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Ablation therapies for thyroid nodules and parathyroid adenomas: What we should know?

Tumay Bekci¹ 
Uluhan Eryuruk¹ 

1. Giresun University, Faculty of Medicine,
Department of Radiology, Giresun, Turkey

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Corresponding Author: Uluhan Eryuruk,
MD., Giresun University, Faculty of Medicine,
Department of Radiology, Giresun, Turkey

Email: uluhaneryuruk@gmail.com

Abstract

Thyroid nodules and parathyroid adenomas are common endocrine disorders that can lead to significant clinical symptoms and necessitate intervention. Traditionally, surgical resection has been the primary treatment for symptomatic or malignant thyroid nodules and parathyroid adenomas. However, surgery carries risks such as hypothyroidism, nerve damage and postoperative complications and may not be suitable for patients, especially those with comorbidities. Recently, non-surgical, image-guided ablation therapies, including ethanol ablation (EA), radiofrequency ablation (RFA), and microwave ablation (MWA), have emerged as viable alternatives for managing benign symptomatic thyroid nodules and parathyroid adenomas. This review highlights the indications, techniques, and outcomes associated with these ablative therapies. While the use of thermal ablation in managing thyroid nodules is well-supported by various guidelines, its application in parathyroid adenomas remains exploratory. The safety and efficacy profiles of these minimally invasive treatments make them promising alternatives to surgery, especially for patients who are high-risk surgical candidates or prefer non-surgical options.

Key words: Thermal ablation; thyroid nodules; parathyroid adenomas; microwave ablation; radiofrequency ablation

Introduction

Thyroid nodules are frequently encountered, appearing in 19%-35% of thyroid ultrasonography (US) studies and 8%-65% of autopsy studies [1]. Despite a significant rise in the incidence of thyroid malignancies over recent decades, the mortality rates for clinically significant thyroid cancers have remained stable for the past 80 years [2]. Consequently, the management of thyroid nodules has become a subject of considerable debate, with guidelines evolving over time. The classification of nodules for specific treatment protocols involves clinical examination, biochemical tests, imaging studies, and cytologic evaluation.

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Traditionally, surgery has been the primary treatment for thyroid nodules with malignant or suspicious cytologic diagnoses or autonomic function. However, there are patients with benign thyroid nodules that may enlarge, causing local pressure symptoms, such as neck pain, choking sensation, dyspnea, or dysphagia. A recent multicenter observational study indicated that up to 15% of benign nodules grow rapidly and continuously, whereas others remain relatively unchanged in size [3]. Historically, surgical resection has been recommended for the treatment of symptomatic benign thyroid nodules. The American Thyroid Association (ATA) guidelines suggest that surgical resection (hemithyroidectomy or total thyroidectomy) when a benign solid or predominantly solid nodule increases in size (>4 cm in diameter) causes local compressive symptoms or raises clinical concerns [4]. Although surgery is generally safe, it carries risks including hypothyroidism, bleeding, infection, hoarseness due to recurrent or superior laryngeal nerve injury, and postoperative hypoparathyroidism. Additionally, surgery poses risks related to general anesthesia and may not be suitable for individuals with underlying medical conditions [5]. Surgery is also the standard treatment for parathyroid adenomas; however, it carries postoperative morbidity and mortality risks, particularly in elderly and chronically ill patients. Furthermore, some patients with symptomatic hyperparathyroidism or symptomatic non-functioning parathyroid cysts either refuse surgery or are unsuitable candidates [6,7].

Non-surgical, image-guided procedures such as ethanol ablation (EA) and thermal ablations have been proposed as less invasive alternatives for managing benign symptomatic thyroid nodules and, to a limited extent, malignant nodules and parathyroid adenomas.

Ethanol Ablation

Ethanol ablation is a commonly used nonsurgical treatment for benign thyroid nodules that are either purely cystic or predominantly cystic (with a cystic portion greater than 50%). In recent years, EA has also been used for the treatment of recurrent thyroid cancer. When dealing with the local recurrence of thyroid cancer, surgery is generally considered the first-line treatment if imaging techniques confirm the recurrence site. However, reoperation can be technically challenging if previous surgeries disrupt the normal tissue plane, leading to fibrosis and scarring in the recurrent cancer area. Surgical complications were also possible.

External radiotherapy (RT) may be considered for

locoregional recurrences that cannot be surgically resected, or in cases with extranodal extension or soft tissue involvement, especially in patients without distant metastases [8]. However, RT can increase morbidity due to potential complications. Therefore, alternative procedures, such as image-guided EA or thermal ablation, have been suggested for patients concerned about RT complications, those who refuse RT, those at risk of serious complications from surgery, or those at high risk for surgery [9,10].

Indications

Cystic or predominantly cystic benign nodules

Ethanol ablation (EA) is recommended for the treatment of benign recurrent pure cysts or predominantly cystic nodules that lead to compression symptoms or neck swelling. EA can achieve a volume reduction of 85-95% in purely cystic nodules and 60-90% in predominantly cystic nodules [11,12]. The results were satisfactory for nodules with less than 20% solid components [13]. The first-line treatment for symptomatic benign pure cysts and predominantly cystic nodules is simple aspiration, although it is associated with a high recurrence rate. Therefore, EA is a reasonable approach for treating patients with recurrent cystic fluid accumulation after aspiration.

A cytological result from simple aspiration can confirm that a pure cystic or predominantly cystic nodule is benign, although cytological results in pure cysts are often non-diagnostic even with repeated examinations. For predominantly cystic nodules with benign ultrasound findings, such as a spongiform appearance or intracyst comet artifacts, EA can be performed after at least one benign fine-needle aspiration (FNA) result. For other predominantly cystic nodules with a solid component, at least two benign FNA results are required before EA is performed. The recurrence rate of thyroid cysts has decreased to less than 20% after EA [12].

Hyperfunctioning thyroid nodules

Ethanol ablation is an alternative to surgery and radioiodine for the treatment of hyperfunctioning nodules [14-17]. It has been reported that nodule size decreases, and hyperthyroidism improves post-EA treatment. However, the therapeutic effect diminishes as nodule size increases [17]. EA is most effective for hyperfunctioning solitary thyroid nodules with a volume of less than 30 mL [14-17]. When ethanol is used for cystic nodules, it remains in the cystic cavity,

resulting in low complication rates. However, injecting ethanol into solid nodules can be challenging because of leakage, which leads to unwanted complications. Additionally, the uneven distribution of ethanol in the nodules necessitates more treatment sessions than thermal ablation for nodules of the same size. Therefore, the use of EA is limited to large solid nodules.

Recurrent thyroid carcinoma

Surgery is the primary treatment for locally recurrent thyroid carcinoma, followed by radioactive iodine and/or thyroid hormone therapy. Minimally invasive treatments, such as RFA or EA, can be alternatives if surgery poses significant difficulty or severe side effects. Percutaneous EA is less invasive than surgery that requires general anesthesia, and repeated procedures are easy and safe, minimizing the risk of complications. While studies on EA's efficacy of EA in treating recurrent thyroid carcinoma are limited, it shows lesser efficacy in the complete disappearance of recurrent nodules and has a relatively higher recurrence rate than RFA [18]. Thus, EA may be recommended for complete ablation in patients with up to three locally recurrent nodules without distant metastases, or for palliative purposes in patients with known distant metastases and growing recurrent tumors.

Symptomatic parathyroid cysts

Simple aspiration was initially used to diagnose and treat symptomatic nonfunctioning parathyroid cysts, although recurrence was reported in 66.7% of cases, necessitating additional treatment. EA can be performed as a subsequent treatment modality for recurrent cases [6].

Standard procedure

It is essential to accurately characterize thyroid nodules and evaluate the surrounding critical anatomical structures using a pre-procedural US examination. The size, proportion, and vascularity of the solid component as well as the internal contents of the cystic component should be carefully assessed using US. Before proceeding, the patient received a thorough explanation of the procedure and provided informed consent, which included potential adverse events (such as pain or voice changes indicative of nerve damage from leakage).

The procedures are typically performed on an outpatient basis. The required materials include a 16-20 gauge needle, a 10-25 mL syringe, and 95-99% ethanol. While some variations exist depending on the operator, the

general method is as follows: the patient is positioned supine with slight neck extension. After sterilization of the skin, a local anesthetic (1-2% lidocaine) is injected into the puncture site. Depending on the viscosity of the cyst's contents, a single 16-20 gauge needle is inserted into the center of the cystic area under US guidance. A transisthmus approach is recommended to prevent needle movement and ethanol leakage when the patient swallows or speaks. Maximum aspiration is performed, and residual debris or colloids are removed via saline irrigation. The operator then slowly injects the appropriate amount of 95-99% ethanol into the cystic cavity, typically around 50% of the aspirated volume. Empirically, the total ethanol volume should not exceed 10 mL, even for large nodules, although more can be used if the ethanol will be removed post-procedure.

There is no definitive consensus regarding the total amount of ethanol required for injection. The exact amount should be based on the lesion size and internal content, the operator's judgment during the procedure, and patient compliance. Kim et al. [19] found a 2-minute ethanol retention time was sufficient due to the rapid cellular reaction of ethanol. However, there is no agreement on whether ethanol should be reaspirated after the procedure. Some studies suggest short ethanol retention times (at least 2 min) and complete removal to minimize patient discomfort and complications from potential ethanol leakage. Kim et al. [20] reported no difference in complications or success between groups in which ethanol was or was not aspirated after injection. Therefore, the choice of ethanol injection, with or without aspiration, depends on the operator's preference.

If the patient experienced pain during the injection, the operator should stop and check for perithyroidal leakage. Proper needle placement in the center of the lesion and avoiding excessive ethanol injection reduce the risk of leakage. If excessive ethanol is used, reaspirating can help alleviate pain. Upon completion of the procedure, the needle was swiftly withdrawn and light compression was applied to the puncture site for 5-10 minutes.

Complications

Ethanol ablation is a safe treatment option for cystic thyroid nodules, with most complications being mild and transient when performed by someone experienced in US-guided procedures. The most common complication is localized pain at the puncture site, but other potential issues include hematoma, facial flushing, feeling of intoxication, hoarseness, dyspnea, and transient

hyperthyroidism. Most patients experience mild pain immediately after the procedure, which can last a few minutes to several hours. This pain often resolves on its own and can be managed with analgesics. Hematoma, a common complication that can cause pain, can be prevented by applying compression to the puncture site for 10 minutes after the procedure.

Radiofrequency and microwave ablation

Radiofrequency ablation (RFA) generates heat through an electric current passing through a focal impedance circuit, causing cell death in the target tissues. Initially used for chronic neurogenic pain, RFA has been expanded to treat conditions such as cardiac ablation, renal sympathetic denervation, and varicose veins.

Heat generation via an electric current, known as the Joule effect, occurs because of frictional forces at the ionic level. Tissue impedance increases with a higher current magnitude and longer duration of flow, leading to coagulation necrosis, and irreversible cell damage starts at temperatures above 46°C for one hour, although this varies by tissue type [21]. Temperatures exceeding 100°C can cause tissue to boil, vaporize and carbonize, limiting heat conduction [22]. RFA for thyroid nodules typically employs 18-gauge needles measuring 7-10 cm with a 5-15 mm active tip, creating a cylindrical ablation zone approximately 2 cm in diameter.

Microwave ablation (MWA) is promising but lacks robust evidence. Studies have reported volume

reductions of 74.6%-90.0% after one year, with MWA potentially carrying higher complication risks due to less energy control and larger applicator diameters than RFA [23,24]. Despite advantages such as greater energy output, larger ablation fields, and shorter treatment times, MWA's broader tumor inactivation and efficacy of MWA in larger nodules are notable. However, meta-analyses, such as that by Qian et al., showed no significant difference in volume reduction between MWA and RFA six months post-operation, with MWA associated with higher major complication rates compared to RFA [25].

Indications

Thermal ablation, including techniques such as RFA, has been addressed by various national and international guidelines for managing both benign and malignant thyroid nodules. While the ATA briefly mentions thermal ablation in its 2015 guidelines, more specific recommendations come from organizations such as the Korean Society of Thyroid Radiology (KSThR), European Thyroid Association (ETA), and European Society of Cardiovascular and Interventional Radiology (CIRSE) (26-29).

For benign symptomatic thyroid nodules, all referenced guidelines suggest considering RFA when the nodules cause compression symptoms or cosmetic concerns. Symptoms such as dysphagia, dyspnea, neck pressure, foreign-body sensation, pain, and cough indicate a potential need for treatment. The KSThR emphasizes that while nodule size matters, location is critical;

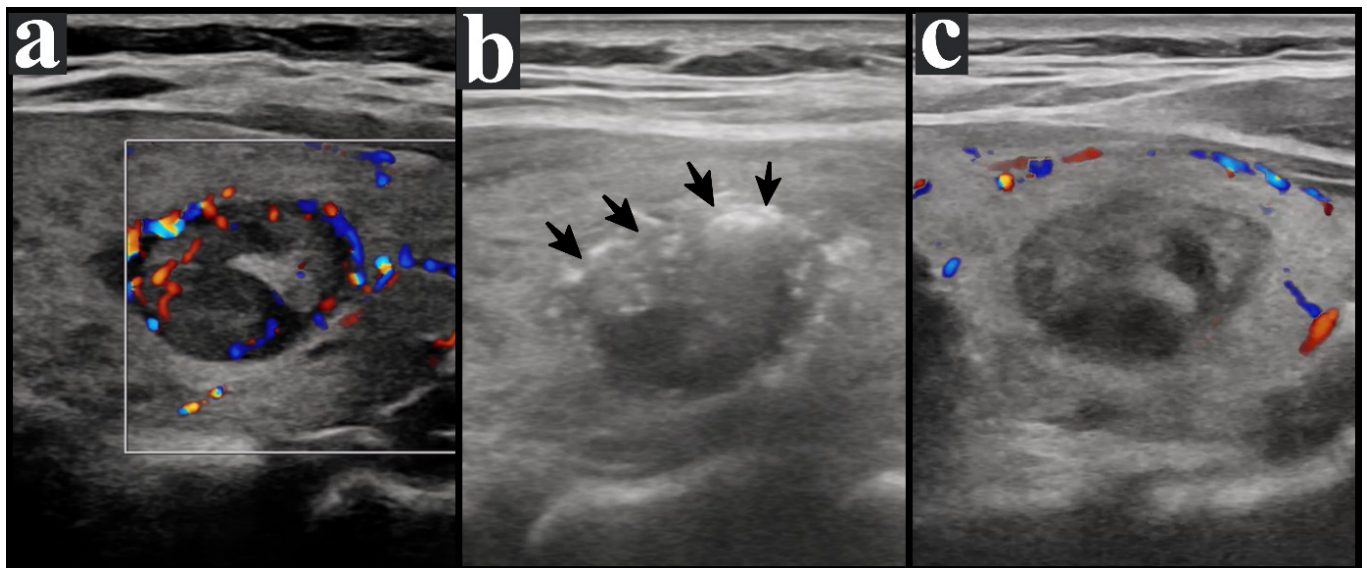


Figure 1. A 48-year-old woman with intrathyroidal parathyroid adenoma in the left thyroid lobe was confirmed by scintigraphy and fine-needle aspiration parathyroid hormone washout test. Figure A shows the internal vascularization of the parathyroid adenoma on preprocedural Doppler ultrasonography. Figure B shows immediate changes, such as echogenic gas bubbles (arrows), and Figure C shows the absence of internal vascularization of the parathyroid adenoma on postprocedure Doppler ultrasonography.

nodules in the isthmus can cause symptoms or cosmetic issues, even if they are smaller than 2 cm [26].

Regarding hyperfunctioning thyroid nodules, the guidelines generally recommend RFA in specific circumstances where surgery or radioactive iodine (RAI) poses risks, such as in patients at risk of prolonged hypothyroidism post-RAI or surgery. Guidelines from the KSThR and CIRSE caution against treating larger or multifocal autonomous nodules with RFA, suggesting RFA as an adjunct in younger patients.

For malignant nodules, the guidelines are less standardized owing to the limited evidence. Thermal ablation may be considered an alternative in patients who refuse or cannot tolerate surgery or in palliative care scenarios for advanced malignancies, as suggested by the KSThR guidelines [26]. ETA and CIRSE recommend minimally invasive techniques based on patient demographics, tumor characteristics, and local technical capabilities [28].

RFA is considered an alternative treatment for recurrent thyroid malignancies when surgery or RAI is contraindicated owing to factors such as previous surgeries or poor general health. This approach is supported by the ATA, ETA, CIRSE, and KSThR guidelines for high-risk surgical patients and those who refuse surgery.

Regarding parathyroid adenomas, while minimally invasive thermal therapies have been proposed as alternatives to surgery (**figure1**), there are currently no guideline recommendations or sufficient data on their efficacy and safety (30).

Standard technique

Thermal ablation procedures, whether using RFA or MWA, are typically conducted as outpatient visits or short hospital stays. These procedures are performed by specialized interventional radiologists skilled in thermal ablation techniques. A detailed overview of the process is as follows.

Thermal ablation involves positioning the patient in a supine position, with the neck extended for optimal access. Sedation levels vary, with local anesthesia often recommended by the KSThR, supplemented by liberal lidocaine injections into the thyroid capsule and nearby subcutaneous tissues, to minimize discomfort [26].

The equipment used includes 18-gauge electrodes for RFA, ranging from 7 to 10 cm with active tips of 5 to 15 mm, selected based on nodule size. MWA utilizes 16-18 G probes tailored to the specific characteristics of the target nodule. Confirmation of the target lesion is done via US, followed by an in-plane oblique approach to enter the thyroid gland and reach the nodule. This

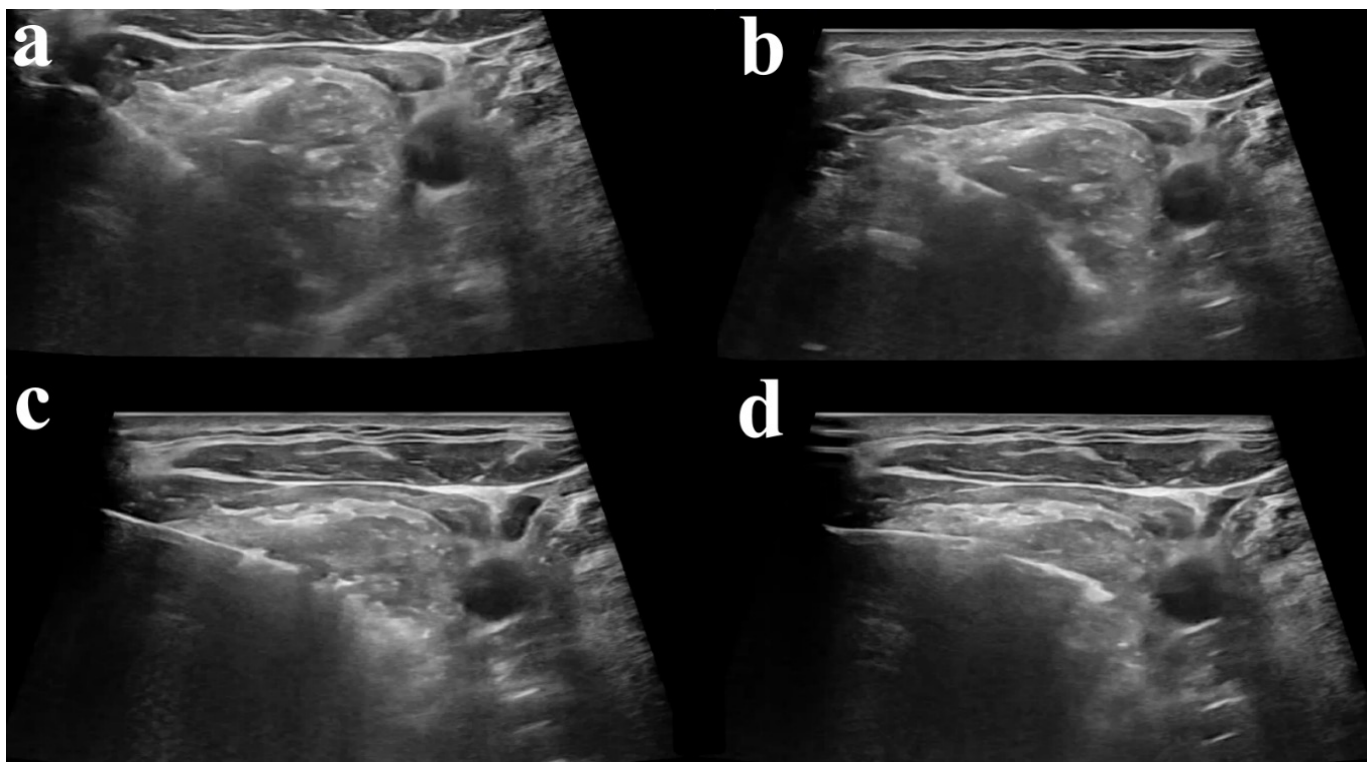


Figure 2. Moving shot technique. The electrode is left in the area until it is surrounded by a transient hyperechoic zone, which is then moved along the nodule from deep to the surface to the next subunit (a-d), and the procedure is repeated until the entire nodule is ablated.

approach ensures real-time confirmation of electrode placement and minimizes the risk of skin burns by increasing the distance between the active tip and skin surface. A transisthmic approach is often preferred to maintain electrode stability and prevent fluid leakage into the surrounding tissues, especially for nodules in the middle and lower thyroid regions.

