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Ultrasonography-guided Peripheral Nerve Blocks in Orthopedic Lower Extremity Surgery: A Narrative Review

Ortopedik Alt Ekstremite Cerrahilerinde Ultrasonografi Kılavuzluğunda Periferik Sinir Blokları: Anlatısal Derleme

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Abstract

In orthopedic lower extremity surgeries, peripheral nerve blocks have gained an important place in anesthesia practice, providing perioperative analgesia, reducing opioid consumption, and enabling early mobilization. During hip, knee, ankle, and foot surgeries, various nerve blocks targeting both motor and sensory functions are applied individually based on the anatomy of the surgical area and the patient's characteristics. Femoral nerve block, pericapsular nerve group block, and suprainguinal and infrainguinal fascia iliaca blocks are frequently preferred in hip and proximal femur interventions, while in knee surgeries, the combination of adductor canal block and interspace between the popliteal artery and the capsule of the posterior knee block stands out. In ankle and foot surgeries, adequate anesthesia and analgesia can be achieved by superficially blocking the tibial, peroneal, sural and saphenous nerves. Nerve blocks performed under ultrasonography guidance reduce the risk of failure due to anatomic variations and decrease complication rates. In this review, the main peripheral nerve blocks used in lower extremity orthopedic surgeries, their anatomical basis, indications, complications, and application techniques are evaluated in light of the current literature.

Keywords: Analgesia, lower extremity, orthopedic procedures, peripheral nerve block, postoperative pain management, ultrasound-guided regional anesthesia

Öz

Ortopedik alt ekstremite cerrahilerinde periferik sinir blokları, perioperatif analjezi sağlama, opioid tüketimini azaltma ve erken mobilizasyona olanak tanıma açısından anestezi pratiğinde önemli bir yer edinmiştir. Kalça, diz, ayak bileği ve ayak cerrahileri sırasında hem motor hem de duyu fonksiyonlarını hedefleyen çeşitli sinir blokları, cerrahi alanın anatomisine ve hastanın özelliklerine göre bireyselleştirilerek uygulanmaktadır. Femoral sinir bloğu, perikapsüler sinir grup bloğu ve suprainguinal ve infrainguinal fascia iliaca blokları kalça ve proksimal femur girişimlerinde sık tercih edilirken, diz cerrahilerinde adductor kanal bloğu ile popliteal arter ile posterior diz kapsülü arasındaki boşluk bloğunun kombinasyonu öne çıkmaktadır. Ayak bileği ve ayak cerrahilerinde ise tibial, peroneal, sural ve safen sinirlerin yüzeyel olarak bloke edilmesiyle etkili bir anestezi ve analjezi sağlanabilmektedir. Ultrasonografi kılavuzluğunda gerçekleştirilen sinir blokları, anatomik varyasyonlara bağlı başarısızlık riskini azaltmakta ve komplikasyon oranlarını düşürmektedir. Bu derlemede, alt ekstremite ortopedik cerrahilerinde kullanılan başlıca periferik sinir blokları; anatomik temelleri, endikasyonları, komplikasyonları ve uygulama teknikleri güncel literatür eşliğinde değerlendirilmektedir.

Anahtar kelimeler: Alt ekstremite, analjezi, ortopedik prosedürler, periferik sinir bloğu, postoperatif ağrı yönetimi, ultrason rehberliğinde rejyonal anestezi

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Introduction

Lower extremity surgeries constitute a significant part of orthopedic practice, encompassing a wide range of procedures, including hip, knee and ankle prostheses, ligament reconstructions, and fracture repairs. During these surgeries, both intraoperative and postoperative pain control are crucial for patient satisfaction, early mobilization, and the reduction of complications. Although general anesthesia and neuraxial blocks are frequently applied, both methods have various disadvantages. Although subarachnoid block and epidural anesthesia/analgesia are successfully applied, there are various problems in patients who are sensitive to sympathetic blockade or who are on anticoagulant use (1,2). Regional anesthesia, which holds an important place in orthopedic operations, has gained significance in recent years with the widespread adoption of ultrasonography (USG).

In recent years, with the widespread use of USG-guided regional anesthesia and techniques, both fascial plane blocks and peripheral nerve blocks (PNBs) can be applied safely and effectively. It has been reported that USG-guided blocks in abdominal operations contribute to postoperative analgesia as well as to mobilization and gastrointestinal functions (3,4). In orthopedic operations, techniques such as femoral nerve block, adductor canal block, sciatic nerve block, and posterior gluteal approaches are widely used to provide adequate anesthesia and analgesia in knee and hip surgeries. These blocks not only reduce postoperative pain but also contribute to lowering healthcare costs by shortening early rehabilitation and discharge times. Their role in multimodal analgesia approaches is particularly noteworthy, as they help in reducing opioid-induced side effects such as nausea, respiratory depression, and sedation. The increasing number of studies on the efficacy and safety of PNBs in lower extremity surgeries, as well as their growing application in both pediatric and adult patients, further underscores their importance (5-7).

In this review, the anatomical basis, technical features, indications, complications, and clinical results of PNBs, which are frequently performed under USG guidance in orthopedic lower extremity surgeries, will be discussed in the context of the current literature.

Method

A literature search was conducted in PubMed, Scopus, and Google Scholar databases for articles published between June 2015 and June 2025 using the keywords “ultrasound-guided”, “peripheral nerve block”, “lower extremity” and “orthopedic surgery”. Randomized controlled trials, observational studies, cohort studies, systematic reviews, and meta-analyses were included in the review. Although no strict inclusion or exclusion criteria were adopted, articles were first evaluated based on their titles and abstracts, followed by an assessment of the full-text manuscripts. In addition, manual search strategies were employed, including screening the reference lists and cited articles in each database. References from key articles were then carefully examined to identify additional relevant sources. Case reports and studies not directly related to lower extremity orthopedic surgery were excluded. This narrative review adhered to the scale for the assessment of narrative review articles checklist to improve reporting quality (8).

PNBs in Hip and Femur Surgery

Anatomical Innervation

The innervation of the hip and femur region is provided by the contribution of multiple nerves originating from both the lumbar and sacral plexus. The anterior hip capsule is innervated mainly by the femoral nerve, the obturator nerve, and the accessory obturator nerve (9). The posterior hip capsule is innervated mainly by the superior gluteal nerve, the inferior gluteal nerve, the quadratus femoris nerve, and branches of the sciatic nerve (10). The femoral skin and periosteum are innervated by branches of the femoral nerve (such as the saphenous nerve) and the obturator nerve. Visceral pain fibers arriving at the hip joint can be transmitted through both somatic and autonomic pathways, which complicates postoperative analgesia. This anatomical diversity may necessitate the use of more than one nerve block or combined techniques to provide adequate analgesia in hip and femur surgeries (11).

Femoral Nerve Block

A femoral nerve block is a peripheral nerve block frequently used to provide adequate analgesia during orthopedic surgeries targeting the anterior region of the hip and femur, as well as the anterior aspect of the knee (12). The femoral nerve originates from the L2-L4 roots and passes through the iliopsoas muscle to reach the femoral triangle region just below the inguinal ligament. In this region, the nerve is located lateral to the femoral artery and can be easily identified with ultrasound guidance due to its superficial course. The block application is effective in reducing both intraoperative and postoperative pain in procedures such as total hip arthroplasty, femoral neck fracture operations, and knee arthroscopies (13). Ropivacaine (0.2-0.5%),

bupivacaine (0.25-0.5%), and levobupivacaine (0.25-0.5%) are frequently used as local anesthetics. While 15-20 mL of local anesthetic is sufficient for a single-shot application, an infusion of 5-8 mL/hour with 0.2% ropivacaine is recommended in cases where a femoral nerve catheter is placed (14). The duration of the block varies depending on the agent used, but it lasts 12-18 hours for bupivacaine and levobupivacaine and approximately 8-12 hours for ropivacaine (15).

USG-guided Femoral Nerve Block Technique

The patient is placed in the supine position. A high-frequency (10-15 MHz) linear probe is placed transversely over the femoral artery, just below the inguinal ligament (Figure 1). In the USG image, the femoral artery appears as an anechoic circle, while the hyperechoic and triangular/oval-shaped femoral nerve is detected laterally (Figure 2). The blocking needle (22G, 50 mm, 80 mm, or 100 mm) is advanced from lateral to medial with an in-plane approach. The needle tip is placed just around the nerve, and local anesthetic is injected after aspiration. Homogeneous spread of the drug around the nerve is an indicator of effective blockade. Depending on the local anesthetic concentration used in the femoral nerve block, mobilization may be delayed due to weakness in the quadriceps muscle. Fall risk should be carefully assessed before initiating mobilization, particularly in elderly patients. Contraindications are infection in the area to be blocked, patient refusal, severe neuropathy, or nerve damage. Coagulopathy and the use of anticoagulants should be considered. Complications include intravascular injection and local anesthetic systemic toxicity (LAST), femoral nerve injury (injection with high pressure should be avoided), hematoma (especially in patients using anticoagulants), local infection, and loss of motor function (a postoperative mobilization plan should be considered).

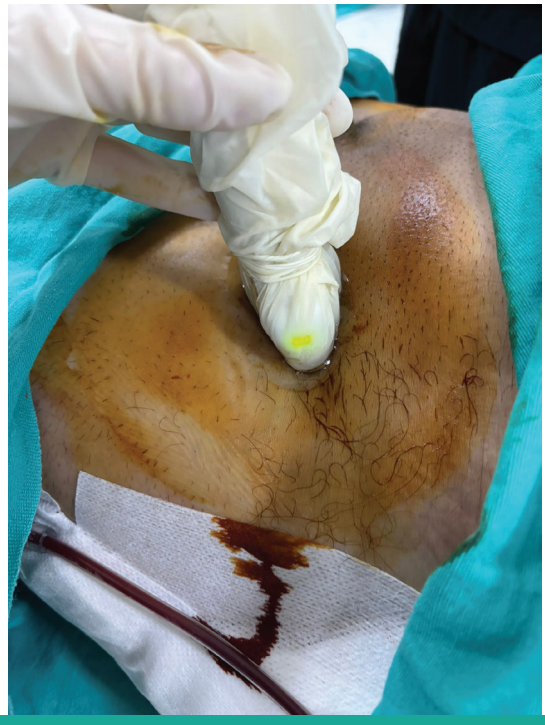

Figure 1. Probe position for femoral nerve block

Fascia Iliaca Compartment Block (FICB)

The FICB is an effective and safe analgesia technique for both intraoperative and postoperative pain control in hip and femur fracture surgeries, targeting the femoral nerve, obturator nerve, and lateral femoral cutaneous nerve. The fascia iliaca is a fascial plane that covers the iliopsoas muscle and provides a potential space for nerves to course. This block aims to provide blockade of more than one nerve by spreading the local anesthetic to the compartment under the fascia iliaca. FICB is particularly suitable for elderly, polymorbid, and opioid-tolerant patients, making it one of the first-choice blocks (16).

There are two basic techniques in FICB: Infra-inguinal and supra-inguinal approaches. In the infra-inguinal approach, the block is performed just below the level of the inguinal ligament; in the supra-inguinal approach, the probe is placed proximal to the ligament and medial to the iliac crest. Ultrasound-guided supra-inguinal fascia iliaca

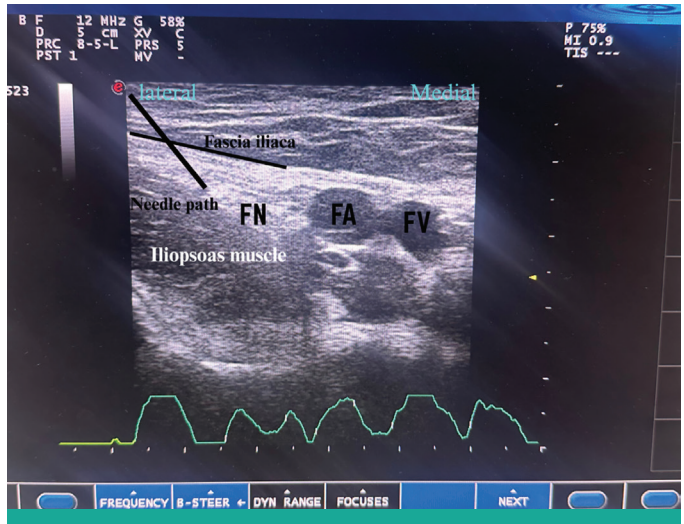

Figure 2. Femoral nerve block

Ultrasound image of femoral nerve block. The black line indicates needle trajectory. Local anesthetic is injected over the nerve. In the infrainguinal fascia iliaca block, local anesthetic is injected into the fascia iliaca under the inguinal ligament. FN: Femoral nerve, FA: Femoral artery, FV: Femoral vein

block (SIFI) can include an obturator nerve block due to the more proximal spread of local anesthetic, providing more extensive analgesia. In the infra-inguinal fascia iliaca block, the high-frequency linear probe is placed 1-2 cm lateral to the femoral artery. The fascia iliaca is visualized as a structure extending between two hyperechoic lines and located above the iliopsoas muscle (Figure 2). The needle is advanced using an in-plane technique. After the needle tip is placed under the iliac fascia, 30-40 mL of local anesthetic (e.g., 0.25-0.5% ropivacaine, bupivacaine, or levobupivacaine) is slowly injected. In SIFI, the injection is made into the wide fascial plane over the iliacus muscle, medial to the iliac crest (Figure 3). The spread of the local anesthetic typically affects the lateral femoral cutaneous nerve first, followed by the femoral nerve, and then the obturator nerve, depending on the volume administered (Figure 4). The duration of analgesia varies depending on the agent used but can last 8-16 hours with ropivacaine and levobupivacaine and 12-18 hours with bupivacaine. It has been reported that SIFI reduces pain more effectively in the early postoperative period (3-8 hours) and achieves higher success rates in nerve blockade compared to the infra-inguinal fascia iliaca block (17). FICB is effective in postoperative analgesia for femur fractures or hip surgery operations, especially in elderly patients, due to its low risk of motor block, broad nerve coverage, and low complication rate.

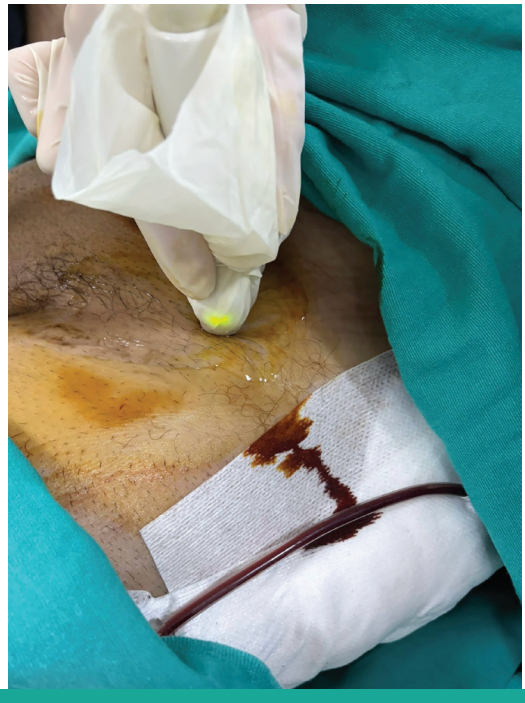

Figure 3. Probe position for suprainguinal fascia iliaca block

Pericapsular Nerve Group (PENG) Block

The PENG block is a new nerve block, defined in 2018, that targets the nerves innervating the anterior capsule of the hip joint and largely preserves motor function. The block targets structures that sense the anterior capsule of the hip joint, such as the femoral nerve, the articular branch of the obturator nerve, and the accessory obturator nerve, if present. It has been reported to be effective and safe in reducing opioid requirements in the perioperative period, especially in elderly patients with hip fractures (18). It reduces the risk of delayed mobilization by affecting quadriceps muscle strength less than traditional femoral or fascia iliaca blocks. When performing a PENG block under USG guidance, the patient is placed in the supine position. The probe is placed in the transverse plane between the anterior inferior iliac spine and the superior pubic ramus. The iliopsoas muscle, femoral artery, and pectineus muscle are identified in the ultrasound image. The needle is advanced from lateral to medial with an in-plane approach. When it reaches the potential area between the iliopsoas muscle and the pubic ramus, the needle tip should stop before approaching the pectineus muscle (Figure 5). Usually, 20-30 mL of local anesthetic (e.g., 0.25-0.5% ropivacaine or bupivacaine) is injected. It should be observed that the local anesthetic spreads under the iliopsoas and reaches the pericapsular area where the nerves are located (18,19). The effect of the PENG block usually begins within 15-30 minutes and can last for 8-16 hours, depending on the agent used. Due to its ease of application in the supine position, low risk of

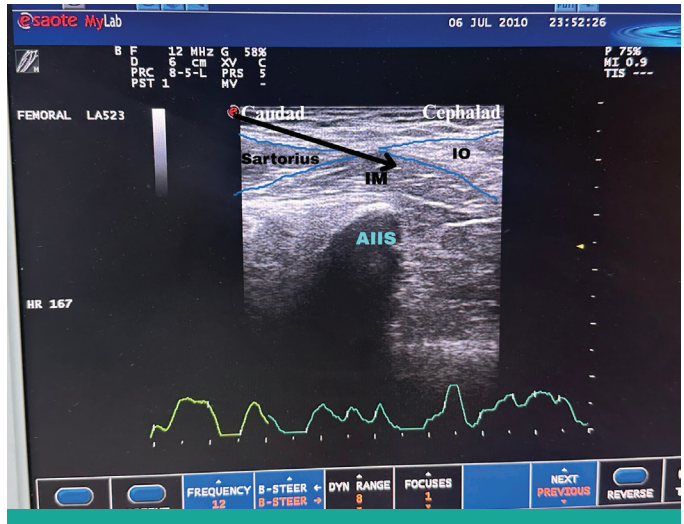

Figure 4. Ultrasound image of suprainguinal fascia iliaca block

The black line indicates needle trajectory. IO: Internal oblique muscle, IM: Iliacus muscle, AIIS: Anterior inferior iliac spine

motor block, and wide coverage, it has become one of the preferred techniques, especially in elderly patients with hip fractures and those at high risk of falling. It can also be used in combination with other blocks (e.g., sciatic nerve block) in major surgeries, such as total hip arthroplasty (18,19).

Psoas Compartment Block (Lumbar Plexus Block)

Psoas compartment block, also known as lumbar plexus block, is applied to block the nerves that innervate the anterior surface of the hip and thigh, such as the femoral nerve, obturator nerve, and lateral femoral cutaneous nerve, with a single injection at the lumbar plexus level. This block provides potent analgesia, especially in large-area orthopedic procedures such as total hip arthroplasty, revision hip surgeries, and femoral fracture fixations. Since it targets more proximal nerve fibers compared to more superficial blocks such as PENG or FICB, a more widespread block is achieved. However, since the application is performed in a deep, anatomically more complex area, the risk of complications is relatively higher (20,21).

In the psoas compartment block, which can be applied under ultrasound guidance or with a nerve stimulator, the patient is positioned in the lateral decubitus position, with the side to be treated facing upwards. A high-frequency or low-frequency (convex) probe is placed at the level of the L3 vertebra. The psoas major muscle is identified on the ultrasound image; hyperechoic nerve structures within the muscle are targeted. The needle is advanced with an in-plane technique, and the location

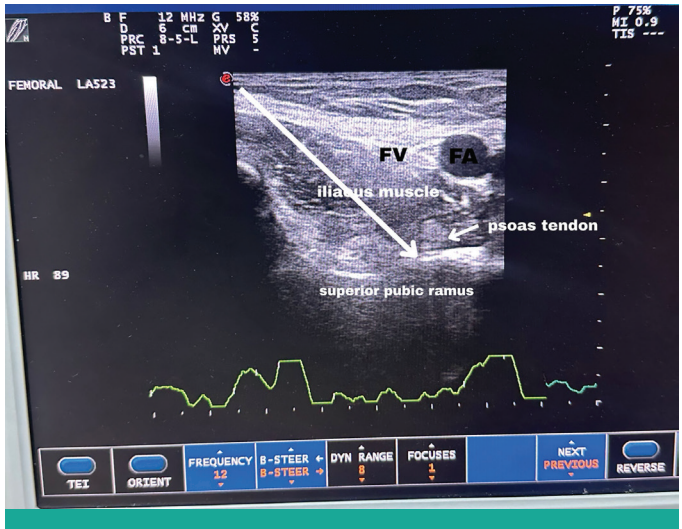

Figure 5. Ultrasound image of pericapsular nerve group block

The white line indicates needle trajectory. Local anesthetic is injected under the tendon of the psoas muscle. FA: Femoral artery, FV: Femoral vein

can be confirmed by obtaining quadriceps contraction with nerve stimulation. Typically, 0.25-0.5% ropivacaine or bupivacaine is used, with a recommended volume of 20-30 mL. The duration of the block's effect varies depending on the agent used but can last up to 12-18 hours. However, due to the risks of complications such as epidural spread, retroperitoneal hematoma, and intravascular injection, this block should only be performed by experienced practitioners and with careful patient selection. This emphasis on careful patient selection and the involvement of experienced practitioners is crucial in ensuring the safety and effectiveness of the psoas compartment block (22).

Sciatic Nerve Block

The sciatic nerve block, a highly effective peripheral block technique, targets the sciatic nerve. This nerve innervates the posterior region of the hip and lower extremity, the posterior aspect of the thigh, most of the leg, and the foot. It is commonly combined with a femoral nerve block, also known as a PENG block, in various surgeries, including hip surgeries, femoral shaft fracture fixations, procedures involving the posterior aspect of the knee, and foot surgeries. The sciatic nerve, originating from the lumbosacral plexus (L4-S3), can be blocked at different anatomical levels as it passes from the gluteal region to the posterior thigh. The subgluteal, parasacral, and popliteal approaches are preferred, with the subgluteal approach often chosen for its technical convenience and more superficial placement between the muscles (23).

When performing a subgluteal sciatic nerve block under USG guidance, the patient is placed in a lateral or prone position. A linear or low-frequency convex probe is placed transversely just proximal to the gluteal fold. On the USG image, the sciatic nerve is defined as a hyperechoic oval structure under the gluteus maximus muscle, between the adductor magnus and quadratus femoris muscles. The needle is advanced from lateral to medial with an in-plane technique. Usually, 0.25-0.5% ropivacaine, bupivacaine, or levobupivacaine is used; a volume of 15-25 mL is sufficient. The effect of the block typically begins 15-20 minutes after administration and can last for 12-18 hours. The most common complications are nerve trauma, hematoma, infection, and, rarely, ischemic neuropathy. Contraindications are active infection, coagulopathy, and traumatic deformation in the application area. High-volume injections should be avoided. It is crucial to apply low pressure and exercise caution during the injection to minimize the risk of nerve damage.

Erector Spinae Plane (ESP) Block and Quadratus Lumborum (QLB) Block

The ESP block, an interfascial block technique introduced by Forero et al. (24), is gaining popularity. This technique involves injecting a local anesthetic into the deep plane of the erector spinae muscle group, located on the transverse processes of the thoracic or lumbar vertebrae. The local anesthetics are believed to provide both somatic and visceral analgesia via the dorsal rami, ventral rami, and rami communicantes. The ESP block, with its potential to provide comprehensive analgesia, has found applications in hip surgeries, pelvic fractures, spinal surgeries, and abdominal procedures. Notably, when applied at the L4-L5 level, it may spread to the lumbar plexus and sacral plexus (25).

The QLB block is a versatile and deeper variant of the transverse abdominis plane block (TAP block). It plays a pivotal role in controlling visceral and deep somatic pain, extending beyond the superficial analgesia achieved in abdominal surgeries. QLB can be performed using four techniques: Lateral (type 1), posterior (type 2), anterior/transmuscular (type 3), and intramuscular (type 4). Particularly in type 3 QLB, a local anesthetic can spread to the plane between the QLB and the psoas major muscle, creating an effective blockade on the lumbar plexus. QLB has been reported to help reduce opioid use, provide visceral analgesia, and offer long-term pain control in hip replacement surgeries and pelvic osteotomies (26).

Both blocks should be performed under USG guidance. In the ESP block, the patient is seated or positioned laterally. The vertebral transverse process is determined with a linear or convex probe. The needle is advanced under the muscle, on the transverse process, with the in-plane technique, and usually 20-30 mL of 0.25% bupivacaine or ropivacaine is injected (Figure 6). In QLB, the probe is placed on the lateral abdominal wall, under the ribs. Especially for type 3, the needle is directed to the plane between the QLB muscle and the psoas major. The duration of effect in both blocks can be up to 12-24 hours, depending on the local anesthetic agent. Complications are rare, but they carry risks such as pleural penetration, retroperitoneal hematoma, and infection, which require anatomical knowledge and skill in the use of USG guidance.

PNBs in Knee Surgery

Anatomical Innervation

The knee joint is innervated by a complex network of nerves originating from both the lumbar and sacral plexus. This innervation encompasses both somatic motor-sensory fibers and articular branches and is of great importance in planning postoperative analgesia. The anterior region of the knee joint is innervated mainly by branches of the femoral nerve (especially the saphenous nerve and vastus medialis), the lateral femoral cutaneous nerve, and the articular branch of the obturator nerve. The posterior capsule is mainly innervated by the terminal branches of the sciatic nerve, the tibial nerve, and the posterior obturator branch (27). The saphenous branch of the femoral nerve, in particular, has a wide sensory distribution in the medial and anteromedial skin regions of the knee and is one of the most frequently targeted nerves in knee surgery. However, the n. vastus medialis and obturator articular branches, which provide deep sensation in the anterior capsule, may not always be adequately blocked with conventional femoral nerve blocks. For effective control of the posterior pain component, techniques such as sciatic nerve block or, more specifically, interspace between the popliteal artery and capsule of the posterior knee (IPACK) block have been reported to be useful (28).

Saphenous Nerve Block

The saphenous nerve is the longest sensory branch of the femoral nerve. It provides extensive sensory innervation to the distal thigh and the anteromedial aspect of the knee, around the patella, and in the proximal tibia region. Since it does not contain motor fibers, it has become an important target for anesthesiologists who want to reduce pain in knee surgeries while preserving quadriceps function. It has

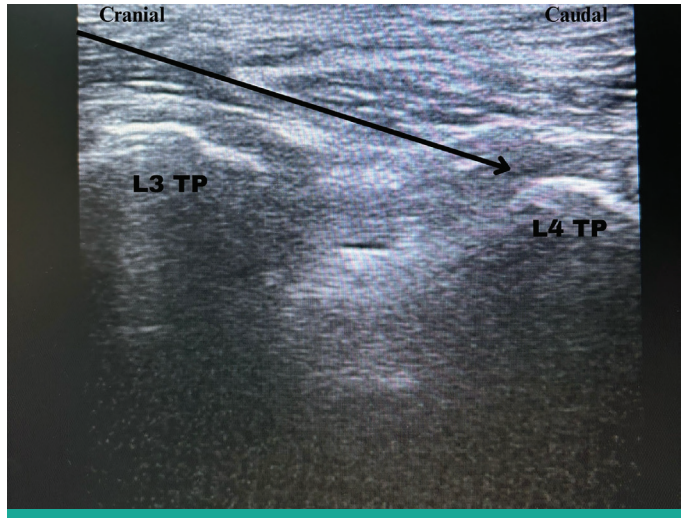

Figure 6. Ultrasound image of lumbar erector spinae plane block

The black line indicates needle trajectory. TP: Transverse process

been reported that isolated saphenous nerve block provides adequate analgesia, especially in anteriorly focused knee procedures such as anterior cruciate ligament surgery, medial meniscus repair, and minimally invasive knee arthroscopies (29).

The USG-guided saphenous nerve block is most commonly performed as an adductor canal block. With the patient in the supine position, a high-frequency linear probe is placed in the mid-thigh region. The femoral artery, sartorius muscle, vastus medialis, and adductor longus/magnus muscles are identified on USG. The saphenous nerve is typically identified as a small hyperechoic structure located laterally or posteromedially to the femoral artery (Figure 7). The block needle is advanced under the sartorius muscle with an in-plane technique, and blockade is achieved with 10-15 mL of 0.25% ropivacaine or bupivacaine. The spread of the local anesthetic around the artery in a ring shape indicates that the block is successful. Saphenous nerve block creates significantly less motor block compared to femoral nerve block, providing advantages in terms of early mobilization, a lower risk of falling, and rapid rehabilitation. Therefore, long-term infusion applications with adductor canal catheters have become widespread, especially in multimodal analgesia protocols. However, in interventions targeting the posteromedial aspect of the knee or the posterior capsule, a saphenous block alone may be insufficient. It should be combined with posterior techniques, such as an IPACK block, if necessary (30).

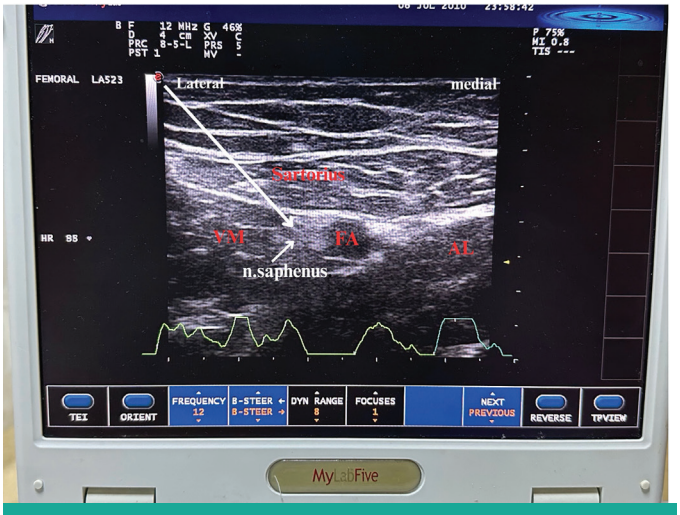

Figure 7. Ultrasound image of saphenous nerve block
The white line indicates needle trajectory. VM: Vastus medialis muscle, FA: Femoral artery, AL: Adductor longus muscle

Popliteal Sciatic Nerve Block

The popliteal sciatic nerve block is an effective technique that aims to block the sciatic nerve at the level just before it divides into the tibial and peroneal branches. It is especially preferred in the posterior region of the knee, as well as in surgeries below the knee and interventions involving the ankle or foot. In knee surgeries, it is applied in combination with femoral or saphenous nerve blocks to control posterior capsular pain. The sciatic nerve divides into two as the tibial and common peroneal nerves in the popliteal fossa, and these branches course in a single sheath before diverging in the distal 1/3 of the thigh. This anatomical unity ensures that the block is effective at this level (31).

During the block application, the patient is usually placed in a prone or lateral position. Under USG guidance, a high-frequency linear probe is placed in the popliteal fossa on the posterior aspect of the thigh, approximately 5-10 cm proximal to the knee joint. The sciatic nerve is targeted at the point where the tibial and peroneal components are visualized as a combined hyperechoic oval structure (Figure 8). The needle is advanced from lateral to medial using an in-plane technique, and 20-30 mL of 0.25-0.5% ropivacaine, bupivacaine, or levobupivacaine is injected around the nerve sheath. The homogeneous spread of the local anesthetic surrounding the nerve is an indicator of the effective block. The duration of effect typically ranges from 12 to 24 hours. The popliteal block should be used with caution in patients planned for early mobilization, as it creates a motor block. However, in terms of providing

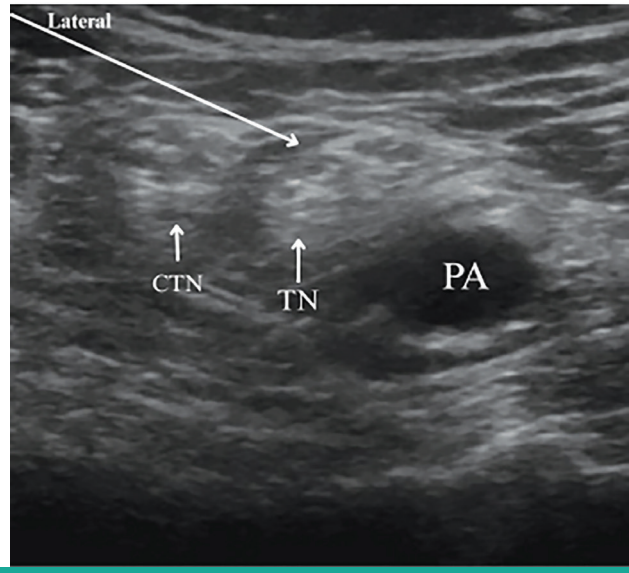

Figure 8. Ultrasound image of popliteal sciatic nerve block
The white line indicates needle trajectory. PA: Popliteal artery, TN: Tibial nerve

analgesia for the posterior capsule of the knee, it can be highly effective in commonly painful procedures, such as total knee arthroplasty, when combined with a saphenous nerve block. It has also been reported that it accelerates recovery by significantly reducing the need for opioids with long-term catheter applications (32).

IPACK Block

The IPACK block, a novel interfascial block technique, is designed to selectively block the nerve fibers innervating the posterior capsule of the knee while preserving motor functions. This unique approach targets structures such as the genicular branches of the tibial nerve, the articular extension of the posterior obturator nerve, and the popliteal plexus. It allows for early mobilization by providing adequate analgesia without causing motor block, particularly in controlling posterior knee pain that develops after total knee arthroplasty. When used in conjunction with the adductor canal block, it effectively blocks both the anterior and posterior knee capsules (33).

When performing an IPACK block under USG guidance, the patient is placed in the supine or lateral position, and a high-frequency linear or low-frequency convex probe is placed in the popliteal region of the knee. The potential space between the popliteal artery and the posterior aspect of the femur and tibia, located just posterior to the artery, is targeted (Figure 9). The needle is advanced in an in-plane technique, from medial to lateral or from lateral to medial.

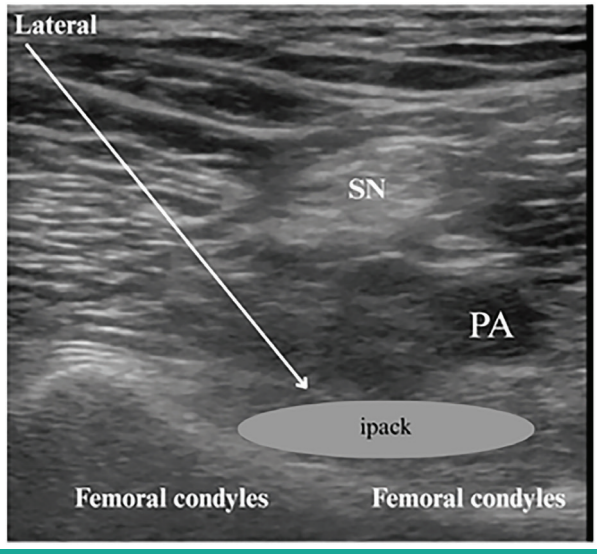

Figure 9. Ultrasound image of interspace between the popliteal artery and capsule of the posterior knee (IPACK) block

The white line indicates needle trajectory. PA: Popliteal artery, SN: Sciatic nerve

No nerve stimulation is required. Injection of 15-20 mL of 0.25% ropivacaine or bupivacaine is usually sufficient. The advantage of the block is that it targets only the posterior sensory branches without affecting the motor nerves, which provides adequate analgesia while minimizing the risk of falls. A well-executed IPACK block not only provides effective pain relief but also significantly reduces opioid requirements, thereby enhancing patient satisfaction and safety.

PNBs in Ankle and Foot Surgery

Anatomical Innervation

Branches of both the tibial and peroneal nerves, as well as other superficial nerves such as the sural and saphenous nerves, provide sensory innervation to the ankle and foot. This anatomical structure shows that complete sensory loss can be achieved by blocking the five primary peripheral nerves around the ankle. These nerves are the tibial nerve, deep peroneal nerve, superficial peroneal nerve, sural nerve, and saphenous nerve. The tibial nerve innervates the medial part of the sole and heel. It can be palpated at the ankle level, medial to the posterior tibial artery, in the retromalleolar region. The deep peroneal nerve is responsible for sensation in the first interdigital space on the dorsum of the foot. Its precise location, adjacent to the anterior tibial artery on the anterior surface of the ankle, is of utmost importance. The superficial peroneal nerve innervates the dorsolateral aspect of the foot; it is primarily located at the subcutaneous level and has a superficial distribution. The sural nerve supplies sensation to the outer side of the foot and the posterolateral aspect of the heel. Its location behind the lateral malleolus is a key point to remember. The saphenous nerve provides superficial sensory branches to the medial skin of the ankle and is an extension of the femoral nerve (34).

Ankle blocks are usually performed for surgical anesthesia (e.g., toe amputations, hallux valgus operations) or postoperative analgesia. Because these five nerves are superficial and easily accessible anatomically, ankle blocks are performed mainly by circumferential injection using anatomical landmarks without the use of USG guidance. However, the use of USG may be preferred, especially for the safe blockade of structures related to arteries, such as the tibial and deep peroneal nerves (35).

Ankle Block Techniques

Ankle block is a superficial and safe technique performed distally in lower extremity surgery. For the block to be successful, five major peripheral nerves—the tibial, deep

peroneal, superficial peroneal, sural, and saphenous nerves—must be blocked separately. Since most of these nerves are superficial and easily identified by anatomic landmarks, ankle blocks are usually performed by subcutaneous injections directed at anatomic points without the need for ultrasound. However, the use of ultrasound may increase safety for structures adjacent to vessels, such as the tibial and deep peroneal nerves. The tibial nerve is located approximately 1-2 cm posterior to the medial malleolus, medial to the posterior tibial artery. Since the nerve courses deeply, it requires deep injection and careful aspiration. 5-8 mL of 0.5% ropivacaine or bupivacaine is sufficient. The deep peroneal nerve courses on the anterior aspect of the ankle, between the extensor hallucis longus tendon and the tibialis anterior tendon, next to the anterior tibial artery.

The nerve is quite superficial at this level; 3-5 mL of local anesthetic is sufficient. Since the superficial peroneal nerve usually spreads laterally in the subcutaneous tissue at the ankle level, it is blocked by a subcutaneous lateral annular injection spreading around the ankle.

The sural nerve is easily localized by palpation, posterior to the lateral malleolus, between the Achilles tendon and the mallear process. A superficial injection of 5 mL of local anesthetic is sufficient for this purpose. The saphenous nerve courses anterior to the medial malleolus, together with the saphenous vein, and usually runs subcutaneously along the medial ankle. Superficial injection of 3-5 mL is also applied here. Effective blockade of all nerves can usually be achieved with a total local anesthetic volume of 20-30 mL. Since the injections are performed near blood vessels, aspiration is essential before each injection. Surgical anesthesia can be achieved in the ankle and distal foot using this block technique; it is also an effective technique for postoperative analgesia, preserving motor functions to a large extent.

Complications of Peripheral Nerve Block

LAST

LAST is a potentially life-threatening complication that may result from intravascular injection of a local anesthetic or from the slow absorption of a high dose of local anesthetic administered perineurally. The clinical presentation and onset of LAST are highly variable, and symptoms may appear rapidly; however, in some cases, they may be delayed for 30 minutes or longer. Neurological toxicity signs usually occur first, followed by cardiac toxicity at higher concentrations. The manifestations of neurotoxicity are subjective and may include dizziness, altered mental status, perioral numbness, and tinnitus (36). These early symptoms can easily be overlooked if the patient is under sedation or general anesthesia. With rising plasma concentrations, muscle twitching and generalized tonic–clonic seizures develop. Ultimately, profound central nervous system depression may occur, leading to decreased consciousness and coma.

The treatment of LAST begins with early recognition of initial symptoms and the intensity of drug accumulation, followed by the urgent administration of intravenous Intralipid emulsion, even in the early stages of patient presentation. Intralipid should be administered as a weight-based bolus, immediately followed by continuous infusion (37). Bolus doses may be repeated, and if the patient remains hemodynamically unstable, the infusion rate can be doubled as indicated in current guidelines (38). The risk of LAST increases when large volumes of local anesthetics are administered simultaneously across multiple nerve distribution sites. Therefore, in PNBs, it is crucial to use the minimum effective dose of local anesthetic required.

Hematoma

During the performance of USG-guided PNBs, inadvertent puncture of surrounding vascular structures may lead to hematoma formation. It is important to avoid performing PNBs in anatomical regions where applying direct pressure to the puncture site is not feasible, as well as in patients with coagulation disorders. The vast majority of hematomas can be controlled by applying direct pressure to the needle puncture site; surgical decompression is rarely required.

Nerve injury

Although rare, nerve injuries may occur following PNBs. Most are transient, lasting from days to months. The incidence of major complications resulting in permanent nerve injury (lasting longer than six months) has been reported to range between 0.015% and 0.09% (39,40). The majority of nerve injuries are thought to occur secondary to intraneural injection. To minimize the likelihood of intrafascicular injection, the injection of local anesthetic should be discontinued if the patient reports paresthesia or if abnormally high resistance is encountered during injection. Under ultrasound guidance, the appropriate spread of the local anesthetic should always be confirmed. Pre-existing neuropathies (including diabetes) may predispose nerves to injury. In addition, nerve injury can also result from the direct neurotoxic effects of certain local anesthetics (41). Clinical manifestations of nerve injury

are primarily sensory (pain, tingling, or paresthesia), but may also include any combination of sensory and motor deficits depending on the affected nerve and the severity of the injury. Most symptoms resolve within six months. If symptoms are severe or persistent, the patient should undergo further evaluation and diagnostic testing.

Block failure

Even in the hands of the most experienced, PNBs carry a risk of failure. Injection of local anesthetics outside the neurovascular sheath may prevent adequate spread to the target nerve. The level of expertise of the anesthesiologist performing the block has been reported to influence the success of the block (42). To maximize success rates, optimization of all patient-related variables is essential. Regardless of block type, patients with a body mass index (BMI) greater than 25 kg/m² have been shown to have a higher likelihood of receiving non-surgical anesthesia compared with those with lower BMI; moreover, block failure rates increase progressively with higher BMI (40). This is likely attributable to the greater difficulty in identifying anatomical landmarks in such patients. Advances in ultrasound guidance and its widespread clinical use have improved success rates, enhanced the quality of sensory blockade, and shortened procedural times by reducing the number of needle passes required to localize the target nerve. Prior to performing a nerve block, the risk of block failure should be discussed with the patient to ensure they are aware of this possibility. As part of this discussion, alternative analgesic strategies (such as alternative blocks, intravenous medications, or oral agents) should be reviewed if the block provides limited pain relief.

Infection

In single-dose PNBs, the risk of infection is considered negligible. The risk increases, however, in hospitalized critically ill patients, trauma patients, immunocompromised individuals, male patients, and when prophylactic antibiotics are not administered. For continuous blocks, the risk of infection can be minimized by removing the catheter within 48 to 72 hours after insertion.

Allergic reaction

The majority of adverse reactions to local anesthetics are non-allergic in nature. Nevertheless, mild allergic manifestations (such as erythema or rash) up to severe reactions progressing to anaphylaxis may occur. Medications and equipment required for symptomatic management should be readily available in locations where PNBs are performed.

Discussion

Ultrasound-guided PNBs are frequently employed for intraoperative anesthesia and postoperative analgesia in orthopedic lower extremity surgeries. In recent years, the description of various new blocks has led to an increase in the number of ultrasound-guided techniques performed (Table 1). In a meta-analysis evaluating the efficacy of the PENG block compared with placebo in total hip arthroplasty, the PENG block was found to significantly reduce early postoperative pain and opioid requirements, while prolonging the time to first opioid administration (43). Another study demonstrated that continuous PENG block provided superior analgesia compared with continuous FICB, better preserved quadriceps muscle strength, facilitated maintenance of motor function, promoted earlier mobilization, and reduced the need for additional analgesics (44). In contrast, a meta-analysis comparing femoral nerve block and FICB in geriatric patients with hip fractures reported no significant difference in opioid consumption within the first 24 hours; however, patients receiving femoral nerve block experienced a significantly lower incidence of side effects such as nausea, vomiting, and sedation (45).

When comparing postoperative analgesic strategies following total knee arthroplasty or traumatic knee surgery, combined and continuous block techniques (such as continuous adductor canal block combined with IPACK or genicular nerve block) have been shown to provide superior analgesia, lower opioid consumption, and improved functional recovery compared with single blocks (46). While a femoral nerve block initially demonstrates high analgesic efficacy, it may cause quadriceps muscle weakness and delay mobilization. In contrast, the adductor canal block has been reported to offer comparable pain control while minimizing this drawback, thereby providing the advantage of motor sparing (47). Furthermore, although the adductor canal block alone provides relatively effective control of anterior knee pain, the addition of an IPACK block has been shown to significantly enhance posterior knee analgesia and facilitate functional mobilization (48).

This narrative review has several inherent limitations. First, although studies from specific databases within a defined time frame were screened, explicit inclusion and exclusion criteria were not applied. Second, unlike systematic reviews with meta-analysis, this review does not provide a quantitative analysis that highlights pooled, calculable outcomes across studies. Finally, the lack of a systematic approach may have led to the exclusion of relevant studies or to disproportionate emphasis on specific findings.