The moving-shot technique is commonly employed during this procedure. This technique involves keeping the electrode in place until it is surrounded by a transient hyperechoic zone and then moving to the next position before the impedance rises sharply (**figure 2**). This ensures thorough nodule ablation while minimizing damage to the adjacent tissues. Care is taken to avoid ablating the outermost layer of benign nodules to prevent harm to nearby structures. In cases of malignancy, efforts are made to ablate the entire nodule.

Power settings typically range from 20 to 50 W and are adjusted based on the sonographic changes observed during the procedure. Continuous US monitoring of the electrode tip ensures effective ablation and prevents complications. Hydrodissection with a 5% dextrose solution is used when nodules are near critical structures, such as the skin surface, cervical muscle groups, carotid artery, or recurrent laryngeal nerve (danger triangle). This technique creates a barrier against thermal energy and minimizes the risk of injury to the adjacent structures (**figure 3**). Immediate sonographic changes, such as echogenic gas bubbles and increased impedance, confirm the effectiveness of ablation [26]. Postprocedural follow-up includes serial US examinations at 1, 6, and 12 months to assess nodule volume reduction and monitor any residual viable tissue.

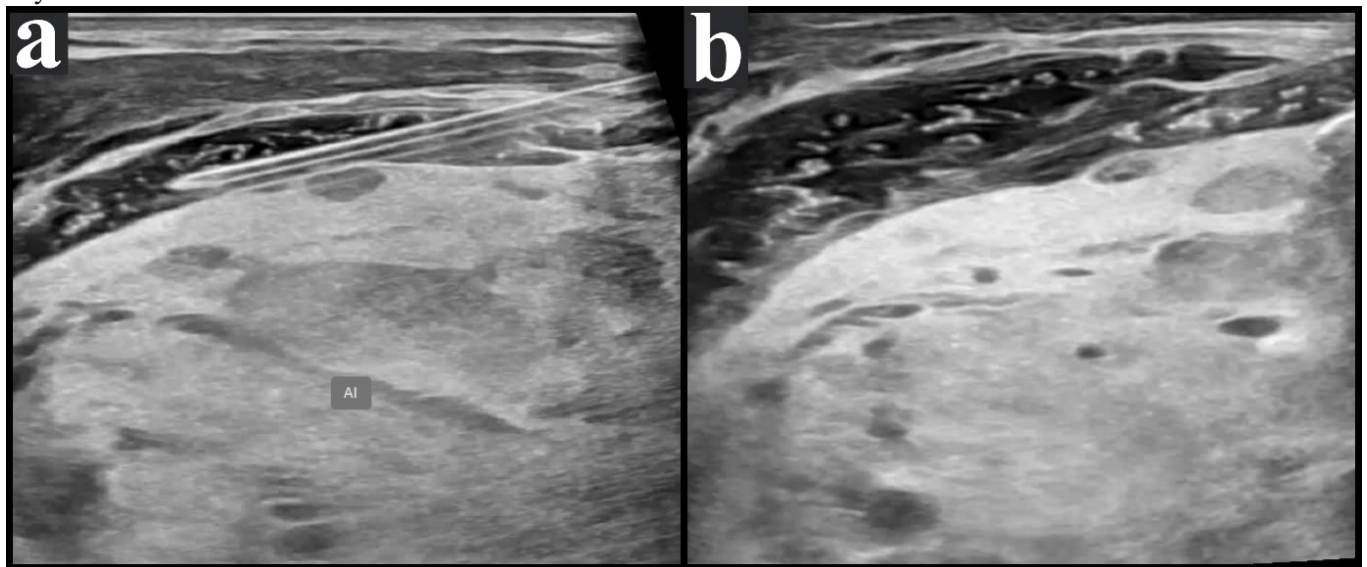


Figure 3. Hydrodissection. Placement of the fine needle outside the thyroid capsule (a) and injection of 5% glucose solution between the capsule and adjacent structures until successful hydrodissection is achieved (b).

Complications

Radiofrequency and microwave ablation are generally safe and well-tolerated procedures for the treatment of thyroid nodules. A meta-analysis of 24 studies and 2421 patients who underwent RFA revealed an overall complication rate of 2.4%, with major complications occurring in 1.4% of the cases [31]. In another study, MWA reported an overall complication rate of 11.5%, with major complications at 5.1% [32]. Both techniques showed comparable outcomes in terms of anesthesia and pain management.

Voice change is the most frequent major complication associated with RFA, occurring in approximately 1.5% of cases, with permanent changes observed in 0.2% of the patients [31]. This complication is attributed to direct thermal injury or laryngeal nerve irritation due to swelling or hematomas. Techniques such as hydrodissection, the moving-shot technique, and the trans-isthmic approach have proven effective in mitigating these risks [26].

Nodule rupture is another major complication of RFA, although rare, occurring in only 0.2% of the cases [31]. It typically results from acute swelling of the nodule due to edema or hemorrhage, leading to capsule rupture and spillage of the nodule contents into the surrounding tissues. Management usually involves conservative measures [33].

Conclusion

Minimally invasive ablative treatments, such as thermal ablation, offer effective and safe alternatives to surgery for the management of both thyroid nodules and parathyroid adenomas. Thermal ablation is particularly effective in

treating benign thyroid nodules, including toxic nodules. There is also a growing interest in its potential application in small primary papillary thyroid cancers, supported by promising outcomes from recent studies. Ethanol ablation and thermal ablation represent significant advancements in providing a more personalized approach to patient care. By carefully selecting suitable candidates, these treatments can achieve therapeutic responses in thyroid nodules and parathyroid adenomas while minimizing the complications and risks associated with surgical interventions.

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Declaration competing interest

The authors declare that they have no competing of interest.

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Anatomical variation of aortic arch branching patterns: An evaluation using digital subtraction angiography

Mustafa Demir¹ 
Suayip Aslan² 

1. University of Health Sciences, Ümraniye Training and Research Hospital, Department of Radiology, Istanbul, TURKEY

2. University of Health Sciences, Sancaktepe Şehit Prof.Dr. İlhan Varank Training and Research Hospital, Department of Radiology, Istanbul, TURKEY

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Corresponding Author: : Mustafa DEMİR,
Ümraniye Eğitim ve Araştırma Hastanesi
Radyoloji Kliniği, Kazım Karabekir mah,
Adem Yavuz Cd F No:10, 34899 Ümraniye/
İstanbul, TURKEY

Email: drmfstfdr1@gmail.com

Abstract

Objective: Anatomical variations in the aortic arch branching pattern are crucial for planning surgical and endovascular procedures. These variations, often detected incidentally during radiological studies, can influence the approach and success rate of interventions. This study explores to retrospectively analyze the variations in the aortic arch branching patterns using digital subtraction angiography [DSA] and compare the findings with existing literature.

Methods: A retrospective analysis was conducted on 221 patients who underwent aortic arch angiography with DSA for neurovascular pathologies at the University of Ümraniye Education and Research Hospital from January 2020 to November 2022. Patients with previous thoracic-vascular surgery were excluded. The aortic arch findings were categorized according to established classifications.

Results: Six distinct aortic arch branching patterns were identified among the 221 patients. The most common type was the normal or classical form [Type 1] found in 78.3% of the patients. Type 2, where the left common carotid artery originates from the brachiocephalic trunk, was observed in 19.9% of the cases. Type 3, characterized by the left vertebral artery originating directly from the aortic arch, was seen in 0.9% of the patients. Other types, including right aortic arch with aberrant right subclavian artery, were less common.

Type 3 variations were more prevalent among females, while other variations showed no significant gender difference.

Conclusion: Variations in the aortic arch branching patterns are common and generally asymptomatic but have significant implications for surgical and interventional procedures. Recognizing these variations is essential for improving procedural success rates and reducing complications in neurovascular interventions.

Keywords: Aortic arch; branching pattern; digital subtraction angiography; anatomical variations; neurovascular interventions

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Introduction

Variations of the aortic arch are categorized according to the output localization and number of vascular structures that originate from the aortic arch. Most prevalent in society are the brachiocephalic trunkus, left main carotid artery, and subclavian artery, from right to left [1].

Depending on chromosomal abnormalities migration and fusion defects, can alter the number and configuration of vascular structures originating from the aortic arch [1,2,3]. Usually asymptomatic and detected incidentally during radiological studies, these variations

gain significance prior to surgical and endovascular interventional procedures. In this study, we retrospectively analyzed the arcus aortographies performed with conventional angiography during diagnostic and therapeutic neurovascular interventions, comparing our results with those from the literature and assessing the association between arch aortic types and neurovascular pathologies.

Methods

Patient selection

The patients who arcus aortography examinations performed with digital subtraction angiography [DSA] for diagnosis or treatment of neurovascular pathologies at the interventional radiology department of the University of Ümraniye Education and Research Hospital between January 2020 and November 2022 were included in this study. Demographical-medical data and the DSA images of the patients were reviewed on the hospital database.

The patients with a previous thoracic-vascular surgery were excluded from this study.

Due to the retrospective nature of the investigation, it was not possible to get formal informed permission from the patients.

DSA technique and image analysis

5 French pig tail catheter was placed in the ascending aorta to obtain an arch aortography. The study included a total of 221 patients. All patients' aortic arch findings were categorized from one to eight according to with the classifications established by the literature (Figure 1) [2,3].

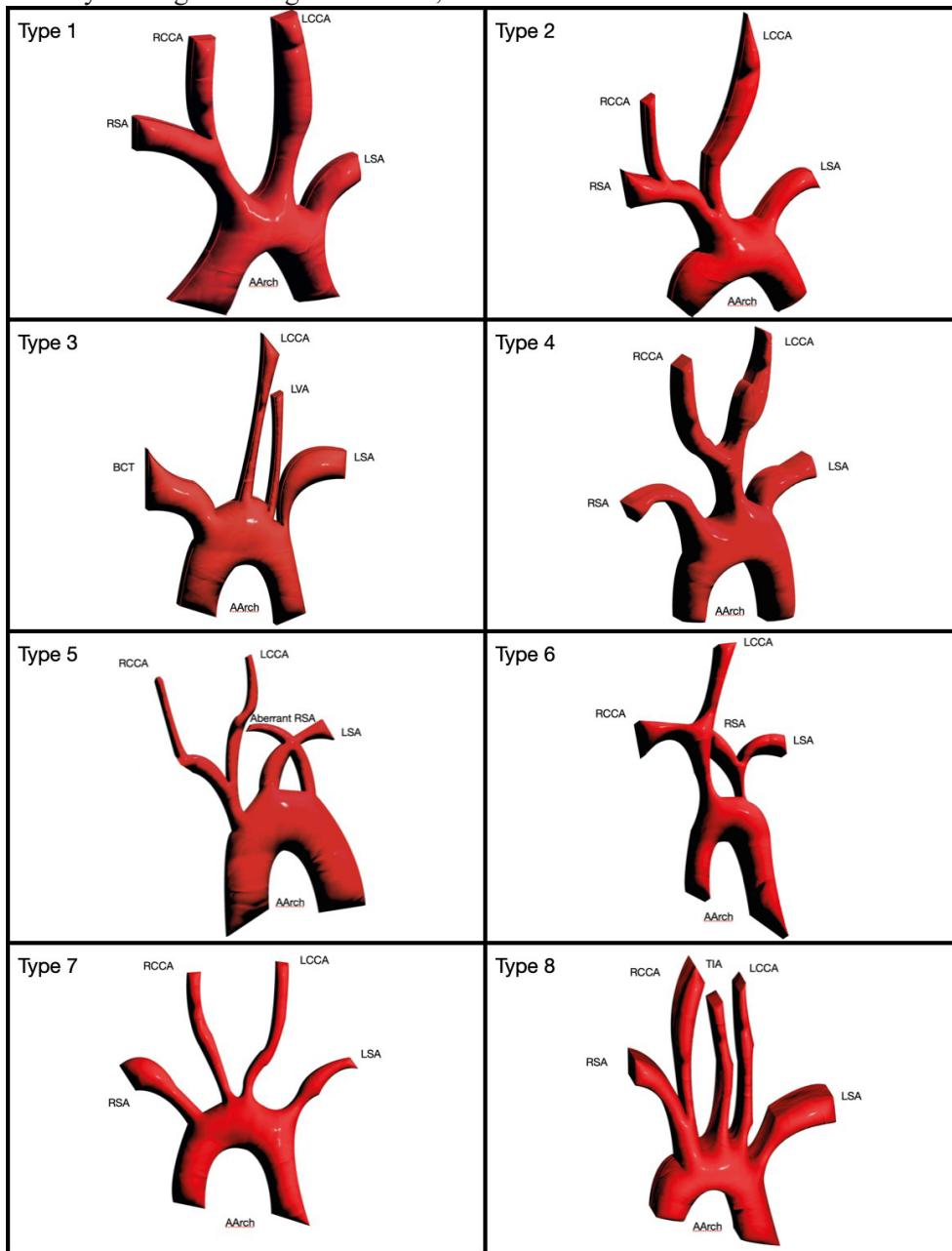


Figure 1. The image depicts the categorization of aortic arch branching patterns.

AArch: Aortic arch; LCCA: Left common carotid artery; LSA: Left subclavian artery; RSA: Right subclavian artery; RCCA: Right common carotid artery; TIA: Thyroide ima artery; Aberrant RSA : Aberrant sol subclavian artery.

Results

Of 221 patients, 116 were female and 105 were male, ranging in age from 19 to 99, with an average age of 57. After analyzing the 221 patients, six distinct aortic arch branching patterns were identified (Table-1). There were 173 patients who had type 1, also known as the normal or classical form. The prevalence of this arch type was 78.3%. The variation known as type 2, in which the left common carotid artery originates from

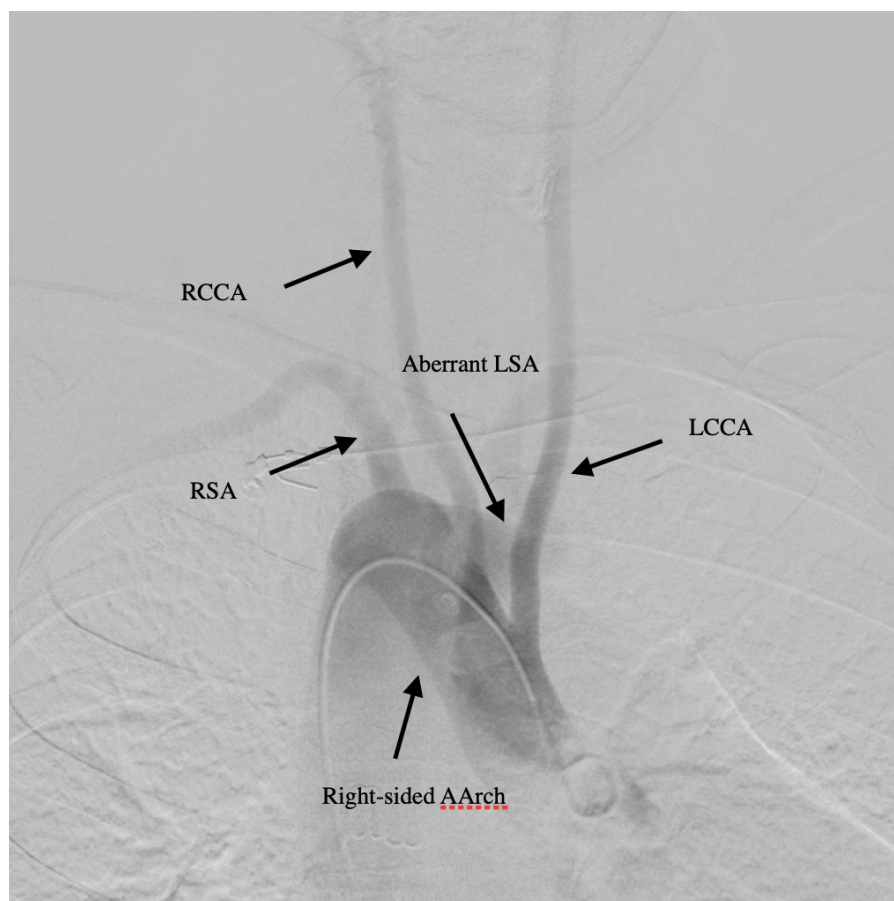


Figure 2: Right aortic arch and aberrant left subclavian artery

AArch: Aortic arch; LCCA: Left common carotid artery; LSA: Left subclavian artery; RSA: Right subclavian artery; RCCA: Right common carotid artery.

the brachiocephalic trunk, was seen in 44 cases, which accounts for 19.9% of the total. In two patient [0.9%], the left vertebral artery originates directly from the aortic arch, as in Type 3 variation. Two patients presented with a right aortic arch and aberrant right subclavian artery [Figure 2]. Overall, it was noted that type 3 variations were more prevalent among females in comparison to males. Conversely, the occurrences of all other types of variations were found to be equivalent in both genders.

Table 2 presents the clinical data on variations in the aortic arch branching pattern.

Discussion

Variations in the aortic arch's branching pattern are common and usually asymptomatic. It is frequently incidentally detected. In our study, no patients exhibited symptoms such as dyspnea or dysphagia that may have been caused by the variant.

The most prevalent type of aortic arch in the population is type 1. Consequently, it is also known as the normal branching pattern. Its incidence varies between 65% and 9% in previous studies [1,2,4,5]. According to the findings of our study, this is the most prevalent form, with an incidence of 78.3%.

Type II is the second most common aortic arch pattern in the literature, and its incidence ranges from 11 to 27%. The common root gives rise to the brachiocephalic trunk and the right CCA. It's also called the bovine arch [2,3,6]. In our series, bovine arch was observed in 19.9% or 44 patients. Those with type 2 aortic arch are more likely to develop thoracic aortic aneurysms, and they typically do so at younger ages [7]. In addition, because catheterization is more challenging during mechanical thrombectomy for acute stroke and endovascular cerebral aneurysm treatment in patients with bovine arch, the procedure takes longer and has a lower success rate [8]. Therefore, the presence of bovine arch detected through radiological imaging techniques performed for another purpose should be noted in the reports.