Table 1. Ultrasonography-guided peripheral nerve blocks performed in lower extremity orthopedic surgeries

Block	Clinical application	Target nerves/ structures	Advantages	Disadvantages	Complication
Femoral nerve block	Hip and femur surgery, anterior knee surgery	Femoral nerve in the inguinal region	Reliable analgesia; easy to perform	Quadriceps weakness, delayed mobilization; fall risk; limited coverage of posterior capsule	LAST, hematoma, infection, neuropathy
Fascia iliaca compartment block	Hip fractures, THA, femur surgery	Femoral, lateral femoral cutaneous, obturator nerves	Broad coverage; low motor block; suitable for elderly patients	Large volume required; variable obturator blockade	LAST, hematoma, local infection
PENG block	Hip fractures, THA	Femoral, obturator, accessory obturator articular branches	Motor-sparing; effective for anterior capsule pain; suitable in elderly and high fall-risk patients	Newer technique; variable learning curve; limited posterior coverage	LAST, infection
Psoas compartment block (lumbar plexus block)	Hip/femur surgery	Lumbar plexus (femoral, obturator, lateral femoral cutaneous)	Wide coverage with single injection	Technically difficult; higher risk of complications; not first-line in elderly	Bleeding and retroperitoneal hematoma, infection epidural spread, LAST, nerve damage
Sciatic nerve block	Hip, femur, knee (posterior), foot/ ankle surgery	Sciatic nerve	Strong analgesia, multiple approaches (subgluteal, popliteal)	Motor blockade	Hematoma, infection, ischemic neuropathy
Erector spinae plane block	Hip and pelvic surgery	Dorsal and ventral rami, lumbar plexus spread	Wide analgesic coverage, relatively safe	Variable spread	Hematoma, local infection pneumothorax (rare)
Quadratus lumborum block	Hip replacement, pelvic osteotomy	Thoracolumbar fascia, lumbar plexus	Provides visceral and somatic analgesia, prolonged effect	Technical variability, limited high-quality evidence	Retroperitoneal hematoma, LAST
Saphenous nerve block	ACL repair, meniscus surgery, TKA	Saphenous nerve	Purely sensory, motor-sparing block	Insufficient for posterior capsule pain	Hematoma, infection and nerve damage
Popliteal sciatic nerve block	Knee (posterior), ankle, foot surgery	Tibial and common peroneal nerves before bifurcation	Reliable coverage of posterior knee and below-knee procedures	Motor block	Hematoma, infection nerve damage, LAST
IPACK block	TKA (posterior capsule pain)	Genicular branches of tibial and obturator nerves	Motor-sparing; selective posterior capsule analgesia	Shorter duration than sciatic block, technical learning required	LAST, vascular puncture (rare)
Ankle block techniques	Foot surgery, toe amputations, hallux valgus	Tibial, deep peroneal, superficial peroneal, sural, saphenous nerves	Covers 5 nerves, motor-sparing; simple technique	Multiple injections required, time-consuming	LAST, vascular puncture, infection

LAST: Local anesthetic systemic toxicity, THA: Total hip arthroplasty, PENG: Pericapsular nerve group, ACL: Anterior cruciate ligament, TKA: Total knee arthroplasty, IPACK: Infiltration of local anesthetic between the popliteal artery and capsule of the knee

Conclusion

USG-guided PNBs are beneficial in reducing systemic side effects associated with general anesthesia and opioid use, while providing adequate analgesia. In orthopedic surgical practice, the choice of the appropriate block for lower extremity procedures should be guided by the specific surgical site, patient anatomy, and clinical considerations. Mastery of PNBs requires a thorough understanding of anatomy, associated risks, and potential complications to

ensure both safety and efficacy. Advances in ultrasound guidance have enhanced the precision and safety of these interventions, making them indispensable in modern anesthetic practice. By adopting these techniques, anesthesiologists can improve perioperative pain management, shorten recovery times, and contribute to the overall quality of patient care in orthopedic surgery.

Ethics

Footnotes

Authorship Contributions

Surgical and Medical Practices: K.A., Concept: K.A., A.S.Ş., Design: K.A., A.S.Ş., Data Collection or Processing: K.A., Analysis or Interpretation: K.A., Literature Search: K.A., Writing: K.A., A.S.Ş.

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ORIGINAL RESEARCH

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A Single-center Experience in Children with Acute Rheumatic Fever

Akut Romatizmal Ateşli Çocuklarda Tek Merkez Deneyimi

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Abstract

Objective: This retrospective study aimed to emphasize the importance of subclinical carditis in children with acute rheumatic fever before the revised 2015 Jones criteria.

Method: Throat culture, antistreptolysin O test, C-reactive protein and erythrocyte sedimentation titers, telecardiogram, electrocardiogram, and Doppler echocardiography findings of each patient were evaluated. Doppler echocardiography, examined by pediatric cardiologists was applied to each patient especially to screen subclinical carditis.

Results: In our study of 54 patients with acute rheumatic fever, the frequency of carditis including cases with subclinical carditis was found to be 74.1% (40 patients). And the other clinical findings were arthritis 70.3% (38 patients), Sydenham's chorea 13% (7 patients), erythema marginatum 1.9% (1 patient), while subcutaneous nodule was not seen in any of our patients. Cardiac involvement was not observed in 14 (25.9%) of 54 cases diagnosed with acute rheumatic fever. Of 54 acute rheumatic fever cases, isolated mitral valve regurgitation in 14 (25.9%), isolated aortic valve regurgitation in 2 (3.8%), and coexistence of mitral and aortic regurgitation in 24 (44.4%) cases were detected. Eighteen patients (45%) with mild carditis detected by echocardiography did not have clinical findings of carditis; these cases were considered as subclinical carditis.

Conclusion: To consider subclinic carditis long before 2015 Jones criteria provided our center to get more favourable outcomes in regard to morbidity and possible mortality in these patients. We think that physicians living in populations with moderate-and high-risk for acute rheumatic fever should pay more attentions to newly publicated issues related to carditis in addition to diagnostic criteria.

Keywords: Acute rheumatic fever, carditis, rheumatic arthritis

Öz

Amaç: Bu retrospektif çalışmanın amacı, revize edilmiş 2015 Jones kriterlerinden önce akut romatizmal ateşi olan çocuklarda subklinik karditin önemini vurgulamaktır.

Yöntem: Her hastanın boğaz kültürü, antistreptolizin O testi, C-reaktif protein ve eritrosit sedimantasyon titreleri, telekardiyogram, elektrokardiyogram ve Doppler ekokardiyografi bulguları değerlendirildi. Özellikle subklinik kardit taraması amacıyla her hastaya pediatrik kardiyologlar tarafından Doppler ekokardiyografi uygulandı.

Bulgular: Elli dört akut romatizmal ateş tanılı hastayı kapsayan çalışmamızda subklinik karditli olgulara dahil edildiğinde kardit sıklığı %74,1 (40 hasta), artrit %70,3 (38 hasta), Sydenham koresi %13 (7 hasta), eritema marjinatum %1,9 (1 hasta) idi. Hiçbir hastamızda deri altı nodül görülmedi. Akut romatizmal ateş tanısı alan 54 olgunun 14'ünde (%25,9) kardiyak tutulum yoktu. Kalp kapağı tutulumu olan 40 olgunun 14'ünde (%25,9) izole mitral kapak yetmezliği, 2'sinde (%3,8) izole aort kapak yetmezliği, 24'ünde (%44,4) mitral ve aort yetmezliği birlikteliği saptandı. Ekokardiyografi ile hafif kardit saptanan 18 hastanın (%45) klinik kardit bulgusu yoktu; bu olgular subklinik kardit olarak değerlendirildi ve romatizmal kardit olarak kabul edilerek tedavi edildi.

Sonuç: Subklinik karditin 2015 Jones kriterlerinden çok daha önce dikkate alınması, merkezimizin bu hastalarda morbidite ve olası mortalite açısından daha olumlu sonuçlar almasını sağlamıştır. Akut romatizmal ateş açısından orta ve yüksek riskli popülasyonlarda yaşayan hekimlerin, tanı kriterlerinin yanı sıra kardit ile ilgili yeni yayınlanmış konulara daha fazla dikkat etmesi gerektiğini düşünüyoruz.

Anahtar kelimeler: Akut romatizmal ateş, kardit, romatizmal artrit

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Introduction

Acute rheumatic fever (ARF) is a late complication of upper respiratory tract infections due to *Group A Beta Hemolytic Streptococcus* and develops as a humoral (antibody-mediated) immune response. ARF mainly involves the joints and heart, less commonly the central nervous system, skin, and subcutaneous tissue. It is an inflammatory disease involving serous and serous surfaces. During the acute phase of rheumatic fever, there can be an increase in morbidity and even death in severe cases. However, in long-term outcomes seen in young adults, the main problem caused by ARF is rheumatic heart disease (RHD) (1-3).

ARF remained the leading cause of acquired heart disease in children until the late 20th century. Improvements in the general standard of living, hygiene and sanitation, a better understanding of the disease, appropriate antimicrobial use, and ease of access to healthcare have been seen with a significant reduction in the incidence of ARF and the prevalence of RHD (3). However, it remains a significant public health problem in moderate and high-risk populations and vulnerable colonies in low-risk populations (4).

With the widespread use of echocardiography in the last 20 years, subclinical (silent) carditis detection has come to the fore. In the 1992 Jones and 2002 World Health Organization (WHO) recommendations, subclinical carditis detected by Doppler echocardiography was not included as a diagnostic criterion (5,6). In 2015, the Jones criteria were updated to include different diagnostic criteria for low-risk and moderate-and high-risk populations. In the moderate and high-risk populations, including Turkey and low-risk populations, subclinical carditis was accepted as the major criterion by Doppler echocardiography (6).

This is a study emphasizing our clinical practice in which patients with subclinical carditis were also included at the time when the 2015 ARF diagnostic criteria were not published yet.

Materials and Methods

The study analysed retrospectively the files of 54 pediatric cases, who were diagnosed with ARF between January 2009 and April 2013. It did not include recurrent ARF cases or cases with uncertain diagnoses.

Ethical approval for this study was obtained from the Ethics Committee of Necmettin Erbakan University (date: 29.01.2013, approval number: 2013/345).

Patients with ARF were diagnosed using the 1992 Modified Jones criteria. Major criteria included carditis, migratory and aseptic polyarthritis, subcutaneous nodules, erythema marginatum, and Sydenham's chorea; minor criteria included PR interval prolongation on electrocardiogram (ECG), polyarthralgia, fever, C-reactive protein (CRP) and erythrocyte sedimentation (ESR) titers increase. In the evidence of preceding *Group A Streptococcal* infection, the diagnosis of ARF was made with the presence of 2 major or 1 major and 2 minor criteria. Polyarthritis was defined as swelling, redness, warmth, and limitation of movement in 2 or more joints. Sydenham chorea was diagnosed after other causes of chorea were excluded (7). Patients considered to have clinical carditis had a pathological murmur with or without heart failure, and also, aortic and/or mitral regurgitations were demonstrated by Doppler echocardiography. Cases without a murmur or clinical findings were screened for subclinical carditis to detect pathological mitral valve regurgitation and/or aortic valve regurgitation according to WHO criteria in Doppler echocardiography (8,9). Subclinical carditis was defined as mild carditis. Patients with moderate valvular regurgitation and murmur but no cardiomegaly were defined as moderate carditis. Patients with severe valvular regurgitation, murmur and cardiomegaly were defined as severe carditis.

Each patient's blood antistreptolysin O (ASO), CRP and ESR, throat culture, ECG, Doppler echocardiography, and telecardiogram findings were evaluated.

Statistical Analysis

Statistical Package for Social Sciences (SPSS for Windows Version 16.00, Chicago, IL, USA) package program was used to evaluate the findings. The conformity of all variables to the normal distribution was investigated using the Shapiro-Wilks test. Pearson chi-square test and Fisher's exact test was used to compare categorical variables between groups. A p-value of <0.05 was considered statistically significant.

Results

A total of 54 patients, including 26 females and 28 males aged 5 to 18 years, were diagnosed with ARF. There were 22 patients aged 5-9 years (40.7%), 25 patients aged 10-14 years (46.3%), and 7 patients over 14 years old (13%). The mean age at the time of diagnosis was 10.1±2.88 years. The follow-up period of 54 ARF cases was 15.12±8.5 months in patients with carditis and 20.8±14.1 months in patients with arthritis.

Among the major criteria, 22 patients (40.7%) had only one major criterion; 9 (16.7%) had isolated carditis, and 13 (24%) had isolated polyarthritis. There were 32 patients (59.3%) with two major criteria; 24 (44.4%) had carditis and polyarthritis, 7 (13%) had carditis and chorea, and 1 (1.9%) had polyarthritis and erythema marginatum. No one had more than two major criteria.

Among the major criteria, the incidence of carditis and Sydenham's chorea was found to be higher in female cases, and polyarthritis was high in male cases ($p<0.05$) (Table 1).

There was no statistically significant difference in the incidence of carditis, arthritis, Sydenham's chorea, and erythema marginatum among all age groups ($p>0.05$).

Among the minor criteria, acute phase reactants increase was observed in 53 patients (98.1%) arthralgia in 41 (75.9%), fever in 7 (13%), and prolongation of PR interval on ECG in 6 patients (11.1%). Considering the distribution of supportive findings of previous streptococcal infection, ASO titre elevation was detected in 53 (98.1%) cases, and streptococcal growth was not observed in the throat culture of all cases. One patient had moderate carditis and Sydenham's chorea, but there was no increase in ASO titer as a supportive finding.

The distribution of the increase of acute phase reactants, the most common minor criterion in our cases, was most frequently observed in ESR titres, followed by the rise in CRP titers.

Cardiac involvement was not observed in 14 (25.9%) of 54 cases diagnosed with ARF. Of 54 ARF cases, isolated mitral valve regurgitation in 14 (25.9%), isolated aortic valve regurgitation in 2 (3.8%), and coexistence of mitral and aortic regurgitation in 24 (44.4%) cases were detected. Of patients with carditis (n=40), there was mild carditis in 18 patients (45%), moderate carditis in 12 patients (30%), and severe carditis in 10 patients (25%). Eighteen patients (45%) with mild carditis detected by echocardiography did not have clinical findings of carditis; these cases were considered subclinical carditis (Table 2).

Table 1. Distribution of major criteria by sex

	Male		Female		p-value
	n	%	n	%	
Carditis	14	53.8	26	92.9	0.001*
Polyarthritis	23	88.5	15	53.6	0.005*
Sydenham's chorea	0	0	7	25.0	0.007**
Erythema marginatum	1	3.8	0	0	0.481**

*: Pearson chi-squared test, **: Fisher's exact test was used to compare categorical variables

Only one of 54 cases diagnosed with rheumatic carditis did not return for a check-up after starting treatment. Therefore, it was not included in the evaluation of valve involvement by echocardiography after treatment. Among cases with carditis (n=39) 9 patients (23%) were completely healed in the cardiac findings at the end of the follow-ups. Carditis in the remaining patients persisted, albeit with a decrease. No ARF attacks were observed as our patients received secondary prophylaxis. When we evaluated mitral and aortic valve regurgitation separately, 10 (27%) of 38 patients with mitral valve regurgitation had improved entirely, 23 (62.2%) had decreased, and 4 (10.8%) had remained at the same level. Of the 32 patients with aortic valve regurgitation, 17 (43.5%) had completely recovered, 9 (23%) had decreased, and 6 (15.3%) had remained at the same level of aortic valve regurgitation (Table 3).

Table 2. Distribution of valve involvement according to clinical degrees at the time of diagnosis

Patient number/percentage		n	%
Subclinical carditis n=18	Mild AR	2	5.0
	Mild MR	7	17.5
	Mild MR+ mild AR	9	22.5
Clinical carditis n=22	Moderate AR	6	15.0
	Severe MR	1	2.5
	Moderate MR+ mild AR	4	10.0
	ModerateMR+ moderate AR	2	5.0
	Severe MR+ mild AR	7	17.5
	Severe MR+ moderate AR	1	2.5
	Severe MR+ severe AR	1	2.5
Total		40	100

MR: Mitral valve regurgitation, AR: Aortic valve regurgitation

Table 3. Distribution of valve involvement according to clinical degrees after treatment

Patient number/percentage	n	%
No valve involvement	9	23
Mild AR	3	7.7
Mild MR	12	30.8
Moderate MR	2	5.1
Severe MR	1	2.6
Mild MR+ mild AR	6	15.4
Moderate MR+ mild AR	3	7.7
Moderate MR+ moderate AR	1	2.6
Mild MR+ moderate AR	2	5.1
Total	39	100

MR: Mitral valve regurgitation, AR: Aortic valve regurgitation

Table 4. Frequency of Modified Jones Criteria detected in studies

		Ravisha et al. (13) n/%	de Loizaga et al. (14) n/%	Karaaslan et al. (15) n/%	Erdem et al. (16) n/%	Yılmaz et al. (17) n/%	Our study n/%
Major criteria	Isolated poliarthritis	101 (40.4%)	208 (30.4%)	88 (32.1%)	47 (12.5%)	11 (16.9%)	13 (24%)
	Isolated carditis	37 (14.8%)	336 (49.1%)	-	56 (14.9%)	49 (75.4%)	9 (16.7%)
	Sydenham's chorea	47 (18.8%)	254 (37.1%)	19 (7%)	14 (3.7%)	-	-
	Subcutaneous nodules	3 (1.2%)	24 (3.5%)	-	-	-	-
	Erythema marginatum	-	59 (8.6%)	-	1 (0.3%)	-	-
	Arthritis, carditis	68 (27.2%)	-	135 (49.2%)	219 (58.1%)	5 (7.7%)	24 (44.4%)
	Carditis, S. chorea	-	-	30 (10.9%)	25 (6.6%)	-	7 (13%)
	Arthritis, E. marginatum	-	-	-	-	-	1 (1.9%)
	Carditis, S. nodules	-	-	2 (0.7%)	1 (0.3%)	-	-
	Carditis, E. marginatum	-	-	1 (0.4%)	1 (0.3%)	-	
	Carditis, arthritis, S. chorea	-	-	-	12 (3.2%)	-	-
Minor criteria	Fever	-	330 (48.2%)	-	194/376 (51.6%)	-	7 (13%)
	Arthralgia	-	131 (19.2%)	-	268/377 (71.1%)	-	41 (75.9%)
	Prolongation of PR interval	-	63 (9.2%)	-	115/297 (38.7%)	-	6 (11.4%)
	APR elevated	-	315 (46.1%)	-	221/312 (70.8%)	-	53 (98.1%)

S. chorea: Sydenham's chorea, S. nodules: Subcutaneous nodules, E. marginatum: Erythema marginatum, APR: Acute phase reactants (C-reactive protein and erythrocyte sedimentation titers) PR interval: The time from the beginning of the P wave to the beginning of the QRS complex in electrocardiography

Discussion

In the 2005 systematic review, there were 471,000 new cases of ARF each year, with 15.6-19.6 million existing RHD cases and 350,000/year ARF deaths as a result of RHD (3). Tibazarwa et al. (10), in a study conducted in 10 countries, found that the average global incidence of ARF was 19/100,000, and the frequency was variable according to geographical regions and societies. Organisation for economic co-operation and development countries were grouped under 3/100,000 cases as a low-risk society, 3-25/100,000 cases as a moderate-risk group, and over 25/100,000 cases as high risk. Turkey was in the moderate-risk group with a prevalence of 21/100,000 (11). In a study of the first attack of 1103 ARF patients in Turkey in 2016, the estimated incidence rate of ARF was 8.84/100,000 (12).

In 2018, WHO identified actions to improve living conditions, effectively treat upper respiratory tract infections, diagnose the disease in its early stages, and prevent recurrent attacks by fully implementing penicillin prophylaxis. ARF and RHD have been unanimously accepted as a global health priority (4).

ARF was seen most commonly in children between the ages of 5-15 years (3). In the study conducted by Ravisha et al. (13) on 550 patients in India between 1971 and 2001, the mean age was 9.6 years. In a retrospective review of 947 cases in 22 US pediatric institutions between 2008 and 2018, the mean age was 9 years (14). In the study conducted by Karaaslan et al. (15) in Konya between 1993 and 1998 on 274 patients, the mean age was 12.7±2.9 years. In a retrospective review of 377 cases diagnosed with ARF in Çukurova/Turkey between 1997 and 2017, the largest age group were between 9 and 12 years and the mean age was 11±2.6 years (16). In our study, the mean age of the patients diagnosed with ARF was 10.1±2.88 years. The youngest patient was 6 years old, and the oldest was 15 years old, which is consistent with the literature.

In the literature, the most common significant clinical finding in ARF was arthritis, while carditis was the second most common clinical finding. Sydenham's chorea occurs in 30% of cases (3). In 1971-2001, Ravisha et al. (13) examined patients with ARF as the most common arthritis, second most commonly carditis. de Loizaga et al. (14) examined in 2008-2018, carditis was the most common in their patients and Sydenham's chorea was the second most common. Karaaslan et al. (15) found the most common arthritis in their patients between 1993-1998 and carditis was the second most common. Erdem et al. (16) found the most common carditis and arthritis was the second most common finding. Yılmaz et al. (17) found the most common carditis in their patients between 2010-2014 (Table 4). Gürses et al. (12) found the incidence of clinical carditis 53.5%, subclinical carditis 29.1%, polyarthritis 52.8%, aseptic monoarthritis 10.3%, polyarthralgia 18.6% and Sydenham's chorea 7.9%. In our study of 54 patients with ARF, the frequency of carditis, when including the cases with subclinical carditis, was 74.1% (40 patients) and then arthritis in 70.3% (38 patients). Sydenham's chorea was in 13% (7 patients) and erythema marginatum in 1.9% (1 patient). At the same time, subcutaneous nodules were not seen in any of our patients. The coexistence of arthritis and carditis was observed in 44.4% (24 patients), the coexistence of carditis and Sydenham's chorea in 13% (7 patients), and the coexistence of arthritis and erythema marginatum in 1.9% (1 patient). Carditis was present in all of Sydenham's chorea patients. We thought that the reason why carditis was detected more often than arthritis was that subclinical carditis was taken into consideration in our centre at that time and that most of the cases with arthritis were treated in primary or secondary care centres. However, cases with suspected carditis were mainly referred to our tertiary health centre.

When we researched the literature, apart from Sydenham's chorea (more common in females), there was no significant sex difference in major findings in other Jones criteria (18). In the study of Karaaslan et al. (15) in 1993-1998, arthritis and carditis showed an equal distribution between the sexes, while Sydenham's chorea was more common in female patients. In the multicenter study of Orsini et al. (19), in which the psychiatric conditions of patients diagnosed with ARF were evaluated, Sydenham's chorea was more common in the female sex. In our study, carditis and Sydenham's chorea incidence was statistically higher in female patients than in males. Although the reason for this association was not completely clear, it can be explained by intrinsic factors such as autoimmune susceptibility.

Of our patients with carditis (n=40), 38 (95%) had mitral valve regurgitation, and 32 (80%) had aortic valve regurgitation. Isolated mitral valve regurgitation was observed in 14 patients (35%), isolated aortic valve regurgitation in 2 patients (5%), and coexistence of mitral and aortic valve regurgitation in 24 patients (60%). In the study of Erdem et al. (16) in 1997-2017, the most commonly affected valve was isolated mitral valve regurgitation (54.9%), followed by a coexistence of mitral and aortic valve regurgitation (34%) and isolated aortic valve regurgitation (5.7%). In the study of Yılmaz et al. (17) in 2010-2014, out of 65 patients diagnosed with ARF, 54 had carditis. Isolated mitral valve regurgitation was observed in 14 patients (21.5%), isolated aortic valve regurgitation in 10 patients (15.4%), and coexistence of mitral and aortic valve regurgitation in 22 patients (33.9%). In our study, compatible with other studies, mitral valve involvement was the most common, followed by the aortic valve.

In 2000, the American Hearth Association (AHA) emphasised the importance of subclinical carditis, which can be detected by echocardiography, as an indicator of ARF. However, the authors concluded that there was insufficient evidence to include subclinical carditis as a diagnostic criterion. It was also emphasised that the detected subclinical carditis might reduce the specificity of Jones criteria and lead to the diagnosis of excessive ARF and the overuse of long-term penicillin prophylaxis due to the diagnosis (20). These prevalence studies have been conducted since then, emphasising the importance of subclinical carditis among patients with ARF. In a meta-analysis of 23 studies in 2007, 16.8% of subclinical carditis was shown in ARF, and 44.7% of these patients had worsened valve involvement over time (21). It had been emphasised that valvular regurgitation findings may represent early RHD due to the pathological prevalence of subclinical carditis detected in Doppler echocardiography according to the diagnostic criteria recommended by WHO for RHD at the time of diagnosis (22).

RHD, the only long-term consequence of ARF, continued unabated among middle-income and low-income communities (22). Subclinical carditis was relatively common in ARF. The reported prevalence of subclinical carditis in ARF was ranges from 0 to 53%. Since 2004, the WHO had recommended echocardiographic screening for RHD and ARF in high-prevalence regions (8,9). In 2005, a joint WHO and National Institutes of Health working party established insufficient experience with normal echocardiographic findings in children and the

concern that echocardiography might be overly sensitive in some children with standard valvular structure and function variation. It had accelerated the development of an internationally validated, evidence-based echocardiographic diagnostic guideline for RHD. The 2012 World Heart Federation aimed to reduce the burden of RHD worldwide by defining minimum echocardiographic criteria for diagnosing RHD (22). Therefore, since we had already performed echocardiography on every ARF patient with arthritis, carditis, and Sydenham's chorea, we accepted subclinical carditis as carditis according to the echocardiographic criteria 2012. After screening for subclinical carditis with Doppler echocardiography, we thought that we missed no case of carditis according to the new Jones criteria. Therefore, we revealed that morbidities and also possible mortalities might be prevented with the follow-up of these patients as carditis long before the 2015 Jones criteria. However, there might be missed cases in patients with isolated monoarthritis or monoarthralgia.

In 2015, the AHA recommended stating the population as low and moderate/high-risk groups with a successful revision, applying echocardiography to patients with suspected ARF, and accepting subclinical carditis as the major criterion in all risk groups (23). In our study between 2009 and 2013, as recommended by WHO, we applied the Doppler echocardiography criteria for pathological mitral and/or aortic valve regurgitation to detect subclinical carditis. Thus, owing to successful management and follow-up of these patients was provided to obtain more favourable outcomes. The Modified Jones Criteria, published later and renewed in 2015, also showed the accuracy of our approach at that time.

Study Limitations

Our study has some limitations. The last patient recruitment was completed in 2013. Unfortunately, we could not collect the 10-year results because some of the patients passed to other centres for follow-up and also transitioned into adulthood.

Conclusion

We suggest that investigating cardiac involvement with Doppler echocardiography is so crucial when any major findings of ARF are suspected, especially in moderate- and high-risk populations. Appropriate treatment and prophylaxis for those with carditis will significantly contribute to the reduction of morbidity and mortality due to RHD. Between 2009 and 2013, we followed and treated our patients by recognising subclinical carditis as a major criterion, showing the accuracy of our approach prior to the 2015 Modified Jones Criteria. Therefore, we think that physicians living in populations with moderate-and high-risk for ARF should pay more attention to newly publicated issues related to carditis in addition to diagnostic criteria.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Ethics Committee of Necmettin Erbakan University (date: 29.01.2013, approval number: 2013/345).

Informed Consent: Consent was obtained from the formal guardians.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: N.B., Concept: N.B., F.Ş., T.B., Design: N.B., F.Ş., T.B., Data Collection or Processing: N.B., Analysis or Interpretation: F.Ş., T.B., Literature Search: N.B., Writing: N.B.

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ORIGINAL RESEARCH

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The Effect of COVID-19 on Laboratory Parameters

COVID-19'un Laboratuvar Parametreleri Üzerindeki Etkisi

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Abstract

Objective: This study aimed to investigate the long-term effects of coronavirus disease-2019 (COVID-19) on semen parameters and hormone levels by dividing the timeline into pre-pandemic, pandemic, and post-pandemic phases.

Method: Between May 2017 and April 2024, we conducted a retrospective study including 10,082 semen analyses from 6.517 patients at our hospital. Patients were divided into three groups according to the World Health Organization (WHO)-defined pandemic start and end dates: pre-COVID-19 (May 2017-March 2020; n=2378), COVID-19 period (March 2020-May 2023; n=5568), and post-COVID-19 (May 2023-April 2024; n=2136). Semen analyses and hormone parameters [total testosterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and prolactin] were examined. However, it was not possible to determine whether each patient had been infected with COVID-19. All semen analyses were performed in accordance with WHO 2010 guidelines.

Results: Sperm concentration, motility, and morphology significantly increased during and after the COVID-19 period compared with the pre-COVID-19 period (p<0.01). Semen volumes remained similar across all three periods (p>0.05). Testosterone levels also showed significant increases during and after the pandemic (p<0.01). In contrast, FSH and LH levels decreased significantly during and after COVID-19 (p<0.001). No significant changes were observed in estradiol levels, whereas prolactin levels increased during and after COVID-19 (p<0.001).

Conclusion: COVID-19 was associated with notable changes in male reproductive health indicators; however, no permanent negative impact on male fertility was identified. Further prospective studies are needed to validate these findings and to elucidate the underlying mechanisms.

Keywords: COVID-19, male fertility, pandemic, semen

Öz

Amaç: Bu çalışma, koronavirüs hastalığı-2019'un (COVID-19) semen parametreleri ve hormon düzeyleri üzerindeki uzun vadeli etkilerini araştırmayı, dönemi pandemiden önce, pandemi sırasında ve pandemi sonrasında olmak üzere üç aşamaya ayırarak incelemeyi amaçlamaktadır.

Yöntem: Mayıs 2017 ile Nisan 2024 arasında, hastanemizde 6,517 hastadan 10,082 semen analizi içeren retrospektif bir çalışma gerçekleştirdik. Dünya Sağlık Örgütü'nün (DSÖ) pandemi başlangıcı ve bitiş tarihlerine göre üç gruba ayırdık. COVID-19 öncesi (Mayıs 2017-Mart 2020): 2,378 hasta; COVID-19 dönemi (Mart 2020-Mayıs 2023): 55,68 hasta ve COVID-19 sonrası (Mayıs 2023-Nisan 2024): 2,136 hasta. Semen analizleri ve hormon parametreleri [toplam testosteron, folikül uyarıcı hormon (FSH), luteinize edici hormon (LH), estradiol ve prolaktin] incelendi. Ancak her bir hastanın COVID-19 enfeksiyonundan etkilenip etkilenmediği belirlenemedi. Tüm semen analizlerini DSÖ 2010 kılavuzlarına uygun olarak gerçekleştirdik.

Bulgular: Sperm konsantrasyonu, motilite ve morfoloji, COVID-19 öncesi döneme kıyasla COVID-19 dönemi ve sonrasında anlamlı bir şekilde arttı (p<0,01). COVID-19 öncesi dönem, pandemi dönemi ve post-pandemi döneminde semen hacmi, COVID-19 dönemlerinden bağımsız olarak benzer kaldı (p>0,05). Testosteron seviyeleri de pandemi döneminde ve sonrasında anlamlı bir artış gösterdi (p<0,01). Aksine, FSH ve LH seviyeleri COVID-19 dönemi ve sonrasında anlamlı bir şekilde azaldı (p<0,001). Estradiol seviyelerinde önemli bir değişiklik gözlenmezken, prolaktin seviyeleri COVID-19 dönemi ve sonrasında arttı (p<0,001).

Sonuç: COVID-19, erkek üreme sağlığı göstergelerinde belirgin değişikliklere neden olmuş olsa da erkek fertilitesi üzerinde kalıcı bir olumsuz etki tespit edilmemiştir. Bu bulguları doğrulamak ve altta yatan mekanizmaları araştırmak için daha fazla prospektif çalışmaya ihtiyaç vardır.

Anahtar kelimeler: COVID-19, erkek doğurganlığı, pandemi, semen

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Introduction

First identified in Wuhan, China, in December 2019, the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) caused approximately 7 million deaths by March 2024. Due to its extreme contagiousness, the World Health Organization (WHO) declared coronavirus disease-2019 (COVID-19) a pandemic in March 2020. However, as of May 2023, the WHO declared it no longer a global emergency (1). According to the data from the Ministry of Health of the Republic of Turkey, the number of confirmed COVID-19 cases is 17,042,722, and the total number of deaths is 101,492. According to the data, 93.38% (57,961,404) of individuals aged 18 and over have received the first dose of the vaccine, while 85.7% (53,195,125) have received the second dose (2). This disease not only affects the respiratory system but also causes histopathological changes in various non-respiratory organs such as the heart, brain, liver, kidneys, and testes (3). Also, studies have reported that men are at a higher risk of contracting COVID-19 compared to women (4). The testes are also easily damaged because sperm does not have much of a defense against oxidative agents. This can cause problems with both the endocrine and exocrine functions of the testes. Therefore, how COVID-19 affects fertility in men has become a subject of research (5).

The human male reproductive system is more susceptible to viral infections due to the blood-testis barrier's inability to completely block virus entry. Researchers have detected 27 different infectious viruses in human semen to date (6). Angiotensin-converting enzyme 2 (ACE-2) receptors let SARS-CoV-2 into the host cell, and it uses transmembrane serine protease-2 (TMPRSS-2), a cellular membrane protease, to help the two cells join together (7,8). It has been reported that ACE-2 and TMPRSS-2 are highly expressed in spermatogonia, as well as in Sertoli and Leydig cells, and this expression inversely correlates with age (4). Accordingly, patients aged 20-30 have the highest levels of ACE-2 expression, while patients aged 60 and above have the lowest levels of ACE-2 expression (9).

The literature reports that COVID-19 affects sperm concentration, motility, and morphology; however, most descriptions of these changes are short-term and temporary (10,11). The aim of this study is to examine semen parameters before and after the COVID-19 pandemic with a high patient volume without reducing the focus to a specific group.

Materials and Methods

Our hospital's clinical research ethics committee approved the study under approval code 2024/03/04/028. Our research included patients who had semen analysis and hormone parameters [total testosterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, and prolactin] examined before, during, and after the COVID-19 outbreak in our hospital. The study excluded patients with testicular trauma, undescended testicle, varicocele, tumor surgery, patients receiving hormone therapy with a diagnosis of hypogonadotropic hypogonadism, and included patients over the age of 18 who did not meet any of these criteria. All patients participating in the study gave their consent.

Accordingly, between May 2017 and April 2024, we included 10,082 sperm analyses from 6.517 different infertility patients who applied to our clinic. The patients were not evaluated separately for whether they were affected by a COVID-19 infection or had a vaccination history. Instead, the patients were categorized according to the periods defined by the World Health Organization. We divided them into three groups based on the WHO's pandemic start and end dates: May 2017-March 2020 (before COVID-19): 2.378 patients; March 2020-May 2023 (COVID-19 period): 5.568 patients; May 2023-April 2024 (post-COVID-19): 2.136 patients. We performed all semen analyses in accordance with WHO 2010 guidelines (12).

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. University of Health Sciences Turkey, İstanbul Bağcılar Training and Research and Hospital's Clinical Research Ethics Committee approved the study under approval code 2024/03/04/028.

Statistical Analysis

We used non-parametric statistics to analyze the numerical data examined according to the COVID-19 periods. The Kolmogorov-Smirnov test evaluated the normal distributions of the variables. We performed Kruskal-Wallis on parameters with non-normal distributions. The significance level in this study was set at 0.05. We calculated the Pearson correlation coefficient to ascertain the presence of a linear relationship between two variables. For the statistical analysis of the data, SPSS (Statistical Package for Social Sciences for Windows, Release ver. 29.0) was used.

Results

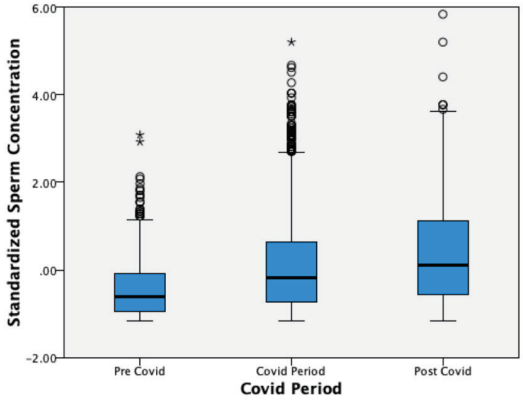
In the pre-COVID-19 period, epidemic period, and post-epidemic period, semen volumes remained similar regardless of COVID-19 periods ($p>0.05$). When sperm concentration was examined, the average sperm concentration was 25.4±21.9 (10^6/mL) in the pre-COVID-19

period, 46.5±38.8 (10^6/mL) in the COVID-19 period, and 56.2±41.3 (10^6/mL) in the post-COVID-19 period. This increase was found to be statistically significant (p<0.01) (Graphic 1).

While the sperm motility rate was 40.5% in the pre-COVID-19 period, it was shown to be 42.54% in the pandemic period and 44.34% in the post-pandemic period, and these changes were shown to be statistically significant (p<0.01). Analysis of the sperm morphology change revealed that the average level was 0.97% in the pre-COVID-19 period, 1.39% in the pandemic period, and 1.85% in the post-pandemic period. This change was shown to be statistically significant (p<0.01). Table 1 and Figure 1 summarize these findings regarding semen analysis.

Testosterone levels were 3.81±1.67 in the pre-COVID-19 period, increased to 4.24±1.85 during the COVID-19 period, and then showed a slight decrease to 4.15±1.72 after the pandemic. The increases in both periods are statistically significant compared to the pre-COVID-19 period (p<0.01). When examining FSH (mIU/mL) and LH (mIU/mL) hormone levels, it was found that the average levels in the pre-COVID-19 period were 11.60±15.21 mIU/mL and 6.75±5.52 mIU/mL, respectively. During the COVID-19 period, these levels were 7.96±8.38 mIU/mL and 7.08±4.91 mIU/mL, respectively. In the post-COVID-19 period, the levels were 6.93±8.36 mIU/mL and 6.81±4.14 mIU/mL, respectively. The decreases in both hormone levels were statistically significant (p<0.001).

While estradiol levels were 29.12±13.40 in the pre-COVID-19 period, they were 31.32±15.04 in the COVID-19 period and 28.46±13.05 in the post-COVID-19 period. There was no statistically significant difference between these levels (p>0.05). Prolactin levels were 11.60±5.84 in the pre-COVID-19 period, 12.72±6.71 during the COVID-19 period, and 11.94±4.50 in the post-COVID-19 period. The levels during and after the COVID-19 period were statistically significantly higher compared to the pre-COVID-19 period (p<0.001). Table 2 and Figure 2 summarize these findings from the hormone analysis.



Graphic 1. Sperm concentrations of individuals according to COVID-19 periods

COVID-19: Coronavirus disease-2019

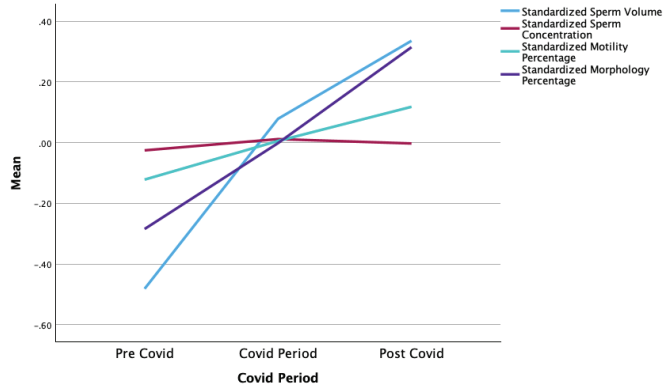


Figure 1. Sperm parameters of individuals according to COVID-19 periods

COVID-19: Coronavirus disease-2019

Table 1. Sperm parameters of individuals according to COVID-19 periods

Parameters	Pre-COVID-19 $\bar{x}$ ± SD (n=2378)	Pandemic period $\bar{x}$ ± SD (n=5568)	Post-COVID-19 $\bar{x}$ ± SD (n=2136)	p-value
Age	30.14±6.75	30.91±7.32	30.72±7.17	-
Sperm volume (mL)	2.78±1.36	2.83±1.38	2.81±1.45	0.174
Sperm concentration (10^6/mL)	25.4±21.9	46.5±38.8	56.2±41.3	**0.001***
Motility (%)	40.5±14.21	42.54±16.08	44.34±17.45	**0.001***
Morfology (%)	0.97±1.20	1.39±1.42	1.85±1.39	**0.001***

Values are presented as mean ± SD. Differences between groups were assessed using the Kruskal-Wallis test. Post-hoc pairwise comparisons were performed where applicable. A p-value <0.05 was considered statistically significant.
SD: Standard deviation, COVID-19: Coronavirus disease-2019, *: p<0.05

Table 2. Hormonal parameters of individuals according to COVID-19 periods

Parameters	Pre-COVID-19 $\bar{x}$ ± SD (n=2378)	During COVID-19 $\bar{x}$ ± SD (n=5568)	Post-COVID-19 $\bar{x}$ ± SD (n=2136)	p-value
Testosterone	3.81±1.67	4.24±1.85	4.15±1.72	**0.001***
FSH	11.60±15.21	7.96±8.38	6.93±8.36	**0.001***
LH	6.75±5.52	7.08±4.91	6.81±4.14	**0.001***
Estradiol	29.12±13.40	31.32±15.04	28.46±13.05	0.126
Prolactin	11.60±5.84	12.72±6.71	11.94±4.50	**0.001***

Values are presented as mean ± SD. Group comparisons were conducted using the Kruskal-Wallis test. Correlations were examined with the Pearson correlation coefficient (r). A p-value <0.05 was considered statistically significant.
SD: Standard deviation, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, COVID-19: Coronavirus disease-2019, *: p<0.05

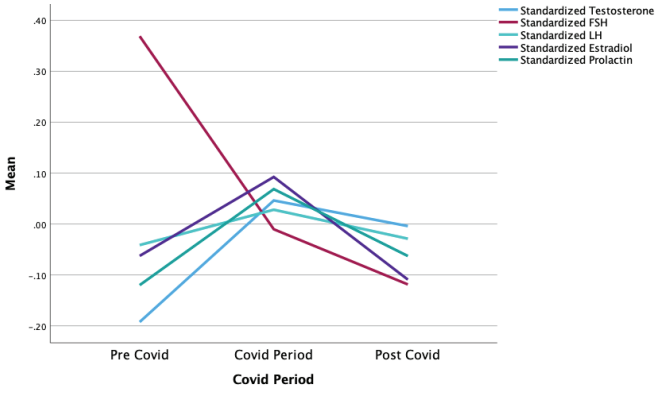


Figure 2. Hormonal parameters of individuals according to COVID-19 periods

COVID-19: Coronavirus disease-2019, FSH: Follicle stimulating hormone, LH: Luteinizing hormone

Discussion

In our study, we examined 10,082 semen analyses from 6.517 different patients, each given at different periods. This is because urology guidelines recommend examining at least two sperm analyses performed at different times to diagnose male infertility.

We predict that during the pandemic period, the restrictions leading to decreased air pollution, reduced water resource pollution, and lowered exposure to free oxygen radicals may result in positive changes in sperm parameters and hormone levels.

The data we obtained show significant changes in individuals' hormone levels during and after the COVID-19 pandemic. Specifically, the decrease in FSH and LH levels may indicate changes in hormonal balance during the pandemic. This situation appears to correlate with the increase in sperm levels and the positive changes in testosterone levels. Fluctuations in estradiol and prolactin levels indicate that stress, health status, and lifestyle changes during the pandemic may impact hormonal health.

In a meta-analysis conducted by Cannarella et al. (13), it was found that there was a significant decrease in sperm concentration and motility in COVID-19 patients compared to healthy individuals. Additionally, a decrease in total testosterone and FSH levels was observed, while increases in LH, prolactin, and estradiol levels were noted. However, sex hormone-binding globulin levels showed no changes (13). One of the differences of this study is that it was conducted only on COVID-19 patients rather than the general population. Another difference is that, due to its short duration, it cannot show long-term results.

In a study conducted by Kadihasanoglu et al. (14) on 265 COVID-19 patients, it was shown that testosterone levels were lower and serum LH levels were higher compared to control groups. It is necessary to demonstrate the long-term changes in these patients after COVID-19. Our study's advantage is that it examined the general population rather than an isolated patient group and demonstrated the long-term changes in this population.

In a study by Zhang et al. (15) on the impact of COVID-19 on sperm quality, it was reported that the infection could lead to a decrease in sperm concentration, particularly after the infection. However, researchers reported that these effects on semen parameters were temporary and gradually recovered within 3-6 months post-recovery (16). These findings appear to be consistent with our study.

In a study conducted by Temiz et al. (17) on COVID-19 patients, a significant decrease in the percentage of normal sperm morphology was demonstrated, and it was suggested that this was due to fever (16). Indeed, other studies have also shown that fever, like inflammation and medications, has negative effects on sperm quality and is temporary (17).

Contrary to the aforementioned example studies, there are also studies in the literature indicating that COVID-19 may have adverse effects on sperm parameters and hormone levels. This discrepancy may have arisen in our study due

to the inability to obtain data on whether each patient was affected by a COVID-19 infection (18-20). However, studies in the literature reflect the short-term effects of COVID-19. In our study, unlike the literature, we evaluated the long-term results.

A meta-analysis reviewing 28 studies found that SARS-CoV-2 was not detected in semen and prostate fluid in 27 studies. A study that examined the semen of 300 patients found SARS-CoV-2 RNA in the semen of only 4 patients (21). The lack of sterile conditions during sample collection led to contamination from aerosols or other bodily fluids from the patients (22). Unlike viruses such as Zika, human immunodeficiency virus, Ebola, hepatit B virus, and hepatit C virus, which can cross the blood-testis barrier and affect semen parameters, it has been shown that SARS-CoV-2, which is 70-100 nm in size, cannot cross the blood-testis barrier and does not affect semen parameters (23,24). All these findings, consistent with the results of our study, indicate that COVID-19 does not have a long-term negative impact on semen parameters.

The COVID-19 pandemic prompted the granting of emergency use authorization for vaccines. This situation raised many concerns regarding the safety of the vaccines. Additionally, misinformation and anti-vaccine campaigns highlighted potential effects on fertility, causing ongoing concerns on social media and the internet. Researchers have examined the impact of mRNA (Pfizer-BioNTech, Mainz, Germany), inactivated virus (Sinopharm, Beijing, China), viral vector (AstraZeneca, Cambridge, UK), and Gam-COVID-Vac (Sputnik V, Gamaleya Institute, Russia) vaccines on semen and hormone parameters, and found no significant changes in these values (25-28). Given that 85% of our study population received at least two doses of the vaccines, long-term hormone and semen analyses reveal no adverse effects on semen parameters.

Study Limitations

According to data obtained from autopsies of individuals who died due to COVID-19 and those who died from various causes after recovering from COVID-19, it has been shown that SARS-CoV-2 infection causes changes in the male reproductive system in the early stages; however, it does not have a long-term impact on male fertility (29). In our study, whether the patients were affected by a COVID-19 infection and their vaccination history were not evaluated, which constitutes one of the limiting factors of the study. Our study's retrospective nature and the absence of semen analyses for all patients in all three periods are other limiting factors. Despite this, our study is significant as it reflects a cross-section of the population.

Conclusion

Although there is sufficient evidence showing changes in the male reproductive system due to SARS-CoV-2 infection, no permanent, long-term effect on male fertility has been identified.

In our study, it was demonstrated that sperm concentration, motility, and morphology showed a significant increase during the COVID-19 period and post-COVID-19 period compared to the pre-COVID-19 period. We also observed significant changes in testosterone, FSH, LH, and prolactin levels. These findings may be attributed to reduced air pollution, decreased contamination of water sources, and lower exposure to free oxygen radicals due to pandemic restrictions.

Given that more than 85% of the population has received two doses of the vaccine, it appears that COVID-19 vaccines do not have harmful effects on male reproductive health. Given the retrospective nature of the study and the large number of patients, population data were adapted for the study. However, we need more randomized, prospective studies to confirm our findings.

Ethics

Ethics Committee Approval: The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. University of Health Sciences Turkey, İstanbul Bağcılar Training and Research and Hospital's Clinical Research Ethics Committee approved the study under approval code 2024/03/04/028.

Informed Consent: All patients participating in the study gave their consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.Y., İ.O.C., İ.H., Concept: S.Y., G.Ç., İ.E.K., Design: S.Y., G.Ç., İ.E.K., Data Collection or Processing: S.Y., F.A., İ.O.C., İ.H., Analysis or Interpretation: S.Y., F.A., İ.O.C., İ.H., Literature Search: S.Y., F.A., İ.O.C., İ.H., Writing: S.Y., İ.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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Civilian Missile and Non-missile Penetrating Spinal Injuries: Experience of A Metropolitan Hospital in Turkey

Sivil Toplumda Ateşli Silah ve Kesici Alet Yaralanmasına Bağlı Gelişen Penetran Spinal Yaralanmalar: Türkiye'de Bir Metropol Hastanesi Deneyimi

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Abstract

Objective: In the civilian population missile and non-missile spinal penetrating injuries and literature on this subject are rare. Injuries were thought to be simpler due to differences in weapons from military. For this reason, we shared our clinical experiences in a center where crime events such as stabbing and shooting are relatively common.

Method: The patients with penetrating spinal injury treated between January 2011 and December 2019 were retrospectively evaluated. Patients were divided into 2 groups according to the type of the injury as missile (MPSI) and non-missile (NMPSI).

Results: Total 23 patients, aged between 1-53 years were evaluated. Two patients were female, 15 had missile and 8 had non-missile injuries. There were 14 thoracic, 4 cervical, 4 lumbar, 1 sacral involvement. Six (40%) of MPSI patients had serious deficits-5 paraplegia due to thoracic lesions, 1 incomplete cauda equine lesion due to lumbar migrating missile and all of these patients were operated for dura repair or removal of migrating missile. 9 patients with MPSI were neurologically normal although 3 of them had vertebral fractures. Four (50%) NMPSI patients had serious deficits, and 2 of them required operations for cerebrospinal fluid fistula. After 11.6±9.9 month follow-up, 7 patients with complete deficits which cause by missile or non-missile injuries did not improve. No problem

Öz

Amaç: Sivil popülasyonda ateşli silah ve kesici aletlerle oluşan penetran spinal yaralanmaları ve bu konuyla ilgili literatür bilgileri nadirdir. Askeri silahlardan farklılıklar nedeniyle yaralanmaların daha basit olduğu düşünülür. Bu nedenle, bıçaklama ve ateş etme gibi suç olaylarının nispeten yaygın olduğu bir merkezdeki klinik deneyimlerimizi paylaştık.

Yöntem: Ocak 2011 ile Aralık 2019 arasında tedavi edilen delici omurga yaralanması olan hastalar geriye dönük olarak değerlendirildi. Hastalar, yaralanma türüne göre ateşli silah (MPSI) ve kesici alet (NMPSI) olmak üzere 2 gruba ayrıldı.

Bulgular: Yaşları 1-53 arasında değişen toplam 23 hasta değerlendirildi. İki hasta kadındı, 15'inde ateşli silah ve 8'inde kesici alet yaralanması vardı. On dört torasik, 4 servikal, 4 lomber, 1 sakral tutulum vardı. MPSI hastalarının altısında (%40) ciddi defisitler vardı - torasik lezyonlar nedeniyle 5 parapleji, lomber göç eden mermi nedeniyle 1 inkomplet kauda ekina lezyonu ve bu hastaların tümü dura onarımı veya yer değiştiren merminin çıkarılması için ameliyat edildi. MPSI olan 9 hasta nörolojik olarak normaldi, ancak 3'ünde omur kırığı vardı. Dört (%50) NMPSI hastasında ciddi defisitler vardı ve 2'si beyin omurilik sıvısı fistülü için ameliyat gerektirdi. 11,6±9,9 aylık takipten sonra, ateşli silah veya kesici alet yaralanmalarının neden olduğu tam defisitli 7 hasta iyileşmedi.

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Abstract

occurred in the follow-up of 13 MPSI and NMPSI patients without deficit, and 3 patients with incomplete spinal cord injury were neurologically improved.

Conclusion: Civilian missile injuries are usually low velocity lesions and have benign course if they do not initially affect spinal cord even they cause fracture of vertebrae. However, non-missile injuries affecting the spinal canal are usually serious because they frequently cause to section the spinal cord. In both cases, we recommend the removal of the foreign object to prevent late complications, infections and toxic effects.

Keywords: Civillian injuries, gunshot wounds, penetrating spinal injuries, stab wounds, spine injury

Öz

Defisiti olmayan 13 MPSI ve NMPSI hastasının takibinde sorun yaşanmadı ve inkomplet omurilik yaralanması olan 3 hasta nörolojik olarak iyileşti.

Sonuç: Sivil ateşli silah yaralanmaları genellikle düşük hızlı lezyonlardır ve omurda kırığa neden olsalar bile başlangıçta omuriliği etkilemedikleri takdirde iyi huylu bir seyir izlerler. Bununla birlikte, omurilik kanalını etkileyen kesici alet yaralanmaları genellikle ciddidir çünkü sıklıkla omuriliğin kesilmesine neden olurlar. Her iki durumda da, geç komplikasyonları, enfeksyonu ve toksik etkileri önlemek için yabancı cismin çıkarılmasını öneriyoruz.

Anahtar kelimeler: Ateşli silah yaralanmaları, kesici alet yaralanmaları, omurga yaralanması, penetran spinal yaralanmalar, sivil yaralanmalar

Introduction

Spinal cord injury (SCI) affects a relatively small proportion of the population compared to other disabling conditions, accounting for only 2.6% of all trauma cases in the United States (1). However, SCI remains a significant medical concern due to the current inability to repair the central nervous system and restore function. Penetrating spinal injury (PSI) is the third leading cause of SCI, following motor vehicle accidents and falls. PSI can be categorized into missile (MPSI) and non-missile (NMPSI) injuries, with the former often caused by gunshot wounds and the latter by stab wounds. These injuries are most prevalent in war zones and areas with high rates of violent crime (2-4).

With the increasing prevalence of firearms in metropolitan areas, missile wounds to the spinal cord are becoming more common than stab wounds. While MPSI may appear more severe due to its high-energy characteristics, isolated MPSI is relatively rare, with its incidence varying across cultures and developmental levels of countries and regions. NMPSI, though often asymptomatic due to the spinal cord's bony protection, can result in irreversible and catastrophic consequences if compromised (1,5,6). Additionally, MPSI is often associated with other systemic injuries, leading to a significantly higher mortality rate compared to NMPSI (1,5,7).

This article aims to share our experiences with PSI in a civilian population to provide insights into the management of this type of injury.

Materials and Methods

This study was approved by the Local Ethics Committee of İstanbul Medipol University Hospital (registration no: 585, date: 07/06/2021).

A retrospective analysis was conducted on all patients with PSI admitted to our neurosurgery clinic in a tertiary training hospital, between January 2011 and December 2019. Patients were categorized into two groups based on the type of injury: MPSI and NMPSI. Data collected included demographic information, cause of injury, injury location, neurological deficits, radiological findings, treatment modalities, and outcomes at the last outpatient examination.

Neurological status was classified into three groups: Normal (no neurological findings), incomplete neurological deficits, and complete neurological deficits (total motor and sensory function loss below the injury level). Cases with incomplete paresis were included in the group.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics (IBM Corp., version 28). Descriptive statistics (frequencies, percentages, means, and standard deviations) summarized patient demographics. We used independent samples t-tests to compare mean ages between MPSI and NMPSI groups. Chi-square tests and Fisher's exact test compared the frequency of neurological deficits and vertebral fractures between groups. A p-value <0.05 was considered statistically significant.

Results

Demographic Data

A total of 23 patients with suspected MPSI or NMPSI were admitted or referred to our clinic during the study period. The female-to-male ratio was 2/21 (91.3% male), with ages ranging from 1 to 53 years (mean 21.0±10.2). Fifteen patients had MPSI, and eight had NMPSI. The mean age for MPSI patients was 23.6±10.4 years, and for NMPSI patients,

it was 18.6±9.5 years. One MPSI patient and one NMPSI patient were female. No correlation was found between injury type and age (p=0.230) or sex (p=0.675).

Seven of the eight NMPSI cases (87.5%) were caused by knife injuries. One 9-year-old female patient with NMPSI presented after her back hit an iron fence.

Injury Levels

There were 14 thoracic, 4 cervical, 4 lumbar, and 1 sacral injuries. The injured levels for MPSI and NMPSI patients are detailed in Table 1.

Neurological Findings

Thirteen patients (9 with MPSI and 4 with NMPSI,) were neurologically normal, 3 had severe incomplete neurological findings, and 7 had total function loss below the injury level (Table 1). Among the MPSI patients, six had serious deficits-five with paraplegia due to thoracic lesions and one with an incomplete cauda equina lesion from a lumbar migrating missile. One of these patients, a 26-year-old male, presented with a gunshot wound that entered 15 cm lateral, from the L1 level and lodged in the spinal canal at the L5 level. On examination, he showed 3/5 weakness in both lower extremities and reported hypoesthesia between T10 and L3, loss of anal sphincter tone, and inability to feel his urine (Figure 1). Four of the eight NMPSI patients had significant neurological deficits: Two with paraplegia from complete lesions at the T5 level, one with quadriparesis from a C5 lesion, and one with right lower extremity paresis from a T8 lesion. Imaging of one of these patients is shown in Figure 2. No significant difference was observed in the frequency of neurological deficits between the two groups.

Injury locations and neurological status were compared between MPSI and NMPSI, in Table 1. No significant correlation was found between injury location and neurological status in MPSI patients (p=0.113). However, in NMPSI cases, neurological deficits were significantly more common in thoracic injuries compared to other locations (p<0.001).

Bony Involvement

Six of the 15 MPSI patients had no vertebral fractures and were neurologically normal. Three patients had vertebral fractures, but were also neurologically normal. Vertebral fractures were present in 6 MPSI patients with neurological findings. The presence of neurological findings was

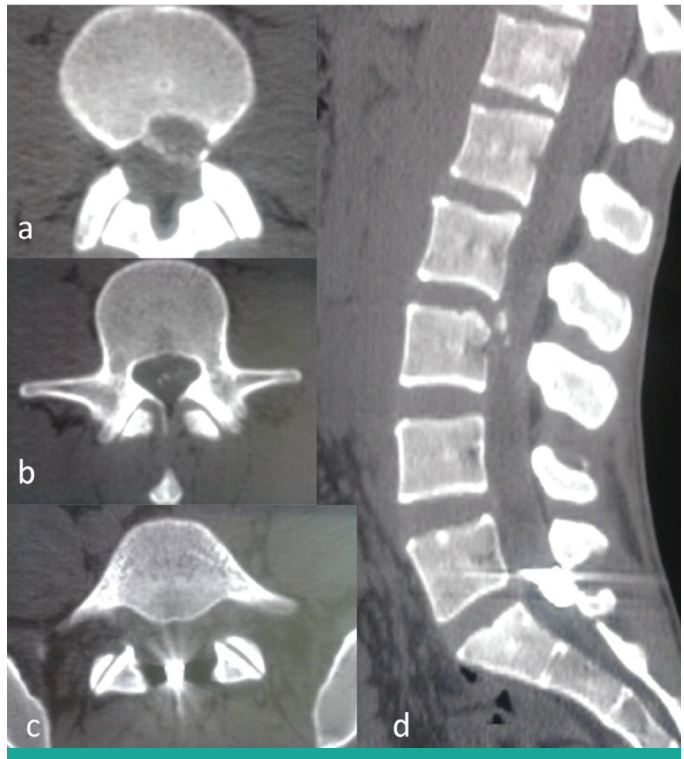

Figure 1. Twenty-seven-year-old male patient with missile injury. Missile penetration site was on 15 cm lateral of left side of L1 spinous process' level. Small bone pieces were seen in left side of spinal canal at L1 level (a) and midline of spinal canal at L3 level (b) and the missile was seen in the spinal canal at S1 level (c and d)

Table 1. Injury levels of the cases

Localization and clinic	Cervical	Thoracic	Lumbar	Sacral	Total
Missile injuries	2 (8.7%)	10 (43.5%)	2 (8.7%)	1 (4.3%)	15 (65.2%)
Normal	2	5	1	1	9 (39.1%)
Incomplete	0	0	1	0	1 (4.3%)
Complete	0	5	0	0	5 (21.8%)
Non-missile injuries	2 (8.7%)	4 (17.4%)	2 (8.7%)	0	8 (34.8%)
Normal	1	1	2	0	4 (17.4%)
Incomplete	1	1	0	0	2 (8.7%)
Complete	0	2	0	0	2 (8.7%)
Total	4 (17.4%)	14 (60.9%)	4 (17.4%)	1 (4.3%)	23 (100%)

significantly higher in patients with vertebral fractures compared to those without vertebral fractures ($p<0.001$). No vertebral fractures were observed in NMPSI patients.

Treatment

Five of the nine MPSI patients without deficits underwent surgery for missile removal. The remaining six MPSI patients with serious neurological deficits (five with paraplegia from complete spinal cord transection at thoracic levels and one with an incomplete cauda lesion from a lumbar migrating missile) underwent surgery for dural repair or removal of the migrating missile causing the neurological deficit. The patient with the incomplete lumbar deficit secondary to lumbar MPSI underwent unilateral hemilaminectomy for decompression, intradural bullet removal, and duraplasty (Figure 3).

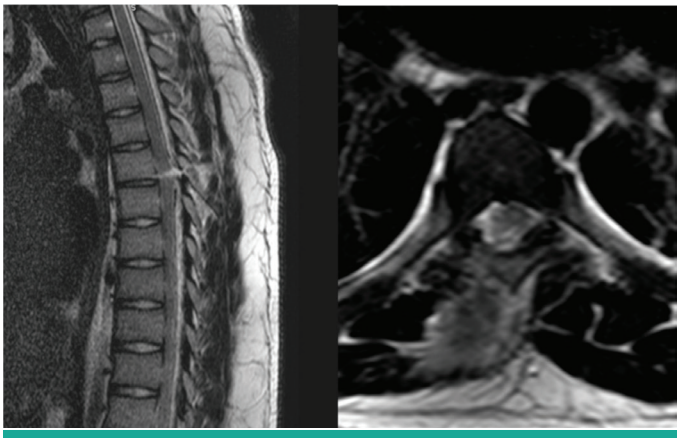

Figure 2. Imaging of the patient with complete dissection of spine in T5 level due to stab wound

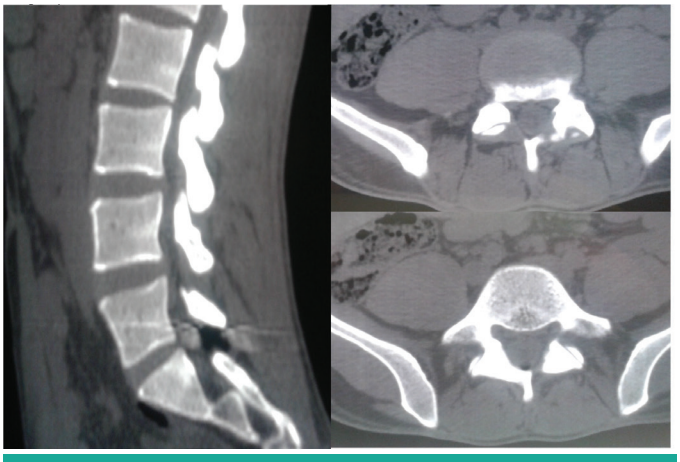

Figure 3. Postoperative computed tomography images of 27-year-old patient who had a missile removed from his spinal cord. The patient underwent unilateral hemilaminectomy for decompression, foreign body removal and duraplasty

Two NMPSI patients with a complete lesion at T5 and an incomplete lesion at T8 underwent surgery for cerebrospinal fluid (CSF) fistulas. The 9-year-old female NMPSI patient underwent surgery for foreign body removal and dural repair. Surgery was not required for the other NMPSI patients.

Follow-up and Outcome

The mean follow-up time was 4±1.5 months (range: 1 month to 1 year). The 13 patients without any neurological deficits remained unchanged during follow-up. Three patients with incomplete SCI showed neurological improvement. One of these patients with the lumbar MPSI, demonstrated neurological improvement after 2 months. His lower extremity strength improved, and he experienced minimal recovery of anal sphincter tone, although bladder sensation remained unchanged. Two NMPSI patients with incomplete lesions also improved after 2 to 6 months. However, no improvement was observed in the 7 patients with complete deficits during follow-up.

Discussion

We analyzed penetrating spinal injuries in a civilian population, categorizing them into missile (gunshot wounds) and non-missile (stab wounds with knives or other sharp objects) injuries.

The most common causes of SCI are motor vehicle accidents and falls from height, with penetrating wounds being the third leading cause. Penetrating SCIs constitute less than 15% of all SCIs. The National Spinal Cord Injury Database (NSCID) estimates approximately 3500 new cases of penetrating SCI in the USA each year (1-3). PSIs can be broadly classified into two groups: missile (MPSI) and non-missile (NMPSI) injuries (2,3,8,9).

While there are cultural variations, MPSI is generally more common than NMPSI. According to the NSCID, approximately 95% of PSIs in the USA are caused by gunshot wounds (3). Burney et al. (1) reported that stab wounds cause only 1% of all SCI cases in the USA. In contrast, Peacock et al. (10) found that NMPSI accounted for 25% of all SCI cases in South Africa.

These findings suggest that penetrating SCI, particularly stab wounds, may be more prevalent among less educated individuals in areas with lower socioeconomic status and in developing countries. In our study, 34.8% of PSI cases were caused by stab wounds. Our clinic is situated in an area with a lower socioeconomic level than other parts

of Istanbul, which may explain the higher incidence of NMPSI, compared to other studies.

Knives are the most common weapons used in NMPSI, accounting for 84% of cases (11). In our study, 87.5% of NMPSI cases were caused by knives. Almost all NMPSI incidents occurred when victims were stabbed from behind.

According to the NSCID, approximately 80% of patients affected by MSCI and NMSCI are male, with a mean age of 29.7 years (3). Our study similarly found that 91.3% of patients were male, with a mean age of 21.0 years, consistent with the literature.

Previous studies on PSI have reported the thoracic spine as the most commonly affected level, accounting for approximately 50-60% of cases (2,3,8,9,12). Specifically, around 50% of MPSI and 60% of NMPSI involve the thoracic spine (1,10,13). Our results align with these findings, with 60.9% of all cases, 66.7% of MPSI cases, and 50% of NMPSI cases affecting the thoracic spine.

In penetrating trauma, SCI can range from normal appearance to complete anatomic destruction. MPSI is associated with a high incidence of neurological damage, caused by multiple mechanisms, primarily, the blast effect and direct mass effect of the missile. Military weapons cause more extensive damage due to the blast and secondary effects of high-velocity missiles. However, in civilian missile injuries, the prognosis is generally better due to the limited blast effect from lower-velocity and smaller-mass missiles (4,12-14). In these patients, the primary causes of damage are missile penetration into the spinal canal and spinal damage from bone fragments due to vertebral fractures (12,13). Our study supports this, as among patients without vertebral fractures, none exhibited any fractures exhibited any clinical findings.

Most studies on the management of spinal gunshot injuries are based on military experiences, and managing MPSI in these studies remains complex, and challenging. However, civilian gunshot wounds to the spine are typically low-velocity injuries, and the incidence of spinal cord involvement is lower than in military injuries. Consequently, conservative management is often sufficient for civilian injuries (8,15). Surgical indications for MPSI include removal of foreign bodies penetrating or compressing the spinal cord, progressive neurological deficits after admission, CSF fistula, or spinal instability. Additionally, late complications such as infections and pain syndromes may necessitate surgery.

In our study, 11 MPSI patients required surgery for exploration or bullet removal. Five of these patients were neurologically normal, and no complications arose during their follow-up. Five of the 11 patients had paraplegia due to complete spinal cord transection and showed no improvement. One patient with an incomplete deficit who underwent surgery on the day of admission for migrating bullet removal showed neurological improvement. In incomplete SCI, some case reports suggest that emergent foreign body removal can improve neurological status. Additionally, removal can prevent future toxic effects from the bullet. Some case reports also indicate that late surgical removal of a foreign body can improve neurological status, whereas others show improvement without surgical removal (7,8,14,15). Many authors suggest that exploration should not be attempted in the early period if there is no CSF leak or neurological deficit (2,9). Nevertheless, the improvement seen in our patient suggests that early surgical removal of a foreign body may have the potential to improve prognosis. However, the improvement seen in our patient with a lumbar injury highlights the potential for favorable outcomes with early surgical intervention. This patient presented with weakness and sensory deficits in the lower extremities, along with abnormal anal sphincter tone and neurogenic bladder. The bullet lodged in the spinal canal and became displaced, continuing to pose a risk of further neurological deterioration. Given the patient's young age and potential for recovery, the decision was made to perform early surgical removal of the bullet and duraplasty. The subsequent improvement in motor function and anal sphincter tone supports our belief that early surgical intervention may provide a significant advantage and should be strongly considered in selected cases of incomplete SCI in which a foreign body is trapped, compressing neural structures.

In stab wounds, SCI is expected to be less common due to the protection provided by the bony structures of the vertebral column. However, in our study, SCI was more common in NMPSI than in civilian MPSI. Most SCIs in NMPSIs result from hemisection of the spinal cord, leading to incomplete neurological deficits. This occurs because, during an assault, the sharp object is often guided along the gutter between the spinous and transverse processes of the vertebra. Consequently, the most common clinical presentation is Brown-Sequard syndrome. In these patients, the prognosis is better than in those with complete deficits (6,16). Conversely, when neurological deficit is complete, it generally does not improve, as it is often caused by complete transection of the spinal cord (17,18).

There is no standardized strategy for removing a foreign body through closed or open surgery in NMPSI, and the decision for surgical exploration remains controversial (8,16,17). However, early debridement and removal of the foreign body can prevent infection, relieve compression, and potentially improve neurological function (18). Furthermore, removing metallic materials, such as the case of our patient who was injured by an iron fence, allows for future magnetic resonance imaging investigations. Additionally, potential toxic effects from the foreign body are avoided.

In our study, four out of nine NMPSI patients underwent surgery because of a CSF fistula. Two of these patients with incomplete neurological deficits showed neurological improvement during follow-up, while the two with complete deficits remained unchanged, which was expected. Recovery from complete neurological deficits is not anticipated in either missile or non-missile injuries. In our study, 7 patients had complete deficits, and none showed neurological improvement. However, cauda equina lesions and incomplete spinal cord deficits may recover, as seen in 3 of our patients. These patients represent the group that requires particular attention from surgeons and prompt treatment decisions. Based on these results, the prognosis for patients with complete deficits is poor. However, incomplete neurological deficits, especially Brown-Sequard syndrome in stab wounds, often improve.

Study Limitations

This study is limited by its retrospective design, small sample size (n=23), and single-center setting, which may affect the generalizability of the findings. The short follow-up period (mean 4 months) may not capture long-term outcomes or late complications. The heterogeneity within the MPSI and NMPSI groups and the lack of a control group and standardized treatment protocols also limit the ability to draw definitive conclusions about treatment efficacy. Future prospective studies with larger samples, longer follow-up, and standardized protocols are needed to further investigate the management of penetrating spinal injuries.

Conclusion

Civilian missile injuries are typically low-velocity lesions and may have a benign course if they do not initially affect the spinal cord or cause vertebral fractures. Stab wounds affecting the spinal canal are less common than missile wounds but can be very serious as they often result in spinal cord transection. Surgical indications include neurological compression causing deficits, intramedullary abscess, and open or closed CSF fistulas. In cases of gunshot injuries where the bullet remains in the body, and penetrating injuries, where a foreign body is present, surgery may be considered to prevent late complications and toxic effects related to the foreign body. Improvements in the prognosis of our patients with incomplete damage who underwent early surgery support this approach. Therefore, we recommend that the missile or foreign body be removed whenever possible.

Ethics

Ethics Committee Approval: This study was approved by the Local Ethics Committee of İstanbul Medipol University Hospital (registration no: 585, date: 07/06/2021).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.D., F.K.G., İ.G., B.E., A.T., N.S.B., C.İ., Ö.Y.A., Concept: E.D., F.K.G., İ.G., B.E., A.T., N.S.B., C.İ., Ö.Y.A., Design: E.D., F.K.G., İ.G., B.E., A.T., N.S.B., C.İ., Ö.Y.A., Data Collection or Processing: E.D., F.K.G., İ.G., B.E., A.T., N.S.B., C.İ., Ö.Y.A., Analysis or Interpretation: E.D., F.K.G., Literature Search: E.D., F.K.G., Writing: E.D., F.K.G.

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ORIGINAL RESEARCH

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Comparison of Sports Awareness in Adolescents and Evaluation of the Effect of Awareness Levels on Sport Oriented Attitudes

Adolesanlarda Spor Farkındalığının Karşılaştırılması ve Farkındalık Düzeylerinin Spora Yönelik Tutumlarına Olan Etkisinin Değerlendirilmesi

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Abstract

Objective: Adolescence is a period characterized by significant psychological and physical changes which can lead to health issues that can be prevented early on through participation in sports. Adolescents' awareness of sports can either encourage or hinder their approach to sports activities. While studies have explored the factors influencing physical activity levels in adolescents, many of them fall short by not examining the motivational factors behind sedentary behavior. This study aims to assess adolescents' sports awareness and evaluate how it impacts their attitudes toward physical activity.

Method: In this cross-sectional study, the sports awareness scale and sport-oriented attitude scale were administered to 400 healthy adolescents, aged 11 to 18, who presented to the adolescent health outpatient clinic of our institution.

Results: Adolescents with higher sports awareness participated in sports at a higher rate, and their sport-oriented attitude scores were significantly higher than those of adolescents who did not engage in sports. A highly significant relationship was found between all subdimension scores and the total scores of both scales.

Conclusion: This study demonstrated that, contrary to popular belief, the role of sports in adolescents' lives and their sports habits are influenced not only by environmental factors but also by their awareness of sports. It is essential to develop and support policies aimed at combating sedentary lifestyles in adolescents, with a particular focus on girls and children from lower-income families, as they are more likely to have

Öz

Amaç: Adolesan dönem, önemli psikolojik ve fiziksel değişimlerle karakterize bir dönemdir; bu değişimlerin sebep olabileceği sağlık sorunlarının bir kısmı, erken dönemde spor alışkanlığı kazanılması ile önlenebilir. Adolesanların spor farkındalığı, spor faaliyetlerine karşı tutumlarını teşvik edebileceği gibi engelleyici bir faktör de olabilir. Adolesanlarda fiziksel aktivite düzeylerini etkileyen faktörler üzerine yapılmış birçok çalışma bulunsa da, bu çalışmaların birçoğu sedanter davranışların arkasındaki motivasyonel faktörleri incelemekte yetersiz kalmaktadır. Bu çalışma, adolesanların spor farkındalığını değerlendirmeyi ve bunun fiziksel aktiviteye yönelik tutumlarını nasıl etkilediğini incelemeyi amaçlamaktadır.

Yöntem: Bu kesitsel çalışmada, hastanemiz ergen sağlığı polikliniğine başvuran 11-18 yaş aralığında olan 400 sağlıklı adolesana spor farkındalık ölçeği ve spora yönelik tutum ölçeği uygulanmıştır.

Bulgular: Daha yüksek spor farkındalığına sahip adolesanlar, spora daha fazla oranda katılım göstermekteydi ve bu bireylerin spora yönelik tutum puanları, spora katılmayan ergenlere göre anlamlı derecede yüksekti. Her iki ölçeğin tüm alt boyut puanları ile toplam puanları arasında istatistiksel olarak anlamlı düzeyde ilişki saptanmıştır.

Sonuç: Bu çalışma, yaygın inanışın aksine, adolesanların yaşamlarında sporun rolünün ve spor alışkanlıklarının yalnızca çevresel faktörlerle değil, aynı zamanda spor farkındalık düzeyleriyle de şekillendiğini ortaya koymuştur. adolesanlarda, özellikle de daha düşük spor farkındalığına sahip olan düşük gelirli ailelerden gelen çocuklar ile kız çocuklarında

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Abstract

lower levels of sports awareness. Efforts should be made to increase adolescents' awareness of sports and provide more opportunities for participation in sports, to foster the development of healthier generations.

Keywords: Adolescent, attitude, awareness, sport

Öz

sedanter yaşam tarzıyla mücadele etmeye yönelik politikaların geliştirilmesi ve desteklenmesi büyük önem taşımaktadır. Adolesanların spor farkındalıklarını artırarak spora katılımları için daha fazla fırsat tanınması, daha sağlıklı nesillerin gelişimine katkı sağlayacaktır.

Anahtar kelimeler: Adolesan, farkındalık, spor, tutum

Introduction

Adolescence is a critical developmental stage marked by the formation of personal identity, the transition from childhood to adulthood, along with a wide range of psychological and physiological transformations. During this period, biological and physiological changes intensify, and adolescents may struggle to adapt to these rapid shifts (1). If not properly managed, such challenges may lead to physical problems such as postural deformities (e.g., idiopathic scoliosis), metabolic syndrome, and emotional instability, which may persist into adulthood and result in long-term health complications (2).

Engaging in regular physical activity during adolescence is essential for mitigating these risks at an early stage, improving physical activity levels, maintaining spinal health, controlling body weight, and supporting mental well-being. It is also crucial for adolescents to develop a consistent exercise routine because it offers numerous benefits, including supporting growth, promoting long-term health, increasing bone density, reducing the risk of osteoporosis, and preventing obesity and various chronic diseases later in life (3).

Lifestyle behaviors significantly influence overall health. In recent years, shifts in societal and environmental conditions have produced substantial changes in lifestyle behaviors, particularly among adolescents (4). These changes often manifest as poor dietary habits, physical inactivity, and sedentary lifestyles. Today's youth are less active, spend more time on screens—whether computers, mobile devices, or televisions—and neglect regular physical activity. This sedentary lifestyle contributes to numerous health concerns, including orthopedic problems, mental health issues, circulatory problems, difficulty managing weight, and premature mortality (5-7). Therefore, it is vital to raise awareness about these detrimental behaviors and their consequences to protect young individuals and foster their healthy development.

Awareness is defined as "being conscious of something". As it is shaped by prior knowledge, personal experience, and reinforcement processes, awareness is inherently subjective (8). Increasing an individual's knowledge and learning enhances theirawareness.

According to the psychological continuum model (9), which was introduced in 2001, awareness leads to allegiance. This hierarchical model consists of four stages: awareness, attraction, attachment, and allegiance. It proposes that a person must first develop awareness of a sports object before forming an emotional or behavioral connection to it. For example, an adolescent who has never played basketball or watched a game is unlikely to become a committed player or fan without first being introduced to the sport and its benefits.

Sports awareness refers to increasing individuals' awareness of sports. In other words, it involves learning about the physical, mental, and social benefits of sports, linking these benefits to various aspects of life, applying this knowledge in real-life situations, and promoting awareness of these benefits within the community (10). Awareness can facilitate or inhibit a person's approach to a sporting object. As a result, the individual will form a stronger psychological connection to it and internalize the concept of the sport object (11). Acquiring the habit of engaging in sports at an early age is crucial for fostering healthy individuals and societies. To achieve this goal, it is essential to identify these behavioral patterns, particularly during childhood and adolescence.

While many studies have investigated factors affecting adolescents' physical activity, they often emphasize demographic or environmental influences (e.g., sex, ethnicity, age, weight status, parenting practices, season, and excessive screen time) overlooking deeper motivational and psychological drivers of inactivity (12-14). This highlights a gap in understanding the motivational determinants of sedentary behavior. It is essential for clinicians to assess adolescents' awareness of the importance and benefits of sports, evaluate the degree of that awareness, and observe how it influences their attitudes toward physical activity.

Only in this way can we help raise healthy generations by increasing young people's awareness of sports and encouraging their regular participation in sports. Therefore, additional research is needed to investigate the connection between awareness and attitude.

This study aims to assess adolescents' awareness and evaluate how it impacts their attitudes and behaviors, to identify key motivational factors that support early and sustained engagement in physical activity.

Materials and Methods

Study Design and Participants

This cross-sectional study included 400 healthy adolescents aged 11-18 years who attended the pediatric outpatient clinic of the Ankara Atatürk Sanatoryum Training and Research Hospital. Participants were categorized into two groups based on their level of sports activity. The "active" group consisted of 200 adolescents who regularly participated in either individual or team sports for at least 40 minutes per day, on a minimum of three days per week, for at least one year. The remaining 200 adolescents who did not meet these criteria were classified as the "inactive" group.

The sample size was calculated using G*Power. Assuming a medium effect size of 0.5 and 95% power, the required number of participants was 105 per group (15,16).

Inclusion criteria for both groups were: Being 11-18 years of age, having no medical condition that contraindicates participation in sports, having a normal body mass index (BMI), and providing informed consent to participate. Adolescents were excluded if they were younger than 11 or older than 18, if they declined to participate, if they had medical limitations preventing physical activity, or if they were classified as obese based on BMI.

Anthropometric measurements were taken during clinical examinations. Body weight was measured using a calibrated digital scale, and height was recorded using a standard stadiometer. BMI was calculated using the formula: BMI = weight (kg)/height $(m)^2$.

Measures

The sports awareness scale (SAS) was developed in line with the psychological continuum model and Bloom's taxonomy theory. Its validity and reliability were established by Uyar and Sunay (10). The scale consists of 30 items across two sub-dimensions: "Sport information and discrimination" (21 items) and "social and individual benefit" (9 items). Responses are scored using a 5-point Likert scale, yielding a total score ranging from 30 to 150. Higher scores indicate greater awareness of the benefits of sports. Awareness levels are categorized as follows: 30-53= "not aware at all", 54-77= "not aware", 78-102= "moderately aware", 103-126= "aware", and 127-150= "fully aware" (10).

The sport-oriented attitude scale (SOAS) was developed by Sentürk in 2015 to assess individuals' propensity to engage in sports, their perspectives on sports, sports habits, and the role of sports in shaping their character—essentially evaluating attitudes toward sports (17). The scale comprises 25 positively scored items, with total scores ranging from 25 to 125. Higher scores indicate a stronger and more favorable attitude toward sports. The scale includes three sub-dimensions: "Giving importance to sport", "being interested in sport", and "engaging in physical exercise or sport" (17). The scale contains no reverse-coded items, which is consistent with research suggesting that negatively worded items may introduce cognitive bias and compromise internal consistency (18).

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics 23, IBM Inc., Chicago, IL, USA). Prior to analysis, datasets were reviewed for missing values and tested for normality (univariate and multivariate), linearity, and multicollinearity to ensure that statistical assumptions were satisfied.

Confirmatory factor analyses were conducted to assess the construct validity of the scales. Differences between the active and inactive groups were evaluated by comparing subscale scores from the SAS and SOAS. Generalized linear models were applied to examine interactions between awareness and attitude levels, with estimated means reported along with 95% confidence intervals. Depending on data distribution, Pearson or Spearman correlation coefficients were calculated to assess the relationships between variables. Group comparisons were performed using either the Student's t-test or the Mann-Whitney U test, based on the assumption of normality. Statistical significance was considered if the p-value was less than 0.05 ($p<0.05$).

Ethical Considerations

This study was conducted in accordance with the Declaration of Helsinki and received approval from the regional Ethics Committee of Ankara Atatürk Sanatoryum Training and Research Hospital (approval number: 2024/482, date: 26.06.2024). All participants were thoroughly informed

about the purpose, procedures, potential risks, and benefits of the study. Written informed consent was obtained prior to enrollment.

Results

This study included a total of 400 healthy adolescents, comprising 200 girls and 200 boys, with a mean age of 14.6±2.2 years. Of these, 200 adolescents reported regular participation in sports activities, whereas the remaining 200 did not engage in any organized physical activity. The majority of participants were high school students, resided in urban areas (city center and central districts), and came from middle-income nuclear families. Additional demographic characteristics are presented in Table 1.

A significant association was observed between age and sports participation; younger adolescents were more likely to engage in sports ($p<0.005$). Similarly, the frequency of physical activity was higher among middle school students than their older peers ($p<0.005$). Adolescents who had close friends who were actively involved in sports and those who resided in urban settings were significantly more likely to participate in physical activity ($p<0.005$ and $p=0.027$, respectively). In contrast, having a family member engaged in sports did not exert a statistically significant influence on adolescents' own participation in sports ($p=0.491$). Furthermore, no significant differences were identified between groups with respect to family type or household income level ($p=0.321$ and $p=0.459$, respectively) (Table 1).

When the scores of both the SAS and the SOAS were compared, statistically significant differences were observed across all dimensions. Higher scores were consistently recorded in the physically active group ($p<0.05$).

Table 1. Demographic data of the study group according to sports activity status

	Total (n=400)	Sport (-) (200)	Sport (+) (200)	p-value
Age (years)[a]	14.6±2.2	15.1±2.1	14.1±2.2	**<0.001**
Weight (kg)[a]	56.7±12.4	58.1±12.4	55.3±12.2	**0.023**
Height (cm)[a]	164.5±10.9	165.5±10.1	163.4±11.5	**0.044**
BMI (kg/m²)[a]	20.8±3.2	21.1±3.4	20.5±2.9	0.083
Gender[b]				**<0.001**
Girls	200 (50%)	123 (61.5%)	77 (38.5%)	
Boys	200 (50%)	77 (38.5%)	123 (61.5%)	
Educational level[b]				**<0.001**
Middle school	129 (32.3%)	46 (23%)	83 (41.5%)	
High school	246 (61.5%)	140 (70%)	106 (53%)	
University	25 (6.2%)	14 (7%)	11 (5.5%)	
Family type[b]				0.321
Nuclear family	350 (87.5%)	172 (86%)	178 (89%)	
Extended family	23 (5.8%)	15 (7.5%)	8 (4%)	
Single-parent family	27 (6.8%)	13 (6.5%)	14 (7%)	
Residential area[b]				0.027
Urban	245 (61.3%)	128 (64%)	117 (58.5%)	
Suburban	144 (36%)	63 (31.5%)	81 (40.5%)	
Rural	11 (2.7%)	9 (4.5%)	2 (1%)	
Family income[b]				0.459
Low	37 (9.3%)	15 (7.5%)	22 (11%)	
Middle	340 (85%)	174 (87%)	166 (83%)	
High	23 (5.7%)	11 (5.5%)	12 (6%)	
Family member involved in sport[b]				0.491
Siblings	107 (26.8%)	51 (25.5%)	56(28%)	
Mother/father	31 (7.8%)	13 (6.5%)	18 (9%)	
None	262 (65.5%)	136 (68%)	126 (63%)	
Close friend involved in sports[b]				**<0.001**
Yes	284 (71%)	110 (55%)	174 (87%)	
No	116 (29%)	90 (45%)	26 (13%)	
Sport licence[b]				**<0.001**
Yes	108 (27%)	0	108 (54%)	
No	294 (73%)	200	92 (46%)	

Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and within-group percentages.
[a]: $p<0.05$ assessed through independent samples t- analysis, [b]: $p<0.05$ assessed through chi-squared analyses, BMI: Body mass index

Table 2. The scores of the scales according to gender and sports activity status

		Sports awareness scale			Sport-oriented attitude scale			
		SID score	SIB score	Total score	GIS score	BIS score	DPES score	Total score
General population	**Sport (-)**	65.6±16.3	36.1±7.1	101.7±21.1	39.2±9.1	21.7±5.1	17.4±4.6	78.3±17.7
	Sport (+)	81.8±11.6	40.8±3.6	122.5±13.4	49.4±6.3	28.1±4.3	24±3.4	101.5±12.3
	p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.007**	**<0.001**	**<0.001**
Girls	**Sport (-)**	**63.9±16.2**	**36.3±6.5**	**100.2±20.3**	**39.8±8.4**	**22±5.2**	**17.4±4.5**	**79.2±16.8**
	Sport (+)	80.4±12.4	41±4	121.5±14.2	49.5±6.2	27.9±4.5	23.3±3.5	100.7±12.6
	p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**
Boys	**Sport (-)**	68.3±16.2	35.7±8.1	104±22.3	38.1±10.2	21.1±5.1	17.4±4.7	76.8±19.2
	Sport (+)	82.6±10.9	40.6±3.4	123.2±12.8	49.3±6.4	28.3±4.1	24.4±3.3	102±12.1
	p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.019**	**0.005**	**<0.001**
Sport (-)	Girls	63.9±16.2	36.3±6.5	100.2±20.3	39.8±8.4	22±5.2	17.4±4.5	79.2±16.8
	Boys	68.3±16.2	35.7±8.1	104±22.3	38.3±10.2	21.1±5.1	17.4±4.7	76.8±19.2
	p-value	0.061	0.529	0.221	0.281	0.210	0.991	0.357
Sport (+)	Girls	80.4±12.4	41±4	121.5±14.4	49.5±6.2	27.9±4.5	23.3±3.5	100.7±12.6
	Boys	82.6±10.9	40.6±3.4	123.2±12.8	49.3±6.4	28.3±4.1	24.4±3.3	101.9±12.1
	p-value	0.196	0.434	0.368	0.784	0.501	**0.025**	0.479
Sport (+)	Sport licence (-)	80±12.5	40.5±3.5	120.4±13.8	47.7±6.7	27.2±4.3	23.5±3.4	98.5±12.7
	Sport licence (+)	83.3±10.5	41±3.7	124.3±12.9	50.8±5.7	28.9±4.1	24.3±3.4	104±11.4
	p-value	**0.040**	**0.267**	**0.038**	**<0.001**	**0.005**	0.083	**<0.001**

Continuous variables were expressed as mean ± standard deviation, SID: Sport information and discrimination, SIB: Social and individual benefit, GIS: Giving importance to sport, BIS: Be interested in sport, DPES: Doing physical exercises or sport

These differences remained evident after stratification by gender: Both male and female adolescents who participated in sports demonstrated significantly higher levels of sports awareness and more favorable attitudes toward sports ($p<0.05$).

However, gender did not significantly influence overall sports awareness or sport-oriented attitudes. However, within the subdimension "doing physical exercises or sports", boys in the sports group scored significantly higher than girls ($p=0.025$). Furthermore, adolescents holding an official sports license demonstrated significantly higher scores on both the SAS and SOAS compared to their non-licensed peers ($p=0.038$ and $p<0.005$, respectively; see Table 2).

No significant associations were detected between most demographic variables (e.g., BMI, education level, family structure, residential area) and total scores on either the SAS or SOAS ($p>0.05$). Nonetheless, younger participants tended to score higher on the SOAS, indicating more favorable attitudes toward sports. In addition, adolescents with close friends who were actively engaged in sports demonstrated significantly higher levels of both awareness and sport-oriented attitudes ($p<0.005$).

Analysis of sports awareness levels—based on the categorical classification of SAS scores—revealed a clear positive correlation between awareness and attitude. As adolescents' sports awareness increased, their sports-oriented attitude scores rose correspondingly ($p<0.005$). Higher awareness was also associated with being male, belonging to middle- to high-income families, having close friends involved in sports, participating in team sports, and holding an official sports license (p-values <0.005, 0.022, <0.005, <0.005, and <0.005, respectively) (Table 3).

No significant associations between sports awareness and BMI, education level, family type, residential location, or the presence of a family member involved in sports were observed ($p>0.05$) (Table 3).

A highly significant positive correlation was identified between all subdimension scores and total scores of the SAS and SOAS in the full sample and within both active and inactive subgroups ($p<0.005$). Adolescents with greater sports awareness—particularly in the dimensions of sport information and discrimination—exhibited stronger sports-oriented attitudes. These individuals were more likely to value sports, display greater interest in sports activities, and engage in regular physical exercise.