According to the literature, Type III aortic arch variation is the third most prevalent variation, with a prevalence of 2.9% to 6.1% [5,9,10]. In contrast, Natsis et al. found the incidence of Type III aortic arch to be 0.79 percent in their study of 633 patients using DSA [2]. In our study, the incidence was 0.9%, which is considerably lower than the average in the literature. It is not clinically asymptomatic, but diagnostic imaging such as Doppler may incorrectly report it as occluded. In addition, catheterization cannot be performed during conventional angiography because it is not in its normal location, and it may be overlooked [11]. Additionally, because

vertebral artery injury complications are common in spine surgery, planning should be done in terms of vertebral artery variations prior to these operations [12].

difficulty swallowing [14,15]. In some cases, the ASDL may also course between the trachea and esophagus or in front of the trachea, potentially causing dyspnea

Table 1.The rate and gender distribution of aortic arch branching pattern variations.

Variation	Description	All (n=221)	Male (n=105)	Female (n=116)
Type 1	Normal aortic arch branching	173 (78.3%)	86 (81.9%)	87 (75%)
Type 2	Bovine aortic arch	44 (19.9%)	17 (16.2%)	27 (23.3%)
Type 3	LVA originating from the aortic arch	2 (0.9%)	1 (1%)	1 (0.9%)
Type 4	Existence of both types 2 and 3	-	-	-
Type 5	Aberrant right subclavian artery	-	-	-
Type 6	Bicarotid trunk coexistence	-	-	-
Type 7	Right and left subclavian and common carotid arteries originate separately.	-	-	-
Type 8	TIA that arises in the aortic arch	-	-	-
	Right aortic arch and aberrant left subclavian artery	2 (0.9%)	1 (1%)	1 (0.9%)

LVA = left vertebral artery ;TIA= thyroidea ima artery

In the literature, a Type IV aortic arch variation is described where the brachiocephalic trunk is absent, and the right and left subclavian arteries arise directly from the aortic arch, with the common carotid arteries emerging from a single bicarotid trunk [9,13]. In the literature, 0.7% incidence of type IV aortic arch has been reported [13]. In our study, type IV aortic arch was not observed. Clinically, the bicarotid trunk is the leading congenital cardiovascular anomaly most frequently responsible for tracheobronchial compression [14,15].

In Type V aortic arch, both common carotid arteries arise from a single trunk, while the left subclavian artery and an aberrant right subclavian artery originate separately [2,5]. This anatomical variation, with an incidence of about 0.7% [6]. The aberrant right subclavian artery is the last branch to emerge from the aortic arch and typically crosses from the left side of the body to the right, often passing behind the esophagus, a condition known as *arteria subclavia dextra lusoria* (ASDL). The incidence of an aberrant right subclavian artery alone is found in 1.4% of people, with reported rates ranging from 0.13% to 25% [10,11]. It can lead to clinical issues such as *dysphagia lusoria*, where esophageal compression causes

or complications during tracheostomy. Additionally, this variation can present challenges during right arm catheterization in angiographic procedures [2,15,16].

Type VI aortic arch variation is comparable to type V, with the exception that both common carotid arteries arise from a single branch. The aortic arch gives rise to two major branches. It is rarely observed [16,17]. Its clinical significance is dependent on the aberrant course of the right subclavian artery, as in type V arch.

In aortic arch type VII, the right subclavian artery, the right common carotid artery, the left common carotid artery, and the left subclavian artery arise independently. It is extremely uncommon and has no clinical manifestations.

In addition to type I aorta, the thyroidea ima artery originates from the aortic arch in type VIII aortic arch. Its incidence was reported to be 0.16 percent [2]. It is clinically silent, but there is a risk of injury during neck-region surgical procedures. It is also susceptible to injury during angiography.

The incidence of right aortic arch anomaly in the

Table 2. The clinical data of variations in the aortic arch branching pattern.

Clinical data	Type 1 (n=173)	Type 2 (n=44)	Type 3 (n=2)	R-A Arch, aRSA (n=2)	Total
AVM	10 (71.4%)	4 (28.6%)	0	0	14
Aneurysm	76 (77.6%)	19 (19.4%)	2 (2%)	1 (1%)	98
CAS	37 (90.2%)	4 (9.8%)	0	0	41
Stroke	18 (69.2%)	7 (26.7%)	0	1 (3.8%)	26
Behçet	1 (100%)	0	0	0	1
SAH	29	10 (25.6%)	0	0	39
Moya Moya	1 (100%)	0	0	0	1
AVF	1 (100%)	0	0	0	1
Total	173 (78.3%)	44 (19.9%)	2 (0.9%)	2 (0.9%)	221

R-A Arch, aRSA =Right aortic arch, aberrant right subclavian artery;AVM=Arteriovenous malformation; CAS=Carotid artery stenosis; SAH=Subarachnoid hemorrhage; AVF=Arteriovenous fistula

population has been estimated between 0.05% and 0.2% [18]. A right aortic arch and a mirror-like arch branching were observed in two cases [%0.9] in our study. According to Terziolu et al.'s study, its prevalence was 0.2%. In two of our patients, the right aortic arch and aberrant left subclavian artery anomaly were described. Left common carotid artery, right common carotid artery, right subclavian artery, and left subclavian artery originate from the aortic aorta, respectively. As the aberrant left subclavian artery moves from right to left in the mediastan, it may pass behind the esophagus and result in compression symptoms. In addition, the left subclavian artery may exhibit an enlargement at the aortic outlet, known as a commereel diverticulum. Its prevalence has been estimated at 0.1% to 0.3% [9,19].

In addition, it has been demonstrated that the risk of cerebrovascular disease increases in certain aortic arch branching variations. Depending on the artery's angle and exit level, the flow hemodynamics in the principal arterial structures originating from the aortic arch vary [Table 2]. According- ly, the death rate from

cerebrovascular disease is higher in type 2 and type 3 aortic arch variations than in type 1 aortic arch variations [20].

This study has several limitations. First, the patient population was limited to those treated at a sin- gle hospital, which may affect the generalizability of the findings. Second, the retrospective nature of the study could introduce bias, and the absence of a control group limits the strength of the con- clusions. Finally, genetic and environmental factors were not considered, which could influence the presence of aortic arch variations.

The prevalence of endovascular treatment for cerebrovascular diseases has increased in recent years. Catheterization of supraaortic arterial structures requires the aortic arch. Particularly in type 2 and type 3 aortic variants, the catheterization time of supraaortic arterial structures and the corresponding radiation dose exposure increase proportionally. In addition, the catheterization time is crucially important for stroke patients undergoing mechanical thrombectomy.

Conclusion



In conclusion, variations in the aortic arch are common in imaging studies. It is essential to recognize these variations because they both set the stage for cerebrovascular diseases and cause symptoms by compressing structures such as the esophagus and trachea. Additionally, it is essential to have a thorough understanding of the aortic arch's anatomy prior to certain surgical interventions and endovascular diagnostic and therapeutic procedures in order to achieve a low complication rate and high procedural success.

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Sedation with chloral hydrate and melatonin in childhood electroencephalography

Betul Diler Durgut¹ 
Emine Tekin¹ 

1. Division of Pediatric Neurology, Giresun University Faculty of Medicine, Giresun, Türkiye

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Corresponding Author: Betül DILER DURGUT, M.D.

Division of Pediatric Neurology,

Giresun University Faculty of Medicine,
Giresun, Turkey

Email: betuldir@hotmail.com

Abstract

Objective: Recording an electroencephalography (EEG) in children is challenging due to their restlessness during the procedure and inability to follow the required instructions. Sleep deprivation and the use of sedative agents are necessary to perform the recording. This study aims to evaluate the need for sedation in patients and to compare the effectiveness and side effects of sedation with chloral hydrate and melatonin.

Methods: Patients who underwent EEG recording between December 2023 and March 2024 were retrospectively evaluated. The chloral hydrate and melatonin groups were formed for the patients requiring sedation. According to the protocol applied in our clinic, chloral hydrate was administered orally at a dose range of 30-50 mg/kg (max 1500 mg), while melatonin was given orally at a dose of 1-3 mg. The sociodemographic information of the patients was recorded from hospital charts, sleeping rates and EEG recording duration were compared.

Results: Of the 471 patients EEG performed, 240 (51%) were female and 231 (49%) were male. The mean age was 9.1 ± 5.1 years, with a median age of 9.5 years. Sleep deprivation was appropriately carried out in 434 patients (92.3%), while 37 patients did not achieve sleep deprivation. Among the 76 patients who received sedation, chloral hydrate was used in 45 (59.2%) and melatonin in 31 (40.8%). Sleeping ratios were 82.2% and 80.6% in the chloral hydrate and melatonin groups respectively; there was no statistically significant difference in sleeping rates ($p: 0.86$). No serious drug-related side effects were observed in either group. Rare gastric complaints, such as gastric discomfort and nausea/vomiting were noted in the chloral hydrate group.

Conclusion: Melatonin and chloral hydrate provided similar rates of sedation. This study showed that either drug can be chosen for the sedation in pediatric EEG recordings.

Keywords: Children; chloral hydrate; electroencephalography; melatonin; sedation

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Introduction

Electroencephalography (EEG) is a valuable method used for the diagnosis and classification of epilepsy, determining the treatment and prognosis.

An ideal EEG recording should include both wakefulness and sleep states in a patient. Sleep EEG is preferred in children because it facilitates compliance, reduces EEG artifacts, and increases the likelihood of diagnosis. In younger children, restlessness during the recording and inability to follow instructions can decrease the success rate of EEG recordings.

Sleep deprivation (decreasing the sleep and keeping the patient awake till the EEG recording for a time appropriate for their age) is used as an activation method because it facilitates falling asleep during the recording and increases the likelihood of detecting interictal discharges [1]. Sedation is required in children who cannot undergo EEG recording despite sleep deprivation. Clinics use different drugs for sedation based on their experience, such as chloral hydrate, melatonin, and hydroxyzine [2-4].

In childhood, both awake and sleep EEG recordings are performed. Sleep deprivation is accepted as an activation method as it increases discharges in EEG. Despite sleep deprivation, patients who have difficulty falling asleep, such as those with autism spectrum disorder, attention deficit hyperactivity disorder, mental retardation, cerebral palsy, and those failing to attain sleep spontaneously may require sedation. Chloral hydrate has been used for many years for sedation purposes. However, chloral hydrate requires close monitoring due to its side effects and long recovery time. To optimize time and resources, alternative agents are necessary to induce sleep effectively. Melatonin is an alternative agent to chloral hydrate because it is considered safe and the recovery time is shorter.

Chloral hydrate is a sedative-hypnotic agent that has been extensively used for inducing sleep during EEG recordings for many years. It can be administered orally or rectally. It is rapidly metabolized by alcohol dehydrogenase in the liver and erythrocytes to its active metabolite, trichloroethanol. This active metabolite crosses the blood-brain barrier and exhibits hypnotic properties. Chloral hydrate has been associated with serious side effects such as oxygen desaturation, delayed apnea, and respiratory arrest [5]. Due to these potential complications, close monitoring of patients is necessary.

Melatonin is a hormone produced in the pineal gland that acts on the suprachiasmatic nucleus of the hypothalamus to induce sleep. It is advantageous due to its low incidence of side effects.

The International League Against Epilepsy (ILAE) recommends partial sleep deprivation for EEG recordings in children aged 12 years and older, as well as in adults. For children under 12 years old, ILAE suggests administering melatonin or conducting sleep deprivation. The recommended dose of melatonin is 1-3 mg given 30-60 minutes before the EEG. In cases where melatonin is not available or partial sleep deprivation is inadequate, chloral hydrate is recommended. Partial sleep deprivation in children under 6 years old involves reducing sleep by 1-3 hours, or by an amount estimated to be necessary for falling asleep at the time of the EEG. For children aged 6-12 years, this includes delaying bedtime by 3 hours and waking up 2 hours earlier than usual, and staying awake until the time of recording. In children aged 12 and older, this involves going to bed 2 hours later (no later than midnight) and waking up at 4:00 AM, remaining awake until the EEG. For adults, it is defined as sleeping between 24:00 and 04:00 before the recording. [6]

In this study, we aimed to determine the need for sedation in our patients and to compare the effectiveness of chloral hydrate and melatonin for sleep induction. The secondary aim of this study is to investigate the side effects associated with the use of chloral hydrate and melatonin during childhood electroencephalography.

Methods

EEG recording

In our clinic, EEG recordings are requested from the pediatric neurology outpatient department. All patients and their families are routinely informed about the importance of sleep deprivation when EEG appointments were scheduled.

Patients with conditions such as autism spectrum disorder, attention deficit hyperactivity disorder, intellectual disability, cerebral palsy for whom EEG recording may be challenging due to anticipated difficulties or inability to sleep despite appropriate sleep deprivation, are sedated for the procedure. Written consent is obtained from families for both EEG recording and sedation. Chloral hydrate or melatonin is preferred for sedation in these cases.

EEG recording is conducted according to the international

10-20 system, which involves the placement of electrodes to capture 18-channels of recordings.

Drugs for sedation

Chloral Hydrate: In our clinic, chloral hydrate is administered orally at a dose range of 30-50 mg/kg (max 1500 mg).

Melatonin: In our clinic, melatonin is administered orally at a dose of 1 mg for patients weighing less than 15 kg, and 3 mg for patients weighing 15 kg or more.

Data Collection:

Patients who underwent EEG recordings in the EEG laboratory between December 2023 and March 2024 were included in the study. Patient data were accessed through hospital charts retrospectively. Information collected included age, gender, sleep deprivation status, need for sedation, and EEG duration. Patients who received sedation were divided into two groups: those administered chloral hydrate and melatonin. Sleeping rates and EEG durations were compared between these groups.

Statistics:

Statistical analyses of the study were performed using the trial version of SPSS 22.0 (SPSS Inc., Chicago, IL) package software. Kolmogorov-Smirnov test was employed to examine whether the quantitative variables were suitable for the normal distribution. Independent groups were compared with the Mann-Whitney U/ Kruskal-Wallis H test in terms of variables that were not normally distributed. The relationship between qualitative variables was examined using chi-square analysis. The descriptive statistics of the quantitative variables that conformed to the normal distribution were

shown as mean \pm standard deviation, and the descriptive statistics of the quantitative variables that were not normally distributed were shown as median (min-max) or mean \pm standard deviation. Descriptive statistics for qualitative variables were expressed as frequency (%). Statistical significance was considered $p < 0.05$.

Ethics Committee Approval:

Ethics committee approval was obtained from local Clinical Research Ethics Committee (Date/Number: 17.07.2024/01)

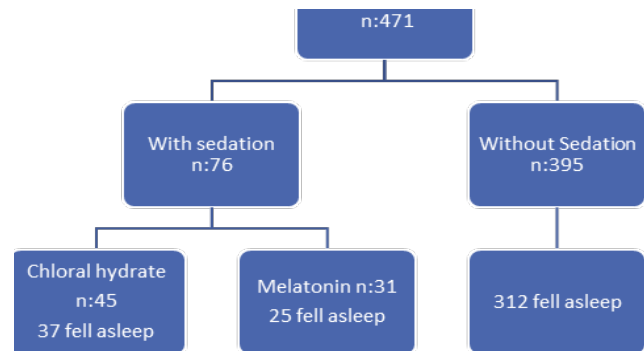


Figure 1: Flow chart of the patients' with EEG recordings

Results

In a three-month period, 471 patients who underwent EEG recordings were included in the study. Of these patients, 240 (51%) were female and 231 (49%) were male. The average age was 9.1 ± 5.1 years, with a median age of 9.5 years. Sleep deprivation was appropriately conducted in 434 patients (92.3 %), while 37 patients failed sleep deprivation. Among the 395 patients who did not require sedation, 312 (76%) fell asleep, whereas 62 (81.6 %) of the 76 patients who received sedation,

Table 1: Characteristics of patients undergoing sedation

	Chloral Hydrate n(%) n:45	Melatonin n(%) n:31	p
Age (year \pm SD)	8.07 \pm 4.49	6.87 \pm 4.31	0.19
Sex			
Boy n(%)	28(62)	19(61)	1.00
Girl n(%)	17(38)	12(39)	
Sedation rate	37 (82.2)	25(80.6)	0.86
Sleep EEG duration (m)	23.35	23,8	0.50

m:minute

fell asleep. Patients requiring sedation, 45 (59.2 %) were in chloral hydrate and 31 (40.8 %) were in the melatonin group. (Figure 1-flow chart)

Children who received chloral hydrate, 82.2% fell asleep, compared to 80.6% in the melatonin group; however, there was no statistically significant difference between the groups ($p=0.86$) (Table 1). The mean EEG recording duration was 32 ± 11.3 minutes, with a median of 35 minutes. No serious drug-related side effects were observed in either group. Rare gastric complaints, such as gastric discomfort and nausea/vomiting, were noted in the chloral hydrate group, observed in 3 patients.”

Discussion

In our study, no significant difference was found in sedation efficacy between melatonin and chloral hydrate groups during EEG recordings ($P= 0.86$). This study demonstrated that chloral hydrate and melatonin, both used for sedation, showed no superiority in inducing sleep over each other. Sedation was required for 76 out of 471 patients, which corresponds to 16.1% of the patients. Side effects were observed only in the chloral hydrate group, with mild gastric discomfort noted in 3 patients.

In the literature, there are studies comparing sleep induction using chloral hydrate and melatonin. Some studies have found chloral hydrate to be more successful than melatonin in inducing sleep, while others have not observed a significant difference [5, 7].

Dirani et al. compared their old and new protocols for EEG recordings in patients aged 6 months to 17.7 years. The old protocol involved the use of chloral hydrate, with a second dose given when necessary. In the new protocol, melatonin, hydroxyzine, and chloral hydrate were sequentially added until sleep was achieved. As a result, the sleep induction rate with melatonin (44.6%) was significantly lower compared to chloral hydrate (95.2%) [5]. In the study, despite using higher doses of melatonin (2.5 mg for children under 5 years old, 5 mg for those 5 years and older), the sleep induction rate with melatonin was notably lower compared to our findings. Unlike our study their patients were kept up late and awakened at the usual morning hour. Our sleep deprivation involved delaying bedtime and waking up earlier than the usual time. We speculated that this difference might account for this disparity. Additionally, in our study, we did not use sequential medications for sedation purposes.

Unlike Dirani et al., Fazli et al. did not find a significant difference in the rates of sedation induction. In their study, which included children aged 6 months to 5 years, they compared 25 mg/kg of chloral hydrate with a dose of 0.4 mg/kg of melatonin [7]. The success rates were found to be similar in the melatonin and chloral hydrate groups, at 92% and 95%, respectively ($p=0.5$). In contrast, in our study, these rates were 80.6% and 82.2%, respectively ($p=0.8$). Our study group consisted of patients aged 4 to 14.2 years. The lower sedation induction rate in our study may be attributed to the difference in patient age groups. As a result, Fazli et al. found melatonin advantageous due to its shorter recovery time and absence of side effects.

Ashrafi et al. randomized 248 uncooperative patients aged 1 month to 6 years for EEG recordings. They compared chloral hydrate and melatonin groups and found similar sleep onset latency. However, the sleep and sedation duration were significantly shorter in the melatonin group compared to the chloral hydrate. Re-dosing was required for 6 patients in the chloral hydrate group and 20 patients in the melatonin group. Both groups experienced few side effects. They recorded the shorter sleep duration and sedation period-drowsiness as two advantages of melatonin over chloral hydrate [8].