Table 3. Level of awareness according to participants' characteristics

	Sports awareness scale					p-value
	Not aware at all (6)	Not aware (18)	Moderately aware (74)	Aware (200)	Fully aware (102)	
GIS[a]	21.7±5.9	26.8±8.9	37±8.3	45.2±6.1	52.7±4.7	**<0.001**
BIS[a]	11.5±4	16.4±5.1	20.3±4.5	25.4±4.3	29.5 ±3.4	**<0.001**
DPES[a]	9±3.3	12±4.5	16.3±3.6	21.3±3.7	25.1±3.2	**<0.001**
Total SOAS[a]	42.2±13.1	55.1±17.3	73.1±13.4	91.9±12.5	107.3±9.4	**<0.001**
BMI[a]	20.2±2.1	20.4±2.8	21.1±3.7	21±3.1	20.4±3	0.530
Gender[b]						**<0.001**
Girls	3 (50%)	12 (66.7%)	48 (64.9%)	96 (48%)	41 (40.2%)	
Boy	3 (50%)	6 (33.3%)	26 (35.1%)	104 (52%)	61 (59.8%)	
Educational level[b]						0.350
Middle school	4 (66.7%)	9 (50%)	19 (25.7%)	63 (31.5%)	34 (33.3%)	
High school	2 (33.3%)	7 (38.9%)	50 (67.6%)	125 (62.5%)	62 (60.8%)	
University	-	2 (11.1%)	5 (6.8%)	12 (6%)	6 (5.9%)	
Family type[b]						0.841
Nuclear f.	6 (100%)	15 (83.3%)	63 (85.1%)	174 (87%)	92 (90.2%)	
Extended f.	0	2 (11.1%)	5 (6.8%)	10 (5%)	6 (5.9%)	
Single parent f.	0	1 (5.6%)	6 (8.1%)	16 (8%)	4 (3.9%)	
Residential area[b]						0.067
Urban	6 (100%)	12 (66.7%)	42 (56.8%)	130 (65%)	55 (53.9%)	
Suburban	0	4 (22.2%)	29 (39.2%)	67 (33.5%)	44 (43.1%)	
Rural	0	2 (11.1%)	3 (4.1%)	3 (1.5%)	3 (2.9%)	
Family income[b]						**0.022**
Low	0	2 (11.1%)	3 (4.1%)	27 (13.5%)	5 (4.9%)	
Middle	6 (100%)	16 (88.9%)	70 (94.6%)	156 (78%)	92 (90.2%)	
High	0	0	1 (1.4%)	17 (8.5%)	5 (4.9%)	
Family member involved in sports[b]						0.571
Siblings	0	6 (33.3%)	16 (21.6%)	60 (30%)	25 (24.5%)	
Mother/father	1	0	7 (9.5%)	15 (7.5%)	8 (7.8%)	
No	5	12 (66.7%)	51 (68.9%)	125 (62.5%)	69 (67.6%)	
Close friend involved in sports[b]						**<0.001**
Yes	2 (33.3%)	7 (38.9%)	37 (50%)	151 (%)	87 (85.3%)	
No	4 (66.7%)	11 (61.1%)	37 (50%)	49 (24.5%)	15 (14.7%)	
Type of sport[b]						**<0.001**
No sport	6 (100%)	15 (83.3%)	48 (64.9%)	64 (32%)	12 (11.8%)	
Individual	0	3 (16.7%)	19 (25.7%)	72 (36%)	40 (39.2%)	
Team	0	0	7 (9.5%)	64 (32%)	50 (49%)	
Sport licence[b]						**<0.001**
Yes	0	0	4 (5.4%)	53 (26.5%)	51 (50%)	
No	6 (100%)	18 (100%)	70 (94.6%)	147 (73.5%)	51 (50%)	

Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and within-group percentages. SOAS: Sport-oriented attitude scale, GIS: Giving importance to sport, BIS: Be interested in sport, DPES: Doing physical exercises or sport, BMI: Body mass index, [a]: p<0.05 assessed through One-Way Analysis of Variance, [b]: p<0.05 assessed through chi-squared analyses

Discussion

To the best of our knowledge, no previous study has directly examined the impact of sports awareness on sports-oriented attitudes among adolescents. Existing research on sports awareness is limited and generally focuses on assessing "recall and knowledge levels" rather than comprehensively evaluating awareness. In contrast, the present study investigated the influence of sports awareness on sports-oriented attitudes and found a strong positive correlation between the two constructs.

Our findings further indicate that adolescents' tendency to engage in sports decreases with age. While sports participation is relatively common during middle school, participation rates decline significantly during high school and university years, likely due to increased academic pressure and risk of burnout. Supporting this, Valenzuela-Moss et al. (19) reported that weekly exercise frequency dropped from 4.0 to 2.3 days and overall participation decreased from 82% to 39% between 7th and 12th grades.

Although they did not differ significantly by grade, school-related burnout was more common among high-school students than among middle-school students (69% vs. 36%) and was higher among girls (19). Similarly, data from the National Health Interview Survey indicated that a greater proportion of boys (56.1%) than girls (52%) participated in sports (20). Consistent with these findings, our study also observed lower participation rates among girls. These results highlight the need for targeted interventions by health professionals and the broader community—including parents, teachers, and coaches—particularly during the transition from middle to high school, to create diverse and supportive opportunities for girls to engage in sports.

Although adolescents who participated in sports demonstrated lower mean height and weight, this finding is likely explained by the higher sports participation rate among younger age groups. Importantly, no significant difference was found in BMI between groups, because obese individuals were excluded to minimize confounding by obesity.

Demographic variables such as age, gender, BMI, grade level, family structure, family income, residential area, and family members' participation in sports did not significantly influence sports participation, sports awareness, or sport-oriented attitudes. While previous studies have emphasized the role of family and socio-economic status in shaping youth sports experiences and have argued that gender should be addressed through policies promoting equitable access (21,22), our findings suggest that sports attitudes are more strongly driven by awareness and intrinsic motivation rather than by external opportunities or environmental influences.

The lack of a significant effect of economic status may also reflect the impact of national policies in Turkey that require local governments to provide basic sports facilities (e.g., swimming pools, gyms, sports fields). The National Youth and Sports Policy aims to distribute sports facilities systematically across the country, enabling individuals of all ages to engage in amateur sports of their choice and ensuring access to expert coaches and qualified staff (23). This infrastructure reduces inequalities in access and supports adolescent sports participation regardless of economic background.

The presence of close friends who participate in sports was identified as a strong motivator, increasing both sports awareness and sports-oriented attitudes. Peer influence is particularly strong during adolescence and significantly shapes decisions and experiences (24). Peers influence sports attitudes in three key ways: Through friendships with specific individuals, through general acceptance within the peer group, and through athletes' self-perceptions relative to their peers. These factors are uniquely linked to the quality of adolescents' sports experiences (25). Another study suggested that a lack of friends with whom to exercise was one reason for low levels of physical activity (22). Thus, having close friends involved in sports not only increases awareness but also fosters positive attitudes toward participation.

All subdimension and total scores of the SAS and SOAS were significantly higher among boys and those who engaged in sports, especially team sports. Licensed athletes also demonstrated higher SAS and SOAS scores than non-licensed individuals. These findings align with previous research showing that participation is closely linked to perceived benefits and knowledge of sports (26). Roth and Stamatakis (27) found that a better understanding of sports guidelines was associated with higher physical activity levels in children aged 11-15. Similarly, awareness has been shown to play a crucial role in promoting active lifestyles (28). Data from the National Health Interview Survey in the United States revealed that, among adolescents, sports participation was higher among boys than among girls (56.1% vs. 52%), although the difference was not statistically significant (20). Another study in Ankara examining sports awareness among regular participants yielded similar results to ours: individuals who regularly engaged in sports had higher sports-awareness scores. Additionally, men and licensed Athletes had higher awareness scores (29). We suggest this result is rooted in the historical perception that sports have been viewed as activities exclusive to men and closely tied to male athleticism. This prevailing societal perspective influences both women's and men's participation in sports and their level of awareness of sports. During sports socialization, families encouraged boys to participate in sports to develop their masculinity, while girls were discouraged from competitive sports to protect their bodies and preserve their feminine qualities. Despite this change in approach in recent years, one study asked students from different social classes to introduce themselves. All male students, regardless of social class, introduced themselves by the sports they practiced or their interests (such as computers or electronics), whereas only female students who were licensed athletes introduced themselves by their athletic identity (30).

A strong correlation was observed among the subdimensions of SAS and SOAS, underscoring the importance of awareness in developing sport-oriented attitudes. Many studies have investigated the factors that drive young people to participate in sports. In most of these studies, achievement in athletics was most strongly related to the perceived value of physical activity as an ascetic experience that provides a medium for social interaction and offers an element of thrill (31-33). Ganakas and Peden (34) evaluated why young Australians participate in sports and ranked the reasons from most to least common as follows: Fun or enjoyment, the desire to try something different or alternative, learning and developing new skills, getting or keeping fit, opportunities for performance or competition, mastering a skill or technique, social reasons, and psychological or mental health benefits (34). Our study demonstrates that sports awareness, which includes understanding the social and individual benefits of sports, sports information, and discrimination, is strongly associated with adolescents' attitudes toward sports. However, as previous studies have shown, awareness and knowledge often lag behind other factors that motivate young people to engage in sports. This underscores the need to raise awareness and highlights the critical role of increased awareness in combating sedentary lifestyles. To raise awareness about sport, thoroughly understanding the benefits of sport is more important than simply having knowledge about it. Sport awareness promotes heightened consciousness and enables adolescents to take action, influencing their approach to sport.

This study is the first to explore the effect of sports awareness on sport-oriented attitudes in adolescents, with the aim of encouraging greater physical activity. Contrary to common assumptions, our findings suggest that sports habits are not solely shaped by environmental and socio-economic factors but are also strongly influenced by individual awareness and motivation.

Strengths of this study include using validated scales to accurately assess sports awareness and sport-oriented attitudes, thereby minimizing measurement bias. Additionally, the large sample size enabled robust analysis of demographic variables and awareness levels across genders. Therefore, our research was exploratory in nature and its results should be taken into account when establishing preventive interventions against sedentary lifestyle in the adolescent population.

Study Limitations

The primary limitation of this study is that it was conducted with participants from a single city, which may restrict the generalizability of the findings to broader populations.

Conclusion

It is crucial to encourage children—particularly adolescents—to adopt regular physical activity as a lifelong habit to foster a healthier society. Achieving this goal requires the implementation and support of comprehensive policies by both local and national authorities. These policies should actively engage families, educators, healthcare providers, and other relevant stakeholders to raise adolescents' awareness of the benefits of sports and expand opportunities for participation.

As highlighted by the findings of this study, strategies aimed at reducing sedentary behavior among adolescents must pay particular attention to girls and individuals from lower socio-economic backgrounds, as these groups are more likely to exhibit lower levels of sports awareness. Furthermore, interventions should capitalize on the influential role of peer relationships in enhancing adolescents' motivation to engage in physical activity.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki and received approval from the regional Ethics Committee of Ankara Atatürk Sanatoryum Training and Research Hospital (approval number: 2024/482, date: 26.06.2024).

Informed Consent: Written informed consent was obtained prior to enrollment.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: G.Ö., Concept: G.Ö., Z.A., Design: G.Ö., Z.A., Data Collection or Processing: G.Ö., Analysis or Interpretation: G.Ö., A.G.G., Z.A., Literature Search: G.Ö., A.G.G., Z.A., Writing: G.Ö., Z.A.

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ORIGINAL RESEARCH

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Evaluation of Visceral Adiposity Index (VAI) and Metabolic Profiles in Patients with Different Body Mass İndex (BMI) Groups

Farklı Beden Kitle İndeksi (VKİ) Gruplarındaki Hastalarda Visseral Adipozite İndeksi (VAİ) ve Metebolik Profillerin Değerlendirilmesi

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Abstract

Objective: The primary objective of this study was to explore the relationship between the visceral adiposity index (VAI) and body mass index (BMI), two critical measures often used to assess individual health and obesity levels.

Method: This retrospective study analyzed data from 141 patients who applied to the Obesity and Internal Medicine Clinic of University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital. Demographic, anthropometric (height, weight, waist, hip circumference, BMI), and biochemical parameters [alanine transaminase (ALT), aspartate transaminase (AST), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, glucose] were assessed. Visceral fat distribution was evaluated using the VAI. Patients were classified into four BMI groups: Normal weight (18.5-24.9), overweight (25-29.9), obese (30-39.9), and morbidly obese (>40), to examine the link between BMI and visceral fat.

Results: The analysis of different BMI groups revealed significant variations in anthropometric and biochemical parameters. Higher BMI was associated with increased weight, waist and hip circumferences, and systolic blood pressure (p<0.001), while height decreased as BMI increased (p<0.001). Platelet count and ALT/AST levels were significantly higher in individuals with higher BMI (p<0.003, p<0.001). HDL cholesterol decreased (p<0.001), while triglycerides and LDL cholesterol increased with BMI (p<0.001, p=0.001). HbA1c levels were also significantly higher in individuals with increased BMI (p<0.001). VAI increased significantly with increasing BMI (p<0.001), indicating greater visceral fat accumulation.

Öz

Amaç: Bu çalışmanın amacı, bireysel sağlık ve obezite düzeylerini değerlendirmek için sıklıkla kullanılan iki kritik ölçüt olan visseral adipozite indeksi (VAI) ile vücut kitle indeksi (VKİ) arasındaki ilişkiyi araştırmaktır.

Yöntem: Bu retrospektif çalışmada Sağlık Bilimleri Üniversitesi, Gazi Yaşargil Eğitim ve Araştırma Hastanesi, Obezite ve İç Hastalıkları Polikliniği'ne başvuran 141 hastanın verileri analiz edildi. Demografik, antropometrik (boy, kilo, bel, kalça çevresi, VKİ) ve biyokimyasal parametreler [alanin transaminaz (ALT), aspartat transaminaz (AST), yüksek yoğunluklu lipoprotein (HDL), düşük yoğunluklu lipoprotein (LDL), trigliserit, glikoz] değerlendirildi. Visseral yağ dağılımı, VAI kullanılarak değerlendirildi. Hastalar, VKİ ile visseral yağ arasındaki bağlantıyı incelemek için dört VKİ grubuna ayrıldı: Normal kilolu (18,5-24,9), fazla kilolu (25-29,9), obez (30-39,9) ve morbid obez (>40).

Bulgular: Farklı VKİ gruplarının analizi antropometrik ve biyokimyasal parametrelerde önemli farklılıklar olduğunu ortaya koydu. Daha yüksek VKİ; artan kilo, bel ve kalça çevresi ve sistolik kan basıncı ile ilişkiliydi (p<0,001), VKİ arttıkça boy azalıyordu (p<0,001). Trombosit sayısı ve ALT/AST düzeyleri daha yüksek VKİ'li bireylerde önemli ölçüde daha yüksekti (p<0,003, p<0,001). HDL kolesterol azalırken (p<0,001), trigliseritler ve LDL kolesterol VKİ ile arttı (p<0,001, p=0,001). HbA1c düzeyleri de artan VKİ'li bireylerde önemli ölçüde daha yüksekti (p<0,001). VAI, VKİ arttıkça önemli ölçüde arttı (p<0,001), bu da daha fazla visseral yağ birikimini gösterdi. Tukey HSD analizi, VKİ grupları arasında, özellikle VKİ 20-25 ve VKİ >40 arasında önemli farklılıklar gösterdi (p<0,001). Bu bulgular, daha yüksek VKİ'nin olumsuz metabolik değişikliklerle güçlü bir şekilde

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Abstract

Tukey HSD analysis showed significant differences between BMI groups, particularly between BMI 20-25 and BMI >40 ($p<0.001$). These findings suggest that higher BMI is strongly associated with adverse metabolic changes, emphasizing the importance of weight management for better health outcomes.

Conclusion: VAI is a key metric for assessing obesity, focusing on visceral fat accumulation rather than just weight and height like BMI. It helps clinicians evaluate metabolic risks more accurately. Increasing awareness of VAI's importance can enhance obesity management and improve patient health outcomes.

Keywords: Body mass index, obesity, visceral adiposity index

Öz

ilişkili olduğunu ve daha iyi sağlık sonuçları için kilo yönetiminin önemli olduğunu göstermektedir.

Sonuç: VAI, obeziteyi değerlendirmek için önemli bir ölçüttür ve VKİ gibi sadece kilo ve boy yerine visseral yağ birikimine odaklanır. Klinisyenlerin metabolik riskleri daha doğru bir şekilde değerlendirmesine yardımcı olur. VAI'nın önemine ilişkin farkındalığın artırılması, obezite yönetimini iyileştirebilir ve hastaların sağlık sonuçlarının daha iyi olmasına katkı sağlar.

Anahtar kelimeler: Beden kitle indeksi, obezite, visseral adiposite indeksi

Introduction

Body mass index (BMI) is a widely used tool for assessing a person's body weight relative to their height; however, it may not always effectively capture the nuances of fat distribution within the body. In fact, the correlation between BMI and the actual body fat ratio can be quite complex. Research has shown that this relationship often follows a curvilinear pattern rather than a straightforward linear one in both men and women. This means that as BMI increases, the corresponding increase in body fat percentage may not be proportional across all individuals, indicating that other factors—such as muscle mass, bone density, and the way fat is distributed—play a significant role in determining overall health and physical composition. Such insights highlight the limitations of relying solely on BMI as an indicator of body fat and emphasize the importance of considering a more comprehensive approach to understanding body composition (1).

However, it is important to recognize that BMI can be influenced by a range of factors, including but not limited to gender, hydration levels, muscle mass, and racial or ethnic background. These variables can skew the accuracy of BMI as an indicator of an individual's body fat percentage, thereby raising concerns about its reliability. As a result, an ongoing debate persists in the scientific community regarding the appropriateness of using BMI as a predictor of cardiovascular risk. Many health professionals question whether it adequately captures the complexities of body composition and its implications for heart health. A notable article published in The Lancet in 2006 highlighted this skepticism, questioning the validity of BMI as a tool for determining cardiovascular risk. This conversation underscores the need for more comprehensive methods that consider individual characteristics beyond simple height and weight measurements (2-4).

The visceral adiposity index (VAI) is a sophisticated empirical mathematical model used to assess visceral fat accumulation in the human body. It is derived from a combination of anthropometric measurements—such as waist circumference and BMI—along with triglyceride (TG) levels in the blood. This index serves as an important tool in the evaluation of health risks associated with excess visceral fat, which is known to contribute to various metabolic disorders, including type 2 diabetes and cardiovascular diseases. By incorporating both physical measurements and biochemical markers, the VAI provides a comprehensive insight into an individual's fat distribution and overall metabolic health (5).

Numerous studies have consistently demonstrated a correlation between an elevated VAI and an increased risk of cardiovascular disease. This index serves not only as a key measurement for assessing the amount of visceral fat, a type of fat that wraps around internal organs, which is often more harmful than subcutaneous fat, but also provides insight into the functionality of visceral adipose tissue and its relationship with insulin sensitivity. Visceral fat is metabolically active and can contribute to inflammation and insulin resistance, factors that are pivotal in the development of various cardiovascular conditions. Therefore, monitoring the VAI can be instrumental in identifying individuals who may be at higher risk for cardiovascular issues, allowing for early interventions. In summary, while the VAI clearly indicates a heightened cardiovascular risk with increased values, it also serves as a crucial metric for evaluating the metabolic health of individuals, particularly concerning their insulin sensitivity (6-8).

The primary objective of this study was to explore the relationship between the VAI and BMI, two critical measures often used to assess individual health and obesity levels. The study aimed to investigate whether variations in BMI correspondingly influence the visceral

adiposity index, which is a more nuanced indicator of fat distribution and associated metabolic risks. By examining how shifts in BMI affect the visceral adiposity index, the research seeks to contribute to a deeper understanding of the dynamics between overall body weight and visceral fat levels, providing insights into potential health implications for individuals with different body compositions.

Materials and Methods

This study included 141 patients who applied to the Obesity and Internal Medicine Clinic of University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital between 01.10.2024/01.01.2025 This study was planned retrospectively. Our study was initiated following the approval of the ethics committee. The University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital's Ethics Committee approval was received on 17/01/2025 under the number 309. The study was approved according to the guide of the Declaration of Helsinki and by the Institutional Review Board and Ethical Committee.

In this comprehensive study, patient information was meticulously gathered from two prominent health data management systems: Nucleus and Fonet. The researchers collected a wide array of demographic data alongside detailed physical measurements, including height, weight, waist circumference, and hip circumference. These parameters were essential for calculating key anthropometric metrics, most notably the BMI. Additionally, the study delved in important hematological parameters, measuring the levels of various blood components such as neutrophils, lymphocytes, platelets, and hemoglobin. The researchers also assessed vital liver enzymes, specifically alanine aminotransferase (ALT) and aspartate aminotransferase (AST), which are crucial indicators of liver function. Furthermore, a complete lipid profile was recorded, including high-density lipoprotein (HDL), low-density lipoprotein (LDL), TG, and glucose levels, providing a holistic view of each patient's metabolic health.

To better understand the distribution of visceral fat, the VAI was calculated for each participant. This study categorized the patients into four distinct groups based on their BMI. Those with a BMI ranging from 18.5 to 24.9 were classified as having a normal weight; individuals with a BMI from 25 to 29.9 were identified as overweight; BMI values between 30 and 39.9 indicated obesity; and patients with a BMI over 40 were classified as morbidly obese. Each group's VAI was then calculated, allowing for a detailed analysis of the relationship between weight classifications and visceral fat distribution. This thorough approach underscores the study's commitment to understanding the complexities of body composition and its implications for health.

The VAI is a gender-specific mathematical model that estimates visceral fat distribution and dysfunction based on BMI, triglycerides, and HDL cholesterol.

VAI Formulation:

VAI (male) = [Waist circumference (cm)/(39.68 + (1.88 x BMI) x (TG (mmol/L)/1.03 x (1.31/HDL (mmol/L)]

VAI (female): [Waist circumference (cm)/(36.58 + (1.89 x BMI) x (TG (mmol/L)/0.81) x (1.52/HDL (mmol/L)] formulated as follows (9).

Statistical Analysis

The descriptive analyses in this study were reported as mean ± standard deviation or as median (minimum-maximum), depending on whether the data followed a normal distribution. Normality was assessed using the Kolmogorov-Smirnov test. To compare differences between multiple groups, a One-Way ANOVA test was used if the data were normally distributed. If the data did not follow a normal distribution, a Kruskal-Wallis test was applied. A p-value of less than 0.05 was considered statistically significant. The analysis of the data of the patients in the study was performed using the SPSS 27.0 software.

Results

The analysis of different BMI groups revealed significant variations in several anthropometric and biochemical parameters (Table 1).

- **Anthropometric measures:** Individuals with higher BMI had significantly increased weight, waist circumference, hip circumference, and systolic blood pressure (SBP) ($p<0.001$). Diastolic blood pressure (DBP) was also significantly different among groups ($p=0.001$). Height decreased as BMI increased ($p<0.001$).
- **Hematological parameters:** Platelet count was significantly higher in individuals with higher BMI ($p=0.003$). Hemoglobin levels were also significantly different across BMI groups, with lower values in the highest BMI category ($p<0.001$).
- **Liver enzymes:** ALT and AST levels varied significantly across groups ($p<0.001$).
- **Lipid profile:** LDL cholesterol was significantly different between BMI groups ($p=0.001$). HDL cholesterol decreased as BMI increased ($p<0.001$), while TG levels

were significantly higher in individuals with higher BMI ($p<0.001$).

- **Glycemic control:** HbA1c levels increased with BMI and were significantly different between groups ($p<0.001$).

These findings indicate that increasing BMI is associated with negative metabolic and cardiovascular changes, highlighting the importance of weight management for better health outcomes.

The VAI showed a significant increase across BMI categories. Individuals with higher BMI had significantly elevated VAI levels [$F(3.138) =7.078$, $p<0.001$], indicating greater visceral fat accumulation as BMI increased. This suggests a strong correlation between BMI and visceral adiposity, emphasizing the metabolic risk associated with higher BMI levels (Table 2).

The Tukey HSD post-hoc analysis revealed significant differences in mean values between BMI groups (Table 3):

- BMI 20-25, vs. BMI >40: A significant mean difference of -8.10 ($p<0.001$) indicates a substantial decrease in the analyzed variable for individuals with BMI >40.
- BMI 20-25 vs. BMI 30-40: A significant mean difference of -4.5 ($p=0.041$) suggests a notable decrease in the BMI 30-40 group.
- Other comparisons (BMI 25-30 vs. BMI 30-40, BMI 30-40 vs. BMI >40, etc.) did not show statistically significant differences ($p>0.05$), indicating relatively smaller variations between these BMI categories.

These results suggest that individuals with higher BMI (particularly BMI >40) exhibit significantly different characteristics compared to those with lower BMI (20-25).

Discussion

A total of 141 patients participated in this study, which aimed to explore the relationship between BMI and visceral adiposity. The participants were carefully categorized into four distinct groups based on their BMI classifications, allowing for a thorough analysis of how varying levels of body mass may influence the distribution of visceral fat. The main focus of the investigation was to assess the correlation between BMI and visceral fat accumulation, providing insights into the potential health implications associated with different body weight categories.

Obesity is a global issue that has experienced a 2- to 3-fold increase worldwide from 1980 to 2014. It is associated with anemia, and research indicates that obesity elevates the risk of developing anemia. In a study by Moafi et al. (10) involving 1,218 participants, the subjects were divided into three groups based on their BMI. The study found a significant relationship between increasing BMI and the prevalence of anemia (10). Recent research has indicated a concerning relationship between BMI and anemia.

Table 1. Descriptive analysis of different BMI groups an One-Way ANOVA results

Measures	BMI 20-25	BMI 25-30	BMI 30-40	BMI >40	p-values
Age	31.71±6.49	33 (19-53)	35.56±9.96	37.05±10.44	0.68
Length	170.4±7.9	173.7±8.6	168.0±10.9	162.6±8.9	<0.001
Weight	62.06±7.51	81.3±8.89	97.5±14.7	118.5±13.04	<0.001
Waist circumference	74.0±7.61	92.1±8.8	107.6±10.9	123.9±12.8	<0.001
Hip circumference	94 (64-110)	103.8±4.7	118.4±6.9	136.2±11.1	<0.001
SBP	99 (80-116)	110.5±8.8	107.5 (91-127)	112.5±8.8	<0.001
DBP	67.1±8.5	74.3±7.0	71 (58-64)	70 (58-88)	0.001
Neutrophils	3.99±1.66	4.22 (2.04-8.77)	4.25±1.41	4.16 (3.31-8.27)	0.209
Lymphocytes	2.29±0.59	2.43±0.69	2.57±0.62	2.53±0.97	0.287
Platelets	259.1±53.7	253 (161-441)	296.0±67.4	315.8±73.8	0.003
Hemoglobin	14.1±1.37	15.2±1.25	14.8±1.33	13.7±1.47	<0.001
ALT	14 (5-68)	27 (11-119)	27.5 (7-111)	17(6-48)	<0.001
AST	19 (13-38)	23 (16-51)	23 (12-69)	16 (10-30)	<0.001
LDL	106.4±28.4	132.3±22.5	119.7±32.8	118.9±31.7	0.001
HDL	50 (31-91)	42 (22-67)	43.8±10.8	41.7±6.4	<0.001
TG	78.6±39.1	133 (60-587)	142.5 (37-392)	135 (66-389)	<0.001
HbA1c	5.3 (3.4-6)	5.6 (5.2-6.4)	5.55 (5.1-6.4)	5.6 (5.1-6.3)	<0.001

SBP: Sistolic blood pressure, DBP: Diastolic blood pressure, ALT: Alanine transferase, AST: Aspartate transferase, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Tryglicerides, BMI: Body mass index

Table 2. One-Way ANOVA analysis of visseral adiposity index for BMI

Measure	BMI 18.5-24.9 (n=49)		BMI 25-29.9 (n=37)		BMI 30-39.9 (n=34)		BMI >40 (n=22)		F (3,138)	h^2
	M	SD	M	SD	M	SD	M	SD		
Visseral adiposity index	2.38	1.5	5.83	5.32	6.63	4.89	10.58	15.48	7.078***	

BMI: Body mass index, ***: p<0.001 (highly significant)

Table 3. Post-hoc results between groups

BMI	BMI	Mean difference	Std. error	Sig.
Normal 18.5-24.9	25-29.9	-3.45	1.55	0.120
	30-39.9	-4.5	1.58	0.041
	>40	-8.10	1.82	0.000
Overweight 25-29.9	18.5-24.9	3.45	1.55	0.120
	30-39.9	-0.80	1.69	0.965
	>40	-4.66	1.91	0.075
Obese 30-39.9	18.5-24.9	4.25	1.58	0.041
	25-29.9	0.80	1.69	0.965
	>40	-3.86	1.94	0.198
Morbid obese >40	20-25	8.10	1.82	0.000
	25-29.9	4.66	1.91	0.075
	30-39.9	3.86	1.94	0.198
	>40	-4.66	1.91	0.097

BMI: Body mass index

Specifically, the findings suggest that for every unit increase in BMI, the likelihood that of developing anemia can significantly increase, potentially rising by as much as 1.6 times. This connection highlights the importance of maintaining a healthy weight, as higher BMI levels may exacerbate the risk of experiencing this blood disorder, which is characterized by a deficiency in red blood cells or hemoglobin. Such insights underscore the need for further investigation into how weight management can play a crucial role in preventing anemia and promoting overall well-being (11). In our study, we found that similar to previous research, changes in hemoglobin and platelet counts were significant as BMI increased, with p-values of <0.001 and 0.003, respectively. However, we did not find any association between changes in leukocyte and lymphocyte counts and BMI, as indicated by p-values of 0.209 and 0.287, respectively.

The relationship between BMI and HbA1c,as well as lipid panel results, has been previously studied. Research indicates a negative correlation between BMI and HDL levels, while a positive correlation is observed with other lipid parameters. In their study involving 296 patients, Babikr et al. (12) found a statistically significant positive correlation between BMI and HbA1c.

In the study conducted by Pituelli Suárez et al. (13), involving 1,043 children and adolescents, the relationship between obesity, BMI, and lipid panel results was investigated, revealing a statistically significant correlation. In our study, we observed that as BMI increased, TG and LDL values tended to rise initially but then decrease, while HDL values tended to decrease. These findings were statistically significant, with p-values of <0.001 for TG, 0.001 for LDL, and <0.001 for HDL. The LDL paradox is a phenomenon observed in morbidly obese patients, and there is a need for more systematic research on this topic. In a study by Vierhapper et al. (14), LDL levels were found to be lower in morbidly obese individuals compared to those with less severe obesity. Similarly, in our study, we observed lower LDL levels in the morbidly obese group, consistent with their findings. Although the trend for LDL values initially increased and then decreased, this aspect was not among the primary focuses of our study, and we did not report post-hoc results between the groups (13). There has been ongoing debate in recent years about whether BMI is an accurate measure of obesity (15). Research has indicated that waist circumference may serve as a more accurate measure than BMI when it comes to assessing abdominal and visceral fat accumulation. This is particularly important because excess visceral

fat, which surrounds internal organs, is closely linked to various health risks, including metabolic syndrome and cardiovascular diseases. Furthermore, the VAI offers a more comprehensive evaluation. This mathematical calculation combines anthropometric measurements, such as waist and hip circumference, with lipid profile data, including levels of triglycerides and cholesterol. By integrating these diverse factors, the VAI provides a more nuanced understanding of an individual's fat distribution and metabolic health compared to relying solely on traditional anthropometric indices like BMI. As such, the VAI may serve as a superior indicator of health risks associated with obesity and fat distribution (16,17). Clinically, the VAI is used as a risk marker in conditions such as metabolic syndrome, cardiovascular disease, type 2 diabetes, polycystic ovary syndrome, and non-alcoholic fatty liver disease. Studies by Amato et al. (18) have demonstrated the association of VAI with these diseases, showing that VAI is a practical, cost-effective, and non-invasive tool for predicting metabolic risks related to visceral fat accumulation. However, since it cannot replace direct imaging methods (computed tomography, magnetic resonance imaging), it should be considered a complementary measure (18-20). In our study, we investigated the relationship between BMI and visceral adiposity. We found a statistically significant change in the VAI and BMI ($p<0.001$). The patients were divided into four groups based on their BMI, and a post-hoc analysis was conducted. The results of the post-hoc analysis revealed significant differences between the group with a BMI greater than 40 and the group with a BMI between 30 and 39.9, as well as between the group with a BMI of 18.5-24.9 ($p<0.001$ and $p=0.041$, respectively).

Study Limitations

One of the primary limitations of this study is its retrospective design, which inherently restricts the ability to draw robust conclusions about causality. Additionally, the sample size is relatively small when compared to the larger studies in the field, which may limit the generalizability of the findings and reduce the statistical power necessary to detect significant effects. This smaller cohort could lead to potential biases and less confidence in the results when extrapolated to broader populations.

Conclusion

The VAI serves as a valuable metric for assessing obesity, similar to the well-known BMI. Unlike BMI, which primarily considers weight and height, the VAI focuses specifically on the accumulation of visceral fat—fat that surrounds the internal organs, which is closely linked to various health risks. Understanding and utilizing this index can help clinicians more accurately evaluate a patient's health status, especially regarding metabolic complications associated with excess visceral fat. Raising awareness among healthcare professionals about the significance and utility of the VAI is crucial for improving obesity management and promoting overall patient well-being.

Ethics

Ethics Committee Approval: The University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital's Ethics Committee approval was received on 17/01/2025 under the number 309. The study was approved according to the guide of the Declaration of Helsinki and by the Institutional Review Board and Ethical Committee.

Informed Consent: Retrospective study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: J.K., İ.S., Concept: J.K., Ö.F.A., İ.S., Design: J.K., İ.S., Data Collection or Processing: Ö.F.A., Analysis or Interpretation: Ö.F.A., İ.S., Literature Search: J.K., İ.S., Writing: J.K., Ö.F.A., İ.S.

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ORIGINAL RESEARCH

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Comparative Analysis of Obstetric Outcomes in Primiparous Versus Multiparous Women Undergoing Vacuum-assisted Delivery

Primipar ve Multipar Kadınlarda Vakum Destekli Doğumun Karşılaştırmalı Olarak Analizi

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Abstract

Objective: To assess and compare maternal and neonatal outcomes of vacuum-assisted vaginal delivery in primigravid versus multigravid women.

Method: This retrospective study analyzed the obstetric outcomes of 65 women who underwent vacuum-assisted vaginal delivery and statistically compared maternal and neonatal outcomes between the primigravid and multigravid groups.

Results: Significant differences were observed between groups in labor duration, neonatal birth weight, and head circumference ($p<0.05$). Primigravid women had significantly longer labors, whereas multigravid women delivered neonates with higher birth weights and larger head circumferences. Episiotomy rates were notably higher in the primigravid group ($p<0.001$); however, no significant differences were found between groups for neonatal intensive care unit admissions, neonatal complications, or maternal complications ($p>0.05$).

Conclusion: This study demonstrated that parity influences outcomes of vacuum-assisted vaginal deliveries, with no significant differences in neonatal outcomes between groups. The use of vacuum assistance in vaginal deliveries appears to prevent, rather than cause, asphyxia by expediting labor. Vacuum-assisted vaginal delivery can serve as an effective intervention to reduce unnecessary cesarean sections.

Keywords: Apgar, asphyxia, complications, normal delivery, vacuum assisted delivery

Öz

Amaç: Vakum yardımlı vajinal doğum gerçekleştiren primigravid ve multigravid kadınlar arasında maternal ve neonatal sonuçlar karşılaştırılarak obstetrik sonuçların değerlendirilmesi amaçlanmıştır.

Yöntem: Çalışma retrospektif olarak 65 vakum yardımlı vajinal doğum yapan gebenin obstetrik sonuçları incelenmiş, primigravid ve multigravid gruplar arasında maternal ve neonatal sonuçlar istatistiksel olarak karşılaştırılmıştır.

Bulgular: Çalışmada travay süresi, yenidoğan doğum ağırlığı ve baş çevresi açısından gruplar arasında anlamlı fark tespit edilmiştir ($p<0,05$). Primigravid kadınlarda travay süresi belirgin şekilde daha uzunken, multigravid kadınlarda doğum ağırlığı ve baş çevresi daha büyük bulunmuştur. Epizyotomi oranları primigravid grubunda anlamlı derecede daha yüksekti ($p<0,001$). Bununla birlikte, yenidoğan yoğun bakım ünitesi kabulü, neonatal komplikasyonlar ve maternal komplikasyonlar açısından gruplar arasında anlamlı fark bulunmamıştır ($p>0,05$).

Sonuç: Bu çalışma, vakum yardımlı vajinal doğum sonuçları üzerinde paritenin etkisini ortaya koymuş; neonatal sonuçlar açısından gruplar arasında anlamlı fark olmadığını göstermiştir. Vakum yardımı, doğum sürecini hızlandırarak asfiksiye neden olmaktan ziyade asfiksiyi önleyici bir müdahale olarak değerlendirilebilir. Vakum yardımlı vajinal doğumlar, gereksiz sezaryen doğumların önlenmesinde etkili bir alternatif olarak kullanılabilir.

Anahtar kelimeler: Apgar, asfiksi, komplikasyonlar, normal doğum, vakum yardımlı doğum

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Introduction

Vacuum-assisted vaginal delivery is an operative vaginal delivery method widely used to facilitate labour. This method is preferred, especially in cases of a prolonged second stage of labour, maternal fatigue, or fetal distress, and constitutes an important part of obstetric practice (1).

If normal spontaneous vaginal delivery is not possible or needs to be accelerated, or if labour has entered the second stage with cervical dilatation of 10 cm, there are two options for delivery: Provide assistance to the mother through instrumental vaginal delivery, or perform a caesarean section (2). However, a caesarean section can be considered only a last resort if instrumental vaginal delivery is unsafe or has failed. It carries maternal morbidity risks, such as greater blood loss and a greater need for postnatal care (3).

Vacuum extraction, performed by applying negative pressure to the fetal head with a vacuum device, carries advantages and risks for both mother and baby (4). The most important risks of vacuum-assisted delivery for the fetus include neonatal head trauma, intracranial haemorrhage, scalp abrasions, and neonatal hyperbilirubinaemia (5). A prospective cohort study from 2022 reported that approximately 13% of vacuum delivery attempts resulted in maternal trauma and 8% resulted in serious neonatal complications such as subgaleal hematoma (4).

For the mother, potential risks include tears in the birth canal, postpartum haemorrhage, need for episiotomy, and anal sphincter injuries. Anal sphincter injuries can lead to anal incontinence and a serious deterioration in quality of life (6,7). Maternal anal sphincter injuries and neonatal traumas are more common following operative vaginal delivery, especially after vacuum and forceps applications (4). Primiparity and instrumental delivery are the main risk factors for this condition (8). However, vacuum-assisted labour has been shown to be a safe and effective option when used for appropriate indications and performed by experienced obstetricians (9).

Benefits of vacuum extraction include shorter labour duration, shorter hospital stay compared with caesarean section, faster postpartum recovery, and lower rates of maternal complications (10). In addition, the use of vacuum-assisted delivery in appropriate cases may alleviate the burden on both individuals and the healthcare system by reducing cesarean delivery rates (11).

While the current literature contains numerous studies on the maternal and neonatal outcomes of vacuum-assisted deliveries, comparative studies of these outcomes across parity groups are limited. In particular, whether variables such as episiotomy rates, neonatal complications, and labor duration differ between primiparous and multiparous groups is important for clinical decision-making.

In this study, maternal and neonatal outcomes were compared between primigravid and multigravid women who underwent vacuum-assisted vaginal delivery. These findings are expected to provide important information to improve understanding of the effect of vacuum-assisted vaginal delivery on obstetric outcomes and to inform clinical practice.

Materials and Methods

This retrospective cross-sectional study included 65 pregnant women admitted to the obstetrics and gynaecology clinic of a rural district state hospital for vaginal delivery between March 2020 and July 2021. Patient data were retrieved from the hospital's digital records and through a review of physical patient files. Primiparous women at or above 34 weeks of gestation and women with previous vaginal deliveries, all with singleton, live, head-presenting fetuses, were included in the study. Exclusion criteria included a history of cesarean section, urinary or anal incontinence, or prior surgery for these conditions. Obstetric history, maternal outcomes, and neonatal outcomes were documented. This study was approved by the Ethics Committee of İstanbul Esenyurt University (approval number E-12483425-299-35347; meeting dated 07.09.2023; protocol number 2023/08-12).

Participants were divided into two groups. Group 1 (n=32) comprised primiparous pregnant women, and Group 2 (n=33) comprised multiparous pregnant women. Obstetric history and maternal and neonatal outcomes were recorded. Patient confidentiality was strictly maintained. All data were anonymized and stored in an encrypted system accessible only to the research team. No personally identifiable information was collected or used in the analysis.

Indications for vacuum extraction were based on the following clinical conditions, consistent with the literature: prolonged second stage of labor (n=28, 43.1%), reduced maternal effort or fatigue (n=19, 29.2%), non-reassuring fetal heart rate pattern (n=12, 18.5%), and other reasons (n=6, 9.2%). These indications were obtained retrospectively from birth records.

Each patient underwent vacuum-assisted delivery using a disposable device known as the "Kiwi Omnicup" (Figure 1), which consists of a silicone or plastic cup attached to a hand pump. Vacuum extraction procedures were performed by specialist physicians experienced in gynecology and actively involved in operative vaginal deliveries.

The cup was positioned on the fetal scalp, and negative pressure (500-600 mmHg) was applied. Delivery was facilitated by gentle traction synchronized with the uterine contractions. Following delivery, the vacuum was gradually released to detach the cup. An average of 2 traction strokes (range: 1-4) was applied during vacuum application, and cases requiring 3 or more traction strokes were carefully monitored. No cases requiring more than four traction strokes were encountered in the study (12). The vacuum head used in all cases was a conventional, disposable, soft-silicone cup. No hard-metal cup was used.

The diagnosis of neonatal asphyxia was made based on the American College of Obstetricians and Gynecologists criteria, and newborns with an Apgar score <7 at 5 minutes and/or an umbilical cord artery pH <7.0 were included in this category. However, because umbilical pH measurement was not available in all cases, the primary assessment was based on the 5-minute Apgar score (13).

Statistical Analysis

Statistical analyses were conducted using the IBM SPSS Statistics 27 software package. Frequency tables and descriptive statistics were utilized to interpret the results. Parametric tests were applied to measurements that were normally distributed. Accordingly, comparisons between two independent groups were performed using the independent-samples t-test (t-table value). For data that did not exhibit a normal distribution, non-parametric methods were employed. In this context, the Mann-Whitney U test (Z-value) was used to compare measurements between two independent groups. Additionally, Spearman's rank correlation coefficient was calculated to examine the relationship between two quantitative variables that were not normally distributed.

Power Analysis

Post-hoc power analysis was performed using G*Power (version 3.0.10) software. Given an effect size of 0.82, an alpha value of 0.05, and power (1-β) =0.90, the minimum sample size was calculated to be 60 participants.

Results

A statistically significant difference was found in age, trauma time (min), fetal weight, and head circumference among gravida classes ($p<0.05$). The duration of trauma (min) was significantly longer in patients with gravida 1 than in patients with gravida ≥2. In addition, weight, and head circumference were significantly higher in participants with Gravida ≥2 than in those with Gravida 1 (Table 1).

There was no statistically significant relationship between gravida groups and neonatal intensive care, complications

Figure 1. Kiwi® OmniCup® complete vacuum delivery system with PalmPump™

(including types of complications), blood TX, and maternal complications (p>0.05). It was determined that the groups were independent and homogeneous with respect to the characteristics mentioned.

A statistically significant correlation was found between gravida groups and episio (χ^2=53.607; p<0.001). It was determined that 31 patients (96.9%) with gravida 1 underwent episiotomy, whereas 31 patients (93.9%) with gravida ≥2 did not undergo episiotomy. It was determined that those with episiotomy were predominantly gravida 1, whereas those without episiotomy were predominantly gravida 62 (Table 2).

Table 1. Comparison of some parameters according to gravida groups

Variable	Gravida 1 (n=32)		Gravida ≥2 (n=33)		Statistical analysis* Probability
	$\bar{X}$ ± SD	Median [IQR]	$\bar{X}$ ± SD	Median [IQR]	
Age	24.09±3.77	24.0 [4.8]	29.88±6.11	30.0 [8.0]	t=-4.610 **p<0.001**
Duration of travay (min)	438.12±249.48	400.0 [258.8]	237.12±240.21	140.0 [315.0]	Z=-3.554 **p<0.001**
Fetal weight	3234.06±489.29	3300.0 [755.0]	3457.27±385.31	3430.0 [360.0]	t=-2.047 **p=0.045**
Fetal lenght	50.43±1.52	50.5 [1.0]	51.18±2.02	51.0 [2.0]	Z=-1.483 p=0.138
Head circumferences	34.78±1.45	35.0 [2.0]	35.67±1.02	36.0 [1.5]	Z=-2.600 **p=0.009**
1st minute Apgar	6.06±2.73	7.5 [5.0]	6.61±1.91	8.0 [2.5]	Z=-0.302 p=0.763
5th minute Apgar	7.96±1.65	8.5 [2.0]	8.06±1.39	9.0 [1.5]	Z=-0.055 p=0.956
pH	7.03±0.17	7.05 [0.2]	7.06±0.12	7.05 [0.1]	t=0.215 p=0.773

*: "Independent Sample's t-test" (t-table value) statistics were used to compare the measurement values of two independent groups for normally distributed data. The Mann-Whitney U test (Z-table value) was used to compare measurements between two independent groups for data that were not normally distributed. IQR: Interquartile range, SD: Standard deviation

Table 2. Examination of the relationships between gravida groups and qualitative characteristics

Gravida group / Variable	Gravida 1 (n=32)		Gravida ≥2 (n=33)		Statistical analysis* Probability
	n	%	n	%	
Episiotomy					
Yes	31	96.9	2	6.1	**p<0.001**
No	1	3.1	31	93.9	
Neonatal intensive care unit					
Yes	14	43.8	14	42.4	χ^2=0.012
No	18	56.2	19	57.6	p=0.914
Complication					
Yes	15	46.9	14	42.4	χ^2=0.130
No	17	53.1	19	57.6	p=0.718
Types of complication					
Asphyxia	8	57.1	8	53.3	p=1.000
Caput sucsadenenum	1	7.1	2	13.3	p=1.000
Cephal heamatoma	1	7.1	1	6.7	p=1.000
Respiratory distress	-	-	3	20.0	p=0.238
Temporary tachypnea	4	28.7	1	6.7	p=0.197
Blood transfusion					
Yes	3	9.4	3	9.1	p=1.000
No	29	90.6	30	90.9	
Maternal complication					
Yes	1	3.1	-	-	p=0.492
No	31	96.9	33	100.0	

*: Cross-tabulation tables and Pearson's χ^2 or Fisher's exact tests were used to examine the relationships between two qualitative variables

Discussion

In this study, maternal and neonatal outcomes of vacuum-assisted vaginal deliveries were compared between primiparous and multiparous women. The findings support the notion that obstetricians should not hesitate to utilize vacuum assistance when clinically indicated.

Since their introduction, disposable vacuum devices have been one of the important options among the limited choices available to clinicians in obstetrics when considering interventional vaginal delivery. Although their mechanism of action is similar to that of metal cup vacuum devices, disposable systems are widely preferred due to their ease of use and their capacity to reduce trauma to both the fetus and the mother (14). Nonetheless, the use of any assisted delivery technique carries potential risks for both maternal and neonatal health. Common maternal complications include anal sphincter injury, postpartum hemorrhage, wound dehiscence, and the need for episiotomy. Among neonates, cephalohematoma, subgaleal hemorrhage, and scalp abrasions are the most frequently reported adverse outcomes (5,6). There is no consensus regarding the relationship between episiotomy and anal sphincter injury across studies. Some studies have shown that vacuum-assisted deliveries increase the likelihood of perineal trauma and are associated with higher episiotomy rates (15,16).

One literature review suggested that routine episiotomy in non-instrumental vaginal deliveries may elevate the risk of sphincter injury (17), while other studies have indicated that, in the context of vacuum delivery, episiotomy may actually protect against anal sphincter damage in primiparous women (16,18-20). Furthermore, some evidence supports that episiotomy reduces the risk of sphincter injury compared to deliveries without episiotomy (18). Although this suggests that episiotomy may reduce serious injuries, no consensus on its necessity, benefits, or routine use has been reached (21). Guidelines recommend that episiotomy be considered in primiparous deliveries when vacuum extraction is used, but the decision should be individualized according to the clinical circumstances (22). The marked difference in episiotomy rates suggests that labor management varies significantly by parity. While the high rate of episiotomies, particularly among primiparous women, is intended to reduce the risk of anal sphincter injuries and advanced perineal tears, the routine applicability of this approach remains questionable. The current literature emphasizes that preventive episiotomy strategies should be considered within the framework of individualized decision-making.

In our study, routine episiotomy was not performed in multiparous women but was routinely performed in primiparous women. No maternal complications related to this approach were observed. Additionally, there was no significant difference in neonatal outcomes between the groups. Although the birth weight of neonates born to multiparous women was statistically higher than that of primiparous women, the need for episiotomy was lower in the multiparous group. These findings suggest that routine episiotomy may not be necessary in multiparous women undergoing vacuum-assisted delivery.

Studies have shown a significant association between vacuum-assisted labour and various neonatal complications. Severe cases of birth asphyxia have been reported in association with vacuum-assisted deliveries; rates of 4.8% for asphyxia and 3.8% for stillbirth suggest that these interventions may worsen fetal outcomes if not performed with caution (23). However, fetal distress is one of the most common indications for vacuum-assisted deliveries, and there is a strong association between the urgency of the intervention and adverse neonatal outcomes, such as labor asphyxia (24). In addition, it has been emphasised that neurological injuries, including intracranial haemorrhage, may occur because of factors such as improper vacuum placement on the fetal head or excessive traction during vacuum extraction (25).

Gupta and Bhagat (26) reported that neonatal complications, such as cephalohaematoma were less common with vacuum-assisted delivery than with forceps delivery, and that, even in cases of fetal distress, timely intervention with vacuum-assisted delivery significantly improved neonatal outcomes.

In this study, the most common neonatal complication reported was asphyxia rather than cephalohematoma. However, this should not be considered a direct result of vacuum application; rather, it should be considered a consequence of the fetal condition during labour that necessitates vacuum use. According to systematic reviews indicating that the incidence of severe neonatal morbidities—including asphyxia, a prolonged second stage, and fetal distress—increases complication rates, it has been stated that vacuum extraction, with appropriate indications may be effective in reducing such adverse outcomes (27). In our study, episiotomy was performed in two multiparous patients to accelerate labour. The neonates

of these two patients required neonatal intensive care and were diagnosed with asphyxia. However, fetal outcomes after vacuum-assisted vaginal delivery were compared between the two groups, and no statistically significant differences were found.

Study Limitations

The single-center design of this study and its limited sample size may reduce the generalizability of the findings. Future multicenter studies with larger samples are important to confirm these findings. In this study, neonatal outcomes, episiotomy rates and related complications could not be compared between patients who underwent non-vacuum-assisted vaginal delivery and those underwent cesarean section after labor.

However, our study shows that vacuum-assisted vaginal deliveries do not increase the incidence of asphyxia or maternal complications; on the contrary, they facilitate labour.

Conclusion

While vacuum-assisted vaginal delivery is an important alternative for the management of difficult labour, the practice of episiotomy should be approached with caution. Studies support the potential benefits of episiotomy in reducing serious lacerations, but potential risks remain controversial, particularly in certain populations, such as nulliparous women. Vacuum-assisted delivery may reduce the risk of developing fetal hypoxia by shortening the second stage of labor; however, prospective studies with larger samples are needed to support this effect. The results of this study suggest that obstetricians should not be reluctant to perform vacuum-assisted vaginal delivery when clinically indicated, because this approach can prevent unnecessary caesarean sections.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of İstanbul Esenyurt University (approval number E-12483425-299-35347; meeting dated 07.09.2023; protocol number 2023/08-12).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.B., E.U., Concept: M.B., E.U., Design: M.B., E.U., Data Collection or Processing: M.B., E.U., Analysis or Interpretation: M.B., E.U., Literature Search: M.B., E.U., Writing: M.B., E.U.

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ORIGINAL RESEARCH

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Evaluation of Knowledge Levels of Nurses Regarding Anaphylaxis Diagnosis, Treatment and Adrenaline Autoinjector Use

Hemşirelerin Anafilaksi Tanısı, Tedavisi ve Adrenalin Otoenjektör Kullanımı Konusunda Bilgi Düzeylerinin Değerlendirilmesi

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Abstract

Objective: Anaphylaxis is the most serious hypersensitivity reaction that begins suddenly, progresses rapidly and can cause death. Correct diagnosis and rapid treatment of anaphylaxis by all healthcare professionals is life-saving. The aim of this study was to assess the knowledge of nurses in our country regarding the diagnosis and treatment of anaphylaxis and the use of adrenaline autoinjectors.

Method: The study was designed as a cross-sectional descriptive study. An online survey was administered to participants to measure their knowledge of the diagnosis and treatment of anaphylaxis and adrenaline autoinjector use.

Results: Two hundred seventy-one nurses participated in the study, mean age was 30.5±8.4 years and mean professional experience was 9±8.7 years. 38.4% of the participants stated that the first-line treatment of anaphylaxis was adrenaline, 42.1% of the participants stated that the correct route of adrenaline administration was intramuscular, 29.5% of the participants knew that the right place of administering adrenaline, 33.6% of the participants knew the correct dose of adrenaline for children, 14.4% of them answered the adrenaline dose correctly for

Öz

Amaç: Anafilaksi, ani başlayan, hızla ilerleyen ve ölümcül olabilen en ciddi aşırı duyarlılık reaksiyonudur. Tüm sağlık çalışanları tarafından anafilaksinin doğru tanısı ve hızlı tedavisi hayat kurtarıcıdır. Bu çalışmanın amacı ülkemizdeki hemşirelerin anafilaksi tanısı, tedavisi ve adrenalin otoenjektörlerinin kullanımı konusundaki bilgi düzeylerini değerlendirmektir.

Yöntem: Çalışma kesitsel tanımlayıcı bir çalışma olarak tasarlandı. Katılımcılara anafilaksi tanısı, tedavisi ve adrenalin otoenjektör kullanımı hakkındaki anlayışlarını ölçmek için çevrimiçi bir anket uygulandı.

Bulgular: Çalışmaya 271 hemşire katıldı, ortalama yaş 30,5±8,4 yıl ve ortalama mesleki deneyim 9±8,7 yıldı. Katılımcıların %38,4'ü anafilaksinin birinci basamak tedavisinin adrenalin olduğunu, %42,1'i adrenalinin doğru uygulama yolunun intramüsküler yol olduğunu, %29,5'i adrenalinin doğru uygulama bölgesini, %33,6'sı çocuklarda doğru adrenalin dozunu, %14,4'ü yetişkinlerde doğru adrenalin dozunu biliyordu. Katılımcıların sadece %13,7'si adrenalin otoenjektörlerinin kullanımını bildiğini belirtti. Adrenalinin doğru uygulama yerini bilen hemşirelerin ortalama meslek yılları istatistiksel olarak anlamlı derecede daha düşük bulunmuştur

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Abstract

adults. Only 13.7% of the participants stated that they knew about the use of adrenaline autoinjectors. The average professional years of the nurses who knew about the correct place of administration of adrenaline were statistically significantly lower (p=0.041). Nurses who received post-graduation training on anaphylaxis; the rate of knowing that the all criteria of anaphylaxis, the correct way and place of administration of adrenaline, the rate of knowing the use of autoinjectors were significantly higher (p=0.003, p=0.008, p=0.019, p=0,022 respectively).

Conclusion: In our study, nurses' knowledge of anaphylaxis and adrenaline auto-injector was found to be insufficient. Nurses can be made more competent in anaphylaxis management by providing postgraduate training.

Keywords: Adrenaline autoinjector, anaphylaxis, knowledge, nurse

Öz

(p=0,041). Anafilaksi konusunda mezuniyet sonrası eğitim alan hemşirelerde; anafilaksinin tüm kriterlerini bilme oranı, adrenalinin doğru uygulama yolu ve yerini, otoenjektör kullanımını bilme oranı istatistiksel olarak anlamlı derecede daha yüksek bulunmuştur (sırasıyla p=0,003, p=0,008, p=0,019, p=0,022).

Sonuç: Çalışmamızda hemşirelerin anafilaksi ve adrenalin otoenjektörü kullanımı hakkındaki bilgilerinin yetersiz olduğu bulundu. Hemşireler lisansüstü eğitim verilerek anafilaksi yönetiminde daha yetkin hale getirilebilir.

Anahtar kelimeler: Adrenalin otoenjektrü, anafilaksi, bilgi, hemşire

Introduction

Anaphylaxis is the most serious hypersensitivity reaction that begins suddenly and progresses rapidly and can cause death. It may occur through various mechanisms and present with different clinical presentations (1,2). Correct diagnosis and rapid treatment of anaphylaxis by all healthcare professionals is life-saving.

The prevalence of anaphylaxis has been reported to be up to 2% in various studies. Emergency department visits due to anaphylaxis are increasing all over the world. However, the mortality rate is extremely low and has not increased in recent years (2,3). A mortality rate of less than 0.5% is reported in those hospitalized or admitted to the emergency department with anaphylaxis (2).

Clinical findings are variable. The most common symptoms are skin and mucosal symptoms such as urticaria and angioedema. Respiratory, cardiovascular and gastrointestinal systems may be affected, with symptoms such as upper and lower respiratory tract symptoms, hypotension, tachycardia, loss of consciousness, vomiting or cramp-like abdominal pain (1,2). The frequency of causes of anaphylaxis varies by age or geographic region. While the most common cause of anaphylaxis in childhood is food, anaphylaxis due to venom and drugs is more common in adults (2,4,5).

There is a possibility of recurrence of anaphylaxis. Therefore, patients presenting with anaphylaxis should be prescribed an adrenaline autoinjector (AAI) and trained in its use (1). Nurses provide treatment services in healthcare institutions at all levels. They are in contact with the patient during and after treatment. It is important for nurses to recognize the signs and symptoms of rare but life-threatening anaphylaxis and know its treatment.

In this study, we aimed to evaluate the knowledge of nurses in Turkey about the diagnosis and treatment of anaphylaxis and the use of AAI.

Materials and Methods

The study was conducted as a cross-sectional descriptive survey between May 2021 and July 2021. The questionnaire was prepared by a pediatric allergist and a nurse who is a faculty member based on current information. The 30-question survey prepared online by the Google forms application was sent to nurses via social media (WhatsApp) and electronic mail. The first part of the survey included the purpose and content of the study and the information and consent part of the researchers. Participants who gave consent answered the survey questions fully.

The questionnaire included questions about demographic information such as gender, professional year, whether they received post-graduation education on anaphylaxis, knowledge and experience in recognizing and treating anaphylaxis, AAI and their knowledge and experience regarding its use. The questionnaire was presented as Supplementary Material 1.

Study Population

It was conducted with nurses working in Turkey. The sample size for the study was determined as a minimum of 198 participants at a 99.9% confidence interval using the t-test (t=3.291, α=0.001). The study was completed with 271 participants.

Statistical Analysis

The data was analyzed by IBM SPSS Statistics 22.0 program. Kolmogorov-Smirnov test was used for the normal distribution of the data. The mean differences of two groups with variables that are not distributed normally was assessed by Mann-Whitney U test. The distribution of categorical variables between groups was analyzed by χ^2 (chi-square) test. Mean, standard deviation, median (1st and 3rd quartiles), frequency and percentage values are given as descriptive statistics. The limit of statistical significance was regarded as $p<0.05$.

Ethical Issues

This study was approved by the Ethics Committee of Bezmialem Vakıf University (date: 30.03.2021, approval number: E.10866). The study was performed according to the Declaration of Helsinki. Consent was obtained from all participants participating in the study.

Results

89.7% (n=243) of 271 participants are women, the average age is 30.5±8.4 years (min-max: 20-58 years) and the average professional experience is 9±8.7 years (min-max: 1-37 years, median: 5 years, Q1-Q3: 3-13 years). While 50.6% (n=137) of the nurses were license degree graduates, 21.4% (n=58) were master's degree graduates, 16.6% (n=45) were high school graduates and 11.4% (n=31) were associate degree graduates. Of the nurses, 22.5% (n=61) were working in primary care, 17.3% (n=47) in secondary care, 52% (n=141) in tertiary care institutions, and 8.1% (n=22) were not currently working as nurses but were involved in administrative and educational duties.

85.6% of the participants (n=232) had received training on anaphylaxis during their education. The rate of receiving postgraduate education on this subject was 29.9% (n=81). More than half of the participants (54.2%, n=147) were actively involved in the treatment of anaphylaxis patients. Demographic characteristics of the participants are given in Table 1.

The proportion of nurses who correctly characterized all three anaphylaxis criteria in the international guidelines [European Academy of Allergy & Clinical Immunology (EAACI) Guidelines] as anaphylaxis was 66.1% (n=179). Of the participants, 38.4% (n=104) stated that the first line drug to be administered in the treatment of anaphylaxis was adrenaline, 42.1% (n=114) stated that the correct route of administration of adrenaline was intramuscular, 29.5% (n=80) stated that the correct site of administration of adrenaline (anterolateral thigh, vastus lateralis muscle), 33.6% (n=91%) stated the correct adrenaline dose in children was 0.01 mg/kg, 14.4% (n=39) stated the correct adrenaline dose in adult patients was 0.5 mg. The correct position to be given to the patient during anaphylaxis (lying the patient on the back and elevating the feet at an angle

Table 1. Participants' demographic information and knowledge about anaphylaxis treatment and AAI

Age, year, mean ± SD	30.5±8.4
Median (Q1-Q3)	27 (24-36)
Professional years (mean ± SD)	9±8.7
Median (Q1-Q3)	5 (3-13)
Educational level, n (%)	
High school	45 (16.6)
Associate degree (2 years)	31 (11.4)
Licence (4 years)	136 (50.2)
Master's degree	58 (21.4)
Institution, n (%)	
Primary care	61 (22.5)
Secondary care	47 (17.3)
Tertiary care	141 (52)
Administrative or educational	22 (8.1)
Postgraduate education, n (%)	
Yes	81 (29.9)
No	190 (70.1)
Participation in anaphylaxis treatment, n (%)	
Yes	147 (54.2)
No	124 (45.8)
Anaphylaxis criteria, n (%)*	
Criterion 1	259 (95.6)
Criterion 2	206
Third criterion	184
Know it all	179 (66.1)
First drug in the treatment of anaphylaxis, n (%)	
Adrenaline	104 (38.4)
Antihistamine	119 (43.9)
Corticosteroids	43 (15.9)
No opinion	5 (1.8)
Adrenaline administration route, n (%)	
Intramuscular	114 (42.1)
Intravenous	101 (37.3)
Subcutaneous	32 (11.8)
No opinion	24 (8.9)
Place of adrenaline administration, n (%)	
IV through the vascular access I can find	96 (35.4)
Intramuscular from lateral thigh	80 (29.5)
Subcutaneous from upper arm	30 (11.1)
Intramuscular from the gluteal region	24 (8.9)
Intramuscular from the deltoid region	13 (4.8)
Subcutaneous from the abdominal area	3 (1.1)
No opinion	25 (9.2)
Knowledge of autoinjector use, n (%)	
Yes	37 (13.7)
No	254 (93.7)
Experience of autoinjector use, n (%)	
Yes	13 (4.8)
No	258 (95.2)

Table 1. Continued

SD: Standard deviation, AAI: Adrenaline autoinjector, *: Clinical criteria for diagnosing anaphylaxis[1]
1. Criteria: Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue or both (e.g., generalized hives, pruritus or flushing, swollen lips–tongue–uvula and at least one of the following)
a. Respiratory compromise [e.g., dyspnoea, wheeze–bronchospasm, stridor, reduced peak expiratory flow (PEF) and hypoxemia]
b. Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction [e.g., hypotonia (collapse), syncope, incontinence]
2. Criteria: Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
a. Involvement of the skin–mucosal tissue (e.g., generalized hives, itch-flush, swollen lips–tongue–uvula)
b. Respiratory compromise (e.g., dyspnoea, wheeze–bronchospasm, stridor, reduced PEF, hypoxemia)
c. Reduced BP or associated symptoms [e.g., hypotonia (collapse), syncope, incontinence]
d. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)
3. Criteria: Reduced BP after exposure to known allergen for that patient (minutes to several hours):
a. Infants and children: low systolic BP (age specific) or >30% decrease in systolic BP*
b. Adults: systolic BP of <90 mmHg or >30% decrease from that person's baseline

of 30-45 degrees if there was no respiratory distress) were known by 60.8% of the nurses (n=165).

Antihistamines were the most frequently selected first-line drug in the treatment of anaphylaxis (43.9%, n=119). More than one third of the nurses (37.3%, n=101) stated that they would administer adrenaline intravenously in the treatment of anaphylaxis. Only 13.7% (n=37) of the participants stated that they knew how to use AAI, 4.8% (n=13) stated that they had used an autoinjector before, and 6.3% (n=17) stated that they had received training on this subject. In our study, there were only 3 school nurses, none of them had experience using AAI, and only one of them stated that she knew how to use AAI. 13.7% (n=37) of the nurses knew that AAI preparation was available in 0.15 and 0.3 mg forms within the scope of reimbursement. The knowledge of the participants regarding anaphylaxis treatment and AAI is presented in Table 1.

There was no statistically significant relationship between the rates of knowing all anaphylaxis criteria, knowing that adrenaline is the first line drug to be used in the treatment of anaphylaxis, knowing the correct route of administration of adrenaline, knowing the correct place of administration of adrenaline, knowing the correct dose of adrenaline in children and adults, and knowing the use of AAI with age, educational level or institution of employment. The mean duration of professional experience of the nurses who knew that adrenaline should be administered anterolateral to the thigh was significantly shorter than those who did not know (p=0.041). There was no statistically significant relationship between professional experience and correct answers to other questions. The rate of nurses who had previous experience in the treatment of anaphylaxis knowing that adrenaline should be administered IM was significantly higher (p=0.012). There was no statistically significant relationship between anaphylaxis treatment experience and correct answers to other questions. Nurses who received postgraduate training on anaphylaxis had significantly higher rates of knowing all anaphylaxis criteria, knowing the correct administration route for adrenaline, knowing the correct administration site for adrenaline, and knowing how to use an AAI (respectively, p=0.003, p=0.008, p=0.019, p=0.022). The statistical relationship between nurses' anaphylaxis diagnosis-treatment knowledge and their age, professional years, education level, institution of employment, postgraduate training on anaphylaxis and involvement in anaphylaxis treatment is presented in Table 2.

Discussion

Anaphylaxis, an acute life-threatening emergency condition, requires immediate treatment in order to prevent further progression and complications. It is important that nurses who are in contact with patients during and after treatment recognize the signs and symptoms of anaphylaxis, which is rare but life-threatening, and know how to treat it.

66% of the participants in our study described all three definitions in the EAACI guide as anaphylaxis (1). These results indicate that the multisystem manifestations of anaphylaxis are not sufficiently known. There may be deficiencies in the diagnosis and treatment of anaphylaxis due to lack of knowledge. Indeed, many studies report that anaphylaxis is underdiagnosed and undertreated (6,7).

In our study, the general knowledge of nurses regarding the treatment of anaphylaxis was found insufficient. Only 38.4% knew that the first-line drug in treatment was adrenaline, 42.1% knew the correct route of administration of adrenaline, 29.5% knew the correct administration place of adrenaline, 33.6% knew the correct dose of adrenaline in pediatric patients, and 14.4% knew the correct application route of adrenaline in adults. In a study conducted with pediatric nurses at a university hospital in our country, the rate of knowing that adrenaline is the first-line drug in the treatment of anaphylaxis was found to be 87-90% in two

Table 2 Comparison of the knowledge levels of nurses according to age, years of employment, educational status, institution of employment, postgraduate education on anaphylaxis and participation in the treatment of anaphylaxis

		All anaphylaxis criteria knowing n=179	Knowing that the first line drug is adrenaline, n=104	Knowing the way to administer adrenaline, n:=14	Knowing the place of administration of adrenaline, n=80	Knowing the dose of adrenaline in a child, n=91	Knowing the dose of adrenaline in adults, n=39	Knowing how to position, n=165	Knowing how to use an autoinjector, n=37
Age (mean ± SD)	Correct	31±8.4	30.4±8.7	29.9±7.3	29.5±6.9	29.9±7.4	29.4±7.7	30.4±8	28.7±6.4
	Incorrect	29.5±8.3	30.5±8.2	30.8±9.1	30.9±8.9	30.7±8.8	30.6±8.5	30.6±9	30.7±8.6
	p*	0.167	0.990	0.362	0.205	0.463	0.392	0.810	0.167
Year of profession (mean ± SD)	Correct	9.5±8.9	9.3±8.9	8±7.3	7.3±7	8±7.7	8.2±7.6	8.8±8.4	7.4±6.1
	Incorrect	8±8.4	8.8±8.7	9.7±9.6	9.7±9.3	9.5±9.2	9.1±8.4-9	9.3±9.4	9.2±9.1
	p*	0.200	0.664	0.121	**0.041**	0.206	0.536	0.670	0.235
Education level n (%)	1. High school, n:45	32 (71.1)	17 (37.8)	16 (35.6)	10 (22.2)	13 (28.9)	3 (6.7)	28 (62.2)	6 (13.3)
	2. Associate degree (2 years), n=31	22 (71)	10 (32.3)	13 (41.9)	6 (19.4)	9 (29)	3 (9.7)	19 (61.3)	4 (12.9)
	3. Licence (4 year), n=136	92 (67.2)	56 (40.9)	62 (45.3)	47 (34.3)	52 (38)	23 (16.8)	81 (59.1)	21 (15.3)
	4. Master's degree, n=58	33 (56.9)	21 (36.2)	23 (39.7)	17 (29.3)	17 (29.3)	10 (17.2)	37 (63.8)	6 (10.3)
	p**	0.378	0.807	0.684	0.241	0.497	0.289	0.936	0.829
Workplace n (%)	Primary care, n=61	39 (63.9)	24 (39.3)	29 (47.5)	17 (27.9)	23 (37.7)	5 (8.2)	41 (67.2)	7 (11.5)
	Secondary care, n=47	36 (76.6)	15 (31.9)	19 (40.4)	12 (25.5)	11 (23.4)	4 (8.5)	24 (51.1)	10 (21.3)
	Tertiary care, n=141	89 (63.1)	54 (38.3)	56 (39.7)	44 (31.2)	48 (34)	26 (18.4)	85 (60.3)	19 (13.5)
	Administration-training, n=22	15 (68.2)	11 (50)	10 (45.5)	7 (31.8)	9 (40.9)	4 (18.2)	15 (68.2)	1 (4.5)
	p**	0.386	0.550	0.747	0.876	0.363	0.148	0.328	0.249
Postgraduate education n (%)	Yes	64 (79)	35 (43.2)	44 (54.3)	32 (39.5)	32 (39.5)	16 (19.8)	53 (65.4)	17 (21)
	No	115 (60.5)	69 (36.3)	70 (36.8)	48 (25.3)	59 (31.1)	23 (12.1)	112 (58.9)	20 (10.5)
	p**	**0.003**	0.285	**0.008**	**0.019**	0.177	0.101	0.317	**0.022**
Participation in anaphylaxis treatment	Yes	99 (67.3)	58 (39.5)	72 (49)	49 (33.3)	54 (36.7)	24 (16.3)	85 (57.8)	24 (16.3)
	No	80 (64.5)	46 (37.1)	42 (33.9)	31 (25)	37 (29.8)	15 (12.1)	80 (64.5)	13 (10.5)
	p**	0.624	0.691	**0.012**	0.134	0.231	0.323	0.261	0.163
Total n (%)		179 (66.1)	104 (38.4)	114 (42.1)	80 (29.5)	91 (33.6)	39 (14.4)	162 (59.7)	37 (13.7)

*: Mann-Whitney U test, **: Chi-square test, SD: Standard deviation

groups divided according to professional experience. These rates are significantly higher than the rates in our study. In the same study, the rate of knowing that adrenaline should be administered intramuscularly was found to be 64-71%, the rate of knowing the correct application site of adrenaline was 48-77%, and the rate of knowing the correct dose was 51-58% (8). In another study conducted with nurses working in a tertiary hospital, their knowledge levels were evaluated before and after in-service training; Before the training, the rate of knowing that the first-line drug in the treatment of anaphylaxis was adrenaline was 84.4%, the rate of knowing the correct application route of adrenaline was 80%, the rate of knowing the correct application site of adrenaline was 50%, and the rate of knowing the correct dose was 64% (9). The knowledge levels in our study are lower than these studies. While approximately half of our participants worked in tertiary healthcare institutions, the inclusion of nurses working in primary and secondary healthcare institutions, as well as in administrative and educational roles may have contributed to this finding. Our study included nurses who had previously been active in nursing but were also in administrative or educational roles at the time the study was conducted. This is one of the limitations of our study. In a study conducted with 1.172 participants, including different healthcare professionals working at different levels in our country, 44.7% of healthcare professionals stated that they would administer adrenaline when they suspected anaphylaxis, 29% specified the correct application route of adrenaline, 23.5% identified the correct application site, and 28.9% of them knew the

correct dose (10). The knowledge levels in this study and our study are relatively similar. In a study conducted in Singapore, 40.3% of emergency room nurses' first choice drug in anaphylaxis was adrenaline, while 47.4% stated that they used the intramuscular route for adrenaline. The rates are similar to our study. In the same study, 50% of nurses knew the correct dose of adrenaline for adults, and this rate was higher than the rate found in our study (11). In our study, the average professional experience of nurses who knew the correct application site of adrenaline was shorter. Professional experience did not have a statistically significant relationship with correct answers to other questions. Contrary to our study, in a similar study by Güneş et al. (8) nurses with more professional experience were more likely to know the correct application site of adrenaline.

There is a possibility of recurrence of anaphylaxis. Therefore, AAI must be prescribed to those that experience anaphylaxis and they should be trained on how to use it. The healthcare professionals that care for the patients at risk for anaphylaxis should also be educated on the use of AAI. Only 13,7% of the nurses in our study stated they knew how to use AAI and 6,3% had undergone training on the use of AAI. Our survey was conducted online and was based on the statements of the nurses so their proficiency in practice could not be evaluated. Therefore comparison with other studies is not aplicable. The rate of knowledge about the presence of AAI was 54% among nurses in Özkul Sağlam and Özkars' (9) study, and 20% among different groups of healthcare professionals in Baççıoğlu and Yılmazel Uçar (10) study.

In studies conducted on healthcare professionals working in primary, secondary or tertiary healthcare centers, it was found that knowledge about the correct use of AAI's was insufficient (12-15). The rate of prescription of adrenaline to patients experiencing anaphylaxis is still inadequate although it has increased in time (16-22).

In our survey the rate of knowledge of the correct route and site of administration of adrenaline and the rate of knowing the use of AAI were higher in the nurses that had undergone postgraduation training on anaphylaxis. This finding clearly displays the need for post-graduate education programs on anaphylaxis for the nurses to update their knowledge. Less than one-fifth of our participants had postgraduate training in anaphylaxis. This was considered to be inadequate. According to these results, the necessity of periodic and comprehensive training to update information should be taken into consideration. In the study of Özkul Sağlam and Özkars (9) nurses' knowledge levels about anaphylaxis diagnosis and treatment were compared before and after training on anaphylaxis, and it was found that their knowledge levels increased after the training. In the study conducted by Sipahi Cimen and Sayili (23) with different groups of healthcare professionals, it was found that participants who received training on anaphylaxis and had experience of anaphylaxis cases responded correctly to questions about adrenaline doses at a higher rate.

Sudy Limitations

The most significant limitation of our study is that it was an online survey. Therefore, participants' knowledge levels could not be verified through a face-to-face interview or practice. While approximately half of the participants worked in tertiary healthcare institutions, there were also nurses working in primary and secondary healthcare institutions, and less than a tenth of the participants were nurses working in educational or administrative roles. This was a limitation of our study even though we found no statistically significant differences in knowledge levels about anaphylaxis across institutions.

Conclusion

As a result of our study, we found that nurses' knowledge regarding the diagnosis and treatment of anaphylaxis is insufficient. The knowledge levels are better in nurses who received postgraduate education. Therefore, implementing post-graduate training programs can help nurses become more competent in dealing with life-threatening anaphylaxis. Nurses' knowledge about AAI treatment is insufficient, and nurses need to be trained on the use of this essential and life-saving drug for people at risk of anaphylaxis.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Bezmialem Vakıf University (date: 30.03.2021, approval number: E.10866). The study was performed according to the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all participants participating in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: L.B., Ö.E., Concept: L.B., M.Y., G.K.E., S.S.Ç., M.A.N., Design: L.B., M.Y., G.K.E., S.S.Ç., M.A.N., Data Collection or Processing: L.B., Ö.E., M.Y., Analysis or Interpretation: L.B., M.A.N., Literature Search: L.B., G.K.E., S.S.Ç., Writing: L.B., M.A.N.

Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary Material 1. Hemşirelerde Anaflaksi Farkındalık Düzeyi

https://d2v96fxpocvxx.cloudfront.net/1e8a7eae-47cf-4a4e-a540-9cee47620b04/content-images/9c8cc639-4fd5-4186-b4d2-7d55bbc07591.pdf

ORIGINAL RESEARCH

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Epidemiological Analysis of Allergic Contact Dermatitis Cases with Positive Patch-test Results Emerging After the COVID-19 Pandemic

COVID-19 Pandemisinden Sonra Alerjik Kontakt Dermatit Şikayetleri Başlayan Yama Testi Pozitif Hastaların Epidemiyolojik Olarak Değerlendirilmesi

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Abstract

Objective: Allergic contact dermatitis (ACD) is a common inflammatory skin disorder caused by extrinsic allergens that reach the skin through direct contact, airborne exposure, or systemic routes. Patch-testing is currently accepted as the gold-standard diagnostic method for ACD. Among the allergens included in the European standard patch-test series is propolis, and it has been suggested that the increased use of personal hygiene products and dietary supplements during the novel coronavirus (COVID-19) pandemic may have led to greater sensitization to this substance. This study aimed to evaluate the frequency of propolis allergy after the COVID-19 pandemic and to investigate possible associations between allergens and demographic or clinical variables.

Method: In this retrospective study, 152 patients who developed symptoms of ACD after the COVID-19 pandemic underwent the European standard patch-test series with 30 different allergens. Of these, 50 patients with at least one positive patch-test result were included in the further analysis. Data were recorded and evaluated according to age, sex, allergen frequency, occupation, hobbies, need for biopsy, and disease duration.

Results: In this study, one of the most striking observations was the notably high rate of propolis patch-test positivity, even surpassing that of nickel. Another key finding was the consistent visibility of propolis reactions: they appeared as early as the initial reading and persisted through day 7, underscoring the allergen's sustained reactivity.

Öz

Amaç: Alerjik kontakt dermatit (AKD), çoğunlukla deriye doğrudan temas, havadan veya sistemik maruziyetler yoluyla ekstrensek alerjenlerin neden olduğu yaygın bir enflamatuvar deri hastalığıdır. Yama testi, AKD tanısında günümüzde kabul edilen altın standart yöntemdir. Avrupa standart yama testi serisinde bulunan alerjenlerden biri propolistir ve yeni koronavirüs hastalığı-2019 (COVID-19) pandemisi döneminde kişisel hijyen ürünleri veya besin takviyelerinin kullanımındaki artış nedeniyle propolise karşı artan bir duyarlılık olabileceği düşünülmektedir. Bu çalışma, COVID-19 pandemisi sonrasında propolis alerjisinin görülme sıklığını ve alerjenler ile demografik/klinik değişkenler arasındaki olası ilişkileri değerlendirmeyi amaçlamaktadır.

Yöntem: Bu retrospektif çalışmada COVID-19 pandemisinden sonra AKD semptomları başlayan 152 hastaya 30 farklı alerjenle Avrupa standart test serisi uygulandı. Pandemi sonrası alerjik semptomları başlayan 152 hastadan yama testi pozitifliği olan 50 hasta ileri incelendi. Elli hastanın verileri yaş, cinsiyet, alerjen sıklığı, meslek, hobiler, biyopsi gerekliliği ve hastalık süresine göre epidemiyolojik dağılım olarak kaydedildi.

Bulgular: Bu çalışmanın en dikkat çekici bulgularından biri, propolis yama testi pozitifliğinin nikel pozitifliğini dahi aşacak düzeyde yüksek olmasıydı. Ayrıca propolis reaksiyonlarının ilk okumada ortaya çıkması ve 7. güne kadar devam etmesi, çalışmanın bir diğer önemli sonucu olarak değerlendirildi.

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Abstract

Conclusion: The findings suggest that the increased use of disinfectants and dietary supplements during the post-COVID-19 period may have contributed to sensitization to propolis. These results indicate that propolis is appearing more frequently as a positive allergen in patch-testing and should be carefully considered during evaluation. Prospective studies are needed to confirm these observations.

Keywords: Allergic contact dermatitis, COVID-19, incidence, nickel, patch-test, propolis

Öz

Sonuç: Bulgular, COVID-19 pandemisi sonrası dönemde dezenfektan ve besin takviyesi kullanımındaki artışın propolis duyarlanmasında rol oynamış olabileceğini düşündürmektedir. Bu durum, yama testlerinde propolisin giderek daha sık pozitifleştiğini ve değerlendirmelerde göz önünde bulundurulması gerektiğini göstermektedir. Prospektif çalışmalarla bu sonuçların desteklenmesi önemlidir.

Anahtar kelimeler: Alerjik kontakt dermatit, COVID-19, insidans, nikel, propolis, yama testi

Introduction

Allergic contact dermatitis (ACD) is a T-cell-mediated type IV hypersensitivity reaction and is common in the general population (1-3). Patch-testing is the gold-standard diagnostic method for ACD (4,5).

During the novel coronavirus disease-2019 (COVID-19) pandemic and its aftermath, various cutaneous manifestations and dermatological conditions have been associated with both vaccination and the infection itself. However, few studies have evaluated changes observed in patch-tests performed for allergic complaints. The existing literature on the COVID-19 pandemic primarily focuses on specific populations, such as healthcare workers, rather than the general population (6).

During the COVID-19 pandemic, people's daily routines have changed dramatically. In this context, the use of dietary supplements, cosmetics, and personal hygiene products increased significantly. Studies conducted in Turkey and various countries have demonstrated a notable increase in consumption of dietary supplements aimed at strengthening the immune system, particularly during the pandemic (7-9). The use of naturally sourced ingredients such as propolis has recently become highly popular in the cosmetics industry. Before the COVID-19 pandemic, the reported frequency of propolis contact allergy in European patch-test cohorts ranged from 1% to 3.5%, and the 2019 inclusion of propolis into the European baseline series (EBS) was based on an overall positivity rate of approximately 2-3% in multicenter studies (10,11). These findings indicate that propolis was a relatively uncommon allergen in the pre-pandemic period. However, during the COVID-19 pandemic, the widespread use of propolis-containing supplements, cosmetics, and hygiene products raised concerns about a potential increase in sensitization. This shift in public behavior formed the main rationale for the present study, which investigates post-pandemic propolis patch-test positivity in a tertiary dermatology center.

This study retrospectively evaluated patch-test positivity among patients from the general population who developed cutaneous complaints after the COVID-19 pandemic and were clinically suspected of ACD. This study aimed to assess patients with ACD who were patch-test–positive for propolis after the COVID-19 pandemic, focusing on epidemiological distribution, allergen frequency, and correlations with demographic and clinical factors.

Although the study does not include a pre-pandemic comparison group, the increased public use of propolis-containing supplements and hygiene products during the pandemic has raised concerns about a possible rise in sensitization. Therefore, the study focuses exclusively on post-pandemic cases and aims to contextualize the observed frequency within pre-pandemic rates reported in the literature.

Materials and Methods

Data from 152 patients whose symptoms began after the COVID-19 pandemic and who were clinically suspected of ACD and who underwent European Standard Patch-testing between March 1, 2023, and May 1, 2023, were retrospectively analyzed. Subsequently, data from fifty patients who tested positive for at least one allergen were examined.

No patient had received topical or systemic steroids or antihistamines on their backs within one month before the patch-test. None of the study participants had a history of atopic dermatitis, and patch-testing was not conducted on individuals with acute dermatitis. In addition, patients using systemic and/or topical immunosuppressive agents, pregnant women, and lactating women were excluded from the study.

Thirty allergens were applied under occlusion using Finn Chambers on the upper back. All patients provided consent and were instructed to avoid showering, wearing tight

clothing, exposure to ultraviolet radiation, exercising, and excessive sweating.

The patients' skin reactions were examined on days two, three, four, and seven. Any findings suggesting irritation were reported. Test readings were recorded as: (-) no reaction; (+/-) faint erythema; (+) mild reaction (erythema, infiltration, and possibly papules); (++) moderate reaction (erythema, infiltration, papules, and vesicles); (+++) severe reaction (erythema, infiltration, papules, vesicles, and bullae) according to the criteria of the International Contact Dermatitis Research Group (12).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for statistical analysis of patient data; $p<0.05$ was considered significant. Descriptive statistics included the mean, standard deviation, minimum, maximum, frequency, and ratio values. Pearson's chi-square test was used to assess associations between categorical variables. Ethical approval for the study was obtained from the Local Ethics Committee of İstanbul Kent University (Scientific Research and Publication Ethics Committee of Health Sciences; approval number: E-10420511-050-26426, date: 02.10.2023), İstanbul, Turkey.

Results

All patients underwent patch-test evaluations on days 2, 3, 4, and 7. Among the 152 patients studied, 102 had negative results for all allergens included in the European baseline patch-test series. Patients who showed positive reactions to at least one allergen remained positive on days 3, 4, and 7. None of these 50 patients exhibited any irritant reactions.

No exacerbation or increase in symptoms or primary skin complaints was observed in any patient during the patch-test period.

Out of the 50 patients with positive patch-test results, 74% (n=37) were female and 26% (n=13) were male (Table 1). The mean age was 34.02±13.94 years; 12% (n=6) of patients were under 18 years, and the mean disease duration was 27.2±9.6 months (Table 1).

Among 50 patients with positive patch-test results, 32% (n=16) were stay-at-home spouses, 18% (n=9) were students, 12% (n=6) were teachers, 8% (n=4) were textile workers, 6% (n=3) cleaning workers, and the rest were other professions. Seventy-four percent (n=37) of the patients had no hobbies; among the 13 patients with a hobby, 76.9% (n=10) reported painting (Table 1).

Skin biopsies were performed in 18% of the 50 patients who tested positive on patch-tests, and no correlation was found between the severity and duration of ACD among those who underwent biopsy. Spongiotic dermatitis was observed in the histopathological examination of all biopsied patients.

Among patients with at least one allergen-positive patch-test, the most frequent allergens were propolis, nickel, fragrance mix I, colophonium, and fragrance mix II (Table 2).

Neomycin sulfate, caine mix III, mercapto mix, epoxy resin, bisphenol A, 2-mercaptobenzothiazole, quaternium-15, tixocortol-21-pivalate, methylisothiazolinone, and formaldehyde were negative in all patients (Table 2).

Pearson's chi-square tests were applied to examine the relationship between patch-test allergen status and patient gender. The patch-test allergen status of the participants did not differ by gender, age, profession, or hobby type ($p>0.05$ for all comparisons) (Table 3).

No statistically significant difference was found between participants' methyldibromo glutaronitrile allergen patch-test results and their age distribution ($p=0.14$).

Of the 50 patients, 17 had a positive propolis patch-test. The severity distribution among the 17 propolis-patch positive patients was as follows: 9 were mild (+), 5 were moderate (++), and 3 were severe (+++) (Table 4). Moreover, all propolis-positive patients continued to exhibit a positive propolis patch-test result on day 7,

Table 1. Frequency table of participants' demographic information

	Frequency	Percentage (%)
Gender		
Female	37	74.0
Male	13	26.0
Age		
<18 years	6	12.0
18-29 years	15	30.0
30-42 years	14	28.0
43-55 years	12	24.0
>55 years	3	6.0
Occupation		
Stay at-home spouse	16	32.0
Student	9	18.0
Teacher	6	12.0
Textile worker	4	8.0
Cleaning worker	3	6.0
Other	12	24.0

Table 2. Participants' allergen status in patch-test

		Negative	+	++	+++
Allergens		**f (%)**	**f (%)**	**f (%)**	**f (%)**
1	Potassium dichromate	48 (96.0)	2 (4.0)	0	0
2	P-phenylenediamine (PPD)	49 (98.0)	1 (2.0)	0	0
3	Thiuram mix	48 (96.0)	2 (4.0)	0	0
4	Neomycin sulfate	50 (100.0)	0	0	0
5	Cobalt (II) chloride hexahydrate	49 (98.0)	0	1 (2.0)	0
6	Caine mix III	50 (100.0)	0	0	0
7	Nickel (II) sulfate hexahydrate	34 (68.0)	5 (10.0)	8 (16.0)	3 (6.0)
8	2-hydroxy ethyl methacrylate	49 (98.0)	0	0	1 (2.0)
9	Colophonium	44 (88.0)	2 (4.0)	3 (6.0)	1 (2.0)
10	Paraben mix	49 (98.0)	1 (2.0)	0	0
11	N-isopropyl-n-phenyl-4-phenylenediamine (I PPD)	49 (98.0)	0	0	1 (2.0)
12	Lanolin alcohol	48 (96.0)	2 (4.0)	0	0
13	Mercapto mix	50 (100.0)	0	0	0
14	Epoxy resin, bisphenol a	50 (100.0)	0	0	0
15	Peru balsam	49 (98.0)	0	1 (2.0)	0
16	4-tert-butylphenolformaldehyde resin	49 (98.0)	1 (2.0)	0	0
17	2-mercaptobenzothiazole	50 (100.0)	0	0	0
18	Fragrance mix 1	44 (88.0)	3 (6.0)	3 (6.0)	0
19	Sesquiterpene lactone mix	49 (98.0)	0	1 (2.0)	0
20	Quatermuim-15	50 (100.0)	0	0	0
21	Propolis	33 (66.0)	9 (18.0)	5 (10.0)	3 (6.0)
22	Methylisothiazolinone + methylchloroisothiazolinone	48 (96.0)	1 (2.0)	0	1 (2.0)
23	Budesonide	49 (98.0)	0	0	1 (2.0)
24	Tixocortol-21-pivalate	50 (100.0)	0	0	0
25	Methyldibromo glutaronitrile	45 (90.0)	4 (8.0)	1 (2.0)	0
26	Fragrance mix II	46 (92.0)	4 (8.0)	0	0
27	Hydroxyisohexyl 3-cyclohexene carboxaldehyde	49 (98.0)	1 (2.0)	0	0
28	Methylisothiazolinone	50 (100.0)	0	0	0
29	Textile dye mix	48 (96.0)	0	0	2 (4.0)
30	Formaldehyde	50 (100.0)	0	0	0

Table 3. Relationship between propolis allergen severity and gender of participants

		Allergen severity					
		Negative	**+**	**++**	**+++**	χ^2	**p**
Allergens		**f (%)**	**f (%)**	**f (%)**	**f (%)**		
Propolis	Female	25 (75.8)	6 (66.7)	4 (80.0)	2 (66.7)	0.482	0.923
	Male	8 (24.2)	3 (33.3)	1 (20.0)	1 (33.3)		

p: Statistical significance

characterized by persistent erythematous papules on their upper back.