In another study, 174 children aged 0-4 years were given melatonin 1 hour before EEG recording, with 3 mg for those weighing less than 15 kg and 6 mg for those weighing 15 kg or more. All children were encouraged to remain sleep-deprived before their sleep EEG. For children over 3 years old, they were kept awake until midnight, then allowed to sleep from 00:00 to 04:00, and were not permitted to sleep until they arrived at the hospital for EEG. The control group was retrospectively composed of patients who received chloral hydrate. The study concluded that melatonin sedation was effective and safe; however, it was found to be less successful in children with developmental and behavioral issues [9].

In the study by Holsakul et al., patients aged between 1 and 5 years, as well as older patients who did not cooperate for EEG recordings, were included. The patients were randomly divided into three groups: the melatonin group (Group A), the melatonin and sleep deprivation combination group (Group B), and the chloral hydrate and sleep deprivation combination control group (Group C). Sleep deprivation was defined as going to sleep 2 hours later than usual, waking up at the usual wake-up time, and not napping during the day. The dose of melatonin used was 3 mg. If the patient

did not fall asleep, the dose was repeated after 1 hour. If sleep still did not occur, chloral hydrate at 25 mg/kg was administered 1 hour after the second dose, with an additional dose of 50 mg/kg if necessary, followed by another 25 mg/kg if needed. In Groups A, B, and C, 5, 3, and 1 patient required a repeat dose, respectively. Unlike our study, this study examined sleep onset latency, defined as the time from drug administration to the onset of stage 2 sleep. Melatonin alone was found to be as effective at inducing sleep as when combined with sleep deprivation. However, the efficacy of melatonin was lower compared to chloral hydrate in combination with sleep deprivation, particularly in terms of sleep onset, latency, and sleep efficiency [10]. These findings are consistent with those of a previous study by Ibekwe et al. in 2017 [9].

In a meta-analysis comparing melatonin with Triclofos (a prodrug pharmacologically converted to an active metabolite similar to chloral hydrate) for EEG recordings, chloral hydrate showed a success rate of 90% and melatonin 76% ($p=0.054$). Although this meta-analysis did not find a significant difference between the groups, it was noted that the chloral hydrate group had longer sleep durations, fewer requirements for a second dose, and more frequent side effects compared to melatonin, suggesting melatonin as a viable alternative for initiation of sleep. Despite weak evidence from current literature, Triclofos and melatonin were considered comparably effective in triggering sleep for EEG recordings in children [4]. In our study, no side effects were observed in patients receiving melatonin, whereas patients receiving chloral hydrate experienced mild gastric symptoms, although no serious side effects were reported. In one of the aforementioned studies [5], vomiting occurred in some patients receiving melatonin, but no side effects were observed in other studies [5, 7, 11]. Chloral hydrate side effects, up to 15% were reported, with gastric complaints being more common; transient bradycardia and desaturation, which resolved with caution, were also reported [5, 7].

Limitations

Small sample size, short study duration, and the retrospective nature of the study may limit the generalizability of the findings. Additionally, the specific age groups included in the study may not fully represent the broader population. Analyzing patients by age groups in a larger sample size may yield more accurate results. Other factors influencing sedation should be considered, and better-designed prospective studies are needed to address these limitations.

Conclusion

This study determined that chloral hydrate and melatonin were not superior to each other in providing sleep induction for EEG recording. The absence of side effects with melatonin use and the lesser need for post-procedural monitoring may make it a preferred choice.

The drugs and drug doses to be used can be selected depending on the experience and preference of the centers.

Conflict of interest

The authors declare no competing interests. The authors declare they have no financial interests.

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The necessity of routine terminal ileum intubation in patients undergoing routine colonoscopy: Is it a must?

Furkan Turkoglu¹ 
Emre Erdogan¹ 

1. Özel Aktif Hospital, Department of General Surgery, Yalova, Türkiye

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Corresponding Author: Furkan Turkoglu,
MD

Özel Aktif Hospital, Department of General
Surgery, Yalova, Türkiye

Email: drfurkanturkoglu@yahoo.com

Abstract

Objectives

Terminal ileal intubation (TII) is a useful procedure during colonoscopy, but its clinical value is controversial in the literature. The aim of this study is to investigate the necessity of terminal ileal intubation during colonoscopy in patients not suspected of having inflammatory bowel disease.

Methods

This study was conducted by retrospectively reviewing data from 872 colonoscopies. Patients with inflammatory bowel disease and those with inadequate bowel preparation were excluded from the study. The demographic data of the patients, colonoscopy results, macroscopic and microscopic findings, and complications were recorded.

Results

The average age of the 763 patients included in the study was 53.26±23.82 years, with 429 (56.22%) male and 334 (43.78%) female patients. A total of 107 patients (14.02%) underwent TII. Of the 107 patients who underwent TII, 56 (52.33%) were female, and 51 (47.67%) were male, with an average age of 49.52±21.69 years. The colonoscopy indications for patients who underwent TII were diarrhea in 46 patients, rectal bleeding in 38 patients, and abdominal pain in 23 patients. Macroscopic pathological findings were observed in 8 patients (7.46%), and microscopic pathological findings in 3 patients (2.80%). The proportion of patients with microscopic pathological findings accounted for 0.39% of all colonoscopies.

Conclusions

Our study suggests that while TII, which requires experience and extends the duration of colonoscopy, may be beneficial for the diagnosis of selected patients, it may not be necessary in routine colonoscopies given its very low diagnostic value.

Keywords: Colonoscopy; terminal ileum; inflammatory bowel disease

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Introduction

Today, colonoscopy is considered the gold standard method for the diagnosis and treatment of colon diseases. The most common reason for performing a colonoscopy is colorectal cancer screening [1]. In addition, colonoscopy is used for the diagnosis of symptoms of irritable bowel syndrome, chronic constipation and diarrhea, iron deficiency anemia, differential diagnosis of abnormal radiological findings in the colon, investigation of occult blood in stool, removal of colon polyps, follow-up after colon cancer treatment, and diagnosis and follow-up of inflammatory bowel diseases [1,2]. Although colonoscopy is a common procedure, it can also lead to many complications [3].

There is uncertainty about whether the terminal ileum (the last part of the ileum) should be routinely intubated during colonoscopy, as its diagnostic value is unclear [4]. Current guidelines do not provide any recommendations for terminal ileum intubation (TII) if there is no suspicion for inflammatory bowel diseases [5]. Although, ileoscopy is not routinely performed, it may be beneficial for some patients in cases such as right lower quadrant pain, unexplained diarrhea, inflammatory bowel disease, hematochezia, and suspected ileocecal tuberculosis [6,7]. Ileocolonoscopy is the preferred procedure for chronic non-bloody diarrhea of unknown origin. Histopathological examination from multiple sites is crucial for diagnosing microscopic colitis [8]. The reported rates of TII during colonoscopy vary widely. Many endoscopy guidelines do not specify a particular rate for TII [9,10].

Given that TII prolongs the duration of colonoscopy and studies have shown that routine TII in patients without symptoms of inflammatory bowel disease does not contribute diagnostically, it becomes clearer why there is debate about the necessity of routine TII during colonoscopy [6,7,11,13]. Therefore, it is often thought that a colonoscopy limited to the cecum meets expectations.

The aim of this study is to determine whether routine TII is necessary in patients without a diagnosis of inflammatory bowel disease.

Methods

This study was conducted by retrospectively reviewing the medical records of patients who underwent colonoscopy at Özel Aktif Hospital between January 2021 and January 2024. The study commenced after receiving approval from the Clinical Studies Ethics Committee (date: 09.08.2024, No: 56). A total of 872 patients who underwent colonoscopy within the specified period were included in the study. Exclusion criteria were defined as having a known history of inflammatory bowel disease or having an incomplete colonoscopy due to contamination or other reasons. As part of our center's routine procedure, informed consent about the colonoscopy procedure is obtained from every patient prior to the colonoscopy. Colonoscopy procedures were performed by three different endoscopist with experienced at least two years and more than 1000 colonoscopy procedures.

For all colonoscopy procedures, patients were positioned in the left lateral position on the examination table, and anal inspection and digital rectal examination were performed before the procedure. The colonoscopy procedures were carried out using the single-hand technique. The colonoscopy was considered successful if the anatomical landmark of the cecum (Mercedes sign), the appendix orifice, or the ileocecal valve was visualized. The decision to perform TII was made by the endoscopist based on the patient's clinical condition. The demographic data of the patients, colonoscopy results, post-colonoscopy complications, and pathology reports if biopsies were taken during the colonoscopy were evaluated and recorded.

Results

A total of 763 patients were included in the study, with an average age of 53.26 ± 23.82 years; 429 patients

Table 1: The results of terminal ileum entubation (SD: standard derivation)

	Total Colonoscopy (n:762)	Terminal Ileum Entubation (n:107)
Age (year) (mean \pm SD)	53.26 \pm 23.82	49.52 \pm 21.69
Gender (Female) (n,%)	334 (43.78%)	56 (52.33%)
Macroscopic ileal pathology (n,%)	8 (1.04%)	8 (7.46%)
Microscopic ileal pathology (n,%)	3 (2.80%)	3 (0.39)

(56.22%) were male, and 334 patients (43.78%) were female. TII was performed in a total of 107 patients (14.02%). Of the 107 patients who underwent TII, 56 (52.33%) were female, and 51 (47.67%) were male, with an average age of 49.52 ± 21.69 years. Colonoscopy was performed for 46 (43.00%) patients due to bloody or non-bloody diarrhea, for 38 (35.50%) patients due to rectal bleeding, and for 23 (21.50%) patients due to isolated abdominal pain. No complications were observed after the colonoscopy, except for one patient who experienced spontaneous rectal bleeding following polypectomy, which resolved on its own.

In patients who underwent TII, biopsies were taken from the terminal ileum in 8 patients (7.46%) with ulcerative lesions or erythematous mucosa observed macroscopically in the ileum (figure 1). The rate of detecting macroscopic pathology in the terminal ileum among all colonoscopy patients was 1.04%. Histopathological examination in three patients with detected macroscopic pathology and who underwent TII revealed terminal ileitis, while no pathological findings were observed in other patients. The rate of pathological findings in microscopic examination was 2.80% among all TII patients, and 0.39% among all patients who underwent colonoscopy.

Discussion

Although TII is not a difficult procedure in experienced

hands, its low diagnostic value, the need for specific experience, the extension of the colonoscopy duration, and the requirement for certain maneuvers and learning curves make it impractical for many centers to implement in clinical practice [14]. In our study, diarrhea was the most common indication for TII, with macroscopic pathology observed in the terminal ileum in 7.46% of patients who underwent TII, and in 1% of all patients. The rate of patients with histopathological findings dropped to 0.4%.

While the current guidelines in the literature recommend routine TII during colonoscopy in patients with suspected inflammatory bowel disease, there is no recommendation regarding TII in colonoscopies performed for reasons other than inflammatory bowel disease [5].

In a large-scale study conducted for colorectal cancer screening, TII was performed in 21% of 6408 colonoscopies, with pathological findings in the terminal ileum observed in 68 patients (1%). Among these 68 patients, abnormal pathological findings were observed in 22 patients (32%) during histopathological examination, and only 3 of them (4.4%) required treatment. When considering all screening colonoscopies, the efficiency of TII was determined to be 0.04% [15]. In our study, the efficiency of TII was found to be 0.39% and had low values as reported in the literature.

In a study evaluating the results of patients who

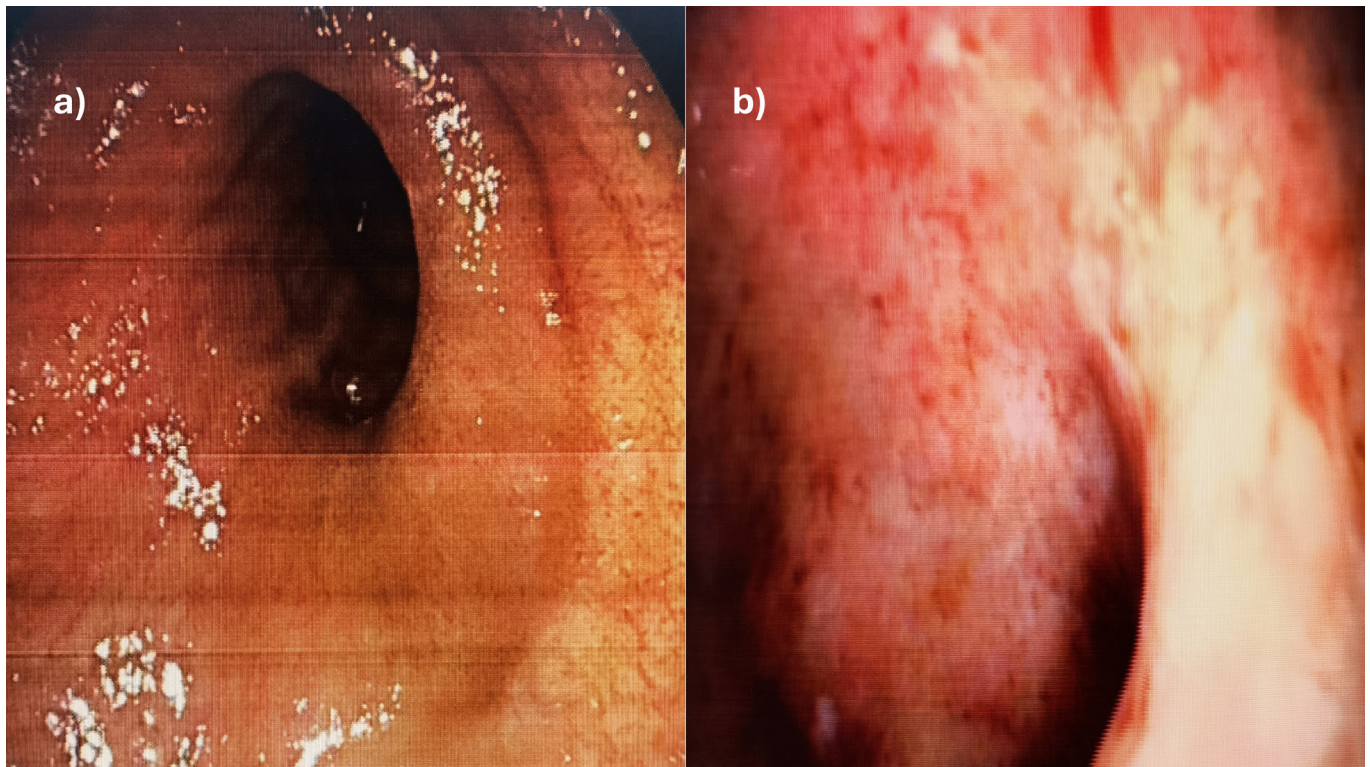


Figure 1: Examples of patients with terminal ileum intubation (a: Normal ileum, b: Ileum with inflamed)

underwent TII, macroscopic abnormalities in the terminal ileum were observed in 54 (20%) of 269 patients who successfully underwent TII, and biopsies in 4 (7.4%) of these 54 patients, and in 1.48% of all TII patients, were positive for Crohn's disease [6]. In a study assessing the necessity of TII in routine colonoscopy procedures, TII was performed in 511 (9.5%) of 5355 colonoscopies, with macroscopic findings identified in 3.52% of these patients. Histopathological examinations of biopsies from patients who underwent TII revealed terminal ileitis in 0.97% of TII patients, and in only 0.09% of all colonoscopies [7]. In a study evaluating 2473 colonoscopies of pediatric and adult patients, the rate of TII was found to be 40.8%, while this rate was reported as 38.2% for adult patients. A macroscopic pathological finding was detected in 3.7%, and microscopic pathology was observed in 1.58% of patients who underwent TII [16]. In our study, macroscopic pathological findings were observed in 7.46% and microscopic pathological findings in 2.80% of patients who underwent TII, which is not much different from the literature.

The limitation of this study is the fact that we are not a center that routinely follows up inflammatory bowel diseases and that the necessity of TII is determined by the endoscopist based on colonoscopic findings may cause an unintentional bias in patient selection. Also, the experience of the endoscopist could influence the TII rates and could change the results.

Conclusion

Our study shows that even in patients who underwent TII, the rate of detecting pathological findings is very low, dropping below 1% when compared to routine colonoscopies. TII, which requires experience and prolongs the colonoscopy procedure, may be beneficial for diagnosing selected patients, but it should not be performed in routine colonoscopies due to its very low diagnostic value. Prospective studies evaluating the necessity and cost-effectiveness of TII, especially in adult patients without a diagnosis of inflammatory bowel disease, will contribute to the literature.

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Histopathological comparison of incision methods in transconjunctival blepharoplasty: A rat model study

Engin Selamioglu¹
Ilker Altundag²
Mustafa Sertac Ocak³
Mehmet Berke Goztepe³
Levent Yildiz⁴
Ahmet Demir³

1. Haliç University Department of Plastic Reconstructive and Aesthetic Surgery, İstanbul, Türkiye

2. İzmir Training and Research Hospital, Plastic Reconstructive and Aesthetic Surgery, İzmir, Türkiye

3. Ondokuz Mayıs University, Department of Plastic Reconstructive and Aesthetic Surgery, Samsun, Türkiye

4. Ondokuz Mayıs University, Department of Pathology, Samsun, Türkiye

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Corresponding Author: Engin Selamioglu
Assistant Professor, M.D.

Haliç University Department of Plastic Reconstructive and Aesthetic Surgery, İstanbul, Turkey

Email: doktorengin@hotmail.com

Abstract

Objectives

The choice of incision method is critical in transconjunctival blepharoplasty, affecting both the wound healing process and aesthetic outcomes. This study aimed to compare the histopathological effects of four different incision methods: scalpel, electrocautery, radiocautery, and laser, on wound healing in an animal model.

Methods

A total of 54 female Sprague-Dawley rats were divided into nine groups, each subjected to different incision methods on their palpebral conjunctiva. Specimens were collected immediately after the incision and at 1- and 2-week intervals to evaluate wound width, depth, vascular proliferation, inflammation, and fibrosis.

Results

Analysis revealed that scalpel and laser incisions resulted in narrower and shallower defects immediately post-operation, while electrocautery and radiocautery produced the most pronounced tissue trauma. By the first week, electrocautery showed the least vascular proliferation, inflammation, and fibrosis, while radiocautery exhibited the most pronounced effects. At the second week, scalpel incisions showed the least inflammation and vascular proliferation, while fibrosis was least observed in radiocautery incisions. Interestingly, despite the initial trauma caused by electrocautery, this method showed less fibrosis over time, suggesting reduced long-term scarring compared to radiocautery. Laser incisions also showed favorable healing outcomes, but with more moderate results compared to the scalpel group. Overall, the study highlights the varying impacts of each incision method on the healing process, indicating that scalpel and laser offer advantages in the early stages of healing, while electrocautery, despite initial trauma, may result in less long-term scarring.

Conclusions

The results highlight the importance of selecting the appropriate incision method to minimize complications and optimize healing in transconjunctival blepharoplasty.

Keywords: Scalpel; electrocautery, laser, transconjunctival blepharoplasty, wound healing

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Introduction

Some incisions are described as exposing the infraorbital rim, orbital floor, or periorcular region. The most used approaches are the subciliary, subtarsal, infraorbital, and transconjunctival approaches [1]. Surgeons are still searching for the best instrument that can achieve the optimal skin incision. This instrument should be easy to use, easy to incise with minimal pressure and tissue tension or minimal inclination, good hemostasis during the incision, less damage to adjacent tissues, less scarring, and rapid sensory recovery [2].

All incisions have advantages and disadvantages. The infraorbital incision is associated with the most complications, including scarring and edema [3]. The subciliary incision rarely leaves a noticeable scar but produces significant temporary lower eyelid retraction [4]. The subtarsal incision is made along the natural crease of the lower eyelid under the tarsal plate and is associated with scarring [1]. A concealed orbital incision and low rates of ectropion have made the transconjunctival approach popular [5-10]. The transconjunctival approach was first described by Bourget in 1924 with the removal of lower eyelid fat [11]. Some authors have suggested that the transconjunctival approach reduces the risk of postoperative eyelid retraction, ranging from scleral demonstration to permanent ectropion [6,12]. However, complications also occur with this approach. The most common complications are lower eyelid avulsion, lower eyelid malposition, lower eyelid retraction, ectropion, and acquired or cicatricial entropion due to adhesion [13-14]. For many years, research has focused on preventing postoperative adhesions. The most important measures to reduce the incidence of adhesions are atraumatic surgical procedure, careful hemostasis, and ischemia [15]. A wide variety of instruments are available for cutting mucosal surfaces, causing varying degrees of tissue trauma, bleeding, and ischemia. Lasers perform tissue cutting by vaporizing the tissue as a result of the absorption of optical energy and its conversion to thermal energy [16]. RF devices generate high energy flow around the electrode tip, which causes less damage to the normal tissue around the lesion [17].

Different devices will have different penetration and thermal effects in the conjunctival mucosa. The aim of this study was to evaluate the effects of incisions made in the palpebral conjunctiva with scalpels, electrocautery, laser, and radiofrequency cautery on wound healing in an animal model. The factors examined included the width and depth of the postoperative wound, vascular

proliferation, inflammation, and fibrosis at the end of the first and second weeks. The clinical application of various devices in the palpebral conjunctiva may be better guided by the different effects on wound healing.

Methods

A total of 54 adult female Sprague-Dawley rats weighing between 200 and 250 grams were used as experimental animals in the study.

The rats were anesthetized by intraperitoneal Ketamine HCl 75 mg/kg and Xylazin 0.2 ml/kg. After monitoring the skeletal muscle tone, the subjects were laid on the workbench. The rats were fixed with 4-0 silk sutures so that their lower eyelid conjunctivas were exposed.

In our study, 15 scalpels, Sharplan 150 XJ SilkTouch CO2 laser, Covidien force FX Electrocautery, Covidien Radiofrequency were used.

In our study, 9 groups were formed and there were 6 experimental animals in each group.

Group 1: An incision was made on the right conjunctiva of the animals with a scalpel and the right sides of all animals were evaluated as the control group. An incision was made on the lower eyelid conjunctiva from the 3 mm inner part of the conjunctival rim with a number 15 scalpel, approximately 1.5 cm long and without reaching the septum. Immediately after the incision, the lower eyelid was completely excised for specimen collection. The right side was the control group, and the trauma zone created by the scalpel around the incision was pathologically evaluated. In this group, the left conjunctiva of the animals was incised with electrocautery. Specimens were taken in the same manner and the burn effect created by the electric current around the incision line (trauma-injury zone) was pathologically evaluated as the length. (Injury distance).

Group 2: The right conjunctiva of the animals was again the control group and incised with the scalpel in the same manner. Specimens were taken immediately for this purpose. Radiocautery was used in the left conjunctiva and the trauma zone was evaluated.

Group 3: The right conjunctiva of the animals was again the control group and incised with the scalpel in the same manner. Specimens were taken immediately for this purpose. Laser was used in the left conjunctiva and the trauma zone was evaluated.

Group 4: The procedures in Group 1 were repeated, but the specimens were taken 1 week later for the evaluation of acute inflammation. The acute inflammatory and vascular proliferation effects of electrocautery were investigated and compared with the control group.

Group 5: The procedures in Group 2 were repeated and the specimens were taken 1 week later to investigate the acute inflammatory and vascular proliferation effects of radio-cautery and compared with the control group and also with electro-cautery studies.

Group 6: The procedures in Group 3 were repeated and the specimens were taken 1 week later to investigate the acute inflammatory and vascular proliferation effects of laser and compared with the control group and also with electro-cautery and radio-cautery studies.

Group 7: The procedures in Group 1 were repeated and the specimens were taken 2 weeks later to evaluate inflammation and fibrosis and the effects of electro-cautery on chronic period healing in transconjunctival blepharoplasty were investigated.

Group 8: The procedures in Group 2 were repeated and the specimens were taken 2 weeks after the operation and the effects of radio-cautery on chronic period healing in transconjunctival blepharoplasty were investigated.

Group 9: The procedures in Group 3 were repeated and the specimens were taken 2 weeks after the operation and the effects of laser application on chronic period healing in transconjunctival blepharoplasty were investigated.

The specimen samples taken from the subjects were fixed in 10% buffered formalin solution. After being washed under running water for 1 day, they were passed through alcohol and xylene series and blocked

in paraffin. The sections taken with a 5µm thickness with a microtome (Leica RM2125RT) were stained with Hematoxylin Eosin for histopathological examination. The evaluation of the results was done with the help of a Nikon Eclipse E600W light microscope. Microscopic photographs were taken with a Nikon DS Camera Head DS-5M.

Statistical Analysis

The statistical analysis of the data was performed using the IBM SPSS 20 statistical package program. The differences between the groups were examined using the Kruskal-Wallis Test in non-parametric data. As a result of the statistical analysis, $p < 0.05$ was considered statistically significant.

Results

4 different methods of incision were made on the eyelids of 54 subjects included in the study. These are (1) Incision with scalpel, (2) Incision with electrocautery, (3) Incision with radiocautery and (4) Incision with laser. Subjects were divided into 9 different groups and the incision methods described in each group were applied. Each subject had a scalpel incision on the right conjunctiva as a control group, 18 subjects were incised with electrocautery, 18 subjects were incised with radiocautery and 18 subjects were incised with laser.

In subjects who underwent surgical intervention; it was investigated whether there was a difference between the width of the defect created by surgery and its depth immediately after the intervention, whether there was a difference between the vascular proliferation, inflammation and fibrosis values after 1 week and whether there was a difference between the vascular proliferation, inflammation and fibrosis values after 2

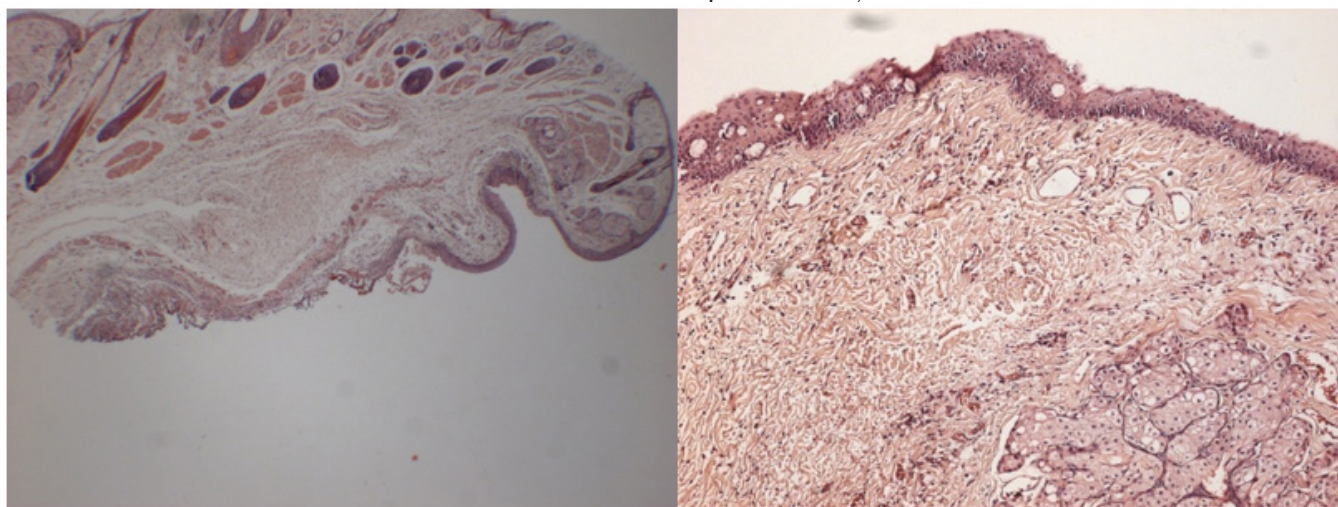


Figure 1. The figure illustrates the variation in tissue response, with differences in vascular proliferation, inflammation, and fibrosis levels after 2 weeks post-incision.

weeks (Figure 1).

In our study, on the day we started the experiment, it can be said that the defect widths in incisions made with scalpel and laser were less than in incisions assisted by radiocautery and electrocautery. In addition, on the same day, the defect depth was observed to be the least in incisions made with scalpel and the most in electrocautery and radiocautery. In the preparations we examined, it can be said that at the end of the first week, histologically, the least vascular proliferation, inflammation and fibrosis occurred in tissue preparations where electrocautery was used. On the contrary, at the end of the first week, the incision method that was detected the most among these histological parameters was radiocautery. In the examinations at the end of the second week, it was determined that the least vascular proliferation and inflammation belonged to the scalpel incision, and fibrosis was observed the least in tissues where radiocautery was used; on the contrary, it was determined that the incision in which these three histological parameters were observed the most belonged to electrocautery.

1-) It can be said with a 5% error that there is a difference in defect widths in the incisions made on day 0 ($\text{sig}<0.05$). In this context, it can be said that (1) Scalpel incision and (4) Laser incision create less defect width than the other two incision methods.

2-) It can be said with a 5% error that there is a difference in defect depths in the incisions made on day 0 ($\text{sig}<0.05$). In this context, it can be said that (1) Scalpel incision creates the least defect depth, and (4) Laser incision is in second place.

3-) It can be said with a 5% error that there is a difference in vascular proliferation, inflammation and fibrosis in the incisions made on week 1 and week 2 in terms of methods ($\text{sig}<0.05$). In this context, it can be said that (1) incision with scalpel causes the least vascular proliferation, and (4) incision with laser is in the second place.

4-) It can be said with a 5% error that there is a difference between vascular proliferation, inflammation and fibrosis in the incisions made in the 1st and 2nd weeks in terms of methods ($\text{sig}<0.05$). In this context, it can be said that (2) incision with electrocautery causes the least inflammation, and (1) incision with scalpel is in the second place.

5-) It can be said with a 5% error that there is a difference between vascular proliferation, inflammation and fibrosis in the incisions made in the 1st and 2nd weeks in terms of methods ($\text{sig}<0.05$). In this context, it can be said that (2) incision with electrocautery causes the least fibrosis, and (1) incision with scalpel is in the second place.

Kruskal-Wallis Test

As a result of the second Kruskal-Wallis test; 1-) In the incisions made in the 1st week, it can be said with a 5% error that there is a statistically significant difference in terms of vascular proliferation, inflammation and fibrosis formation in terms of incision methods ($\text{sig}<0.05$). In this context, it can be said that incisions made with electrocautery in the 1st week revealed the least vascular proliferation, inflammation and fibrosis.

As a result of the second Kruskal-Wallis test;

1-) In the incisions made in the 2nd week, it can be said with a 5% error that there is a statistically significant difference in terms of vascular proliferation in terms of incision methods ($\text{sig}<0.05$). In this context, it can be said that incisions made with scalpel in the 2nd week revealed the least vascular proliferation, and secondly, incision with Laser revealed the least vascular proliferation.

2-) In the incisions made in the 2nd week, it can be said with a 5% error that there is no statistically significant difference in terms of inflammation and fibrosis in terms of incision methods.

Discussion

On the day we started the experiment in our study, it can be said that the defect widths in the incisions made with scalpel and laser were less than in the incisions assisted by radiocautery and electrocautery. In addition, on the same day, the defect depth was observed to be the least in the incision made with scalpel and the most in the incisions made with electrocautery and radiocautery. In the preparations we examined, it can be said that at the end of the first week, histologically, the least vascular proliferation, inflammation and fibrosis occurred in the tissue preparations where electrocautery was used. On the contrary, at the end of the first week, the incision method that was detected the most among these histological parameters was the use of radiocautery. In the examinations at the end of the second week, it was determined that the least vascular proliferation and inflammation belonged to the scalpel

incision, and fibrosis was observed least in the tissues where radiocautery was used; conversely, the incision where these three histological parameters were observed the most was found to be electrocautery. This also suggests that long-term scarring will be greater in tissues where electrocautery was used. However, in the study conducted by Pruksapong et al., long-term scar results of Colorado needle-tip cautery and classical scalpel in upper eyelid blepharoplasty were compared, and it was observed that cautery did not have worse results [2]. In the article by Laurence et al., the use of CO2 laser, electrocautery and scalpel was compared specifically for blepharoplasty surgery, and no difference was found between the three incisions in terms of scar quality, color, size and structure [18]. Rokhsar et al. used CO2 laser and Colorado needle-tip cautery in upper and lower blepharoplasty and compared them in terms of scarring. Histological examination showed that CO2 laser caused more thermal damage; however, there was no difference in scar width on the 30th postoperative day [19]. Again, Carqueville and Chesnut, in their article comparing upper blepharoplasty incisions, found that heat artifacts, thermal damage and epidermal necrosis related to this were more in histological specimens of CO2 laser compared to microdissection cautery and classical scalpel [20]. In the study conducted by Liboon et al. by incising pig mucosa, it was stated that the least histological damage was in the tissues where scalpel was used [21]. Fisher et al. stated in their article that less scar tissue was formed and healing occurred faster in laser-created wounds compared to wounds opened with traditional scalpel [22]. In the experimental study conducted by Sinha et al. on the oral mucosa of guinea pigs, straight scalpel, ultrasonic scalpel, monopolar and bipolar were compared. At the end of 28 days, it was observed that the best tensile strength and the fastest re-epithelialization were in the incisions made with the classical and ultrasonic scalpels, and that complete resolution of inflammation was again in the classical and ultrasonic scalpels in 14 days [23]. Barbi et al. compared radiofrequency and scalpel incisions in upper blepharoplasty and observed no difference in scar vascularity, elasticity or pigmentation after a six-month follow-up [24].

Conclusion

This study highlights the varying effects of scalpel, electrocautery, radiocautery, and laser incisions on wound healing in transconjunctival blepharoplasty. Scalpel and laser incisions caused less tissue trauma and faster healing in the short term, while electrocautery

and radiocautery produced more pronounced tissue damage initially but led to reduced inflammation and fibrosis over time. At one week, electrocautery showed the least vascular proliferation and fibrosis, whereas radiocautery caused the most tissue trauma early on. By the second week, scalpel incisions resulted in the least inflammation, and radiocautery had the least fibrosis. These findings suggest that while scalpel and laser may be preferable for short-term healing, electrocautery offers potential benefits in minimizing long-term scarring, underlining the importance of selecting the appropriate incision method based on both immediate and long-term outcomes.

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Ethical Declaration: Ethics approval for the study was obtained from the Ondokuz Mayıs University Animal Experiments Ethics Committee (date: 23.06.2005, no: 2005/070)

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Regional fat distribution as a predictor of carotid atherosclerosis: Insights from mediastinal and cervical fat analysis

Sevde Nur Emir¹

Servet Emir²

1. University of Health Sciences, Umraniye Training and Research Hospital, Department of Radiology, Istanbul, Turkey

2. University of Health Sciences, Umraniye Training and Research Hospital, Department of Internal Medicine, Istanbul, Turkey

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Corresponding Author: Sevde Nur EMİR

University of Health Sciences, Umraniye Training and Research Hospital, Department of Radiology, Istanbul, Turkey

Email: drsevdenuremir@gmail.com

Abstract

Objective

Atherosclerosis is a leading cause of cardiovascular diseases such as myocardial infarction and stroke. Obesity, particularly regional fat distribution, is known to play a significant role in the pathogenesis of atherosclerosis. The aim of our study is to investigate the relationship between the anterior mediastinal fat tissue areas, posterior cervical subcutaneous fat tissue thickness, and the presence of carotid plaque.

Methods

This retrospective study included 273 patients who underwent carotid CT angiography between 2021 and 2023. Patients under 18 years, with malignancy, or within adequate image quality were excluded. Anterior mediastinal fat tissue area was measured manually on axial CT images, and posterior cervical subcutaneous fat thickness was measured on sagittal images. Statistical analyses included the Mann-Whitney U test, Spearman's correlation, and logistic regression.

Results

There was a significant positive correlation between mediastinal fat area and carotid plaque presence ($r_s = 0.3417$, $p < 0.05$). The optimal cut-off value for mediastinal fat area to detect carotid plaque was 575 mm^2 , with 78.79% sensitivity and 62.67% specificity. No significant correlation was found between cervical fat thickness and carotid plaque presence.

Conclusion

The anterior mediastinal fat tissue area is a moderate predictor of carotid plaque presence and can be easily measured during routine CT scans. This measurement may help identify patients at risk of atherosclerosis and guide further diagnostic evaluations.

Keywords: Carotid artery stenosis; fatty tissue; atherosclerosis; cardiovascular risk; computed tomography

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Introduction

Atherosclerosis is the leading cause of cardiovascular diseases, including myocardial infarction and stroke, and remains a significant global health issue [1]. According to the World Health Organization, atherosclerosis accounts for 32% of all deaths, making it the primary cause of mortality worldwide [2]. The pathogenesis of atherosclerosis is closely linked to chronic inflammation, driven by risk factors such as dyslipidemia, diabetes, obesity, hypertension, and smoking [3].

In both developed and developing countries, obesity is among the most preventable contributors to morbidity and mortality related to atherosclerosis. Consequently, recent research has increasingly focused on understanding the pathophysiological connections between obesity and cardiovascular conditions such as hypertension, dyslipidemia, and glucose intolerance. Current evidence suggests that fat distribution may be a more accurate indicator of cardiovascular risk than overall obesity itself [4].

Abdominal visceral fat accumulation, in particular, has been identified as a key factor in the heightened risk of cardiometabolic and inflammatory events [5,6]. In addition to this, studies have increasingly explored the role of specific fat depots, such as pericardial, epicardial, and perivascular fat, in cardiovascular risk, revealing associations with atherosclerosis [7,8,9]. Adipose tissue, known to secrete proinflammatory mediators, plays a crucial role in activating macrophages, T cells, and cytokines, thereby fostering an inflammatory environment that promotes the development of atherosclerosis [10].

Thus, beyond the commonly used measures like body mass index (BMI) or total fat volume, the distribution of fat in specific regions is critical for understanding the link between obesity and atherosclerosis. Regional fat measurements, including abdominal visceral fat and epicardial fat, often require specialized imaging techniques. In contrast, our study focuses on more easily accessible measures, specifically the anterior mediastinal fat tissue area and posterior cervical subcutaneous fat tissue thickness, to assess their relationship with the presence of carotid plaque. To our knowledge, no previous research has investigated the association between mediastinal fat tissue area, posterior subcutaneous fat tissue, and carotid plaque formation.