In these analyses, Pearson's chi-square tests were applied to examine associations between propolis allergen severity and gender, age, and profession. There were no differences in propolis allergen severity by gender (p=0.858; Table 3), age distribution (p=0.711; Table 4), or profession (p=0.458; Table 5) among the participants.

When the relationship between propolis allergen and rash localization was examined in patients, dermatitis

Table 4. Relationship between propolis allergen severity and age of participants

		Allergen severity					
		Negative	+	++	+++	χ^2	p
Allergens		f (%)	f (%)	f (%)	f (%)		
Propolis	<18	4 (12.1)	2 (22.2)	0	0	8.035	0.782
	18-29	9 (27.3)	3 (33.3)	2 (40.0)	1 (33.3)		
	30-42	10 (30.3)	2 (22.2)	2 (40.0)	0		
	43-55	8 (24.2)	2 (22.2)	1 (20.0)	1 (33.3)		
	>55	2 (6.1)	0	0	1 (33.3)		

p: Statistical significance

lesions were most frequently localized to the head and neck region. The Pearson chi-square test was applied to examine the relationship between patients' propolis allergen positivity and localization. Accordingly, no association was found between the participants' propolis allergy and localization (p=0.658). In addition, patients with positive patch-tests to propolis had involvement in all body regions, but none had genital complaints or lesions (Table 6).

An ANOVA was performed to evaluate the relationships among severity of sensitivity to propolis allergen, body mass index (BMI), and disease duration among participants. No statistically significant association was found between propolis allergen severity and either BMI (p=0.841) or disease duration (p=0.262) (Tables 7 and 8).

The Pearson's chi-square test was used to examine the association between propolis allergen severity and histopathological results. The severity of propolis allergen sensitivity did not differ significantly based on the histopathological results (p=0.247).

The Pearson chi-square test was used to assess the association between propolis allergen severity and types of hobbies. No significant difference in propolis allergen severity was observed among hobby types (p=0.879).

When examining other allergens that were positive alongside propolis in participants, 6% also tested positive for thiuram mix, cobalt (II) chloride hexahydrate, nickel (II) sulfate hexahydrate, paraben mix, 4-tert-butylphenol formaldehyde resin, sesquiterpene lactone mix, and methyldibromo glutaronitrile, while 12% tested positive for colophonium (Table 9).

Discussion

ACD is a common inflammatory skin disease characterized by a type IV hypersensitivity reaction. Clinical findings and history are essential in the diagnosis of ACD, but the allergen cannot be detected using clinical or histopathological methods (1,12,13). Patch-testing is currently considered the gold-standard diagnostic method for ACD (4,5). Propolis, a potent allergen, was added to the EBS patch-test as an allergen in 2019 (11).

The COVID-19 pandemic led to a significant increase in the use of systemic dietary supplements and personal hygiene products, including products containing propolis. This trend has raised concerns regarding their dermatological impacts, as highlighted by the increased propolis positivity observed in this study. During the COVID-19 pandemic, the consumption of propolis-

Table 5. Relationship between participants' propolis allergen severity and occupation

		Allergen severity					
		Negative	+	++	+++	χ^2	p
Allergens		f (%)	f (%)	f (%)	f (%)		
Propolis	Stay at-home spouse	12 (36.4)	1 (11.1)	2 (40.0)	1 (33.3)	12.677	0.627
	Student	6 (18.2)	3 (33.3)	0	0		
	Teacher	3 (9.1)	1 (11.1)	1 (20.0)	1 (33.3)		
	Textile worker	4 (12.1)	0	0	0		
	Cleaning worker	3 (9.1)	0	0	0		
	Other	5 (15.2)	4 (44.4)	2 (40.0)	1 (33.3)		

p: Statistical significance

Table 6. Relationship between propolis allergen and lesion localization of participants

		Negative	Positive	χ^2	p
Allergens		**f (%)**	**f (%)**		
Propolis	Head-neck	13 (39.4)	9 (52.9)	3.276	0.658
	Upper extremity	10 (30.3)	6 (35.3)		
	Trunk	3 (9.1)	0		
	Lower extremity	2 (6.1)	0		
	Head-neck and upper extremity	2 (6.1)	1 (5.9)		
	Upper and lower extremity	3 (9.1)	1 (5.9)		

p: Statistical significance

Table 7. Comparison of propolis allergen severity and BMI of participants

	Propolis allergen severity	n	Mean ± SD	M (min-max)	F	p
BMI	Negative	33	27.48±5.41	27.5 (16.71-40.82)	0.404	0.751
	+	9	25.07±7.19	22.06 (14.79-35.86)		
	++	5	26.18±8.82	23.44 (16.22-39.06)		
	+++	3	26.44±3.27	25.39 (23.83-30.11)		

BMI: Body mass index, SD: Standard deviation, M: Median, Min-max: Minimum-maximum, p: Statistical significance

Table 8. Comparison of propolis allergen severity and disease duration of participants

	Propolis allergen severity	n	Mean ± SD	M (min-max)	F	p
Disease duration	Negative	33	27.52±8.63	29 (6-36)	1.457	0.239
	+	9	28.67±12.48	36 (3-36)		
	++	5	19.40±10.51	19 (9-36)		
	+++	3	32.0±6.93	36 (24-36)		

SD: Standard deviation, M: Median, Min-max: Minimum-maximum, p: Statistical significance

Table 9. Concurrently positive allergens with propolis allergen positivity in participants

		Negative	Positive
Allergens		**f (%)**	**f (%)**
3	Thiuram mix	16 (94.1)	1 (5.9)
5	Cobalt (II) chloride hexahydrate	16 (94.1)	1 (5.9)
7	Nickel (II) sulfate hexahydrate	16 (94.1)	1 (5.9)
9	Colophonium	15 (88.2)	2 (11.8)
10	Paraben mix	16 (94.1)	1 (5.9)
16	4-tert-butylphenolformaldehyde resin	16 (94.1)	1 (5.9)
19	Sesquiterpene lactone mix	16 (94.1)	1 (5.9)
25	Methyldibromo glutaronitrile	16 (94.1)	1 (5.9)

containing dietary supplements and hygiene products markedly increased, reflecting the public's growing preference for natural, immune-supporting ingredients (8,14). Furthermore, the use of naturally sourced ingredients has become highly popular in the cosmetics industry. Propolis stands out as a key component, used both in natural cosmetic products and dietary supplements. Because of its antibacterial effects, this substance is also used as a preservative in the cosmetics industry (15,16).

Propolis is produced by bees through the combination of the tree resins they collect with beeswax and saliva, and is described in the literature as a potent contact allergen (10,17). The chemical composition of propolis varies depending on its geographical origin, water sources, and other factors. However, it is not known whether these differences affect the tendency of propolis to cause contact allergy. A 2021 study investigated the frequency of contact allergy to four types of propolis from different geographical origins and found similar frequencies across all types. However, for each propolis type, half of the patients who reacted did so exclusively to that type. Nevertheless, 50% of patients who developed contact dermatitis to a given propolis type reacted only to that type (10). In our study, the majority of patients who tested positive for propolis had unknowingly used over-the-counter products during the pandemic.

Published pre-pandemic patch-test studies have reported propolis sensitization rates generally ranging from 1% to

6% in European and Nordic cohorts. In a large Swedish multicenter analysis, propolis from different geographical origins produced positivity rates between 1.3% and 5.8% (10,18). Similarly, a retrospective study from Western Sweden conducted before 2020 reported a sensitization rate of 6.2% among 722 patch-tested patients (19). More recently, a 4-year retrospective evaluation following the inclusion of propolis in the EBS reported an overall positivity rate of 9.5% for 2019-2023 (11), still far below the rate observed in our post-pandemic cohort (34%). Although our study does not include a pre-pandemic comparison group, this sharp divergence from historical data suggests that increased pandemic-era exposure to propolis-containing supplements, disinfectants, and cosmetic products may have contributed to heightened sensitization. This interpretation aligns with global reports demonstrating a marked increase in public use of natural immune-boosting products, including propolis, during the COVID-19 pandemic (8,14). In our study, all patients with positive propolis patch-test results were asked whether they had used propolis systemically, topically, or both during the COVID-19 pandemic. None of the patients knew whether the cosmetic or personal hygiene products they used contained propolis. Among the 17 patients with positive propolis patch-test results, 10 (approximately 59%) reported purchasing over-the-counter products from pharmacies, markets, or online platforms during the COVID-19 pandemic to boost their immune systems. These products were reported to contain propolis. However, they could not recall the brand names or the dosage in milligrams. Consequently, no information could be obtained regarding the origin of the propolis. In addition, all patients reported using disinfectants and some antimicrobial sprays to increase their personal hygiene during the COVID-19 pandemic. Although they did not specify brand names, they reported using multiple brands and products.

The key finding of this study was that 17 patients had positive patch-test reactions to propolis. Propolis positivity among the patients was apparent at 48 hours and persisted through day 7. In Chaudhry's cohort, the patch-test, which had been negative on previous days, became positive on the seventh day (20). However, in our study, positivity was detected at the first reading and persisted for seven days. The underlying reason for this issue remains unclear, as the source and dosage of propolis used systemically by the patients were unknown. Furthermore, the patients were unaware of the composition of the topical product they applied.

Patch-test evaluations are routinely performed at 48 and 96 hours, with delayed readings if necessary. According to the literature, 7-14% of patients may exhibit delayed reactions to certain allergens, including metals (e.g., gold), topical antibiotics, preservatives (e.g., formaldehyde), compounds (e.g., cocamide diethanolamine and p-phenylenediamine), and topical corticosteroids. Therefore, delayed assessments on the seventh day may be conducted for some patients (20,21). In our study, all patients were routinely evaluated on the seventh day; no increase in the severity of positive reactions was observed. This situation may be explained by the synergistic topical and systemic effects of propolis (20). However, in our study, since the majority of patients used a combination of dietary supplements, cosmetic products, and disinfectants, it was impossible to determine exactly which factor contributed to this condition. Among our patients with positive reactions to propolis, one also reacted to thiuram mix; one to cobalt (II) chloride hexahydrate; one to nickel (II) sulfate hexahydrate; two to colophonium; one to paraben mix; one to 4-tert-butylphenol formaldehyde resin; and one to methyldibromo glutaronitrile. However, fragrances I and II were not detected in any patient with a positive patch-test to propolis. Numerous haptens have been identified in propolis, with caffeic acid and its ester derivatives suggested as the primary haptens. Because propolis is partly of botanical origin, it is common to observe concurrent positive patch-test reactions to both propolis and fragrances or plant-derived test preparations in the baseline series, which are often essential oils, colophonium, *M. pereirae* resin, and fragrances (10,11). Although propolis and colophonium were both positive in two of our patients, this finding did not apply to other substances. It is difficult to determine whether the reaction was solely due to propolis or cross-reactivity with these allergens. However, in our study, nine patients were exclusively allergic to propolis, with no sensitivity to other allergens. This shows that propolis alone can be a stimulus in ACD. Additionally, this finding highlights the importance of delayed readings on day seven, particularly in suspected cases, as the persistent positivity to this lesser-known substance warrants further investigation. Clinicians should specifically inquire about propolis-containing supplements or topical agents when evaluating ACD, particularly in post-pandemic cases.

In the case of propolis, the slow release of flavonoids and the prolonged retention of caffeic acid derivatives in the epidermis may contribute to prolonged and, in some cases, delayed positive reactions (22,23). Additionally, propolis has been extensively studied as a potent hapten that triggers an immune response (15,24). In our cohort, the persistent

positivity of propolis reactions at the day-7 reading provides important insights not only for clinical practice but also for the safety evaluation of propolis-containing cosmetic and food products. From an immunological perspective, T-cell-mediated sensitization to propolis may underlie the prolonged clinical course observed in some patients. The combination of an early reaction at the first reading and sustained positivity at day 7 in our patients is consistent with an initial release of allergenic compounds followed by their slower, continued release from the skin.

Especially during the pandemic, the widespread use of natural ingredients such as propolis for immune support may lead to sensitization in susceptible individuals, without their awareness. This emphasizes the importance of detecting propolis positivity in patch-tests at both early (48 hours) and late (day 7) time points. In our study, two patients had a history of propolis-induced systemic contact dermatitis related to prior systemic or topical exposure. No systemic reactions occurred during the patch-testing period. The patients' histories included use of multiple cosmetic products and dietary supplements. Therefore, a causal link between propolis and systemic contact dermatitis was not established. Cases related to systemic and local propolis use have been reported in the literature; however, these are case reports rather than studies (25,26). There is a need for large-scale studies to elucidate this condition.

It is known that systemic exposure, including from certain foods, and topical products (such as fragrances, powders, wet wipes, corticosteroids, personal-hygiene or perfumed sprays, or lubricants) may cause contact dermatitis in the anogenital area (3). In our study, 10 of the 17 patients with propolis positivity reported using propolis-containing products for immune support during the pandemic, suggesting that systemic use may have contributed to this sensitivity. However, the lack of information regarding the brands and contents of these products is a major limitation of our study. Additionally, our study found that the distribution of propolis-positive patients was homogeneous across age, gender, and occupational groups, and the severity of positivity was unrelated to these parameters. This finding suggests that propolis may be a common allergen across all segments of society. For instance, dermatitis lesions, frequently found in the head and neck area, may support the possibility that propolis was used both topically and via inhalation. The absence of anogenital involvement limits our ability to draw firm conclusions about the clinical impact of systemic exposure in our cohort. However, studies with a large number of participants, in which systemic and/or topical use is clearly defined at the patient level, are needed for confirmation.

In our study, eight allergens were positive alongside propolis; among them, colophonium and the sesquiterpene lactone mix were of plant origin and consistent with the literature. Because propolis is not among the allergens in the T.R.U.E.® test series but is included in another commonly used patch-test series, the observed propolis positivity rate—particularly after the COVID pandemic—suggests that propolis sensitization may have a higher incidence than nickel sensitization, as seen in our study.

An intriguing finding of this study is the lack of an association between propolis patch-test positivity and factors such as age, gender, BMI, occupation, hobbies, or disease duration. This observation suggests that propolis may be a potent allergen capable of affecting all populations equally, irrespective of these parameters. This is likely due to the increased use of disinfectants, personal hygiene products, and dietary supplements across all demographic groups during the COVID-19 pandemic (14,27-29). However, further multicenter studies are needed to substantiate the aforementioned hypothesis.

No studies in the literature have investigated positive patch-test reactions to propolis since the COVID-19 pandemic. Therefore, our study may raise awareness that substances such as nutritional supplements and disinfectants, whose use has increased significantly, especially during the COVID-19 pandemic, may not be innocuous.

An important aspect of our findings is that all propolis-positive reactions remained detectable on day 7. Although the evaluation of late readings was not originally defined as part of the primary aim, the consistent day-7 positivity emerged as an important complementary finding that provides additional clinical insight. This temporal persistence directly aligns with the goal of distinguishing true allergic responses from irritant or transient reactions. In standard patch-testing, allergic reactions typically intensify or persist at the day-7 reading, whereas irritant reactions resolve earlier. Therefore, the sustained positivity observed in our cohort strengthens the interpretation that the increased rate of propolis reactions reflects genuine ACD rather than irritant responses. This feature distinguishes our study from pre-pandemic series, in which late readings were either not routinely performed or, when performed, reported much lower persistence rates.

Study Limitations

This study has several limitations, including the lack of detailed data on the specific brands and compositions of propolis-containing products used by patients, the retrospective design, the small patient population, and the unknown duration of product use. We would like to emphasize once again that the findings should be supported by larger, prospective studies. Moreover, this study does not compare pre- and post-pandemic patch-test results; instead, it focuses solely on patients whose dermatological symptoms began after the COVID-19 pandemic. Therefore, the findings represent a cross-sectional evaluation of post-pandemic cases rather than a temporal comparison.

Conclusion

As expected, we observed that patients showed increased sensitivity to some allergens due to excessive use of disinfectants, cosmetic and personal hygiene products, and supplements since the start of the pandemic. We believe that sensitization to these allergens may still be on the rise over time.

The principal finding of this study is that increased sensitization to propolis was detected during the COVID-19 period; contrary to expectations, this was independent of occupation or hobbies. This study revealed a significant increase in positive patch-test reactions to propolis during the COVID-19 pandemic. Notably, positivity persisted from the first to the seventh day, emphasizing the need for delayed patch-test readings in suspected or borderline cases.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Local Ethics Committee of İstanbul Kent University (Scientific Research and Publication Ethics Committee of Health Sciences; approval number: E-10420511-050-26426, date: 02.10.2023), İstanbul, Turkey.

Informed Consent: The study employed a retrospective design.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: N.C., B.İ.D., Concept: N.C., B.İ.D., Z.T., Design: N.C., M.T., Z.T., Data Collection or Processing: N.C., B.İ.D., M.T., Analysis or Interpretation: N.C., B.İ.D., Z.T., Literature Search: N.C., B.İ.D., M.T., Writing: N.C., B.İ.D., Z.T.

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ORIGINAL RESEARCH

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The Impact of Proper Use of the Death Notification System on Health Statistics: The Case of İstanbul

Ölüm Bildirim Sisteminin Doğru Kullanılmasının Sağlık İstatistiklerine Etkisi: İstanbul Örneği

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Abstract

Objective: This study aims to evaluate how death reports submitted to the death reporting system in İstanbul province affect statistics, investigate the reasons for improperly completed documents, and identify areas requiring improvement for more accurate use of the system, thereby facilitating further work in these areas.

Method: In this study, death certificates reported to the death notification system in İstanbul province in 2023 were accessed on May 12, 2024, with institutional permission. A sample of 2.351 documents was examined. The documents were selected from the 2023 DNS database using simple random sampling. Documents requiring correction were exported to Excel, and each section was analyzed separately. For documents deemed unsuitable, the returned sections and their percentages, the reasons for return, the correction times for returned documents, and the total completion time for these documents were examined. The study was conducted in 2024 at the Public Health Directorate in İstanbul.

Results: Of the documents examined, 70.7% were found to be correctly issued, while 29.3% were incorrect or incomplete. Of the incorrect documents, 11 were found to have been returned to the same physician. The most common errors or omissions on death certificates (80%) were found in the cause of death section.

Conclusion: Several areas need to be addressed to ensure more complete and accurate death certificates. It is important that these improvements be carried out jointly with all relevant institutions. Efforts

Öz

Amaç: Bu çalışmada İstanbul ilinde ölüm bildirim sistemine yapılan ölüm bildirimlerinin incelenerek uygun düzenlenmeyen belgelerin nedenlerinin araştırılması ve sistemin daha doğru kullanılması için ihtiyaç duyulan konuların tespit edilmesi, bu konularda çalışmalar yapılmasının sağlanması amaçlanmıştır.

Yöntem: Yapılan bu çalışmada İstanbul ilinde 2023 yılında ölüm bildirim sistemine bildirimi yapılan ölüm belgelerine 12.05.2024 tarihinde alınan kurum izni ile ulaşılmıştır. Örneklem olarak 2,351 adet belge incelenmiştir. Belgeler 2023 DNS veri tabanından basit rastgele örnekleme ile seçilmiştir. Belgelerden düzeltme talep edilen belgeler Excel'e aktarılarak belgelerdeki her bir bölüm ayrı birer parametre olarak incelenmiştir. Uygun bulunmayan iade edilen belgelerde, iade edilen bölümler ve bunların oranları, iade nedenleri, iade edilen belgelerin düzeltme süreleri ve bu belgelerin toplam tamamlanma süreleri incelenmiştir. Çalışma İstanbul ilinde Halk Sağlığı Başkanlığı'nda 2024 yılında yapılmıştır.

Bulgular: İncelenen belgelerden %70,7'sinin doğru düzenlendiği, %29,3'ünün hatalı ya da eksik düzenlendiği görülmüştür. Hatalı olan belgelerden aynı hekime 11 kez iade edilen belge olduğu tespit edilmiştir. Ölüm belgelerinde en çok ölüm nedenleri kısmında (%80) hata ya da eksiklik olduğu görülmüştür.

Sonuç: Ölüm belgelerinin daha eksiksiz ve hatasız düzenlenebilmesi için bazı konularda çalışmalar yapılmasına ihtiyaç vardır. Bu iyileştirmeye yönelik çalışmaların ilgili tüm kurumlar ile ortak yapılması önemlidir. Bu

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Abstract

to achieve this should be directed at individuals and institutions involved in the process from the inception of the document to its registration.

Keywords: Death certificate, death notification system, health statistics

Öz

yönde yapılacak çalışmaların belgenin düzenlenmesinin başlangıcından tescil edilmesine kadar olan süreçte rol alan kişi ve kurumlara yönelik olması gerekir.

Anahtar kelimeler: Ölüm belgesi, ölüm bildirim sistemi, sağlık istatistikleri

Introduction

Determining a country's level of development, establishing health policies and priorities, and planning, organizing, controlling, and implementing intervention programs are related to statistical data. For this reason, it is essential that health statistics be based on accurate and regularly collected data. One of the most important of these statistics is mortality. Death certificates contain important information such as age, gender, manner of death, place of death, and causes of death. Accurate determination of causes of death is particularly important for identifying mortality trends, analyzing diseases causing death, and identifying preventable causes of death (1,2). Cause-of-death statistics are an important source of data for explaining mortality patterns with respect to time and place, establishing population projections, supporting public health programs, and generating hypotheses for research. In addition, these data are necessary for public health evaluations and form the basis of the public health statistics system (3). These results guide health managers and policymakers.

Mortality statistics have been compiled by Turk Stat since 1931. Until the end of 1949, 25 provincial centers were included; between 1950 and 1956, all provincial centers were included; and after 1957, all provincial and district centers were included. Since 2009, cause of death statistics have been published separately. During the European Union (EU) harmonization process, the Turkish Statistical Institute and the Ministry of Health initiated a project entitled "Cause of Death Statistics" to harmonize cause-of-death statistics with EU standards. The aim of this project is to improve the quality and reliability of cause-of-death statistics, ensure comparability between countries, and produce cause-of-death statistics in accordance with international standards. In this context, a new death certificate was developed in accordance with the World Health Organization (WHO) standards. Effective January 1, 2009, the new death certificate was implemented. With the new document, information on infant and maternal deaths, as well as on the causes and duration of those deaths, has begun to be compiled. Coding of diseases in the sections used to determine the cause of death follows the International Classification of Diseases (ICD)-10, and the underlying cause is determined by applying the rules of the WHO. Accurate recording of deaths has become a problem for many countries. The 2007 study reports completeness and accuracy sufficient to enable comparisons between most European countries (4).

In 2012, the death notification system (DNS) was developed by the Ministry of Health; it enables the electronic registration of death certificates, collects data in a common pool, and authorizes only physicians to issue death certificates. It entered into force on 01/01/2013. Since 2013, death certificates have been issued electronically via the DNS (5).

The reliability of the information in death certificates, which constitute the data for death statistics, is of utmost importance. The information on death certificates is based on the individuals who issued the certificates and on the nature of the data they provided. The issuing physician is responsible for the accuracy of the information in the form. When not all sections of death certificates are completed as intended, mortality statistics may be affected. In the cause-of-death section of death certificates, the actual cause of death is often not recorded; instead, a result related to the cause is recorded, rather than the primary cause (6,7).

Death certificates contain sections A, B, C, D, E, F, G, and H. Section A contains the identity and residence information of the deceased. Part B consists of the date, hour, minute, and place of death. Section C records the manner of death. This section must correctly state whether the manner of death was due to an infectious disease and whether it was a forensic death. For deaths resulting from diseases within the scope of the Notifiable Diseases included in Annex-1 of the Communiqué on the Notification and Notification System of Infectious Diseases, published by the Ministry of Health in the Official Gazette dated 06.11.2004 and numbered 25635, the type of death should be recorded as "infectious disease" (8). If the manner of death is considered forensic, it must be specified in this

section. Because the forensic process typically begins with the physician's suspicion of death, this examination is perhaps the most important for clarifying forensic cases involving death (9).

Section D indicates whether the death occurred as a result of injury; Section E indicates whether an autopsy was performed and, if so, provides autopsy information. Following Section E, information about the person who provided details about the deceased must be recorded. It is considered inappropriate for persons under the age of 18, who are ineligible to carry out official transactions without a parent or legal guardian, to serve as the informant on the death certificate valid for official transactions (10). However, when no first-degree relatives are available, other officials involved in the event of a death, such as hospital health workers, nursing-home staff, police, security guards, the gendarmerie commander, and a mukhtar, may also be recorded.

The information provided by the authorized person filling out the document includes the physician's details. Section F opens to the infant death information form interface. If the person who died is a woman and between the ages of 15-60, section G must be filled in, which is the section

that includes information on whether the death is a maternal death. Section H is the section where the causes and duration of death are written.

Since the information on death certificates directly affects death statistics, inaccurate cause-of-death statistics in a country are an important source of concern. According to the latest mortality data announced by the Turkish Statistical Institute, the total number of deaths in Turkey in 2022 was 504,839 (11). In İstanbul, it is 87,252 (ÖBS, 2022). Approximately 18% of the total deaths in Turkey occur in İstanbul. Therefore, accurate death notification in İstanbul significantly affects Turkey's mortality statistics. Because these results are derived from the physicians who prepare death certificates, those physicians play a central role in the formation of death statistics. Correcting the causes of death in incorrectly or incompletely prepared documents is important, as it affects mortality statistics.

This study aimed to examine death notifications made to the DNS in İstanbul province and to evaluate how they affect the statistics; to investigate reasons for documents not being issued appropriately; and to identify issues requiring attention to improve the accuracy of system use and to ensure that further studies address these issues.

Materials and Methods

A total of 82,287 deaths occurred in İstanbul in 2023. Death statistics are obtained from data in documents reported to the DNS. In this study, death certificates that were reported to the DNS in İstanbul in 2023 were accessed retrospectively after institutional permission was obtained from the İstanbul Provincial Health Directorate on May 12, 2024. The sample size was calculated as $n = (82.287 \times 1.96^2 \times 0.5 \times 0.5) / [(0.05^2 \times 82.286) + (1.96^2 \times 0.5 \times 0.5)] = 383$, using the sampling method formula and taking into account a 95% confidence level and a 5% margin of error. This calculated sample size was deemed sufficient to represent the population. In the study, a total of 2.351 documents were examined, exceeding the predetermined sample size intended to increase analytical power and further reduce the margin of error. The documents were selected from the 2023 DNS database using simple random sampling.

The study was conducted in 2024 at the Public Health Directorate in İstanbul. The study was approved by the Üsküdar University Non-Interventional Research Ethics Committee at its meeting No. 3, held on March 26, 2024, and institutional approval was obtained on May 12, 2024.

Results

According to DNS data, examination of sample documents revealed that 70.7% (1.662) of the sample documents were completed correctly, whereas 29.3% (689) were completed incorrectly or incompletely. Documents prepared incorrectly or incompletely were not approved and were returned to the physicians who prepared them. Of the documents that were not approved, 52.7% (363) were legal documents. 47.3% (326) were documents from other institutions (Table 1).

Of the 434 physicians whose documents were examined as a sample, 54.8% (238) had their documents returned for correction. Analysis of the number of documents returned to physicians showed that between one and eleven documents were returned to the same physician (Table 2).

A total of 122 institutions issued 2,351 documents. documents were returned for correction to 114 institutions (93.4%); no documents were returned to 8 institutions. Each of the institutions to which documents were returned received between 1 and 16 documents (Table 2).

Eighty percent of the retrieved documents addressed correction of causes of death. The documents returned in

the causes of death section are usually those in which the ICD code for the actual cause of death was not written, the ICD codes were not ordered according to cause and effect, or the durations of the diagnoses were not written correctly.

The rate for other reasons is 20%. The rates of corrections were 8.2% in the address section and 1.5% in the informant section; in addition, 2.5% of the infant death certificates were returned to add the Turkish ID number to the system. One of the most important sections of death certificates is the manner of death. The rate of documents returned for the manner of death section is 6%. In the documents examined for this research, the deceased's educational level and occupational information were not provided (Table 3).

Among the sampled documents, none were returned to physicians for correction of more than one parameter.

Discussion

Although 12 years have passed since the DNS was implemented—developed to increase the quality and reliability of cause-of-death statistics, to facilitate comparisons between countries, and to conform to the WHO standards—many problems continue to be

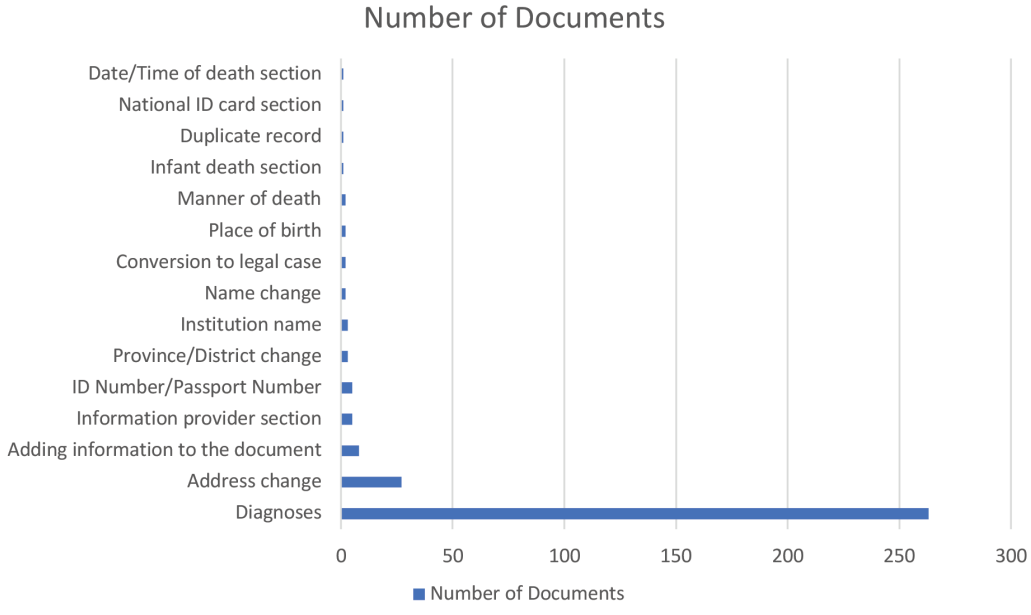
Table 1. Approval and return status of documents

Document status	Number	% (Total)	% (Subcategory)
Approved documents	1.662	70.7	-
Unapproved documents	689	29.3	-
- Documents returned to doctor	326	-	47.3
- Legal documents	363	-	52.7
Total	2.351	100	100

Table 2. Distribution of returned documents by physician and ınstitution

	Number	%	Min	Max	Median
Number of physicians who issued documents	434	100	-	-	-
Number of physicians to whom documents were returned	238	54.8	1	11	1
Number of institutions where documents were issued	122	100	-	-	-
Number of institutions to which documents were returned	114		1	16	2

Table 3. Return reasons for returned documents



encountered in the issuance of death certificates. This study found that 29.3% of the sampled documents were not approved for various reasons. The extent to which these documents, if approved, could affect health statistics warrants investigation.

Identifying issues related to document organization and developing solutions are crucial to preventing these errors from recurring. Furthermore, 11 documents were returned to one physician and 16 to the same institution, suggesting a problem specific to the physician or institution. For this reason, it is necessary to examine the causes of incorrect or incomplete death certificates from multiple angles.

Another important type of information derived from death records is demographic data. Incorrect recording of demographic data, which are important for mortality statistics, can lead to miscalculations of life expectancy in a region. Life tables calculated from mortality data are the most important indicators of differences in demographic and health conditions across countries. Hoşgör's (12) study reports that death records are insufficient or inaccurate because of underreporting; that research is being conducted, particularly in developing countries, to inform the development of appropriate policies; and that efforts are underway to eliminate the causes of underreporting. The success of these efforts is also related to countries' level of development (12). 20% of the documents returned to physicians for correction in Turkey concern demographic data.

In 2019, To prevent potential gaps or inaccuracies in demographic data, the Ministry of Health, the General Directorate of Population and Citizenship Affairs (NVİGM), under the Ministry of Interior, and the Turkish Statistical Institute collaborated to integrate their systems. When a death certificate is issued and the deceased person's Turkish ID number is entered into the system, the demographic data registered with the NVİGM are automatically retrieved. In this case, entering the Turkish ID number correctly or ensuring that the information in the population records is accurate is sufficient to access accurate demographic data. A 2022 study found inconsistencies between demographic information on 14.8% of death certificates and corresponding records in the Central Population Administration System (MERNİS) (13). The same study reported inconsistencies between death certificates and MERNİS records for 72.6% of addresses, 8.4% of death dates, 1.7% of parents' names, and 0.5% of ages. The rate of documents returned to physicians for address changes in the documents covered by this study was 8.2%. In this case, the information in the MERNİS records for İstanbul province can be assumed to be more accurate. One document was returned regarding the date of death, and no documents were returned for the parents' names and age information. This further supports the conclusion that the population records for İstanbul province contain accurate information.

That the deceased person's educational status and occupation information were not filled in suggests that these sections are not mandatory. In particular, the inclusion of occupational information in the documents will provide important data for linking the cause of death to occupational groups. The same situation occurs in Beirut, where the literature shows that occupational information is missing from almost all death certificates (14). Information on educational status, on the other hand, enables comparison of individuals' educational levels with their ages at death.

Following integration with the NVİGM, physicians register documents electronically. If corrections to demographic data are required after registration, NVİGM must cancel the registration. Corrections can be made to the documents after the registration has been removed. Since this situation requires multiple steps to approve the documents, the approval process is time-consuming. It is also thought that physicians may not notice the returned documents in the system, may not know how to correct them, or may experience delays in correcting them because of technical issues. Documents requiring urgent correction can be addressed promptly with appropriate communication and support. Article 11(d) of the DNS circular states that "Returned documents must be corrected and updated by the physician who completed them within one (1) business day at the latest" (15). One of the most important parameters in mortality data is the cause of death. The cause of death must be correctly recorded and ranked. Determining the leading cause of death in a country depends on the correct organization of this section. A study on this subject noted that records should be maintained using internationally accepted diagnostic classifications to ensure reliable analysis of death statistics (16).

This study found that 80% of the sections requiring correction in documents that were incorrectly or incompletely organized concerned causes of death. In a study by Çilingiroglu et al. (17), the rate of inconsistency between the causes of death listed in patients' discharge summaries and those in death certificates was 36.72%. The study by Shantibala et al. (18) found major errors between

death certificates and causes of death in 38.3% of cases. A study evaluating death records at the Isparta provincial center reported a 16.8% inconsistency in the recorded cause of death (13). Errors in the cause-of-death section were mainly due to inconsistencies between the ICD code for the actual diagnosis and the ICD code for the cause of death. In a study comparing the ICD codes of diagnoses in the hospital automation system with the ICD codes on death certificates [Korkmaz and Balaban (19)], it was noted that the highest consistency between the ICD codes and the causes of death on death certificates was found in MI cases, and that the highest inconsistency was also found here because "cardiopulmonary arrest" was still listed as the cause of death. In this study, the high rate of errors or omissions in the cause-of-death section may be due to a lack of information, insufficient sensitivity to the subject, or physicians' heavy workload.

Another element to examine on death certificates is the cause-of-death section. Recording the cause of death as an infectious disease when it is not, or as a non-infectious disease when it is, is misleading for the management of pandemics or endemics within a country. In this study, the return rate for correction of cause-of-death information (0.6%) is low. Particular attention has been paid to ensuring the correct recording of this section during the pandemic.

Another important issue to consider regarding the cause of death is the role of forensic cases. Of the certificates returned to physicians for correction, 52.7% are forensic. There appear to be different practices among physicians regarding the recording of death certificates for forensic cases. Article 9 of the DNS circular dated 2021/7 states: "If the death is determined by the physician to be judicial, it is recorded as such in the DNS and a judicial incident report is made" (15). Particularly in cases of judicial deaths occurring in emergency departments, physicians prepare only judicial reports and do not create a DNS record. In such cases, deaths in which the body is not sent to the forensic medicine institution for autopsy and burial is carried out solely on the basis of a prosecutor's report are not recorded in the system. Because documents are not recorded electronically in the system, deaths go unrecorded and, consequently, the person appears to be alive. This process needs to be clarified in practice. Cases in which a deceased person appears alive in the records, or a living person appears dead in the system, present significant problems. The DNS has standardized mortality data. Sustaining this standard requires that all relevant institutions to clearly and completely record data in the system. Furthermore, keeping the system constantly updated will ensure rapid access to accurate data (20).

The accuracy of death statistics depends on the quality of the data provided by the physician who issues the death certificate. Therefore, solutions must be developed to ensure that physicians are thoroughly informed about the system's content and technical aspects and made aware of their duties and responsibilities in accordance with the DNS circular.

Study Limitations

The use of only 2023 data and the examination of deaths occurring in İstanbul province can be considered limitations of the study. The documents were first categorized as either suitable or unsuitable. Unsuitable documents were transferred into Excel, and each document section was examined as a separate parameter. For documents rejected as unsuitable, the rejected sections and their proportions, the reasons for rejection, the correction periods, and the total completion periods were examined.

Conclusion

While education is the primary solution, the specifics and significance of issuing death certificates must be planned carefully, such as whether they should be taught as a course in medical schools, covered during residency, or whether physicians should be required to review training documents before being granted basic permissions to access the DNS. It is particularly important that physicians working in emergency and intensive care units have a thorough understanding of this issue.

It is also important to ensure that physicians have a clearer understanding of the process of reporting forensic cases to prevent discrepancies in practice. To ensure deaths buried with a prosecutor's report are recorded in the death reporting system, the cemetery administration could be required to request a burial certificate in addition to the prosecutor's report.

The system progresses when the mandatory fields on death certificates have been completed. If the deceased's education and occupation are also included in the mandatory fields, death statistics will be evaluated from this perspective.

The system can be configured to issue warnings when a single cause of death is listed, or when diagnoses that cannot be considered the sole cause of death are listed. In cases of death at home, the physician issuing the death

certificate can access their e-pulse information to ensure that the cause of death is determined accurately.

Death certificates issued by physicians are approved by authorized controller physicians at Provincial or District Health Directorates. To prevent incorrect or incomplete documents from being approved by controller physicians without detection, an algorithmic guide could be developed.

Ethics

Ethics Committee Approval: The study was conducted in 2024 at the Public Health Directorate in İstanbul. The study was approved by the Üsküdar University Non-Interventional Research Ethics Committee at its meeting No. 3, held on March 26, 2024, and institutional approval was obtained on May 12, 2024.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: K.K., S.P., A.S.E., T.Ü.S., S.Ç., Design: S.P., A.S.E., Data Collection or Processing: K.K., T.Ü.S., S.Ç., Analysis or Interpretation: K.K., A.S.E., T.Ü.S., Literature Search: K.K., S.P., A.S.E., S.Ç., Writing: K.K., S.P., A.S.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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Evaluation of the Predictive Value of the Delta Neutrophil Index for Chorioamnionitis in Pregnancies with Preterm Premature Rupture of Membranes

Delta Nötrofil İndeksin Erken Membran Rüptürü Olan Gebeliklerde Koryoamniyoiniti Belirleme Gücünün Değerlendirilmesi

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Abstract

Objective: Chorioamnionitis is an intra-amniotic infection involving the fetal membranes, amniotic fluid, or placenta, and is associated with adverse perinatal outcomes, particularly in pregnancies complicated by preterm premature rupture of membranes (PPROM). After membrane rupture; the risk of infection increases early diagnosis is essential to reduce the risks of neonatal sepsis, preterm birth, and maternal morbidity. Conventional diagnostic approaches are limited due to reliance on clinical signs and non-specific biomarkers. The delta neutrophil index (DNI), which reflects circulating immature granulocytes, has emerged as a rapid inflammatory marker. This study aimed to assess the diagnostic performance of DNI in predicting clinical chorioamnionitis in PPROM.

Method: Three hundred singleton pregnancies with PPROM diagnosed between 24+0 and 33+6 weeks were retrospectively analyzed at a tertiary perinatology center between May 2020 and July 2023. Patients were classified according to the presence of clinical chorioamnionitis using the American College of Obstetricians and Gynecologists criteria. Maternal blood samples were obtained within one hour of admission and before administration of antenatal corticosteroids. DNI values were automatically calculated as the proportion of circulating immature granulocytes.

Öz

Amaç: Koryoamniyonit, fetal membranları, amniyotik sıvıyı veya plasentayı içeren intra-amniyotik bir enfeksiyon olup, özellikle preterm erken membran rüptürü (PPROM) ile komplike gebeliklerde olumsuz perinatal sonuçların önemli bir nedenidir. Membran rüptürü sonrası enfeksiyon riski artar ve erken tanı yenidoğan sepsisi, preterm doğum ve maternal morbiditenin önlenmesinde kritik öneme sahiptir. Rutin tanı yöntemlerinin doğruluğu klinik bulgulara ve özgül olmayan belirteçlere dayanması nedeniyle sınırlıdır. Dolaşımdaki immatür granülosit düzeyini yansıtan delta nötrofil indeksi (DNI), enfeksiyon için hızlı bir biyobelirteç olarak öne çıkmaktadır. Bu çalışma, PPROM olgularında klinik koryoamniyoniti öngörmede DNI'nın tanısal performansını değerlendirmeyi amaçlamaktadır.

Yöntem: Mayıs 2020-Temmuz 2023 arasında, üçüncü basamak bir perinatoloji merkezinde 24+0 ile 33+6 hafta arasında PPROM tanısı almış 300 tekil gebelik retrospektif kesitsel olarak incelendi. Hastalar, Amerikan Kadın Hastalıkları ve Doğum Derneği kriterlerine göre klinik koryoamniyonit varlığına göre sınıflandırıldı. Maternal kan örnekleri başvurudan sonraki ilk bir saat içinde, antenatal kortikosteroid uygulanmadan önce alındı. DNI, hematoloji analizörü tarafından dolaşımdaki immatür granülosit oranı olarak otomatik hesaplandı.

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Abstract

Results: Maternal DNI levels were significantly higher in the chorioamnionitis group than in controls (p<0.01). Receiver operating characteristic analysis yielded an area under the curve of 0.627 (95% confidence interval: 0.515-0.739; p=0.026). At a cut-off of 0.11, sensitivity, specificity, likelihood ratios were 74.2%, 57.1%, 1.73, and 0.45, respectively. In the multivariable logistic regression model, platelet count, DNI, and international normalized ratio were identified as independent predictors of clinical chorioamnionitis.

Conclusion: DNI is significantly associated with clinical chorioamnionitis in PPROM and may support early detection of intrauterine infection. However, its diagnostic performance is limited, and DNI should not be used alone. Combined evaluation of clinical and laboratory findings is recommended. Larger prospective studies are needed to validate these results and clarify the role of DNI in infection risk assessment.

Keywords: Chorioamnionitis, delta neutrophil index, DNI, obstetric infection, preterm premature rupture of membranes

Öz

Bulgular: Maternal DNI düzeyleri, koryoamniyonit grubunda kontrol grubuna kıyasla anlamlı olarak daha yüksekti (p<0,01). Alıcı çalışma karakteristiği analizinde eğri altında kalan alan 0,627 bulundu (%95 güven aralığı: 0,515-0,739; p=0,026). 0,11 eşik değeri ile duyarlılık %74,2, özgüllük %57,1, pozitif olasılık oranı 1,73 ve negatif olasılık oranı 0,45 olarak hesaplandı. Çok değişkenli lojistik regresyon analizinde trombosit sayısı, DNI ve uluslararası düzeylendirilmiş oran, klinik koryoamniyonit ile bağımsız olarak ilişkili bulundu.

Sonuç: DNI, PPROM ile komplike gebeliklerde klinik koryoamniyonit ile anlamlı şekilde ilişkili olup intrauterin enfeksiyonun erken tanısında yardımcı bir biyobelirteç olabilir. Bununla birlikte tanısal gücü sınırlıdır ve tek başına kullanılmamalıdır. Klinik ve laboratuvar parametreleriyle birlikte değerlendirilmesi daha uygundur. Bulguların doğrulanması ve DNI'nın perinatal enfeksiyon risk değerlendirmesindeki rolünün netleştirilmesi için daha geniş, prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Delta nötrofil indeksi, DNI, erken membran rüptürü, koryoamniyonit, obstetrik enfeksiyon

Introduction

Preterm premature rupture of membranes (PPROM) is an important obstetric complication associated with high rates of perinatal morbidity and mortality (1). Inflammatory processes are increasingly recognized as key contributors to the pathogenesis of PPROM, and maternal inflammatory biomarkers such as interleukin (IL)-6 have been reported to correlate with the risk of intrauterine infection (2).

The delta neutrophil index (DNI) is a hematological parameter that reflects the proportion of circulating immature granulocytes and has been recognized as a valuable marker in the early detection of sepsis and systemic inflammatory conditions (3). Given its role in systemic inflammation, DNI has also been investigated as a potential biomarker for intrauterine infection. Previous studies have primarily evaluated its predictive value for histological chorioamnionitis in pregnancies complicated by PPROM (4), whereas data focusing on clinically diagnosed chorioamnionitis remain limited.

Chorioamnionitis is a serious clinical condition associated with significant maternal and neonatal complications, and timely diagnosis and management are essential to improving outcomes. In this context, DNI may serve as a rapid, non-invasive, cost-effective adjunct for the early identification of infection-related complications in PPROM. The aim of this study was to evaluate the clinical utility of DNI in predicting clinical chorioamnionitis among women with PPROM.

Materials and Methods

This retrospective, cross-sectional study included 300 pregnant women diagnosed with PPROM who were admitted to the Obstetrics and Gynecology Department of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital between May 2020 and July 2023.

The inclusion criteria were as follows:

- Maternal age between 18 and 45 years
- Singleton, live pregnancies between 24+0 and 33+6 weeks of gestation
- PPROM confirmed by speculum examination showing active leakage, pooling of amniotic fluid in the posterior fornix, vaginal pH >5, or a positive AmniSure® test.

Exclusion criteria included multiple gestations, major fetal anomalies (incompatible with life or requiring prenatal or postnatal surgery), intrauterine fetal demise, chromosomal or genetic syndromes, placental anomalies, systemic maternal infections, hematological or autoimmune disorders, and maternal smoking, alcohol use, or illicit drug use.

Maternal demographic and clinical data (age, parity, gestational age at delivery, vital signs, and laboratory parameters) and neonatal outcomes (1- and 5-minute Apgar scores) were retrieved from electronic hospital records.

Blood sampling and laboratory analysis: Maternal blood samples were collected within the first hour of admission and prior to administration of antenatal corticosteroids.

Complete blood count (CBC), DNI, white blood cell count (WBC), neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP) were obtained. Samples were drawn into EDTA tubes and analyzed in the hospital laboratory. In addition to these parameters, maternal procalcitonin levels were measured.

DNI was measured using the ADVIA 2120 Hematology System (Siemens Healthcare Diagnostics, Forchheim, Germany). The DNI was automatically calculated by the analyzer as the difference between leukocyte subfractions measured in the myeloperoxidase and nuclear lobularity channels, which reflects the proportion of circulating immature granulocytes.

Treatment protocol: Following PPROM diagnosis, patients were managed according to institutional protocols based on international guidelines. Antenatal corticosteroids (betamethasone 12 mg intramuscularly, two doses 24 h apart) were administered for fetal lung maturation. Antibiotic prophylaxis consisted of intravenous ampicillin 2 g every 6 h for 48 h, followed by oral ampicillin 250 mg every 8 h for 5 days, in combination with a single oral dose of azithromycin 1 g (5). Vital signs were monitored regularly; clinical signs of infection (e.g., fundal tenderness, foul-smelling discharge) were assessed; and daily CBC and CRP measurements were obtained in patients with suspected infection.

Delivery planning: Unless urgent obstetric indications were present, delivery was planned for 34 weeks' gestation. Rescue corticosteroid therapy was administered if the initial course had been completed more than 14 days before delivery. Magnesium sulfate infusion (1 g/h for 24 h) was administered for fetal neuroprotection between 24 and 32 weeks of gestation.

Diagnostic criteria for chorioamnionitis: Clinical chorioamnionitis was diagnosed according to the American College of Obstetricians and Gynecologists criteria: Maternal fever ≥38.0 °C accompanied by at least two of the following—maternal tachycardia (>100 bpm), fetal tachycardia (>160 bpm), uterine tenderness, foul-smelling vaginal discharge, or maternal leukocytosis (>15.000/mm^3) (6).

Ethics: The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital (approval no: 2023-610, date: 27.11.2023).

Statistical Analysis

Statistical analyses were performed using NCSS 2007 (Number Cruncher Statistical System, Kaysville, Utah, USA). Descriptive statistics (mean, standard deviation, median, frequency, percentage, minimum, maximum) were calculated. Normality was assessed using the Shapiro-Wilk test. Group comparisons were made with the Mann-Whitney U test for continuous variables and chi-square tests for categorical variables.

A post-hoc power analysis was performed using G*Power (version 3.1). Assuming a large effect size (d=0.8), α=0.05, and power =0.985, the required sample size was calculated to be n=300. Since the study cohort consisted of exactly 300 participants, the achieved statistical power was considered adequate.

Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curve analysis: The area under the curve (AUC), the standard error, the 95% confidence interval (CI), the p-value, and the positive and negative likelihood ratios (LR^+, LR^-) were calculated. Logistic regression was performed to identify independent predictors of chorioamnionitis. In the logistic regression model, the dependent variable was coded as 0 for chorioamnionitis (–) and 1 for chorioamnionitis (+), following the standard binary coding approach. Therefore, regression coefficients (B) greater than zero correspond to odds ratios (OR) above 1 and indicate an increased likelihood of chorioamnionitis. Variables were selected for multivariate analysis if they demonstrated statistical significance in univariate testing or had established clinical relevance (inflammatory, coagulation, or hemodynamic parameters). OR with 95% CIs and p-values were reported. A p-value 0.05 was considered statistically significant.

Results

A total of 300 patients met the inclusion criteria and were analyzed. The mean maternal age was 30.12±6.40 years, and the mean gestational age at delivery was 30.65±3.06 weeks. Descriptive statistics for maternal demographics, laboratory findings, and perinatal outcomes are summarized in Table 1.

Among the patients included in the study, 39.3% (n=118) were primigravida, 18% (n=54) had two pregnancies, 20% (n=60) had three pregnancies, and 22.7% (n=68) had four or more pregnancies. In terms of parity, 46.7% (n=140) of patients were nulliparous, 20% (n=60) had one previous delivery, 22% (n=66) had two previous deliveries, and 11.3% (n=34) had three or more previous deliveries.

Amniotic fluid assessment revealed anhydramnios in 8.7% (n=26), normal amniotic fluid volume in 53.3% (n=160), oligohydramnios in 36% (n=108), and polyhydramnios in 2% (n=6) of patients. Regarding the mode of delivery, 52.7% (n=158) had a primary cesarean section, 24% (n=72) had a repeat cesarean section, 2% (n=6) had an induced vaginal delivery, and 21.3% (n=64) had a spontaneous vaginal delivery.

Table 1. Baseline maternal demographics, laboratory findings, obstetric characteristics, and neonatal outcomes in the study population (n=300)

	Mean ± SD	Min-max (median)
Age (years)	30.12±6.4	18-46 (29)
Height (cm)	161.61±5.58	149-175 (162)
Weight (kg)	75.85±13.71	44-119 (75)
Body mass index (kg/m^2)	29.06±5.29	18.510-45.31 (28.52)
Hemoglobin (g/dL)	11.36±1.27	7.4-13.8 (11.5)
Hematocrit (%)	34.25±3.35	25.5-41.8 (34.25)
Platelet count (10^9/L)	246.71±70.8	92-466 (244)
Neutrophils (10^9/L)	13.4±16.65	3.29-89.8 (8.91)
White blood cell (10^9/L)	12.17±3.46	5.7-24.92 (11.67)
Lymphocytes (10^9/L)	2.05±0.85	0.46-8.9 (2.01)
DNI (10^9//L)	0.14±0.14	0.02-0.96 (0.1)
DNI % (%)	1.13±0.94	0.2-5.7 (0.85)
CRP (mg/dL)	13.41±22.25	0.04-172.9 (6.1)
Procalcitonin (ng/mL)	0.06±0.05	0.02-0.42 (0.05)
PT (sec)	8.08±0.55	6.6-10.1 (8)
INR	0.93±0.06	0.8-1.1 (0.9)
aPTT (sec)	26.32±3.22	19.2-38.9 (26.2)
Birth weight (g)	1657.77±628	550-3230 (1690)
Apgar 1st min	5.29±2.12	0-8 (6)
Apgar 5th min	7.21±1.58	0-9 (7)
Gestational age at delivery (weeks)	30.65±3.06	24.14-34 (31.14)
Cervical length (mm)	32.35±9.6	10-50 (35)
Umbilical PI	0.98±0.23	0.45-1.83 (0.96)
Length of hospital stay (days)	14.23±11.86	2-60 (10)
Maternal temperature (°C)	36.02±0.14	36-38.8 (36)
Maternal systolic blood pressure (mmHg)	110.5±10.66	83-160 (110)
Maternal diastolic blood pressure (mmHg)	65.63±10.81	41-125 (61)

DNI: Delta neutrophil index, SD: Standard deviation, Min-max: Minimum-maximum, PI: Pulsatile index, PT: Prothrombin time, CRP: C-reactive protein, INR: International normalized ratio, aPTT: Activated partial thromboplastin time

Comorbidities were present in 17.3% (n=52) of patients; 82.7% (n=248) had no known comorbidities. Fetal growth restriction (FGR) was identified in 6% (n=18) of the patients; 94% (n=282) of the patients did not exhibit FGR.

Regarding antenatal corticosteroid use, 86% (n=258) received a full course, 8.7% (n=26) received a single dose, and 5.3% (n=16) received no steroids. Erythrocyte suspensiontransfusion at delivery was required in 7.3% (n=22) of patients; 92.7% (n=278) did not require transfusion. Placental abruption occurred in 16% (n=48) of patients, whereas placental separation was not observed in the remaining 84% (n=252).

As shown in Table 2, there were no statistically significant differences between the chorioamnionitis and non-chorioamnionitis groups with respect to maternal age, body mass index, hemoglobin, hematocrit, neutrophil count, WBC count, lymphocyte count, procalcitonin levels, or prothrombin time (PT) (all p>0.05).

In contrast, platelet count (PLT), DNI, DNI percentage, and CRP level were significantly higher in the chorioamnionitis group compared with the non-chorioamnionitis group (p=0.045, p=0.029, p=0.019, and p=0.018, respectively). The international normalized ratio (INR) and maternal body temperature were significantly higher in the chorioamnionitis group compared with the non-chorioamnionitis group (p=0.008 and p=0.017, respectively). Maternal diastolic blood pressure was also significantly elevated in the chorioamnionitis group (p=0.020). In contrast, no statistically significant differences were observed between the groups in terms of birth weight, Apgar scores at 1 and 5 minutes, duration of PPROM, gestational age at delivery, cervical length, umbilical artery pulsatility index (PI), length of hospital stay, or maternal systolic blood pressure (all p>0.05) (Table 3).

Correlation analysis further demonstrated a strong positive correlation between DNI and maternal fever (r=0.694, p<0.01), and a moderate positive correlation with maternal systolic blood pressure (r=0.578, p<0.05). No significant correlations were found between DNI and CRP, procalcitonin, PT, INR, aPTT, birth weight, Apgar scores, gestational age at delivery, cervical length, umbilical artery PI, length of hospital stay, or maternal diastolic blood pressure (all p>0.05). ROC analysis results and AUC values are summarized in Table 4.

Table 2. Comparison of measurements according to chorioamnionitis status

Parameters	Chorioamnionitis (+) (n=30)	Chorioamnionitis (-) (n=270)	p-value
Age (years)	27.77±6.85 (19-46; 25)	28.71±3.98 (18-35; 30)	0.056
BMI (kg/m^2)	28.74±6.17 (18.51-44.14; 27.89)	29.02±5.29 (11.69-45.31; 28.91)	0.401
Hb (g/dL)	11.47±1.14 (8.7-13.5; 11.6)	11.33±1.31 (7.4-13.8; 11.5)	0.788
Hct (%)	34.61±3.03 (27.7-39.9; 34.6)	34.30±3.43 (25.5-41.8; 34.2)	0.559
PLT (10^9/L)	**272.39±86.77 (92-439; 259)**	**240.03±64.79 (118-466; 236)**	**0.045***
Neutrophils (10^9/L)	14.78±19.33 (3.29-89.8; 10.75)	13.04±30.95 (4-85.6; 8.8)	0.322
WBC (10^9/L)	13.12±4.31 (5.7-24.92; 12.22)	11.93±3.17 (6.45-24.05; 11.53)	0.123
Lymphocytes (10^9/L)	2.00±0.60 (1.03-3.12; 1.99)	2.07±0.90 (0.46-8.9; 2.05)	0.774
DNI (10^9/L)	**0.27±0.29 (0.02-0.96; 0.12)**	**0.13±0.10 (0.02-0.66; 0.09)**	**0.029***
DNI (%)	**1.84±1.80 (0.11-5.7; 1.0)**	**0.93±0.68 (0.02-4.5; 0.7)**	**0.019***
CRP (mg/dL)	**22.16±47.03 (1.6-172.9; 5)**	**13.79±31.78 (0.04-172.9; 3.2)**	**0.018***
Procalcitonin (ng/mL)	0.05±0.04 (0.02-0.19; 0.04)	0.06±0.05 (0.02-0.42; 0.05)	0.456
PT (sec)	8.24±0.66 (7.4-10.1; 8.1)	8.05±0.51 (6.6-9.9; 8.0)	0.180

*: p<0.05, Hb: Hemoglobin, Hct: Hematocrit, BMI: Body mass index, PLT: Platelet count, WBC: White blood cell count, DNI: Delta neutrophil index, CRP: C-reactive protein, PT: Prothrombin time

Table 3. Comparison of measurements according to chorioamnionitis status

		n	Mean ± SD	Min-max (median)	p
INR	**With**	30	0.96±0.07	0.9-1.1 (0.9)	0.008**
	Without	270	0.92±0.06	0.8-1.1 (0.9)	
aPTT (sec)	**With**	30	27.35±3.99	19.2-38.9 (27.1)	0.087
	Without	270	26.05±2.95	19.2-35 (26.1)	
Birth weight (g)	**With**	30	1808.55±623.66	660-3100 (1800)	0.103
	Without	270	1618.49±625.76	550-3230 (1630)	
Apgar 1st min	**With**	30	5.42±2.2	1-8 (6)	0.672
	Without	270	5.25±2.11	0-8 (6)	
Apgar 5th min	**With**	30	7.32±1.6	2-9 (7)	0.728
	Without	270	7.18±1.58	0-9 (7)	
Gestational age at delivery (weeks)	**With**	30	29.74±3.01	24.29-34 (29.43)	0.300
	Without	270	30.76±3.06	24.14-34 (31.57)	
Cervical length (mm)	**With**	30	32.83±8.39	14-48 (33.5)	0.805
	Without	270	32.21±9.96	10-50 (35)	
Umbilical PI	**With**	30	1.01±0.17	0.84-1.83 (0.98)	0.446
	Without	270	0.97±0.11	0.45-1.5 (0.98)	
Length of hospitalization (days)	**With**	30	14.9±12.18	3-44 (9)	0.822
	Without	270	14.05±11.83	2-60 (10)	
Maternal temperature (°C)	**With**	30	38.55±0.23	38-39.4 (38.7)	0.017*
	Without	270	36.01±0.14	36-36.8 (36)	
Maternal systolic blood pressure (mmHg)	**With**	30	114.39±11.1	100-138 (130)	0.492
	Without	270	109.49±10.35	83-160 (110)	
Maternal diastolic blood pressure (mmHg)	**With**	30	65.1±13.75	44-125 (60)	0.02*
	Without	270	65.77±9.96	41-109 (61)	

*: p<0.05, **: p<0.01, SD: Standard deviation, Min-max: Minimum-maximum, PI: Pulsatile index, INR: International normalized ratio, aPTT: Activated partial thromboplastin time

A DNI cut-off value of 0.11 yielded a sensitivity of 74.2% and a specificity of 57.1% for predicting chorioamnionitis, representing a clinically relevant threshold that may contribute to early detection and proactive management strategies in PPROM cases (Table 4). Figure 1 illustrates the corresponding ROC curve, further demonstrating the diagnostic performance of DNI in distinguishing pregnancies complicated by chorioamnionitis.

Building upon the diagnostic performance demonstrated by the ROC analysis, a multivariate logistic regression model was subsequently applied to further delineate independent predictors of chorioamnionitis, the results of which are presented in Table 5.

A multivariable logistic regression analysis was performed to identify independent predictors of clinical chorioamnionitis. The overall model was statistically significant (χ^2=24.294, p=0.001), indicating an acceptable model fit. The explanatory power of the model was modest but clinically meaningful (Nagelkerke R^2=0.180).

Among the hematological and coagulation parameters evaluated, PLT, DNI, and INR were identified as independent predictors of chorioamnionitis. Higher PLT values were associated with a small but statistically significant increase in risk (OR=1.007, 95% CI: 1.001-1.013; p=0.016). DNI demonstrated the strongest association with chorioamnionitis (OR=53.255, 95% CI: 5.170-548.559; p=0.001), consistent with its role as an inflammatory marker.

INR was also significant (OR=7,956.218, 95% CI: 1.21–5.2×10^7; p=0.042), but its wide confidence interval indicates substantial variability and suggests the estimate should be interpreted with caution.

Overall, the model indicates that hematological inflammatory markers and coagulation parameters may serve as independent predictors of chorioamnionitis in pregnancies complicated by PPROM (Table 5).

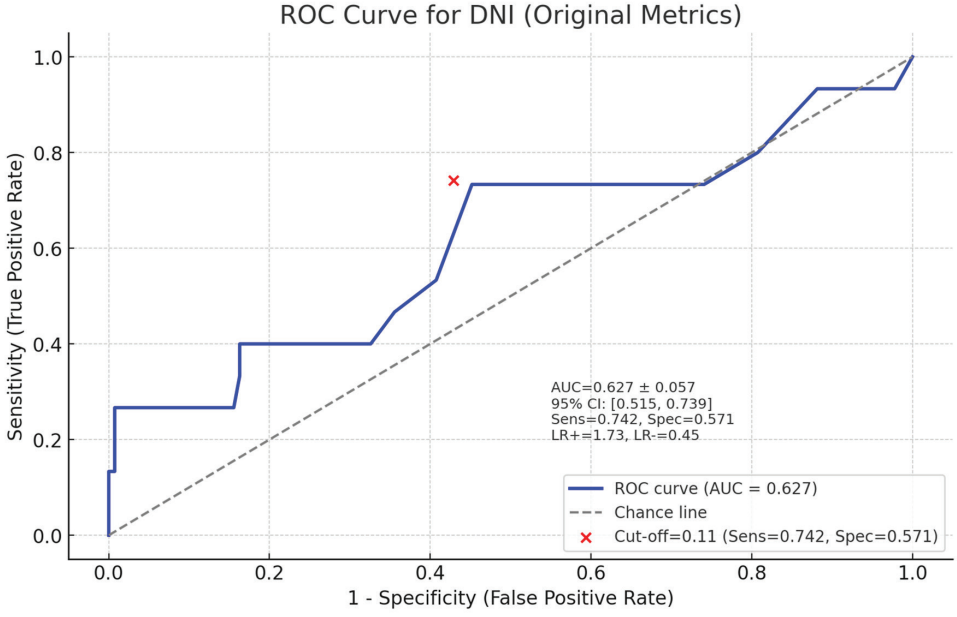

Figure 1. ROC curve of DNI for predicting chorioamnionitis in pregnancies complicated by PPROM

ROC: Receiver operating characteristic, DNI: Delta neutrophil index, AUC: Area under the curve, CI: Confidence interval, PPROM: Preterm premature rupture of membranes, LR: Likelihood ratios

Table 4. ROC analysis results and AUC values

Parameter (10^9/L)	Sens. %	Spec. %	Cut-off	AUC (95% CI)	SE	p-value	LR^+/LR^-
DNI	74.2	57.1	0.11	0.627 (0.515-0.739)	0.057	0.026*	1.73/0.45

*: p<0.05, LR: Likelihood ratios, ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, SE: Standard error, DNI: Delta neutrophil index

Table 5. Predictors of chorioamnionitis identified by multivariate logistic regression

		Multivariable				
Model	**Variables**	**B**	**SE**	**Exp(B)**	**95% CI**	**p**
	PLT	0.007	0.003	1.007	1.001-1.013	0.016*
	DNI (10^9/L)	3.975	1.190	53.255	5.170-548.559	0.001**
	INR	8.982	4.486	7956.218	1.21-5.2×10^7	0.042*
	R^2=0.180					
	X^2=24.294, p=0.001**					

*: p<0.05, **: p<0.01, DNI: Delta neutrophil index, SE: Standard error, PLT: Platelet count, CI: Confidence interval, INR: International normalized ratio

Discussion

This study highlights the potential role of the DNI as a biomarker for the early detection of chorioamnionitis in pregnancies complicated by PPROM. In clinical practice, where timely and reliable diagnostic tools are essential, DNI provides several practical advantages. It is derived automatically from a standard CBC, incurs no additional cost, requires no specialized laboratory processing, and can be reported in real time, thereby providing an accessible adjunct to infection surveillance protocols (7).

Our findings showed that DNI values were significantly elevated in patients with chorioamnionitis, consistent with DNI's proposed role as a marker of the release of immature granulocytes during acute inflammatory responses. This early hematologic shift may precede elevations in conventional markers such as CRP, WBC count, or procalcitonin (8). Unlike these delayed systemic markers, DNI reflects the an early increase in immature granulocytes of the innate immune system, thereby allowing earlier recognition of subclinical intrauterine infection.

Consistent with our results, Cho et al. (4) reported that increased DNI levels were independently associated with histological chorioamnionitis in patients with PPROM, suggesting its predictive utility in obstetric populations. Moreover, other hematologic indices, including platelet-to-lymphocyte and NLRs, have been investigated for their diagnostic value in PPROM and threatened preterm labor, further underscoring the relevance of readily available hematologic parameters in this context (9). Collectively, our data support the use of simple inflammatory indices, including DNI, as adjunctive tools in the evaluation of infection risk in PPROM.

Furthermore, the integration of other hematologic parameters—PLT, INR, and maternal diastolic blood pressure—into our predictive model strengthens the rationale for a combined assessment using routine hematologic parameters for early identification of chorioamnionitis. The association with elevated PLTs is noteworthy, raising the possibility that thrombocytosis reflects an active hematological response to systemic inflammation rather than a coincidental finding (10). This observation is consistent with the broader concept that platelets act as immunomodulatory cells in inflammatory cascades, rather than merely serving hemostatic functions (10).

Our findings suggest that incorporating DNI into routine assessment may help clinicians recognize infection earlier in the course of PPROM. The routine use of DNI—alone or in combination with complementary biomarkers—may allow obstetricians to anticipate infection, initiate timely interventions, and reduce neonatal exposure to inflammatory insults.

Inflammatory biomarkers such as CRP and procalcitonin have long been used in the diagnostic workup of chorioamnionitis; however, their delayed rise in levels and limited specificity reduce their reliability. By contrast, the DNI reflects early granulocytic activation and can be measured rapidly and at no additional cost as part of a standard CBC (11). In our study, CRP levels were significantly higher in the chorioamnionitis group, in line with previous reports. However, CRP is a non-specific acute-phase reactant that may increase in diverse infectious and non-infectious conditions, including tissue injury and autoimmune disorders (12). This inherent lack of specificity underscores the need for adjunctive biomarkers, with DNI offering a promising alternative.

Chorioamnionitis is a common complication of pregnancies with PPROM and an established risk factor for adverse fetal and neonatal outcomes. The inflammatory cascade underlying this condition is initiated by maternal immune activation—whether triggered by microbial invasion or sterile inflammation—and is characterized histologically by neutrophil infiltration of the amniotic membranes (13). In line with this pathophysiological

process, our findings revealed significantly higher DNI values in patients diagnosed with chorioamnionitis (p=0.029), suggesting enhanced neutrophil mobilization and increased levels of circulating immature granulocytes. This observation reinforces DNI's potential as a marker for early intrauterine inflammatory activity (7).

Collectively, these findings support the broader concept of using blood-based inflammatory indices—such as the NLR, CRP, lymphocyte count, and particularly DNI—in the early detection of chorioamnionitis during preterm labor. These markers are non-invasive, rapidly obtainable, and cost-effective, making them especially attractive in high-volume or resource-limited clinical settings. Ridout et al. (14) have emphasized the diagnostic potential of NLR in preterm labor management, particularly in low-income countries. In a similar vein, our data suggest that DNI, due to its higher specificity than traditional markers, may represent a more effective screening tool for early identification of chorioamnionitis in PPROM. The ability to intervene at an earlier stage could translate into reduced maternal and fetal morbidity.

These findings have meaningful clinical implications. Early administration of antibiotics for confirmed or suspected chorioamnionitis has been shown to significantly reduce rates of neonatal sepsis and maternal complications (15). The diagnostic cut-off of 0.11 identified for DNI via ROC analysis may provide a practical reference point for clinicians. This threshold, with its balanced sensitivity and specificity, could assist in risk stratification, guide timely initiation of antibiotic therapy, and even inform decisions regarding the optimal timing of delivery in at-risk pregnancies.

In our study, the significantly elevated maternal diastolic blood pressure observed in chorioamnionitis may reflect the interplay among systemic inflammation, sympathetic activation, and endothelial dysfunction. Pro-inflammatory cytokines (IL-6, TNF-α, IL-1β) are known to impair endothelial tone and promote vasoconstriction, while systemic inflammation can activate the sympathetic nervous system and increase vascular resistance (16). Placental inflammation and hypoperfusion may further contribute to maternal hemodynamic instability, suggesting that chorioamnionitis extends beyond intrauterine infection and exerts systemic cardiovascular effects during pregnancy (17).

The incidence of chorioamnionitis in our cohort was 10% (n=30), aligning with reported rates of 1-5% at term and 20-30% in preterm pregnancies (18). This relatively high incidence likely reflects the tertiary referral nature of our center, where high-risk pregnancies are concentrated. In addition, INR values were slightly but significantly higher in affected patients, although still within normal limits. This finding may indicate subtle cytokine-mediated alterations in hepatic synthetic function or early coagulopathy, consistent with previous reports linking chorioamnionitis to coagulation disturbances (18,19).

Our study contributes to the limited literature on DNI in PPROM by combining a relatively large, well-characterized cohort with comprehensive hematologic profiling. These results reinforce the potential of DNI—together with dynamic markers such as PLT, INR, and blood pressure parameters—as part of an integrated, real-time infection surveillance strategy in obstetric practice.

Study Limitations

This study has some limitations. Its retrospective and single-center design may limit the generalizability of the results. Because of the retrospective design, an a priori power analysis could not be performed; however, a post-hoc power calculation demonstrated that the sample size (n=300) provided adequate statistical power to detect large effect sizes. In addition, DNI values were obtained using a specific hematology analyzer (ADVIA 2120), and inter-laboratory variations cannot be completely excluded. Another limitation is that DNI was measured only once during hospitalization, which did not allow for evaluation of temporal changes. Nevertheless, these findings provide meaningful preliminary evidence supporting the potential role of DNI in PPROM, and future multicenter prospective studies are needed to confirm and expand upon our results.

Conclusion

Our findings suggest that the DNI may serve as a useful biomarker for identifying the risk of chorioamnionitis in pregnancies complicated by PPROM. An elevated DNI level was significantly associated with infection, highlighting its potential role in early diagnosis. Because DNI is rapid, cost-effective, and easily accessible through routine blood counts, it may represent a practical adjunct in clinical decision-making. When interpreted together with other inflammatory markers, DNI could contribute to a more accurate and timely assessment of infection risk and guide prenatal management strategies in cases of PPROM. Nonetheless, confirmation in larger, multicenter prospective studies is essential before the integration of DNI into standardized care protocols can be recommended.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital (approval no: 2023-610, date: 27.11.2023).

Informed Consent: This study was conducted retrospectively, Independent Ethics Committee University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital approved the waiver of informed consent. Patient confidentiality was maintained throughout the study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: T.A., Concept: T.A., K.K.B., Design: T.A., K.K.B., Data Collection or Processing: T.A., K.K.B., Analysis or Interpretation: T.A., Literature Search: T.A., Writing: T.A.

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ORIGINAL RESEARCH

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Efficacy of Ultrasound-guided versus Palpation-guided Techniques in Spinal Anesthesia: A Randomized Controlled Trial

Ultrason Rehberli ile Palpasyon Rehberli Spinal Anestezi Tekniklerinin Etkinliği: Randomize Kontrollü Bir Çalışma

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Abstract

Objective: This study aims to assess and compare the effectiveness of spinal anesthesia administered through traditional palpation and ultrasound (US) guidance by analyzing the precision of needle placement, procedural success, patient satisfaction, and complication rates.

Method: A prospective, randomized clinical trial was conducted involving 135 patients (American Society of Anesthesiologists I-III) scheduled for lower limb surgery. Participants were randomized into two groups: The palpation group (n=65) and the US-guided group (n=66). Parameters including the accuracy of needle entry point, the number of attempts required to obtain cerebrospinal fluid (CSF), patient satisfaction levels, and the incidence of complications were documented and evaluated.

Results: The success rate of CSF identification on the first attempt was 83.0% in the palpation group and 89.3% in the US guided group (p=0.6). While 28.4% of the spinal punctures in the palpation group were conducted outside the intended intervertebral space, all procedures in the US guided group were accurately localized (p<0.05). There were no statistically significant differences between the groups concerning the total number of attempts, complication occurrence, or patient satisfaction (p>0.05). However, among patients with a body mass index exceeding 30, the US guided group demonstrated a significantly higher success rate and required fewer attempts compared to the palpation group (p<0.01).

Conclusion: US imaging enhances the accuracy of spinal level determination, although both techniques yield comparable overall

Öz

Amaç: Bu çalışma, spinal anestezinin geleneksel palpasyon ve ultrason (US) rehberliği ile uygulanmasının etkinliğini; iğne yerleştirme doğruluğu, işlem başarısı, hasta memnuniyeti ve komplikasyon oranları açısından analiz ederek değerlendirmeyi ve karşılaştırmayı amaçlamaktadır.

Yöntem: Alt ekstremite cerrahisi planlanan, Amerikan Anestezistler Derneği I-III sınıfında 135 hastanın yer aldığı prospektif, randomize bir klinik çalışma yürütüldü. Katılımcılar iki gruba randomize edildi: palpasyon grubu (n=65) ve US rehberli grup (n=66). İğne giriş noktasının doğruluğu, beyin omurilik sıvısına (BOS) ulaşmak için gereken deneme sayısı, hasta memnuniyet düzeyleri ve komplikasyon insidansı gibi parametreler belgelenip değerlendirildi.

Bulgular: İlk denemede BOS elde edilme başarısı, palpasyon grubunda %83,0, US rehberli grubunda ise %89,3 olarak bulundu (p=0,6). Palpasyon grubunda spinal ponksiyonların %28,4'ü hedeflenen intervertebral aralığın dışında gerçekleştirilirken, US rehberli gruptaki tüm işlemler doğru lokalize edilmiştir (p<0,05). Toplam deneme sayısı, komplikasyon insidansı ve hasta memnuniyeti açısından gruplar arasında istatistiksel olarak anlamlı bir fark gözlenmedi (p>0,05). Ancak, beden kitle indeksi 30'un üzerinde olan hastalar arasında, US rehberli grupta anlamlı derecede daha yüksek başarı oranı elde edilmiş ve daha az girişim gerekmiştir (p<0,01).

Sonuç: US görüntüleme, spinal seviye belirlemede doğruluğu artırmaktadır; ancak her iki teknik de genel başarı ve güvenlik profili açısından benzer sonuçlar vermektedir. US'nin avantajları özellikle obezite

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success and safety profiles. The advantages of ultrasonography are particularly evident in patients with obesity or challenging anatomical landmarks. Therefore, its use is recommended as a complementary approach in complex cases. Further large-scale studies are needed to validate these outcomes and support the development of standardized protocols for routine US use in spinal anesthesia.

Keywords: Palpation, spinal anesthesia, ultrasonography

veya anatomik belirteçlerin zor ayırt edilebildiği hastalarda belirgin hale gelmektedir. Bu nedenle, US kullanımı karmaşık olgular için tamamlayıcı bir yaklaşım olarak önerilmektedir. Bu sonuçların doğrulanması ve spinal anestezide rutin US kullanımına yönelik standart protokollerin geliştirilmesi için daha büyük ölçekli çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Palpasyon, spinal anestezi, ultrasonografi

Introduction

Spinal anesthesia, a regional anesthesia technique, involves the temporary interruption of nerve conduction by injecting an anesthetic solution into the cerebrospinal fluid (CSF). Due to its numerous advantages over general anesthesia, spinal anesthesia has been a trusted method for almost a century, particularly favored for surgeries of the lower abdomen, perineum, and lower limbs (1).

In routine clinical practice, the selection of the appropriate intervertebral space for the central lumbar block is critically dependent on the identification of the L4 vertebra through anatomical landmarks. Notably, the intercristal line—also referred to as Tuffier's line—crosses the spine at the L4 vertebra or the L4-L5 intervertebral space. This line is a vital reference point for anesthesia placement, especially useful in ensuring the puncture is performed at a safe level considering the termination of the adult medullary cone at the lower edge of the L1 vertebral body (2-4).

The palpation method, a traditional technique for administering spinal anesthesia, utilizes landmarks such as the iliac crest and spinous processes. However, the visibility of these landmarks may be compromised by factors including obesity, previous spinal surgeries, pregnancy, and age-related degenerative changes, which can increase the difficulty of the procedure and the risk of complications (5).

To overcome these challenges and improve the precision and safety of identifying the correct intervertebral space, ultrasonography has increasingly been integrated into spinal anesthesia practices in recent years (6).

Studies have employed various intervertebral spaces for spinal anesthesia, such as L2-3 and L3-4 in numerous patients, and occasionally L4-5 or L5-S1 depending on the surgical requirements (7-9). It is crucial to note that the conus medullaris, the lower end of the spinal cord, may extend down to the L3 vertebra in adults, which poses additional risks during puncture (10). Consequently, our study primarily utilized the L3-L4 and L4-L5 intervertebral spaces for punctures, as these spaces are typically safer and provide adequate room for maneuvering, away from the conus medullaris (11).

This study aims to evaluate the efficacy of spinal anesthesia performed using traditional palpation guidance versus ultrasound-guided (US guided) techniques in terms of success rates, anatomical accuracy, the impact of body mass index (BMI) on procedural outcomes, patient satisfaction, and potential complications.

Materials and Methods

This randomized, prospective study was conducted in the operating rooms of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital after receiving approval from the Clinical Research Ethics Committee (date: 24.01.19, approval no: 61). Our research adhered to the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants.

Participants

The study included 135 patients aged 18-75 years with an American Society of Anesthesiologists score of 1-2-3 who were scheduled to undergo orthopedic lower extremity surgery. Exclusion criteria included the presence of uncontrolled systemic diseases (such as diabetic neuropathy or hypertensive nephropathy), inability to assume a sitting position, a history of vertebral surgery, and contraindications to regional anesthesia (such as coagulopathy or sepsis). During the procedure, four patients developed syncope and were subsequently excluded from the analysis.

Group Assignment

Patients were allocated into two groups using a computer-generated block randomization method. Group assignments were concealed using sequentially numbered, opaque, sealed envelopes. Group palpation (n=65) underwent the traditional palpation technique to identify the needle insertion site for spinal anesthesia, while Group US guided (n=66) utilized US guidance. The flow

diagram of the patient population is presented in Figure 1. Demographic data, including age, gender, height, weight, and BMI, were recorded for all participants.

Procedures

For patients in Group palpation, spinal anesthesia was administered by an anesthesiologist with at least four years of experience using the classical palpation method. For patients in Group US guided, an anesthesiologist experienced in US identified the needle insertion site and subsequently performed the spinal anesthesia. The SonoSite® M-turbo linear probe with a frequency range of 6-13 MHz was used for ultrasonographic measurements in B mode. To ensure imaging standardization, all ultrasound scans were performed by the same experienced anesthesiologist using a standardized protocol. The probe was positioned in the sagittal plane over the lumbar spine to identify the midline structures, with consistent probe orientation and contact pressure. Bony landmarks such as the spinous processes and iliac crests were used for alignment in each case.

In Group palpation, patients were positioned in a seated posture. For the needle insertion site, the vertebral space along the imaginary Tuffier's line between the crests of the iliac bones or the nearest caudal space to this line was marked. A 25-gauge Quincke spinal needle was used for the procedure. The appearance of CSF confirmed a successful block. After the procedure, the needle insertion site was covered with a small sterile sponge. Following the

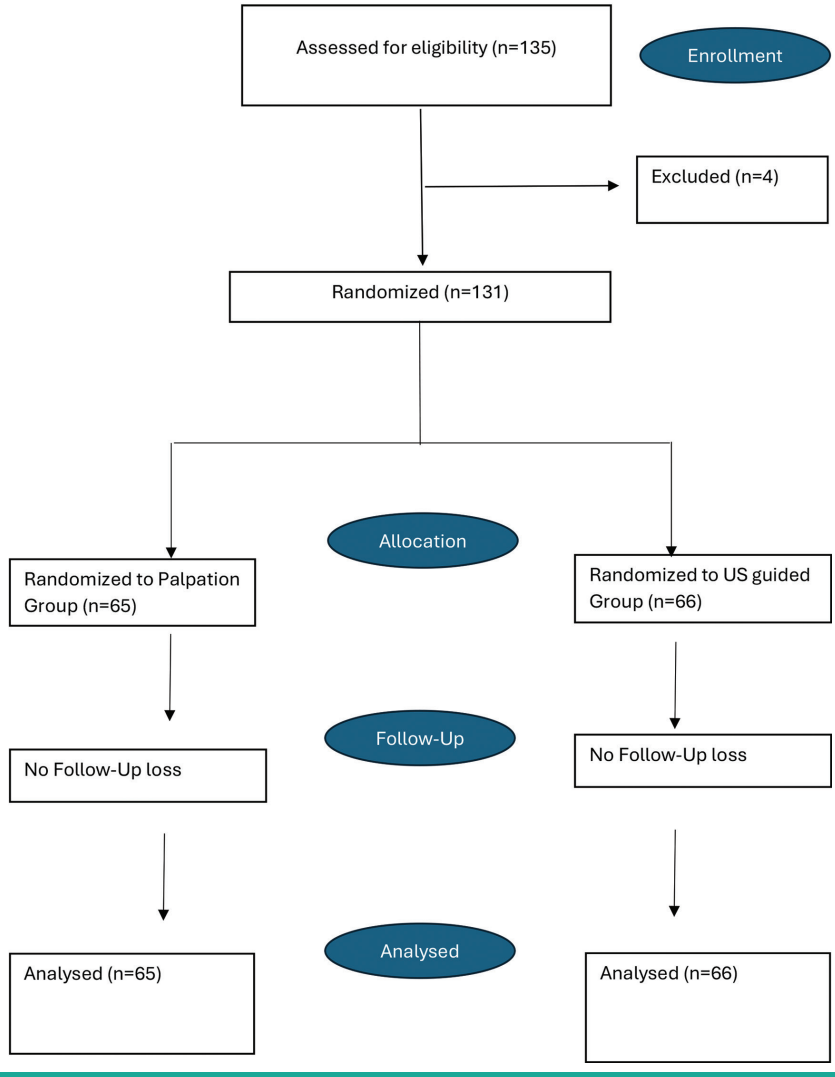

Figure 1. Flow diagram of patient population
US: Ultrasound

operation, patients were repositioned in a seated posture in the post anesthetic care unit, and US was used to identify the vertebral space based on the location of the sterile sponge.

In Group US guided, the US probe was placed sagittally on the sacrum, and as the probe moved towards the neck, spinal landmarks such as the L5 vertebra and the L5-S1 intervertebral space were identified. The desired needle insertion site (L3-4 or L4-5 intervertebral space) was marked at the midpoint between spinous processes. The same spinal needle and procedure were followed as in Group palpation.

Anesthetic medication prepared with 13 mg isobaric bupivacaine (Buvacin®, Vem Ilac Turkey) and 20 mcg fentanyl (Talinat®, Vem Ilac Turkey) was administered intrathecally to both groups. Needle insertion attempt was defined as the removal and reinsertion of the needle through the skin. Adjustments made after the initial needle insertion were not considered as separate attempts.

Outcome Measures

For both groups, we recorded the needle insertion levels, the number of attempts to achieve CSF flow, patient satisfaction and differences in complications. Patient satisfaction was evaluated using a simple 4-point Likert-type scale (1-not satisfied, 4-very satisfied) developed by the authors. All postoperative complications—such as headache, back pain, and neurological deficits—were assessed through daily in-person clinical evaluations conducted during the 72-hour postoperative hospitalization period.

Statistical Analysis

Based on a power analysis (assuming a Kappa agreement coefficient of 0.40 for accuracy determination, an alternative coefficient of 0.60, with 80% power and a 5% margin of error), the required sample size was determined to be 127 patients.

The data obtained were recorded using the statistical package program (SPSS, version 24.0, SPSS, Chicago, USA). As descriptive statistics, the numbers (n), percentages (%), mean ± standard deviations, and median (interquartile range) values were given. The Pearson chi-square test and Fischer's exact test were used for the analysis of the categorical variables. The normal distribution of the data for the continuous variables was evaluated by Shapiro-Wilk, the normality test, and Q-Q graphs. In comparing the continuous variables of the two groups, the independent sample t-test was used for variables with a normal distribution, and the Mann-Whitney U test was used for variables with a non-normal distribution. The evaluations were made within a 95% confidence interval, and $p<0.05$ was considered statistically significant.

Results

The demographic data of the patients are presented in Table 1. No significant differences were observed between the groups in terms of age, weight, height, BMI, or gender ($p>0.05$).

In the palpation group, the success rate for locating CSF on the first attempt was 83.0%, decreasing to 12.3% on the second attempt and 1.5% on the third attempt. In the US guided Group, the success rate on the first attempt was 89.3%, with 10.7% on the second attempt, and no patients requiring a third attempt. Both groups achieved comparable success rates ($p=0.6$).

In the palpation group, postoperative evaluation of the levels revealed that in 18 patients (28.4%), the procedure was performed outside the safest ranges according to the literature. In contrast, in the US guided Group, as the levels were pre-determined, spinal anesthesia was successfully administered within the safe ranges in all 65 patients (100%). The difference between the groups was statistically significant ($p<0.01$). A detailed analysis of the vertebral level ranges is presented in Table 2.

In the palpation group, spinal anesthesia could not be performed in 2 patients despite 3 repeated attempts, necessitating a switch to general anesthesia. Similarly, in the US guided Group, 1 patient required a transition to general anesthesia after 3 unsuccessful attempts.

Both groups demonstrated similar palpability of anatomical landmarks, and the number of needle insertion attempts was likewise comparable.

To evaluate the impact of BMI on the success of spinal anesthesia, needle attempt rates were compared across different BMI categories in the palpation and US guided groups.

In the palpation group, patients with a BMI >30 required ≥2 attempts in 10 patients, whereas only 6 patients successfully received spinal anesthesia with <2 attempts. Conversely, among patients with a BMI ≤30 in the same group, only 1 required ≥2 attempts, while 38 achieved success with <2 attempts.

In the US guided group, patients with a BMI >30 showed a more favorable distribution, with only 5 requiring ≥2

attempts and 13 achieving success with <2 attempts. Similarly, among patients with a BMI ≤30 in the US guided group, 3 required ≥2 attempts, while the majority (35 patients) succeeded with <2 attempts.

The results, summarized in Table 3, demonstrated statistically significant differences between the groups (p<0.01).

Patient satisfaction levels did not refer significantly between the groups, indicating comparable experiences across both techniques (p=0.12).

Similarly, postoperative complication rates remained consistent between the palpation and ultrasound-guided groups, with statistical analysis revealing no discernible difference (p=1.00).

Discussion

In our study, the efficacy of spinal anesthesia performed using traditional palpation guidance versus US guided techniques was evaluated in terms of success rates, anatomical accuracy, the impact of BMI on procedural outcomes, patient satisfaction, and potential complications.

Firstly, no significant demographic differences were observed between the groups regarding age, weight, height, BMI, or gender ensuring that the observed differences in outcomes were not confounded by patient characteristics. This consistency in baseline characteristics allows for a fair comparison between the two techniques in spinal anesthesia.

Spinal anesthesia can be safely administered at any level below the termination of the spinal cord. In our study, the L3-L4 and L4-L5 intervertebral spaces were chosen as the

Table 1. Comparison of demographic characteristics of group palpation and group US guided

	Group palpation	Group US guided	p-value
Age (year)	47.77±15.29	46.38±15.31	0.60†
Weight (kg)	79.85±14.35	81.30±15.01	0.57†
Length (m)	1.70±0.09	1.71±0.09	0.61†
BMI (kg/m²)	26.40 (5.55)	27.40 (5.38)	0.55†
Gender			
Female n (%)	24 (63.15%)	14 (36.85%)	0.05†
Male n (%)	41 (44.0%)	52 (56.0%)	0.05†

†: The Pearson chi-square test and Fischer's exact test have been used, US: Ultrasound, BMI: Body mass index

Table 2. Comparison of preoperative and postoperative vertebral levels in group palpation and group US guided

Vertebral level	Group palpation	Group US guided	p-value
L1-L2	4 (6.3%)	0 (0.0%)	
L2-L3	13 (20.6%)	0 (0.0%)	
L3-L4	29 (46.0%)	22 (33.8%)	<0.01*
L4-L5	16 (25.3%)	43 (66.2%)	
L5-S1	1 (1.5%)	0 (0.0%)	
Total (percent)	63 (100.0%)	65 (100.0%)	

*: Mann-Whitney U test has been used, US: Ultrasound

Table 3. Comparison of attemp rates based on BMI* in the palpation and US guided groups

Groups	Attemps ≥2	Attemps <2	p-value
Group palpation (BMI >30)	10 (62.5%)	6 (37.5%)	
Group palpation (BMI ≤30)	1 (2.6%)	38 (97.4%)	
Group US guided (BMI >30)	5 (27.8%)	13 (72.2%)	<0.01
Group US guided (BMI ≤30)	3 (7.9%)	35 (92.1%)	

*: Mann-Whitney U test has been used, BMI: Body mass index, US: Ultrasound

reference levels due to their greater distance from the conus medullaris and their wider anatomical dimensions (12).