Methods

This study was approved by our hospital's institutional

review board. We retrospectively screened patients who underwent carotid CT angiography between 2021 and 2023 using our hospital's Picture Archiving and Communication System (PACS). The inclusion criteria required that the scans contain the level where the aorta

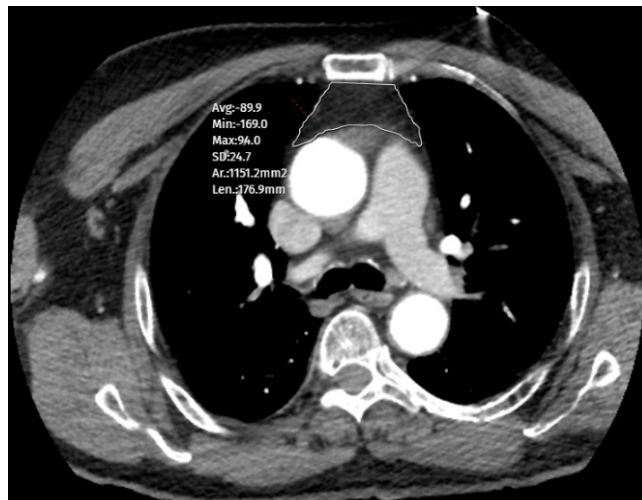


Figure 1: The measurement of the anterior mediastinal fat tissue area on the axial CT image.

and pulmonary artery are side by side, as this is the reference level for measuring the anterior mediastinal fat tissue area. Patients under 18 years of age, those with a history of malignancy or thoracic surgery, or those whose image quality was compromised due to artifacts were excluded from the study.

All CT scans were acquired using the same 128-multidetector CT scanner (GE Healthcare), with



Figure 2: The measurement of the posterior cervical subcutaneous fat tissue thickness on the sagittal CT image.

intravenous contrast administered via bolus injection. A radiology specialist with 11 years of experience performed all measurements on a high-resolution monitor. We divided the patients into two groups: those with carotid plaque and those without [11]. The anterior mediastinal fat tissue area was measured on the

axial plane. A free-hand region of interest (ROI) was used to manually measure the mediastinal fat tissue at the level where the aorta and pulmonary artery are situated in the anterior compartment, and these measurements were recorded in square millimeters (mm^2) (see Figure 1). For posterior cervical subcutaneous fat tissue thickness, measurements were taken in the sagittal plane. The thickness was assessed at the level of the C7 vertebra, where a perpendicular line was drawn from the bone margin to the skin (see Figure 2).

We performed statistical analyses using the NCSS (Number Cruncher Statistical System) 2007 software (Kaysville, Utah, USA). Descriptive statistics such as maximum, minimum, and mean values of mediastinal fat area and cervical fat thickness were calculated for both groups. The Shapiro-Wilk test was applied to determine whether the data followed a normal distribution. As the data were not normally distributed, group comparisons were conducted using the Mann-Whitney U test. Additionally, Spearman's rank correlation coefficient was used to assess relationships between carotid plaque presence, mediastinal fat area, and cervical fat thickness. Logistic regression analysis was performed to examine the impact of mediastinal fat area and cervical fat thickness on carotid plaque presence, adjusting for confounding factors such as age and gender. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 273 patients were included in our study, consisting of 114 women and 159 men. The average age was 59 for men and 61 for women. When we divided the patients into two groups based on the presence of carotid plaque, 198 patients had carotid plaque while 75 did not. Table 1 summarizes the age, anterior mediastinal fat area, and cervical fat thickness statistics for both groups.

According to the Spearman correlation analysis, we found a moderate correlation between the presence of

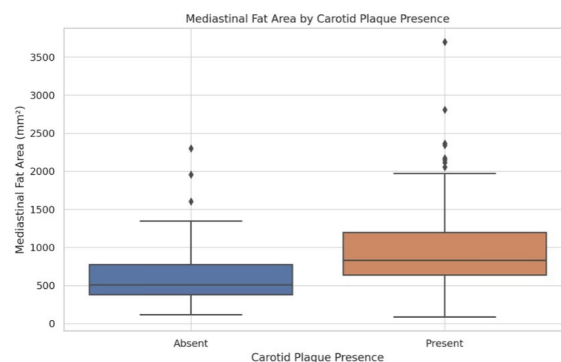


Figure 3: This plot compares the mediastinal fat area between patients with and without carotid plaque.

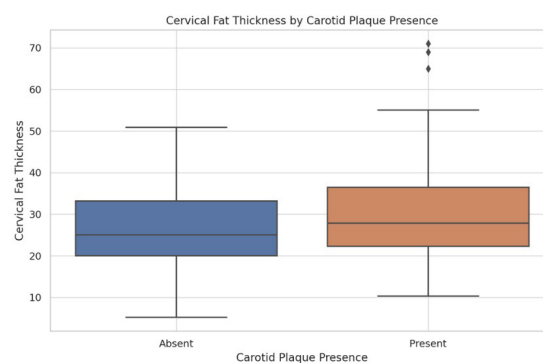


Figure 4: This plot compares the cervical fat thickness between patients with and without carotid plaque.

carotid plaque and the mediastinal fat tissue area ($r_s = 0.3417$), indicating a significant relationship between these variables (Figure 3). However, the correlation between carotid plaque and cervical fat thickness was weaker ($r_s = 0.1390$) (Figure 4). Additionally, the correlations of age with carotid plaque presence, mediastinal fat tissue area, and cervical fat thickness were found to be very weak.

In the logistic regression analysis, an increase in mediastinal fat area was significantly associated with a higher likelihood of carotid plaque presence ($p = 0.000045$). Being male was also significantly related to

Table 1: Summary statistics of age, anterior mediastinal fat area and cervical fat tissue thickness between individuals with and without carotid plaque

	Number	Age Mean \pm SD	Anterior mediastinal fat area Mean \pm SD	Cervical fat tissue thickness Mean \pm SD
Carotid Plaque Absent	75	59.36 \pm 9.34	623.27 \pm 405.05	26.08 \pm 9.76
Carotid Plaque Present	198	60.56 \pm 8.36	954.61 \pm 522.34	29.75 \pm 10.92

a higher likelihood of having carotid plaque ($p = 0.045$). However, no significant relationship was observed between cervical fat thickness and the presence of carotid plaque ($p = 0.219$). The ROC analysis showed that the area under the curve (AUC) for mediastinal fat tissue area in detecting carotid plaque was 0.721 (95% CI), as shown in Figure 5. The optimal cut-off value for mediastinal fat area, determined by the Youden index, was 575 mm². At this cut-off, the sensitivity was 78.79%, and the specificity was 62.67%.

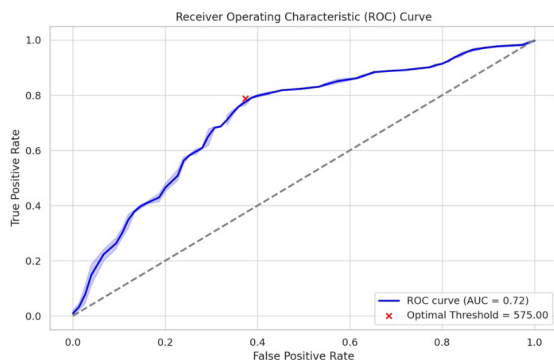


Figure 5: The Receiver Operating Characteristic (ROC) curve analysis for anterior mediastinal fat area.

Discussion

Obesity is characterized by abnormal fat accumulation due to excessive energy intake, and it is well established that obesity significantly increases the risk of myocardial infarction and stroke through its contribution to atherosclerosis. Adipose tissue plays a key role in promoting vascular inflammation by producing adipokines and inflammatory mediators, which affect vascular elasticity and atherogenesis. These mediators influence gene expression and cell functions in endothelial cells, arterial smooth muscle cells, and macrophages, fostering atherosclerosis development [12, 13].

In recent years, the focus has shifted towards the importance of local fat accumulation, independent of total fat volume or BMI. Research has emphasized the roles of epicardial and perivascular fat in particular, highlighting their significant local effects as cardiovascular risk factors [13,14]. However, it is known that these measurements are not routinely included in diagnostic screening reports and often require dedicated workstation assessments. For this reason, we aimed to investigate the relationship between carotid plaque presence and two parameters that can be easily measured

in routine practice: anterior mediastinal fat tissue and posterior cervical subcutaneous fat thickness.

In daily practice, non-contrast thoracic CT scans are frequently performed for various reasons, such as pain, cough, infection, and nodule follow-up. Given that we consistently evaluate the anterior mediastinal fat tissue in these scans, we sought to determine whether it could serve as an indicator of atherosclerosis. The key finding of our study is that the anterior mediastinal fat tissue area demonstrated moderate performance in predicting the presence of carotid plaque, with a threshold value of 575 mm² proving to be significant. This finding suggests that during routine thoracic CT evaluations, measuring the anterior mediastinal fat tissue area can help identify patients at risk for carotid plaque. This information could be shared with clinicians to recommend further evaluation via carotid Doppler ultrasound, particularly in male patients, potentially reducing the incidence of carotid stenosis and embolic stroke.

A study by Bekin Sarıkaya et al. found no significant relationship between thoracic aortic plaque and mediastinal fat area [15], but their study had a smaller sample size and examined thoracic aortic plaques, which are less clinically significant compared to carotid plaques [16]. Thus, we believe our study adds important value to the literature.

When evaluating thoracic CT, cervical CT, and cervical spinal MRI, we routinely use the sagittal plane. During this process, posterior cervical subcutaneous fat thickness can be easily measured. In a study by Piche et al., the relationship between posterior cervical subcutaneous fat thickness and body mass index (BMI) was explored, and fat thickness measured at the C7 level was found to have the strongest correlation with BMI ($r=0.583$, $p<0.05$) [17]. Based on these findings, we measured the subcutaneous fat thickness at the C7 level in our study. However, no significant relationship was found between the presence of carotid plaque and subcutaneous fat thickness in our analysis. The literature includes studies suggesting that cervical subcutaneous fat accumulation is associated with cardiovascular disease risk factors, independent of BMI and visceral fat tissue [18,19]. However, the lack of association in our study may be attributed to the multifactorial nature of atherosclerosis pathophysiology, which involves numerous factors beyond fat tissue alone. Therefore, we believe that further studies are needed in this area.

Our study has certain limitations. First, selection bias may be present, as the measurements were taken

from carotid CT angiographies performed for specific complaints and symptoms. Second, biochemical blood inflammation markers and lipid profiles of the patients were not evaluated. Including these parameters could yield more detailed results. Additionally, while we excluded patients with malignancies, other systemic inflammatory conditions such as diabetes mellitus and hypertension were not excluded from the study.

Conclusion

In conclusion, despite certain limitations, our study demonstrated a positive correlation between increased anterior mediastinal fat and the presence of carotid plaque. Routine evaluation of anterior mediastinal fat tissue during thoracic CT may help identify individuals at risk for atherosclerosis. Referral for carotid Doppler ultrasound in at-risk individuals, particularly men, could facilitate early detection and intervention, potentially reducing complications related to carotid stenosis and embolic stroke.

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Ethical Declaration: Ethics approval for the study was obtained from the Umraniye Research and Training Hospital Scientific Research Ethics Committee (date: 11/07/2024, no: 210)

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Association of helicobacter pylori infection with coronary artery disease and the severity of angiographic lesions

Nur Ozer Sensoy¹
Selman Unverdi²

1. University of Health Sciences Bursa City Training and Research Hospital Department of Internal Medicine and Nephrology, Bursa Turkey

2. Türkiye Dr. Suat Günsel Girne University Hospital University of Kyrenia Hospital Department of Internal Medicine and Nephrology, Girne Cyprus

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Corresponding Author: Nur Ozer SENSOY, MD. University of Health Sciences Bursa City Training and Research Hospital Department of Internal Medicine and Nephrology, Bursa Turkey

Email: nurozer_@hotmail.com

Abstract

Objective: There are controversies evaluating the association between different strains of *Helicobacter pylori* (HP) and occurrence of coronary arterial disease (CAD). HP may facilitate gastric ulcers and gastrointestinal bleeding. As angiographic lesions of high thrombus burden needs more potent and risky antithrombotic treatment regimens, we aimed to investigate the role of different strains of HP for angiographic lesions with high thrombus burden.

Methods: Medical and drug history of 109 consecutive patients who were candidate for coronary angiography were taken. Blood samples were obtained to measure anti HP (Ig) immunoglobulin G and anti-CagA (cytotoxin-associated gene) IgG antibody. According to angiography reports, participants were divided into three groups. Normal (n = 34), lesions with no thrombus (n=38) and lesions with thrombus (n = 37). To measure the association between CagA positive and less virulan strains of HP with the severity of CAD, ordinal logistic regression tests were used by adjusting age, sex, history of hypertension, diabetes mellitus, dyslipidemia and smoking.

Results: The mean ages of patients with and without CAD were 59±14. The prevalence of seropositivity to HP IgG titer was 69% (n=75). Fifty nine (79%) subject had CagA IgG seropositivity. Positive CagA IgG serology was 67% (n=50) and 44% (n=15) in CAD and control groups respectively. While HP IgG serology wasn't associated with lesion severity; CagA IgG serology was independently associated with lesion severity (OR: 2.4 (1.1-5.6) p=0.03).

Conclusion: Colonization of CagA positive HP was an independent risk factor for angiographic lesion severity.

Keywords: Helicobacter Pylori; coronary arterial disease; atherosclerotic lesion severity

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Introduction

Atherosclerosis represents a prevalent vascular condition that can lead to numerous clinical problems. Among these are coronary artery disease (CAD), ischemic stroke and peripheral tissue necrosis [1,2]. Numerous studies have identified factors such as diabetes, hypertension, smoking, and hypercholesterolemia as significant contributors to the development of atherosclerosis. However, the precise processes that initiate and drive the progression of atherosclerotic plaques are not yet fully understood. Interestingly, atherosclerosis can occur without conventional risk factors. Inflammation plays a key role in CAD pathogenesis, highlighting chronic infections as possible triggers of inflammatory responses. In the last ten years, significant effort has been directed toward researching to uncover potential links between chronic infections and atherosclerosis [3,4]. Several pathogens have been detected within atherosclerotic plaques, leading to the hypothesis that these infectious agents may trigger vascular inflammation through persistent infection or immune-mediated [5,6].

Helicobacter pylori (HP) infection is closely associated with various medical conditions, including peptic ulcer disease, potentially dangerous gastrointestinal bleeding, atrophic gastritis, and gastric cancer [7]. Recent research has also indicated a possible connection between HP infection and CAD. A case-control study found a notably higher rate of seropositivity to HP among patients with coronary artery stenosis, as confirmed through coronary angiography, compared to the general population [8]. Although certain studies have corroborated these findings [9,10], other research shows conflicting evidence regarding the link between HP infection and CAD [11,12]. Factors such as age, smoking habits, and social class, which are related to both HP infection and CAD risk, may contribute to these inconsistent results [4]. On the other hand, investigations examining the impact of more virulent strains of HP particularly those harboring the cytotoxin-associated gene A (CagA) pathogenicity island, have yielded more promising findings. A significant association between infection sustained by those strains and vascular damage have been shown [13].

Effective long-term antiplatelet and antithrombotic treatments are essential for patients with CAD, especially for those presenting with significant thrombus burden in angiographic assessments. In addition to the inflammatory mechanisms involved in atherosclerosis, HP infection has been shown to elevate

the risk of gastrointestinal bleeding [14]. The increased cytotoxicity of certain HP strains, coupled with the enhanced risk of digestive tract complications arising from the use of aspirin or dual antiplatelet therapies, underscores the crucial role HP plays in the context of CAD management.

We therefore conducted a cross-sectional study to assess the association between various markers of previous infection with HP (IgG) and angiographically confirmed CAD, controlling simultaneously for a variety of potential confounders. Specifically, we wanted to assess whether chronic infection with HP was associated with angiographic lesion severity and whether this association was related to the presence of the more virulent HP CagA-positive strain. Thus, we will contribute to the literature on the extent of the risk that long-term antiplatelet therapy may pose in ischemic heart disease.

Methods

Patients and Control Subjects

Consecutive patients undergoing elective and urgent coronary angiography in the Department of Cardiology, Ankara Training and Research Hospital, Turkey with various manifestations of ischaemic heart disease including the acute coronary syndrome patients were included in the study. All patients were considered potential cases of CAD based on clinical symptoms or findings from non-invasive diagnostic tests such as electrocardiography, a treadmill exercise test, and radionuclide myocardial test. Participation was on a voluntary basis, and written informed consent was obtained from all participants. The study protocol received approval from the ethics committee of the Ankara Training and Research Hospital, Turkey. The inclusion period was from February to August of 2014. A total of 34 patients with acute coronary syndrome and 75 patients with evidence of ischemia (34 patients with normal angiographic coronary arteries) were studied.

The case group was consisted of 75 angiographically confirmed CAD patients who had stable or unstable symptoms. The control group consisted of 34 symptomatic patients admitted to the hospital with angiographically normal coronary arteries. No participant showed clinical signs of connective tissue disease, liver dysfunction, hypothyroidism, severe chronic heart failure or severe renal disease (eGFR < 30 mL/min/1.73 m²) and malignant diseases. Moreover, patients were excluded if they had an acute or chronic infection or inflammation,

had undergone any surgery in the four weeks prior, had a history of upper gastrointestinal tract surgery or coronary artery bypass surgery, were using nonsteroidal anti-inflammatory drugs, or if their data was incomplete. Additionally, none of the 109 participants enrolled in the study irrespective of stable or unstable symptoms had undergone eradication therapy for HP infection or received any antibiotic treatment during the study period.

All subjects underwent standardized interviews conducted by trained interviewers. Demographic information and CAD risk factors were documented for all participants. Participants were asked about medical history, including specific questions related to physician-diagnosed hypertension, diabetes, heart failure and gastro duodenal disease. Furthermore, current medication, socio-demographic data, and lifestyle habits, including smoking and alcohol consumption, were recorded. Individuals with an income below twice the national minimum wage were classified as having a lower socioeconomic status. Education levels were categorized into two groups: those with less than 10 years of education and those with 10 or more years of education.

Cardiovascular risk factors included a family history of CAD in first-degree relatives under 55, hypertension (blood pressure $>140/90$ mm Hg or use of antihypertensive medication), diabetes (fasting glucose >126 mg/dL or use of antidiabetic drugs/insulin), and hyperlipidemia (LDL cholesterol ≥ 130 mg/dL or use of lipid-lowering medication). Twenty cigarettes per month were smokers and renal dysfunction was defined as creatinine plasma concentrations of >1.3 mg/dL.

Effort angina was defined as chest pain during walking that was relieved within 10 minutes of stopping, indicated by ST segment depression on a 12-lead ECG during pain, or a positive stress test. Acute myocardial infarction (AMI) diagnosis followed the related Society of Cardiology criteria [15].

Laboratory methods

Blood testing before coronary angiography was evaluated using an auto-analyzer. Blood was centrifuged at $3000g$ for 10 minutes till frozen at -70°C until analysis. Specific anti-HP IgG and Anti-CagA IgG antibodies were measured using a commercial ELISA kit (Radim Diagnostics, Rome, Italy) following the manufacturer's instructions. Titers were classified as positive or negative with a cutoff of 30 UR/mL. The test sensitivity and specificity were 88% and 93.8%, respectively [16].

Determination of CAD

Coronary arteries were demonstrated in the left and right oblique planes with cranial and caudal angulations. Iohexol injections opacified the coronary arteries at each position. Based on the results of coronary angiography, the patients were classified into CAD (including the acute coronary syndrome patients) and control groups. The CAD group was divided further into thrombotic and non-thrombotic groups.

Normal coronary artery has been defined as absence of angiographically visible atherosclerotic plaques, thrombi, ectasia, myocardial bridging, or congenital coronary artery anomalies. Abnormal coronary artery has been defined as stenosis of at least one major epicardial coronary vessel. The assessment of stenosis severity is based on the percentage decrease in the vessel's diameter. Abnormal angiograms were categorized as one, two, or three vessel disease based on the presence of stenosis greater than 50% in a significant epicardial vessel. Additionally, the severity of visual lesions was classified according to their thrombotic characteristics. Thrombotic lesions included intraluminal, rounded filling defects that were largely detached from the vessel wall, evidence of embolization from this material, haziness of the lesions, irregular shapes with poorly defined edges, intraluminal staining at sites of total occlusion, and other filling defects that did not correspond with calcification.

Statistical analysis

Demographic and clinical characteristics in patients and control subjects were compared in a descriptive way. We employed the Shapiro-Wilk test to evaluate the normality of numeric variables. The Student *t* test, and the chi-square (χ^2) tests (or Fisher's exact test if any expected cell count was <5) were used to compare baseline characteristics, HP serology, and the presence of CAD. Comparisons of parametric values among the normal, thrombotic and non-thrombotic groups were performed by 1-way analysis of variance (ANOVA). Tukey Honest Significant Difference (HSD) was used as a post hoc test for multiple comparisons between the groups. Binary regression was used to investigate the relation between HP serostatus and coronary disease, while accounting for any confounding variables including age, sex, smoking, hypertension, hyperlipidemia and diabetes mellitus. Results are expressed mean \pm SD, percentages and as odds ratio (OR) with 95% confidence intervals (CI) as appropriate.

Proportional-odds ordinal logistic-regression models

Table-1. Main Characteristics of Our Study Group

	Overall (n=109)	CAD (n=75)	Control (n=34)	p-value
Age, (years)	59±14	62±13	53±12	0.001
Female, n (%)	45 (41)	28 (37)	17 (50)	0.21
Family history of CAD, n (%)	64 (59)	51 (68)	13 (38)	0.003
Socioeconomic status, n (%)				
Low	38 (35)	25 (33)	13 (38)	0.62
Middle-High	71 (65)	50 (67)	21 (62)	
School education <10 years, n (%)	52 (48)	38 (51)	14 (41)	0.36
Diabetes, n (%)	46 (42)	41 (55)	5 (15)	<0.0001
Hypertention, n (%)	67 (61)	57 (76)	10 (29)	<0.0001
Dyslipidemia, n (%)	54 (49)	46 (61)	8 (23)	<0.0001
Current smoker, n (%)	58 (53)	45 (60)	13 (38)	0.03
Daily alcohol consumption, n (%)	26 (24)	21 (28)	5 (15)	0.13
Heart failure, n (%)	22 (20)	22 (29)	0 (0)	<0.0001
Renal dysfunction, n (%)	16 (15)	15 (20)	1 (3)	0.015
Gastroduodenal disease, n (%)	55 (50)	37 (49)	18 (53)	0.73
Income level, n (%)				
Poor	38 (35)	25 (33)	13 (38)	0.62
Medium-Good	71 (65)	50 (67)	21 (62)	
Helicobacter pylori IgG seropositivity, n (%)	75 (69)	51 (68)	24 (71)	0.78
CagA IgG seropositivity, n (%)	65 (60)	50 (67)	15 (44)	0.026
Helicobacter pylori IgG titer	53.8±45.6	54.2±46.1	52.7±45.1	0.87
CagA IgG titer	81.6±89.7	92.4±91.8	57.6±81.1	0.06

CAD; Coronary arterial disease Data are expressed as mean±SD or number (%).

were used to assess the independent association of a positive antibody titer against HP with multiple severity categories of CAD, while simultaneously controlling for age, sex, smoking, history of hypertension,

Table-2. Relationship Between Helicobacter Pylori CagA Seropositivity and The Severity of Coronary Atherosclerotic Lesions

	Overall (n=109)	CagA IgG seropositive (n=65)	CagA IgG seronegative (n=44)	p-value
CAD, n (%)	75 (69)	50 (77)	25 (57)	0.03
CAD type, n (%)				
Stable CAD	75 (69)	44 (68)	31 (70)	0.76
ACS	34 (31)	21 (32)	13 (29)	
Number of arteries with lesions, n (%)				
1	24 (22)	13 (20)	11 (25)	0.14
2	21 (19)	14 (21)	7 (16)	
3	28 (26)	21 (32)	7 (16)	
Thrombotic lesion, n (%)	37 (34)	26 (40)	11 (25)	0.07

ACS; Acute coronary syndrome, CAD; Coronary Arterial Disease.

Table-3. General Characteristics of Our Study Group According to Angiographic Lesion Severity

	Control n=34	Non-thrombotic n=38	Thrombotic n=37	p-value
Age, (years)	53±12	62±14	63±14	0.003 * †
Female, n (%)	17 (50)	15 (39)	13 (35)	0.43
Family history of CAD, n (%)	13 (38)	25 (66)	26 (70)	0.01
Socioeconomic status, n (%)				0.07
Low	13 (38)	8 (21)	17 (46)	
Middle-High	21 (62)	30 (79)	20 (54)	
School education <10 years, n (%)	14 (41)	17 (45)	21 (57)	0.38 †‡
Diabetes, n (%)	5 (15)	22 (58)	19 (51)	<0.0001 †‡
Hypertention, n (%)	10 (29)	30 (79)	27 (73)	<0.0001 †‡
Dyslipidemia, n (%)	8 (23)	24 (63)	22 (59)	0.001 †‡
Current smoker, n (%)	13 (38)	22 (58)	23 (62)	0.10
Daily alcohol consumption, n (%)	5 (15)	10 (26)	11 (30)	0.30
Heart failure, n (%)	0 (0)	11 (29)	11 (30)	0.002 †‡
Renal dysfunction, n (%)	1 (3)	8 (21)	7 (19)	0.06
Gastroduodenal disease, n (%)	18 (53)	22 (58)	15 (40)	0.30
Helicobacter pylori infection, n (%)	24 (71)	25 (66)	26 (70)	0.88
CagA IgG seropositivity, n (%)	15 (44)	24 (63)	26 (70)	0.03 *§
H. Pylori IgG titer	53±45	59±49	49±42	0.75
CagA IgG titer	57±81	97±99	87±85	0.15
CAD type, n (%)				<0.0001 †‡
Stable CAD	34 (100)	25 (66)	16 (43)	
ACS	0 (0)	13 (34)	21 (57)	

ACS; Acute coronary syndrome, CAD; Coronary Arterial Disease. Values are expressed as mean ± standard deviation. * $p < 0.05$ between non-thrombotic and control groups, § $p < 0.05$ between thrombotic and control groups, † $p < 0.01$ between thrombotic and control groups, ‡ $p < 0.01$ between non-thrombotic and control groups.

hyperlipidemia and diabetes. This approach fits a uniform log cumulative odds of progression across our three categories of severity as a function of a positive antibody titer against HP at admission and other covariates. The proportional odds assumptions were met for these

regression models. A P-value ≤ 0.05 was considered statistically significant. Statistical tests were two-sided. All analyses were performed with IBM SPSS 14 (SPSS Statistics version 14, IBM Corp).

Results

Study population

The main characteristics of our study group are summarized in Table 1.

Patients showing CAD at coronary angiography presented more frequently with arterial hypertension, hypercholesterolemia, and diabetes mellitus as compared with controls, and were more frequently current smokers. Control subjects were slightly younger; and showed higher HDL cholesterol levels.

Approximately sixty-nine percent of the patients (69%) had CAD by coronary angiography, 69% had SAP and 31% had acute coronary syndrome (ACS). Thrombotic coronary lesions were detected in 34% of patients (Table 2).

General characteristics of our study patients stratified into three groups according to angiographic lesion severity are shown in Table 3.

Patients with normal coronary arteries were younger, had lower rate of comorbidities and family history of CAD compared to other groups.

HP Infection

The prevalence of seropositivity to HP (IgG titer) was 69% (n=75) and 59 (79%) subject had CagA IgG seropositivity. HP CagA IgG antibody titers in females and males were 92.8 ± 88.9 vs. 73.7 ± 90.2 , respectively ($p=0.3$). There was no association between age groups and both of the HP serostatus. The prevalence of

seropositivity to HP (IgG titer) was not significantly different between the CAD and control groups but CagA IgG seropositive patients were more likely to have CAD (Table 1 and 3). The percentage of seropositivity to HP CagA IgG in HP IgG seropositive patients according to angiographic lesion severity is shown in Figure-1.

CagA IgG titers in SAP and ACS groups were 75.2 ± 85.9 vs. 95.6 ± 97.4 ; $p > 0.05$ respectively. Patients with positive CagA IgG serology were more likely to be females and to have lower socioeconomic status. Diabetes mellitus, heart failure and gastro-duodenal disease were the most prevalent comorbidities in the CagA IgG seropositive group than the seronegative group (Table-4).

Predictors of CAD and lesion severity

Table 5 presents the results of univariable and multivariable logistic regression analyses in which the association between HP CagA IgG serostatus and CAD was adjusted for age, sex and for a variety of other potential confounders.

The OR for CAD given a positive HP CagA status remained to be statistically significant after adjustment for cardiovascular risk factors and other confounding factors. The association between HP CagA IgG serostatus and angiographic lesion severity was also assessed. In fully adjusted analyses HP CagA IgG serostatus was independently associated with lesion severity in addition to gender, hypertension and smoking (OR: 2.4, 95% CI: 1.1-5.6, $p=0.03$). CagA IgG serostatus was not a predictor of CAD type (OR: 1.1, 95% CI: 0.5-2.6, $p=0.76$).

Discussion

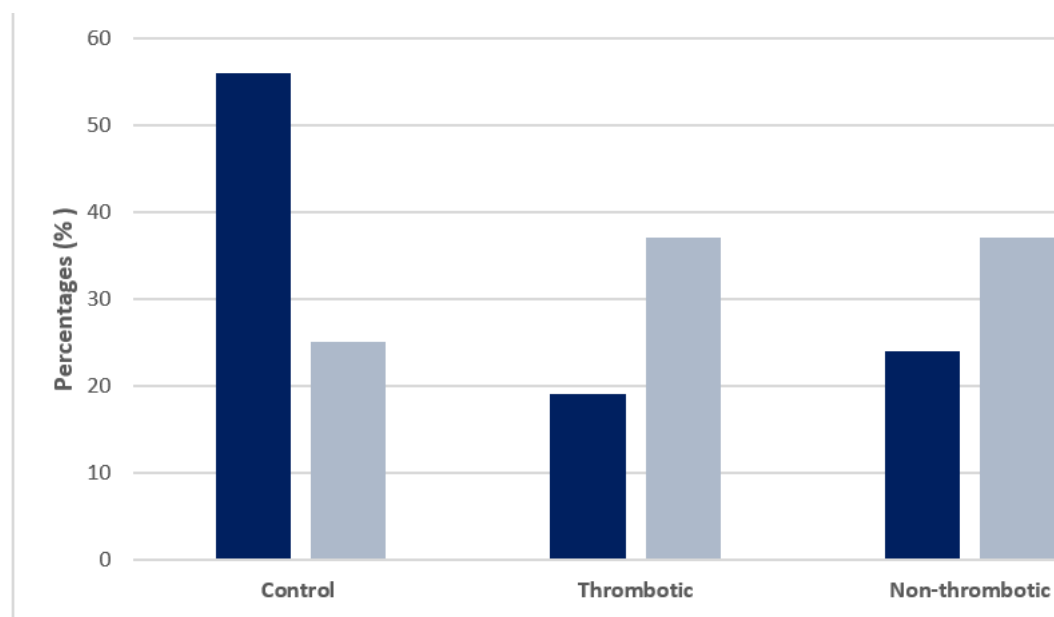


Figure-1: The percentage of seropositivity to HP CagA IgG in HP IgG seropositive patients according to angiographic lesion severity

In our study we have not demonstrated an association between serologic evidence of HP infection and angiographic evidence of CAD. On the other hand we found moderate associations between CagA IgG seropositivity to HP and the presence of angiographically confirmed CAD and lesion severity, which persisted to be statistically significant

Table-5. Univariate and Multivariate Logistic Regression Analysis of the Association Between The Confounding Multiple Variables and CAD.

Variables	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P Value
Age	1.0 (1.02-1.08)	0.001	1.04 (0.98-1.1)	0.21
Female gender	0.6 (0.3-1.3)	0.21	0.2 (0.05-0.72)	0.02
School education <10 years	1.5 (0.6-3.3)	0.36	-	-
Lower socioeconomic status	1.2 (0.5-2.8)	0.62	-	-
Hypertention	7.6 (3.0-18.8)	<0.0001	6.8 (1.7-26.4)	0.005
Diabetes mellitus	6.9 (2.4-20)	<0.0001	2.7 (0.7-10.3)	0.15
Dyslipidemia	5.1 (2.0-12.9)	<0.0001	1.9 (0.5-7.5)	0.34
Current smoker	2.4 (1.1-5.6)	0.037	4.5 (1.3-16.2)	0.02
Family history of CAD	1.3 (0.6-2.9)	0.6	-	-
Daily alcohol consumption	2.2 (0.8-6.6)	0.14	-	-
CagA IgG seropositivity	2.5 (1.1-5.8)	0.028	3.6 (1.1-12.3)	0.04
Helicobacter pylori IgG seropositivity	0.89 (0.36-2.14)	0.79	-	-

CAD; Coronary arterial disease.

after controlling for a variety of potential confounders.

As a widespread global infection, HP impacts over half of the world's population [7]. In Turkey, a developing country, seroprevalence of HP IgG is between 41% to 83% [17]. Our seropositivity rates were consistent with the previous findings. We found, 79% seropositivity for HP CagA IgG. In previous research, almost all strains isolated from samples collected in East Asian countries tested positive for CagA, in contrast to only about half of the strains from Western countries displaying CagA positivity [17]. This research found no significant variation in the rate of HP IgG seropositivity based on age or gender. However, CagA IgG seropositivity was notably higher in females compared to males. This finding is different from the study of Jafarzadeh et al. [18] that CagA positivity was more prevalent in males.

Although, some studies found HP infection as being one of the risk factors for CAD, separate from diabetes mellitus, dyslipidemia, and hypertension; existing research on the connection between HP infection and stable, chronic cardiac conditions has produced inconsistent findings

[19,20]. These conflicting findings might be attributed to the varying methodologies employed in these studies. These studies primarily relied on Enzyme-linked Immunosorbent Assay (ELISA) tests to detect HP IgG antibodies, which can indicate a current or past infection but do not confirm an active HP infection. Kowalski et al [21] discovered that subjects with CAD were significantly more likely to test seropositive for both HP and CagA IgG antibodies compared to the control group. Conversely, Sandifer et al. [22], demonstrated a negative correlation between the death rate from CAD and the seroprevalence of HP antibodies. Additionally, other studies have not confirmed any relationship between HP infection and the progression of CAD [23]. However, these authors did not examine the significance of anti-CagA seropositivity, which is known to be a marker for a heightened potential to trigger a systemic immune response. This inconsistency may partly be explained by Pasceri et al.'s hypothesis that only cytotoxic, CagA-positive *H. pylori* strains might be associated with CAD [13,24]. CagA seropositivity, as opposed to CagA seronegativity, has been shown to be linked with an increased susceptibility to CAD [13,24]. Furthermore, in a cross-sectional study

conducted by Niccoli et al [25], the anti-CagA antibody titer emerged as the sole independent predictor of the extent of coronary atherosclerosis. In our study, the rate of anti-CagA antibody seropositivity was consistent with the aforementioned studies, and this group alone demonstrated a significant association with CAD.

Another controversial subject is the relation between HP infection and unstable forms of cardiac syndromes. Such a significant, positive association between CagA IgG seropositivity and the occurrence of ACS was confirmed in a meta-analysis [26]. Similarly no significant relation was demonstrated between HP IgG seropositivity and the risk of acute myocardial infarction and stroke among 29,876 middle-aged Japanese patients in 12 year period. Only CagA IgG seropositivity exhibited a trend toward correlation with acute myocardial infarction [27]. In contrast, a relatively small study reported the higher seroprevalence of HP IgG in ACS patients than the control group while CagA IgG seroprevalence was similar in both groups [18]. These studies primarily utilized Enzyme-linked Immunosorbent Assay (ELISA) tests to detect HP IgG antibodies, which indicate current or past infection but do not confirm ongoing infection. This discrepancy between the investigations may be attributed to cohort heterogeneity due to the presence of probable active HP infection rate. In studies concerning the relationships between HP seropositivity and ACS, the CAD patients were frequently followed in relation to ACS occurrence. After ACS, being on acute infection period by HP can be responsible for platelet aggregation and local inflammation within the vascular wall that diminish along with plaque stabilization during subsequent weeks. The significant association of HP seropositivity with the risk of only short-term outcomes, rather than long-term outcomes; may emphasize the importance of acute infection in unstable forms of cardiac syndromes [28]. Although our analysis did not reveal any significant differences between stable and unstable cardiac syndromes based on pathogen HP serology, we did find a higher prevalence of thrombotic lesions in cases that were CagA seropositive. Unfortunately, we are unable to assess the potential influence of acute HP infection on our results.

Potent combined and long-term antithrombotic therapies are the mainstay of treatment in ACS, particularly in those with lesions of high thrombus burden. One of the hypothesized mechanisms connecting HP infection to the development of ACS is the stimulation of thrombotic processes through the perpetuation of a low-level chronic inflammatory response. [29]. By observing an association

between CagA IgG seroprevalence and lesion severity according to the presence of thrombogenic lesions, we have confirmed this finding. The involvement of HP infection in causing gastrointestinal (GI) bleeding is well documented. Furthermore, GI bleeding following ACS is linked to higher rates of morbidity and mortality [30]. In patients with CAD who are on dual antiplatelet therapy, better outcomes will be influenced by effective prevention of both ischemic events and bleeding complications. At present, it is recommended that patients at risk undergo HP testing and receive eradication therapy as a preventative measure against primary gastrointestinal bleeding [31,32].

The higher prevalence of HP infection in lower socioeconomic groups can be attributed to the greater percentage of infected individuals in developing countries (up to 82.5% of the general population) compared to developed countries (less than 20% of the general population) [17,33]. Low socioeconomic status is a known risk factor for atherosclerosis [33]. Studies indicating a connection between HP infection and CAD without accounting for socioeconomic factors are considered to be biased, as no link between HP seropositivity and future AMI has been detected among individuals of similar socioeconomic backgrounds [34]. In our study although we detected higher rates of low socioeconomic status in CagA IgG seropositive group, no effect of socioeconomic status was found on CAD.

It has been proposed that the link between CAD and HP infection is influenced by shared risk factors that predispose individuals to both conditions [30,35]. Diabetes mellitus, a significant contributor to the rise in CAD cases, is associated with a higher prevalence of HP infection [35]. A recent meta-analysis conducted by Wang et al [36] demonstrated a stronger correlation between HP infection and type 2 diabetes mellitus compared to type 1 diabetes mellitus. The association has been attributed to the delayed gastric emptying caused by autonomic diabetic neuropathy, which facilitates bacterial colonization of the gastric mucosa Tobacco smoking, a significant risk factor for atherosclerosis, has been suggested as a key factor in promoting HP transmission and exacerbating its detrimental effects on gastro-duodenal mucosa and extragastric manifestations, including ACS [30,37]. On the other hand, Brown [38] showed in his review that the majority of studies have not found tobacco use or alcohol consumption to be risk factors for HP infection. In our study while history of Diabetes mellitus, heart failure and gastroduodenal disease were the covariates associated with positive

CagA IgG serostatus, dyslipidemia, smoking and alcohol consumption were not associated with it. In fact, the relation between HP CagA IgG seropositivity and CAD remained to be significant even after adjustment for potential confounding factors. While HP infection may not be as significant a risk factor for CAD as traditional risk factors, even a slight increase in risk could have notable epidemiological consequences. This might be clinically important as the infection can be eradicated by specific antibiotic treatments [39].