In the study by Furness et al. (13), magnetic resonance imaging (MRI) validation demonstrated a 71% correlation in patients where US was used for localization, compared to only 30% with the conventional palpation method.

Radiographic methods or MRI are considered the gold standard for accurately identifying vertebral levels. However, in the operating room setting, US offers a more practical and objective alternative. Broadbent et al. (14) and Whitty et al. (15) previously reported the inaccuracies associated with the palpation method, highlighting that anesthetists often misidentify the correct intervertebral space. Broadbent et al. (14) found that accurate localization occurred in only 29% of patients, with more than half of the placements being at a higher level than intended. Similarly, Whitty et al. (15) reported that 44% of spinal blocks were performed at a different level than predicted, with an accuracy rate of only 52%.

Consistent with the literature, one of the most noteworthy findings in our study was the challenge of accurately identifying vertebral levels. In the palpation group, 28.4% of procedures were performed outside safe anatomical boundaries, whereas all procedures in the US guided Group were conducted within safe limits. This finding highlights a fundamental limitation of the palpation method, suggesting that it may be less reliable, particularly in patients with less prominent or difficult-to-palpate anatomical landmarks.

In the study by Chin et al. (16) on spinal anesthesia using US, successful block placement was achieved in 84% of patients on the first attempt, 14% on the second attempt, and 2% on the third attempt. Similarly, Lahham et al. (17), in their study on lumbar puncture, reported no significant difference between the US guided and conventional palpation groups in terms of the number of attempts required. In the systematic review conducted by Young et al. (18), it was demonstrated that the use of preprocedural ultrasound improved efficacy indicators such as the first-pass success rate, without leading to an increase in procedure time. In another systematic review conducted by Makino et al. (19), it was also demonstrated that the US-guided technique improves the success rate.

In our study, success rates were comparable between the groups (83.0% in the palpation group and 89.3% in the US guided Group). Although a small subset of patients in both groups required a second attempt, none of the patients in the US guied Group required a third attempt. This finding suggests that US imaging may provide a significant advantage in facilitating accurate needle placement. Previous studies have also demonstrated that ultrasound guidance can enhance precision in neuraxial anesthesia procedures, thereby reducing the need for multiple needle insertions (16,17).

The technical difficulty of spinal anesthesia is closely related to the palpability of anatomical landmarks (3). The quality of these landmarks serves as an indicator of whether regional anesthesia will be challenging (20). In the study by Chin et al. (16), successful spinal anesthesia was achieved using US in 38% of patients despite non-palpable anatomical landmarks. Furthermore, in another study by Chin et al. (16), among 60 patients in whom the spinal level was identified using US, only one patient resulted in failure. This patient was classified as morbidly obese (BMI >35) and had non-palpable anatomical landmarks. In a study conducted by Kalagara et al. (21), it was demonstrated that preprocedural ultrasound facilitates the accurate identification of the midline, vertebral level, and depth, thereby enabling optimal trajectory planning and improving the success of neuraxial block placement with fewer needle passes, particularly in patients with challenging anatomical features. In a randomized controlled trial conducted by Bilge and Başaran (22) in 2025, prepuncture ultrasound imaging was shown to be beneficial in spinal anesthesia for pregnant women with class 3 obesity, particularly in cases where anatomical landmarks were not clearly identifiable using conventional palpation techniques.

In our study, fewer attempts were required in patients with a higher BMI under ultrasound guidance, which is consistent with the findings reported in the literature.

In the meta-analysis conducted by Perlas et al. (23), it was demonstrated that the use of US in spinal and epidural anesthesia increases procedural success while reducing the number of needle insertions and technical difficulties. In our study, despite the advantages offered by the US technique in anatomical localization, overall success rates and complication rates were found to be statistically similar between the two groups. The need for conversion to general anesthesia occurred at comparable rates in both groups (2 patients in the palpation group and 1 patient in the US guided group). Additionally, no statistically significant difference was observed between the groups in terms of the palpability of anatomical landmarks or the total number of needle insertion attempts. These findings

suggest that while US guidance enhances accuracy, the palpation method remains an effective option in patients with easily identifiable anatomical landmarks.

Postoperative patient satisfaction and complication rates were also found to be similar. The proportion of patients without complications was 90.7% in the palpation group and 87.8% in the US guided Group. This finding is consistent with the results reported by Grau et al. (24) and Ansari et al. (25). Multiple needle insertions may increase the incidence of complications such as post-dural puncture headache, paresthesia, hematoma, and infection, all of which can lead to greater intraoperative discomfort and reduced overall patient satisfaction. Therefore, patient satisfaction during spinal anesthesia appears to be influenced not only by the technique used, but also by factors such as the clinician's experience, the number of needle passes, communication with the patient, and the overall comfort of the procedure (26).

Study Limitations

This study has several limitations. First, being a single-center study, the generalizability of the findings to other healthcare institutions may be limited. Additionally, long-term complications following spinal anesthesia were not evaluated; instead, only early postoperative patient satisfaction and complication rates were analyzed. Furthermore, the additional time required for US guidance was not assessed, which could be a crucial factor in clinical practice, particularly in emergency surgical settings. Another limitation is the use of a non-validated, study-specific 4-point Likert-type scale to assess patient satisfaction. Although similar subjective scales have been employed in other studies—such as the 5-point verbal scale reported by Chen et al. (26)—the absence of a standardized, validated tool may limit the reliability and comparability of our satisfaction data. Moreover, our study population did not include morbidly obese patients (BMI >40), making it difficult to draw definitive conclusions regarding the efficacy of US guidance in this specific patient group. Lastly, the clinical feasibility of ultrasound-guided spinal anesthesia was not comprehensively evaluated in terms of training requirements, procedure duration, and cost-effectiveness. These factors are especially relevant in high-volume operating environments, where efficiency and resource allocation are critical. Future multicenter studies with larger and more diverse patient populations are needed to overcome these limitations and provide more robust evidence on the clinical utility and practical implementation of US guidance in spinal anesthesia.

Conclusion

In conclusion, our findings indicate that while palpation and ultrasound US-guided spinal anesthesia techniques offer similar success rates and patient outcomes, US guidance provides superior accuracy in identifying vertebral levels. This technique appears to be particularly advantageous in patients with a high BMI.

Given the potential of US guidance to enhance procedural precision and reduce the risk of mislocated spinal anesthesia, it should be considered as an adjunct to palpation, especially in complex patients where anatomical landmarks are difficult to identify.

Ethics

Ethics Committee Approval: This randomized, prospective study was conducted in the operating rooms of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital after receiving approval from the Clinical Research Ethics Committee (date: 24.01.19, approval no: 61).

Informed Consent: Our research adhered to the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants.

Footnotes

This manuscript benefited from language editing and grammatical refinement provided by ChatGPT-4o.

Authorship Contributions

Surgical and Medical Practices: A.E.B., E.A., Concept: A.E.B., Design: A.E.B., Data Collection or Processing: A.E.B., Analysis or Interpretation: A.E.B., E.A., Literature Search: A.E.B., E.A., Writing: A.E.B.

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ORIGINAL RESEARCH

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Comparison of Regional and General Anesthesia in Ureterorenoscopic Management of Distal Ureteral Stones: A Prospective Randomized Study

Distal Üreter Taşlarının Üreterorenoskopik Tedavisinde Bölgesel ve Genel Anestezinin Karşılaştırılması: Prospektif Randomize Bir Çalışma

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Abstract

Objective: To compare the effects of regional (spinal) and general anesthesia (GA) on surgical outcomes, perioperative complications, postoperative pain, and surgeon comfort in patients undergoing ureterorenoscopy (URS) for distal ureteral stones.

Method: This prospective, randomized clinical study included patients undergoing URS for distal ureteral calculi at a tertiary academic center between January 2024 and March 2025. Patients were allocated to either the GA or regional anesthesia (RA) group. Baseline demographics, operative parameters, postoperative pain scores [visual analogue scale (VAS)], analgesic requirements, and surgeon comfort were recorded and statistically compared.

Results: A total of 180 patients were included (90 in each group). Demographic and stone characteristics were similar between the two groups. The mean operative time was significantly shorter in the GA group (22.9±8.3 vs. 27.9±9.5 min, p=0.001). VAS were significantly lower in the GA group at the 6th and 12th hours: median VAS scores were 5.0 [interquartile range (IQR) 4.0-6.0] vs. 6.0 (IQR 5.0-6.3) at 6 hours (p=0.001), and 4.0 (IQR 3.0-5.0) vs. 6.0 (IQR 4.0-6.8) at 12 hours (p=0.001), respectively. Surgeon comfort scores were also significantly higher in the GA group (p=0.001). Success and complication rates did not differ significantly between groups.

Öz

Amaç: Distal üreter taşları için üreterorenoskopi (URS) uygulanan hastalarda bölgesel (spinal) ve genel anestezinin (GA) cerrahi sonuçlar, perioperatif komplikasyonlar, postoperatif ağrı ve cerrah konforu üzerindeki etkilerini karşılaştırmaktır.

Yöntem: Bu prospektif, randomize klinik çalışmaya Ocak 2024 ile Mart 2025 arasında üçüncü basamak bir akademik merkezde distal üreter taşları için URS uygulanan hastalar dahil edildi. Hastalar GA veya bölgesel anestezi (RA) grubuna ayrıldı. Başlangıç demografik özellikleri, operatif parametreler, postoperatif ağrı skorları [görsel analog skala (VAS)], analjezik gereksinimleri ve cerrah konforu kaydedildi ve istatistiksel olarak karşılaştırıldı.

Bulgular: Toplam 180 hasta çalışmaya dahil edildi (her grupta 90 hasta). Demografik özellikler ve taş özellikleri iki grup arasında benzerdi. Ortalama ameliyat süresi GA grubunda anlamlı olarak daha kısaydı (22,9±8,3 dakika vs. 27,9±9,5 dakika, p=0,001). Ameliyat sonrası ağrı skorları, 6. ve 12. saatlerde GA grubunda anlamlı olarak daha düşüktü: medyan VAS skorları 6. saatte 5,0 [çeyrekler arası aralık (ÇAA) 4,0-6,0] ve 6,0 (ÇAA 5,0-6,3) (p=0,001) ve 12. saatte sırasıyla 4,0 (ÇAA 3,0-5,0) ve 6,0 (ÇAA 4,0-6,8) (p=0,001) idi. Cerrah konfor skorları da GA grubunda anlamlı olarak daha yüksekti (p=0,001). Başarı ve komplikasyon oranları gruplar arasında anlamlı bir fark göstermedi.

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Abstract

Conclusion: Both general and RA are safe and effective for URS in distal ureteral stone management. However, GA is associated with shorter operative times, reduced postoperative pain in the early period, and improved surgeon comfort. These findings suggest that anesthetic modality may influence both clinical and surgical aspects of endourological procedures.

Keywords: Distal ureteral stones, general anesthesia, postoperative pain, regional anesthesia, ureterorenoscopy

Öz

Sonuç: Hem genel hem de RA, distal üreter taşı yönetiminde URS için güvenli ve etkilidir. Ancak, GA daha kısa ameliyat süreleri, erken dönemde postoperatif ağrının azalması ve cerrah konforunun artması ile ilişkilidir. Bu bulgular, anestezi yönteminin hem endoürolojik prosedürlerin klinik hem de cerrahi yönlerini etkileyebileceğini düşündürmektedir.

Anahtar kelimeler: Bölgesel anestezi, distal üreter taşı, genel anestezi, postoperatif ağrı, üreterorenoskopi

Introduction

Ureterorenoscopy (URS) is a well-established and widely used minimally invasive endoscopic procedure in urological practice worldwide (1). Numerous parameters related to this treatment, such as success rates and complications, have been extensively investigated; however, the relationship between the type of anesthesia administered and these outcomes has not been adequately assessed (2).

Although general anesthesia is more commonly used in URS procedures for the treatment of ureteral and renal stones, these procedures can also be performed under regional anesthesia (3). General anesthesia offers advantages over spinal anesthesia (SA) with respect to better control of procedure duration, reduced respiratory motion, and improved intraoperative patient cooperation (4). On the other hand, SA may be more advantageous because it is associated with a lower incidence of complications, such as venous thromboembolism and bleeding (5). We hypothesize that the advantages and disadvantages of each type of anesthesia may vary according to the localization of the ureteral stone. Therefore, we believe that investigating the potential benefits and drawbacks of different anesthesia modalities in relation to stone localization would provide valuable insights.

Although URS procedures for the treatment of urinary system stones have been widely studied with respect to factors such as success rates and complications, our aim in this study is to compare regional and general anesthesia specifically for distal ureteral stones. We focus on evaluating their effects on surgical success, perioperative complications, and surgical comfort.

Materials and Methods

This prospective, comparative study was conducted at a tertiary academic hospital between January 2024 and March 2025. Patients over 18 years of age who underwent URS for distal ureteral calculi were included in the study. Patients were divided by computer-assisted randomization into two groups: General anesthesia and regional anesthesia. The study was initiated after obtaining local ethical approval of University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital (approval no: 242-2023, dated: 20 December 2023) and was designed in accordance with the principles of the Declaration of Helsinki.

The sample size was calculated based on the study by Sahan et al. (6), which reported that 78 patients (39 per group) would be sufficient to detect significant differences between anesthesia types with 80% power and a 5% alpha error. Accordingly, we included 180 patients (90 per group) to enhance statistical reliability and allow subgroup analyses.

Patients with American Society of Anesthesiologists (ASA) physical status ≥III, those with multiple or bilateral stones, those with prior urinary diversion, those with active urinary tract infection or anatomical anomalies preventing retrograde access, and those who were not eligible for regional or general anesthesia were excluded.

Patient demographic data [age, gender, body mass index (BMI), ASA score, comorbidities, and stone characteristics] were recorded. Intraoperative data were recorded during the procedure. Operative time was recorded as the duration of the endourologic surgical procedure. Anesthesia administration times were not included in the operation time. Success was defined as being completely stone-free without requiring additional intervention. Perioperative complications were noted. All data were compared between the groups.

Primary Outcome

The primary outcome of this study was to compare the surgical success rates between patients undergoing URS with general anesthesia and those receiving regional anesthesia for the treatment of distal ureteral stones.

Secondary Outcomes

The secondary outcomes included operation; time; postoperative pain evaluated via visual analogue scale (VAS) at 1, 6, 12, and 24 hours; requirement for additional non-steroidal anti-inflammatory drugs (NSAIDs); hospitalization time; perioperative complications; and surgeon comfort scores rated on a standardized scale immediately after the procedure.

Anesthesia Techniques

All anesthetic procedures were performed by certified anesthesiologists with at least five years' experience. Preoperative prophylaxis included administration of 1 g of intravenous ceftriaxone 30 minutes before the procedure.

General anesthesia: Intravenous access was established using an 18-20 G cannula. Patients were preoxygenated with 100% O_2 for 4-5 minutes. Induction was achieved with fentanyl (2 µg/kg), propofol (2-3 mg/kg), and rocuronium (0.5 mg/kg). Anesthesia was maintained with 1% sevoflurane in 50% oxygen. Controlled mechanical ventilation was provided at a tidal volume of 8-10 mL/kg and a respiratory rate of 10-12 breaths/min.

Regional anesthesia: SA was performed at the L3-4 or L4-5 interspaces using a 25-26 G spinal needle. Upon confirmation of cerebrospinal fluid, 2 mL of 0.5% hyperbaric bupivacaine was injected. Sensory block was verified via pinprick test, with surgery commencing upon attainment of a T6-T8 dermatome level.

Surgical Procedure

All procedures were conducted in the lithotomy position using standardized endourological instruments. After the insertion of a hydrophilic guidewire, a 9.5-Fr semi-rigid ureteroscope was advanced to access the stone. Fragmentation was achieved using a holmium:YAG laser with energy settings tailored to stone size and location. Stone clearance was confirmed endoscopically, and a 4.8-Fr double-J stent was inserted post-procedure in all patients. Operative time was defined as the duration of the endoscopic procedure, excluding anesthesia preparation and induction times.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 27 (IBM Corp., Armonk, NY, USA) was used. The normality of the distribution of the variables was assessed using the Shapiro-Wilk test and Q-Q plots. Data showing a normal distribution were compared using the independent-samples t-test, and data not showing a normal distribution were compared using the Mann-Whitney U test. Quantitative data are shown as mean ± standard deviation or median [interquartile range (IQR)]. Discrete data were compared using the chi-square test. The data were analyzed at a 95% confidence level.

Results

Patient demographic data are summarized in Table 1. The mean age was similar between the general anesthesia group (41.8±13.5 years) and the regional anesthesia group (38.7±12.2 years, p=0.107). Gender distribution, BMI, ASA score, and the presence of comorbidities, including hypertension, diabetes mellitus, and coronary artery disease, were comparable between the groups (p>0.05 for all). Similarly, no significant differences were observed in Hounsfield units, presence of hydronephrosis, history of previous stone surgery, laterality of the affected side, or preoperative creatinine levels. The mean stone size was also similar between the two groups (12.2 mm vs. 11.5 mm, p=0.191).

Operative data revealed a significantly shorter mean operation time in the general anesthesia group than in the regional anesthesia group (22.9±8.3 vs. 27.9±9.5 minutes; p=0.001). However, no significant differences were observed between the two groups regarding hospitalization duration (median 24 hours in both groups; p=0.768), procedural success rates (95.6% vs. 91.1%, p=0.232), or overall complication rates (3.3% vs. 2.2%, p=0.650) (Table 2).

Postoperative pain assessments showed that the general anesthesia group had significantly lower VAS scores at 6 and 12 hours postoperatively compared with the regional anesthesia group. The median VAS score at 6 hours was 5.0 (IQR 4.0-6.0) in the general group and 6.0 (IQR 5.0-6.3) in the regional group (p=0.001). At 12 hours, the values were 4.0 (IQR 3.0-5.0) versus 6.0 (IQR 4.0-6.8) (p=0.001). No significant differences were noted at 1 and 24 hours. The need for additional NSAID administration was higher in the regional anesthesia group (28.9% vs. 15.5%, p=0.031). Furthermore, surgeon comfort scores were significantly higher in the general anesthesia group (8.8±2.3 vs. 6.3±1.7, p=0.001) (Table 3).

Discussion

When intervention is required for ureteral stones, the most commonly selected procedure is URS, involving lithotripsy and/or stone extraction with a basket (7). Performing URS in the distal ureter offers several technical advantages.

Table 1. Comparison of preoperative data between groups

	General anesthesia (n=90)	Regional anesthesia (n=90)	p-value
Age (years)*	41.8±13.5	38.7±12.2	0.107
Sex, n (%)			0.654
Male	47 (52.2%)	50 (55.6%)	
Female	43 (47.8%)	40 (44.4%)	
BMI (kg/m²)*	26.5±4.4	26.6±4.2	0.934
ASA score*	1.4±0.6	1.4±0.6	0.626
Comorbidities, n (%)			
Hypertension	13 (14.4%)	11 (12.2%)	0.661
Diabetes mellitus	11 (12.2%)	12 (13.3%)	0.823
Coronary artery disease	8 (8.9%)	6 (6.7%)	0.578
Stone size (mm)*	12.2±3.4	11.5±3.6	0.191
Presence of hydronephrosis, n (%)	65 (72.2%)	71 (78.9%)	0.298
Previous stone surgery, n (%)	23 (25.6%)	24 (26.7%)	0.865
Side, n (%)			0.233
Right	48 (53.3%)	40 (44.4%)	
Left	42 (46.7%)	50 (55.6%)	
Hounsfield unit**	873.0 (614.3-1100.0)	857.5 (559.5-1107.0)	0.450
Preoperative creatinine (mg/dL)**	1.0 (0.8-1.2)	0.9 (0.8-1.3)	0.938

*: Mean ± standard deviation, **: Median (IQR), BMI: Body mass index, ASA: American Society of Anesthesiologists, IQR: Interquartile range

Table 2. Comparison of operation data, success and complication rates between groups

	General anesthesia (n=90)	Regional anesthesia (n=90)	p-value
Hospitalization time (hours)**	24 (16-28)	24 (17-27)	0.768
Operation time (endoscopy) (min)*	22.9±8.3	27.9±9.5	**0.001**
Success, n (%)	86 (95.6%)	82 (91.1%)	0.232
Complications, n (%)	3 (3.3%)	2 (2.2%)	0.650

*: Mean ± standard deviation, **: Median (IQR), IQR: Interquartile range

Table 3. Comparison of postoperative VAS scores and surgeon comfort between groups

	General anesthesia (n=90)	Regional anesthesia (n=90)	p-value
Additional NSAID requirement, n (%)	14 (15.5%)	26 (28.9%)	**0.031**
VAS score**			
Postoperative 1st hour	3.0 (2.0-5.0)	4.0 (2.0-5.0)	0.384
Postoperative 6th hour	5.0 (4.0-6.0)	6.0 (5.0-6.3)	**0.001**
Postoperative 12th hour	4.0 (3.0-5.0)	6.0 (4.0-6.8)	**0.001**
Postoperative 24th hour	3.0 (2.0-4.0)	4.0 (2.0-5.0)	0.329
Surgeon comfort*	8.8±2.3	6.3±1.7	**0.001**

*: Mean ± standard deviation, **: Median (IQR), VAS: Visual analogue scale, NSAID: Non-steroidal anti-inflammatory drug, IQR: Interquartile range

These include easier and faster access compared with proximal stones and a reduced impact of respiratory movements (inspiration and expiration) on the procedure (8). Based on these factors, we hypothesize that the disadvantages associated with SA—such as reduced patient compliance, increased postoperative pain, and decreased surgeon comfort—may pose a lower risk in URS procedures targeting distal ureteral stones.

Postoperative pain is one of the factors that can prolong the length of hospital stay and negatively affect patients' quality of life (9). The type of anesthesia administered can influence the intensity of postoperative pain and the need for NSAIDs for pain relief. Çakici et al. (10) found no significant difference in postoperative pain levels between two anesthesia modalities in patients undergoing URS. In contrast, our study revealed that VAS scores at 2 hours postoperatively were significantly higher in the regional

anesthesia (RA) group, although no significant difference was observed at 24 hours. Similarly, the need for additional postoperative NSAID administration was significantly higher in the RA group than in those who received general anesthesia via a laryngeal mask airway (LMA). We attribute this to the higher incidence of colicky pain due to obstruction caused by ureteral stones, increased nociceptive signaling in obstructed ureters, and a relatively lower likelihood of obstruction in URS procedures targeting renal stones. Nonetheless, the absence of significant differences in pain levels at 24 hours postoperatively suggests that SA may be a viable alternative to LMA for URS targeting distal ureteral stones.

Postoperative pain is significantly influenced by the type of anesthesia used during URS. In our study, patients in the regional anesthesia group reported significantly higher VAS scores at 6 and 12 hours postoperatively. A possible explanation is that SA primarily provides intraoperative sensory blockade, but its analgesic effect diminishes within a few hours postoperatively. In contrast, general anesthesia—especially when combined with systemic opioids—may offer more prolonged pain control in the early postoperative period.

In endoscopic interventions for ureteral stones, the use of intraluminal energy—especially lasers—carries risks of tissue damage and suboptimal stone fragmentation due to challenges in laser targeting. These factors may prolong the procedure and, consequently, increase energy exposure time. Additionally, respiratory movements that affect the maneuverability of the URS device within the lumen can prolong operative time (11). In their study, Cai et al. (12) reported no significant difference in operative time between anesthesia types used during URS procedures. In our study, the mean operative time was significantly shorter in the general anesthesia group. This finding may be attributed to several factors. First, the use of muscle relaxants during general anesthesia ensures complete immobility, allowing for more efficient endoscopic maneuvering and laser lithotripsy. Second, controlled ventilation minimizes respiratory-induced motion artifacts, facilitating accurate targeting of stones and more rapid fragmentation. Additionally, higher surgeon comfort scores in the GA group suggest that the operative environment was more favorable, potentially leading to shorter procedure times. In contrast, during regional anesthesia, even minor voluntary or involuntary patient movements — such as coughing, muscle tension, or discomfort — may prolong the operative procedure by disrupting scope control or laser precision.

SA carries potential drawbacks that may significantly impact the surgeon's comfort, including increased sensitivity to inspiratory and expiratory movements, patient instability, and involuntary movements such as coughing or sneezing, all of which can impede optimal laser targeting (13). In a study by Sahan et al. (6) evaluating surgeon comfort during URS, general anesthesia provided significantly better conditions than SA. In contrast to their findings, our study found that surgeons' comfort was significantly higher in the SA group. We attribute this difference to the greater susceptibility of renal procedures to respiratory motion, due to the kidney's proximity to the diaphragm, and to the higher likelihood of movement triggered by coughing or sneezing. In the distal ureter, these disadvantages are markedly reduced, which may explain the improved surgical experience.

Our study is unique in that, unlike previous research comparing anesthesia types for ureteral stone surgery, it specifically focuses on the distal ureter.

Study Limitations

However, there are several limitations. First, the sample size was small and the study had a retrospective design. Pain evaluation was limited to the first 24 hours postoperatively, and no long-term assessment was conducted. Additionally, cost analysis was not included in our study.

Conclusion

In conclusion, both SA and LMA are effective and safe anesthetic techniques for URS procedures. However, our study demonstrated that the endoscopy duration was significantly shorter, and surgeon comfort was significantly better, in the SA group than in the LMA group. We recommend that these findings be further validated through large-scale, prospective, randomized controlled trials.

Ethics

Ethics Committee Approval: The study was initiated after obtaining local ethical approval of University of Health Sciences Turkey, İstanbul Haseki Training and Research Hospital (approval no: 242-2023, dated: 20 December 2023) and was designed in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: U.Ç., A.A., Ö.Ş., F.Ö., Concept: M.K., Ö.Ş., F.Ö., Design: M.K., Ö.Ş., Ö.S., Data Collection or Processing: R.Y., Ö.S., Analysis or Interpretation: U.Ç., Ö.S., Literature Search: R.Y., A.A., F.Ö., Writing: M.K., R.Y., A.A.

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CASE REPORT

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Postoperative Hepatic Inflammatory Pseudotumor in Autoimmune Pancreatitis: Hepatic Involvement of IgG4-related Disease

Hepatik Enflamatuvar Psödotümör Gelişen Opere Otoimmün Pankreatit Olgusu: IgG4 İlişkili Hastalığın Karaciğer Tutulumu

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Abstract

Autoimmune pancreatitis (AIP) is a rare subtype of chronic pancreatitis with IgG4-positive lymphoplasmacytic infiltration and storiform fibrosis, often mimicking pancreatic cancer. A 69-year-old male presented with abdominal pain, jaundice, elevation of cholestatic enzymes, and elevated CA 19-9. Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography demonstrated diffuse pancreatic enlargement, T1 hypointensity, and delayed enhancement. Malignancy could not be excluded; pancreaticoduodenectomy confirmed Type I IgG4-related AIP. Two months postoperatively, MRI detected a cystic-cavitary hepatic lesion. Infectious causes were excluded, and corticosteroid therapy for presumed hepatic inflammatory pseudotumor (IPT) achieved complete resolution. AIP may closely resemble pancreatic adenocarcinoma clinically and radiologically, particularly in focal disease. Accurate diagnosis requires integrated evaluation of MRI morphology, ductal configuration, and enhancement behavior. Although uncommon, hepatic IPT is a key extrapancreatic manifestation of IgG4-related disease and should be recognized as a benign, steroid-responsive entity to avoid unnecessary surgical intervention.

Keywords: Autoimmune pancreatitis, hepatic inflammatory pseudotumor, IgG4-related disease, pancreatic mass

Öz

Otoimmün pankreatit (OİP), kronik pankreatitin nadir bir alt tipidir. Bu olgu sunumunda, Tip I otoimmün pankreatitli bir hastada Whipple operasyonu sonrası gelişen hepatik enflamatuvar psödotümörün radyolojik ve klinik özellikleri tartışılmıştır. Altmış dokuz yaşında erkek hasta, karın ağrısı ve sarılık şikayetleri ile başvurdu. Laboratuvar testlerinde karaciğer fonksiyon testlerinde bozulma ve CA 19-9 yüksekliği saptandı. Manyetik rezonans görüntüleme (MRG) ve manyetik rezonans kolanjiyopankreatografide pankreasta difüz boyut artışı ve konturlarda düzleşme, geç fazda yoğun kontrast tutulumu izlendi. Klinik değerlendirme sonucunda Whipple prosedürü uygulandı. Patoloji Tip I IgG4 ilişkili OİP ile uyumlu bulundu. Postoperatif ikinci ayda karaciğerde kistik-kaviter lezyon gelişti. Enfeksiyon dışlandı ve hepatik enflamatuvar psödotümör (EPT) ön tanısıyla steroid tedavisi başlandı. Takip MRG incelemelerinde lezyon tamamen geriledi. OİP, klinik ve radyolojik olarak pankreatik adenokarsinomu taklit edebilir. Özellikle fokal tutulum durumlarında ayırıcı tanıda MRG bulguları, pankreatik kanal morfolojisi ve kontrast tutulum paternlerinin dikkatle değerlendirilmesi gereklidir. Hepatik EPT, nadir olmakla birlikte, IgG4 ilişkili hastalık spektrumunda düşünülmelidir.

Anahtar kelimeler: Hepatik enflamatuvar psödotümör, IgG4 ilişkili hastalık, otoimmün pankreatit, pankreatik kitle

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Introduction

Autoimmune pancreatitis (AIP) is a rare subtype of chronic pancreatitis classified into two distinct types (1). Type I is more frequently observed in men and is associated with IgG4 and with antinuclear, anti-smooth muscle, anti-lactoferrin, and anti-carbonic anhydrase antibodies (2). Extrapancreatic inflammatory findings and the coexistence of other autoimmune diseases are commonly encountered in Type I AIP. This entity is defined as IgG4-related systemic disease. Type II, however, is not associated with specific autoantibodies or extrapancreatic manifestations. Serum IgG4 levels above 135 mg/dL are useful in differentiating AIP pancreatitis from other pancreatic disorders; however, such elevation may also occur in pancreatic carcinoma and chronic pancreatitis (2).

AIP may coexist with other autoimmune diseases, such as ulcerative colitis or autoimmune hepatitis. Radiological findings of AIP may include a focal mass, a normal-sized pancreas, or diffuse, uniform enlargement with loss of lobulated contours (3). Mild localized lymphadenopathy is frequently observed, most commonly involving the pancreatic head. In pancreatic carcinoma, abrupt ductal narrowing with distal smooth dilatation may help differentiate the two entities (4). Diagnostic criteria for AIP have been developed, incorporating radiological, laboratory, and histopathological assessments (5-7). Within the spectrum of IgG4-related AIP, hepatic inflammatory pseudotumor (IPT) subtypes characterized by fibrohistocytic and lymphoplasmacytic inflammation have also been described (6). This case report aims to highlight the radiological diagnosis of AIP and present a case of hepatic IPT that developed after Whipple surgery.

Case Report

A 69-year-old male presented to the general surgery outpatient clinic with abdominal pain. On physical examination, a midline surgical scar was present, but no palpable mass was detected. The sclerae were icteric. Laboratory analysis revealed elevated aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, and alkaline phosphatase levels; mildly increased CA 19-9; direct hyperbilirubinemia; and elevated C-reactive protein.

Upper abdominal magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) demonstrated a hydropic gallbladder and diffuse dilatation of the intrahepatic bile ducts. The common hepatic duct and proximal common bile duct measured up to 17 mm in diameter, with an abrupt narrowing of the intrahepatic portion of the common bile duct (Figure 1d). On contrast-enhanced MRI, the pancreas appeared diffusely enlarged with smooth contours, hypointense on T1-weighted images, and encapsulated. Diffusion restriction and intense delayed-phase enhancement were also observed (Figures 1a, 1b, 1c). These findings were highly suggestive of AIP; however, malignancy could not be excluded, and the patient underwent a Whipple procedure. Pathological examination confirmed Type I IgG4-related AIP.

Follow-up and Treatment Response

On follow-up MRI at two months, a cystic-cavitary lesion with peripheral enhancement was observed in hepatic segment 4b, raising suspicion for hepatic IPT. Infectious markers were negative, and corticosteroid therapy was initiated (Figure 2). At three months, the lesion appeared more solid and slightly enlarged, prompting an adjustment to the steroid regimen (Figure 3).

By eight months, MRI demonstrated complete resolution of the hepatic lesion, confirming a favorable response to corticosteroid therapy and supporting the diagnosis of hepatic IPT.

Discussion

Type I AIP is widely recognized as the pancreatic manifestation of IgG4-related disease. In contrast, Type II is characterized by unique histopathological and clinical features and typically lacks elevated serum IgG4 levels or associated autoantibodies (2). The IgG4-associated form of AIP is defined by dense periductal infiltration of IgG4-positive plasma cells accompanied by fibrosis. Imaging or clinical evaluation may reveal either diffuse or localized pancreatic enlargement with irregular ductal narrowing. Progressive acinar atrophy and fibrosis lead to the loss of normal lobular architecture (2,8).

IgG4-related AIP occurs in approximately 2-8% of patients with chronic pancreatitis (3). It predominantly affects middle-aged and elderly men, with a male-to-female ratio of 3-7:1 (3). Although patients with AIP do not present with specific symptoms, some may experience abdominal pain, obstructive jaundice, weight loss, new-onset diabetes, pancreatic enlargement, or, rarely, extrapancreatic lesions (3). MRI plays a critical role in diagnosis. In cases of diffuse involvement, homogeneous enlargement of the entire

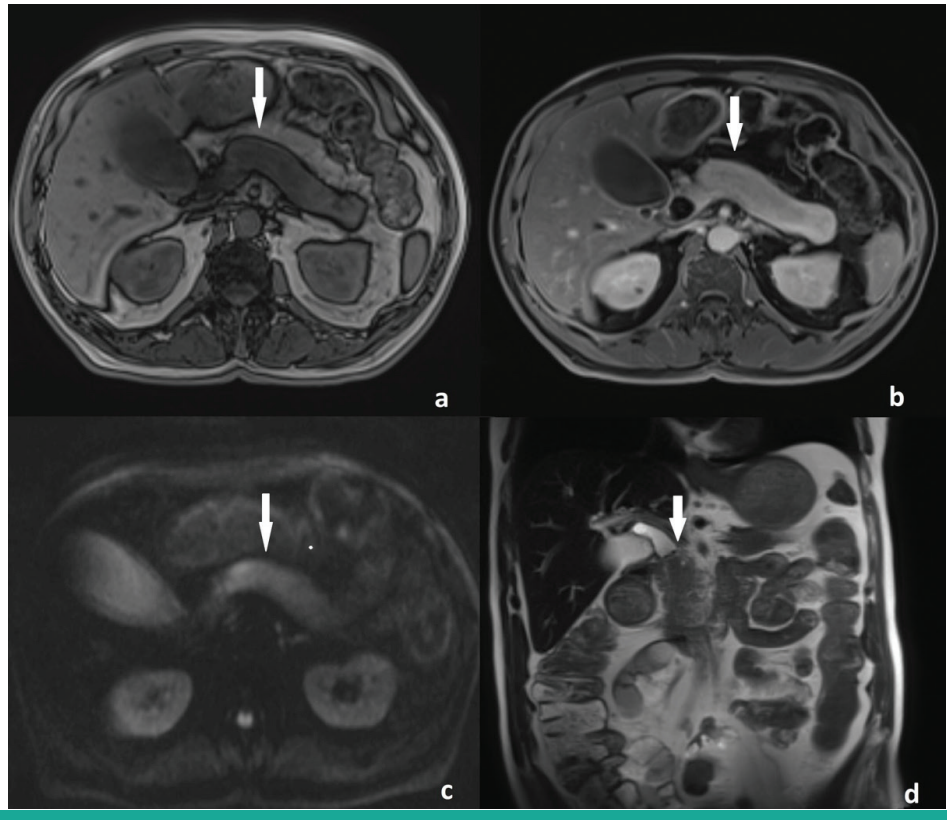

Figure 1. Axial T1 out of phase image (1a) demonstrates diffuse enlargement of the pancreas with smooth contours and decreased T1 signal intensity (arrow). Post-contrast axial T1-weighted image (1b) shows homogeneous enhancement of the pancreas (arrow). The axial diffusion-weighted image (b=1500 s/mm^2) (1c) reveals a uniform diffusion hyperintensity consistent with inflammatory activity (arrow). Coronal T2-weighted image (1d) demonstrates upstream dilatation of the common bile duct proximal to its intrapancreatic segment (arrow)

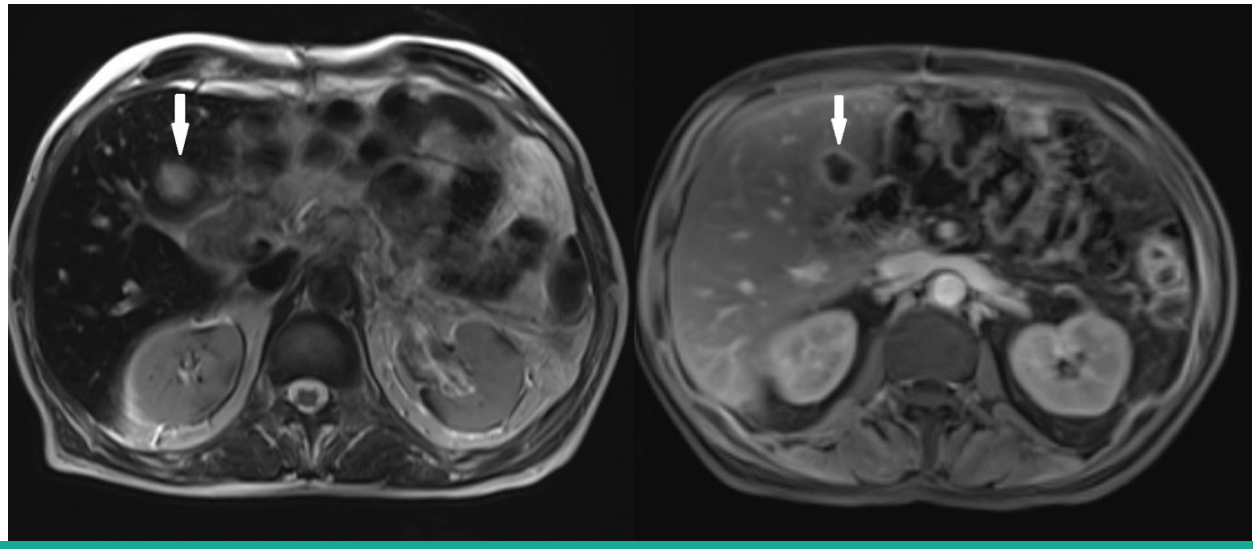

Figure 2. Contrast-enhanced MRI obtained two months after surgery. Axial T2-weighted image (left) shows a thick-walled, cystic, cavitary lesion in hepatic segment 4B (arrow). Axial post-contrast T1-weighted image (right) demonstrates peripheral wall enhancement with a non-enhancing cystic center (arrow). No diffusion restriction was observed (not shown), a finding consistent with hepatic inflammatory pseudotumor

MRI: Magnetic resonance imaging

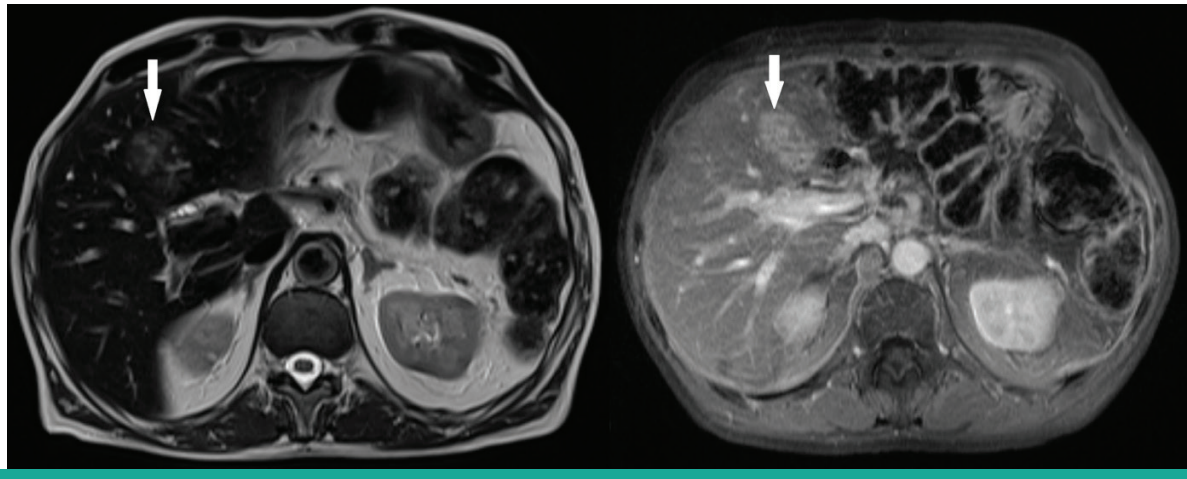

Figure 3. On the follow-up MRI obtained three months after surgery. Axial T2-weighted image (left) demonstrates that the cystic component of the lesion has transformed into a solid component (arrow). On axial post-contrast T1-weighted images (right), the lesion shows diffuse, homogeneous enhancement, confirming its solid nature (arrow)

MRI: Magnetic resonance imaging

gland is observed, with decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted sequences. On contrast-enhanced MRI, the delayed phase shows striking, homogeneous, intense enhancement. Together with findings such as "diffuse enlargement" and a "capsule-like rim", this appearance strongly supports the diagnosis of AIP (6). With focal involvement, a mass-like lesion is observed in a limited portion of the pancreas, most commonly in the pancreatic head. This appearance may mimic pancreatic adenocarcinoma, particularly if associated with target-like peripheral enhancement. AIP lesions typically demonstrate more homogeneous and more delayed enhancement than adenocarcinoma. The Desmoplastic reaction is less pronounced. Furthermore, MRCP may reveal multiple sequential ductal narrowings and dilatations or the so-called "penetrating duct sign", in which the duct continues through the lesion, gradually tapering. These findings suggest an inflammatory process and help differentiate it from malignancy (6-8). In AIP, the main pancreatic duct typically appears long, irregular, and narrowed, whereas in adenocarcinoma, the narrowing is usually abrupt, short, and accompanied by marked distal dilatation. Therefore, the presence of a focal mass is not a direct indicator of malignancy; rather, signal characteristics, ductal morphology, and enhancement patterns must be assessed together (6-8).

The diagnosis of AIP remains challenging, as a subset of cases closely mimics pancreatic adenocarcinoma. Approximately 3-9% of patients undergoing resection for suspected carcinoma are ultimately diagnosed with AIP (4). Various diagnostic criteria have been proposed internationally. The Japanese Pancreas Society first introduced diagnostic criteria including imaging findings, serology (elevated IgG4), and characteristic histopathological features (5). Subsequently, additional diagnostic parameters were proposed (7). In 2011, the International Association of Pancreatology published the International Consensus Diagnostic Criteria for Type I AIP, which defined five key features: Pancreatic imaging (parenchymal and ductal), serology (IgG4), histopathology and immunostaining, involvement of other organs, and response to steroid therapy (5,7,8).

Differentiating hepatic IPT from metastasis or abscess can be challenging due to overlapping imaging characteristics. Nevertheless, certain radiological and clinical clues may assist in making the distinction. IPTs are typically solitary lesions with delayed homogeneous enhancement and mild diffusion restriction, corresponding to their fibroinflammatory histology. In contrast, hepatic abscesses commonly demonstrate central diffusion restriction with peripheral rim enhancement and are usually accompanied by fever and marked leukocytosis. Metastatic lesions are often multiple, show heterogeneous enhancement with surrounding edema, and frequently exhibit early arterial enhancement followed by washout in delayed phases (9).

Although hepatic involvement in Type I AIP is rare, hepatic IPTs may present as an important extrapancreatic manifestation. Limited case series have described histological features of dense IgG4-positive plasma cell

infiltration, fibroinflammation, and obliterative phlebitis. These lesions frequently mimic malignancy; however, their rapid response to corticosteroid therapy confirms the diagnosis. For instance, Kamisawa et al. (10) reported two cases in which both AIP and hepatic pseudotumor responded to steroids. These findings suggest that hepatic inflammatory lesions represent a benign, treatment-responsive entity within the systemic spectrum of IgG4-related AIP.

Conclusion

This case represents a pathologically confirmed case of Type I AIP, consistent with the literature in terms of age, sex, laboratory findings, and radiological findings. The hepatic lesion that subsequently developed was diagnosed as an IPT, a rare manifestation. Cross-sectional imaging not only plays a pivotal role in diagnosing pancreatic involvement but also enables early detection of multi-organ manifestations, such as hepatic IPT.

Ethics

Informed Consent: Informed consent was obtained from the patient for sharing the clinical and radiological findings included in this case report. The patient understood that all data presented would be anonymized and that no personally identifiable information would be disclosed. Written consent was documented and archived in accordance with institutional and ethical guidelines.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.U., A.A.K., Concept: A.U., Design: A.U., Data Collection or Processing: A.U., A.A.K., Analysis or Interpretation: A.U., A.A.K., Literature Search: A.U., A.A.K., Writing: A.U.

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