Limitations

This is a cross-sectional investigation that establishes an association between HP CagA seropositivity and CAD but not causality. Therefore, CagA seropositivity may not directly cause CAD or lesion severity, but instead serves as a marker for an unknown risk factor. Consequently, the study's conclusions should be viewed as preliminary and hypothesis-generating. In addition, we didn't assess active HP infection based on the examination of biopsy specimens obtained during endoscopy or HP stool antigen and ¹³C-urea breath tests. Even if an active HP infection is not confirmed in seropositive patients, the possibility remains that the atherogenic impact of the infection, once triggered, may continue. Additionally, the duration of infectivity and the impact of HP infection on inflammatory and autoimmune responses were not taken into account.

Conclusion

These findings underscore the clinical significance of previous research that identified a connection between more virulent HP strains and more severe CAD, although the exact mechanism remains unclear. In this context, eradication and gastroprotective treatment of ischemic heart patients with more virulent H. pylori strains and receiving antiplatelet therapy will come to the fore in clinical practice.

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The effect of hypertension on cognitive dysfunction in female patients with fibromyalgia syndrome

Mehmet Alptekin Karacesme¹

Manolya Ilhanli²

Ilker Ilhanli³

1. *Physical Medicine and Rehabilitation State Hospital, Samsun, Turkey*

2. *Ondokuz Mayıs University Faculty of Dentistry, Multidisciplinary Clinic, Samsun, Turkey*

3. *Ondokuz Mayıs University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Samsun, Turkey*

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Corresponding Author: Manolya ILHANLI, Dt., PhD. in Oral and Maxillofacial Radiology, Ondokuz Mayıs University Faculty of Dentistry, Multidisciplinary Clinic, 55139, Samsun, Turkey

Email: manolya_dmrnc@hotmail.com

Abstract

Objective: To evaluate the effect of the presence of hypertension (HT) on cognitive dysfunction in female patients with fibromyalgia syndrome (FM).

Methods: A total of 36 female patients diagnosed with FM were included in the study and the patients were divided into 4 equal groups. Group 1 was HT with impaired cognition, Group 2 was HT with normal cognition, Group 3 was non-HT with impaired cognition and Group 4 was non-HT with normal cognition. Mini mental status examination test (MMSE) was used to assess cognitive function. Groups were compared in terms of age, FM disease duration, education, and MMSE scores. Also, the correlation of variables was investigated within the hypertensive and non-hypertensive patient groups.

Results: The median age was 51 (41-77) years and median FM disease duration was 60 (3-336) months. There was no significant difference between the groups in terms of age and disease duration ($p=0.423$ and $p=0.308$, respectively). Median MMSE value was 23.5. Between the groups with normal cognition (groups 2 and 4), MMSE median value was similar ($p=0.203$). Median value of MMSE was also similar ($p=0.192$) between the groups with impaired cognition (groups 1 and 3). Also, the median MMSE value in patients with HT was similar to in those without HT ($p=0.414$). When the correlation of variables was investigated within the hypertensive and non-hypertensive patient groups, no significant correlation was detected

Conclusion: In conclusion, in our cohort, which included a group of middle-aged patients, there was no evidence that HT increases cognitive dysfunction in female FM patients.

Key words: Fibromyalgia syndrome; hypertension; cognitive dysfunction

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Introduction

Fibromyalgia syndrome (FM) is a chronic disease of unknown cause, characterized by widespread pain and tender points in the musculoskeletal system, and may be accompanied by sleep and mood disorders, fatigue, and cognitive dysfunction [1]. Cognitive functions such as focus, attention and memory are affected in patients with FM [2, 3]. Cognitive dysfunction is one of the diagnostic criteria of FM and is used to determine the severity of the disease [4]. Problems related to memory and focus are called fibrofog [2, 3, 5]. Fibrofog refers to cognitive impairment such as forgetfulness, blurring of mental activity, sensory overload, difficulty in thinking, decreased ability to process information or follow conversations [6]. Approximately 80% of patients diagnosed with FM have cognitive complaints [5].

The general definition of Hypertension (HT) is systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg [7]. In more than 90% of cases with HT, no underlying cause can be identified and this is called primary HT, while 5-10% have an underlying cause and this is called secondary HT. HT is a serious medical condition that significantly increases the risk of cardiovascular, cerebral, renal and other organ dysfunction, but cognitive impairment is relatively less important [8, 9]. However, HT is a risk factor that negatively affects cognitive functions [10]. Cognitive functions are affected by blood pressure. Studies have proven that cognitive impairment is common in HT [11]. In particular, high blood pressure in middle age has been shown to increase the risk of cognitive decline and dementia in elderly [12]. Hypertensives exhibit decreased cerebral blood flow and metabolism in certain brain regions, particularly the frontal and temporal lobes and subcortical areas [13]. There are reports that hypertensives show smaller cerebral blood flow responses than normotensives during memory tasks [14]. Neurochemical transmission and basic cellular functions in the brain are also affected by hypertension. Therefore, various neurophysiological changes in hypertensives may explain their loss of cognitive function. High blood pressure is found to be related to smaller total and regional brain volumes which can be contributed to cognitive impairment [15]. This atrophy can be due to cortical neuronal apoptosis related to subcortical vascular pathologies. Endothelial damage due to high blood pressure can also disrupt the blood-brain barrier and allow toxic substances to enter the brain [13]. Also, HT is a serious risk factor for small vessel disease of the brain, and can lead to

microbleeds of brain, lacunar infarcts and white matter hyperintensities [15]. This small vessel disease can result in vascular dementia or interact with Alzheimer's pathology. In addition, HT was found to be associated with the beta amyloid deposition which may lead to cognitive impairment [15].

Cognitive dysfunction develops in the presence of HT and the dysfunction has been shown to be more severe in the presence of HT. Since cognitive impairment is associated with FM disease severity, it can be concluded that HT affects cognitive function in FM patients [16]. Although cognitive dysfunctions in HT and FM have been investigated separately, we have not found a study in the literature investigating the relationship between HT and FM according to the cognitive function. The aim of this study was to evaluate the effect of the presence of HT on cognitive dysfunction in patients with FM.

Methods

To determine the sample size, G*Power 3.1.9.4 (Duesseldorf, Germany) was used [17]. According to F tests, the total sample size for 4 groups was calculated as 36, with an effect size of 0.54, $\alpha = 0.05$ and 95% power [18]. A total of 36 female patients over 18 years of age who applied to Ondokuz Mayıs University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation and who were diagnosed with FM according to American College of Rheumatology-2016 FM diagnostic criteria and who gave written consent to participate in the study were included in the study. Exclusion criteria were as follows: cognitive impairment that prevents patients from answering the questionnaire, psychiatric diagnosis, systemic diseases other than HT, secondary HT and patients who were taking medication for FM. Patients were divided into 4 equal groups. Group 1 was HT with impaired cognition, group 2 was HT with normal cognition, group 3 was non-HT with impaired cognition and group 4 was non-HT with normal cognition. Patients diagnosed by a specialist were considered to have HT. Age, education and disease duration of the patients were recorded.

The Mini Mental State Examination Test (MMSE) was used to evaluate cognitive function. It was developed to quantitatively assess cognitive performance [19]. Its subsections include time and space orientation, recording memory, attention and concentration, recall and language. It is scored by summing the scores obtained from each item. The MMSE, which can be administered in 10 minutes under outpatient clinic conditions, is scored over a total of 30 points [19].

A score of ≤ 23 is considered cognitive impairment [20]. Turkish reliability and validity was conducted by Güngen et al [21].

For statistical analysis SPSS 22 (IBM, USA) was used. Kolmogorov-Smirnov, skewness-kurtosis and histogram-plots were used for evaluating normal distribution. Descriptive statistics were used. Median (min-max) values were given for non-normally distributed data. Kruskal Wallis and Mann Whitney U test were used to evaluate the difference between groups in terms of continuous variables. The chi square test was used to evaluate the difference in frequencies between groups. Also, MANOVA test was used to find the difference originated between which groups. Levene's test was used to analyse the equality of variances. For Post Hoc analysis, when the variance of the dependent variable is equal across groups Tukey's test was used

considered very high correlation [22]. Significance level was set $p < 0.05$.

Results

The total number of patients was 36, 9 in each group. All were female and married. The median age was 51 (41-77) years and median FM disease duration was 60 (3-336) months. There was no significant difference between the groups in terms of age, disease duration and education ($p=0.423$, $p=0.308$ and $P=0.322$, respectively). Table 1 shows the comparison of the groups according to demographic variables. Median MMSE value was 23.5. Between the groups with normal cognition (groups 2 and 4), MMSE median value was similar ($p=0.203$). Median value of MMSE was also similar ($p=0.192$) between the groups with impaired cognition (groups 1 and 3). Table 2 shows the comparison of the groups according to MMSE score. Also, the median MMSE score in patients

Table 1. Comparison of the groups according to demographic variables.

		Total N=36	Group 1 N=9	Group 2 N=9	Group 3 N=9	Group 4 N=9	P value
Age, years, Median (min- max)		51 (41-77)	55 (49-77)	51 (43-65)	50 (41-72)	51 (42-58)	0.423 ¹
Education, N	Literate	2	1	0	1	0	0.322 ²
	Primary school	24	7	6	6	5	
	Secondary school	2	1	0	1	0	
	High school	6	0	2	0	4	
	University	2	0	1	1	0	
Disease duration, months, Median (min-max)		60 (3-336)	84 (24- 246)	60 (3-120)	72 (12- 144)	120 (6-336)	0.308 ¹

* Significance level $p < 0.05$, ¹ Kruskal-Wallis test, ² Chi-Square test, Group 1: Hypertension with impaired cognition, Group 2: Hypertension with normal cognition, Group 3: Non- Hypertension with impaired cognition, Group 4: Non- Hypertension with normal cognition, min: minimum, max: maximum, N: subject number.

for correction and when the variance of the dependent variable is not equal across groups Tamhane's test was used for correction. Spearman correlation coefficient analysis was done to evaluate the correlations between age, disease duration and MMSE scores. A value between 0 and 0.3 was considered negligible correlation, a value between 0.3 and 0.50 was accepted as low correlation, a value between 0.51 and 0.7 was considered moderate correlation, a value between 0.7 and 0.9 was considered high correlation, and a value between 0.9 and 1.00 was

with HT was similar to in those without HT ($p=0.414$, Table 3). A significant, low, negative correlation was found between age and MMSE scores when all patients were considered (Table 4). On the other hand, when the correlation of variables was investigated within the hypertensive and non-hypertensive patient groups, no significant correlation was detected (Table 5 and 6). Variance analysis showed no difference between groups according to age and disease duration, but MMSE (Table 7).

Table 2. Comparison of the groups according to Mini mental status examination test score.

	Total N=36	Group 1 N=9	Group 2 N=9	Group 3 N=9	Group 4 N=9	P value
MMSE, score, Median (min-max)	23.5 (12-28)	21 (17-23) ^{2,a}	24 (24-28) ^{2,b}	20 (12-22) ^{2,a}	24 (24-25) ^{2,b}	<0.001 ^{1,*}
	Group 1 vs. Group 2					<0.001 ^{2,*}
	Group 1 vs. Group 3					0.192 ²
	Group 2 vs. Group 3					<0.001 ^{2,*}
	Group 2 vs. Group 4					0.203 ²
	Group 3 vs. Group 4					<0.001 ^{2,*}

* Significance level $p < 0.05$, ¹ Kruskal-Wallis test, ² Mann-Whitney U test, while same letters show no significance, different letters show significant difference, Group 1: Hypertension with impaired cognition, Group 2: Hypertension with normal cognition, Group 3: Non-Hypertension with impaired cognition, Group 4: Non- Hypertension with normal cognition, MMSE: Mini mental status examination test, min: minimum, max: maximum, N: subject number.

Table 3. Comparison of the hypertensive and non- hypertensive patients according to age, disease duration and Mini mental status examination test score.

	Hypertensive patients N=18	Non- Hypertensive patients N=18	P value
Age, years, Median (min-max)	54 (43-77)	50.5 (41-72)	0.326 ¹
Disease duration, months, Median (min-max)	60 (3-246)	78 (6-336)	0.372 ¹
MMSE, score, Median (min-max)	23.5 (17-28)	23 (12-25)	0.414 ¹

* Significance level $p < 0.05$, ¹ Mann-Whitney U test, MMSE: Mini mental status examination test, min: minimum, max: maximum, N: subject number.

Table 4. Correlation of variables among the patients (N=36).

Spearman's rho		Disease duration	MMSE score
Age	R	,238	-,337*
	P value	,162	,045
Disease duration	R	1,000	-,200
	P value	.	,243

* Significance level $p < 0.05$, MMSE: Mini mental status examination test, N: subject number, R: Correlation Coefficient.

Table 5. Correlation of variables among the hypertensive patients (N=18).

Spearman's rho		Disease duration	MMSE score
Age	R	,392	-,431
	P value	,108	,074
Disease duration	R	1,000	-,399
	P value	.	,101

* Significance level $p < 0.05$, MMSE: Mini mental status examination test, N: subject number, R: Correlation Coefficient.

Table 6. Correlation of variables among the non-hypertensive patients (N=18).

Spearman's rho		Disease duration	MMSE score
Age	R	,136	-,269
	P value	,590	,280
Disease duration	R	1,000	,035
	P value	.	,889

* Significance level $p < 0.05$, MMSE: Mini mental status examination test, N: subject number, R: Correlation Coefficient.

Table 7. Variance analysis to explore the differences between groups.

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	p	Partial Eta Squared
Between groups	Age	224,750	3	74,917	1,072	,375	,091
	Disease duration	21972,750	3	7324,250	1,577	,214	,129
	MMSE	232,111	3	77,370	17,826	,000	,626

* Significance level $p < 0.05$, MMSE: Mini mental status examination test

Discussion

In our study, MMSE score in FM patients with HT was similar to in those without HT. A significant, low, negative correlation was found between age and MMSE scores when all patients were considered. On the other hand, when the correlation of variables was investigated within the hypertensive and non-hypertensive patient groups, no significant correlation was detected. Variance analysis showed no difference between groups according to age and disease duration, but MMSE.

It is known that the cognitive functions are affected in patients with FM [2, 3]. Some studies have reported that cognitive dysfunction in FM is not much different from

other chronic painful conditions. In a study conducted by Dick et al., although FM patients showed significantly higher levels of anxiety than the rheumatoid arthritis and musculoskeletal pain patient groups, FM patients did not appear to have more severe attentional problems than other chronic pain patients. Furthermore, FM patients did not perform more poorly than patients with rheumatoid arthritis or musculoskeletal pain patients on any of the investigated domains of attention and cognitive function [Dick]. However, cognitive dysfunction is still one of the diagnostic criteria of FM and is used to determine the severity of the disease [4].

Hypertension is one of the most common comorbid

conditions in FM patients [23]. Cognitive dysfunction develops in the presence of HT and, it can be concluded that HT may affect cognitive function in FM patients [16]. However, we did not find significant differences in FM patients with and without HT according to cognitive functioning.

Since simple and rapid tests that can be used to evaluate cognitive functions in FM patients are limited in clinical practice, it is suggested that self-report can be used instead of complex tests [24]. However, scales that evaluate global cognitive function, such as the MMSE, come to the fore in investigating the effects of systemic diseases, including HT, on cognitive functions [25]. In our study, we used MMSE to investigate cognitive function and created subgroups according to the MMSE cut-off value.

Pulse pressure is a well-established predictor of cognitive variability in aging [26-28]. Similar to our study, Kircher et al. [29] used MMSE and the same cutoff value in the assessment of cognitive function in their study. However, unlike our study, they excluded those with cognitive dysfunction according to the MMSE score. The main hypothesis of their study was that systolic blood pressure, diastolic blood pressure, and pulse pressure would have an impact on the ability to solve daily life problems in older adults, beyond the contribution of demographic and neuropsychological variables. However, it was hypothesized that a concomitant FM condition would be a significant predictor of the ability to solve daily life problems. This assessment was made by applying the Everyday Problems Test to patients whose cognitive function was considered normal according to the MMSE score [29]. Their results revealed that higher systolic blood pressure and higher pulse pressure were both related to better everyday problem solving- real-world functioning on cognitive tasks of daily living, but no significant relation was found between presence of FM and worse performance in everyday problem solving [29]. In the study of Reyes del Paso et al. [30] in the healthy subjects, but not in the FM patients, blood pressure was found to be inversely associated with mental performance. In a meta-analysis conducted by Gifford et al. [25] small to modest correlations found between increasing blood pressure and poorer episodic memory and global cognitive performances as well as the modest correlation between increasing blood pressure and enhanced attention performances. It should be noted that some studies were designed to evaluate the relationship

between hypertension and cognitive function, while some studies were designed to evaluate the relationship between blood pressure and cognitive function [13]. Results of studies examining the relationship between hypertension and cognitive function indicate that hypertensives perform worse than normotensives in almost all areas of cognitive function, including learning and memory, attention, abstract reasoning, executive functions, and visuospatial, perceptual, and psychomotor skills. However, hypertension has generally not been associated with verbal intelligence or language skills [13]. Our hypothesis was similar to these findings however, we did not find an effect of HT on cognitive functioning in FM patients. Results of studies examining the relationship between blood pressure and cognitive function generally show that increases in blood pressure are associated with gradual decreases in cognitive function. Interestingly, however, a few studies have found that lower blood pressure levels are associated with poorer cognitive function [13]. Contrary to the literature [25], Kircher et al. [29] found that higher blood pressure was associated with better everyday problem solving in older adults. So, the both high and low blood pressure are seemed to be associated with lower cognitive function [31].

Hypertensive patients are usually not clinically affected on cognitive tests [13]. They do not have the severe cognitive impairment known as dementia, and their test performance is usually within the normal range. However, the effect of hypertension on cognition may be considered clinically significant [13]. We can attribute the fact that the median value of the MMSE score in our study was so close to the cut-off value and that we did not find a significant difference in cognitive function between FM patients with and without HT to this situation.

Furthermore, meta-analysis reported by Gifford et al. [25] suggests that high blood pressure is associated with worse aspects of cognitive aging before the onset of clinical dementia or stroke, independent of important demographic variables (e.g., age, education) and medical or vascular comorbidities (e.g., diabetes, cholesterol, other prevalent cardiovascular disease). In our study, patients with systemic diseases other than HT were excluded and so this argument has not been investigated. In our study, increasing age was found to be correlated with deterioration in cognitive functions. However, this association was not present in the

subgroups of patients with and without HT. Also, the FM patients with and without HT did not differ according to the cognitive function.

Although, some studies have shown that HT at an early age can also affect cognitive functions [32], it is known that, especially high blood pressure in middle age increases the risk of cognitive decline and dementia in elderly [12, 33]. And also, HT affects cognitive function more in the elderly [34, 35]. One study reported lower memory test scores in those diagnosed with HT at age <55. They found that HT was associated with a decrease in global cognitive function score and memory test score [32]. Most of the patients in our study were middle aged. Despite the FM patients are generally from the middle age group FM disease can also be seen in the elderly, and new studies can be conducted among elderly FM patients [35].

Typically, HT patients in studies investigating the effects of HT on cognitive function are either not taking medication or have stopped taking their antihypertensive medications before cognitive testing, because antihypertensive medications can have small but significant effects on cognitive function on their own [13]. In spite of strong evidence of biological mechanisms, studies do not strongly show that the antihypertensive therapy should be better for cognition [15]. Also, animal experiments have shown that angiotensin-I inhibitors can cause FM-like symptoms in mice [37]. Although antihypertensive medications and cognitive function and FM seem to be so intertwined, medication was ignored in our study because the evidence was not strong and the possible effects were relatively small. However, it should be kept in mind that this situation may have affected the results of our study.

Depression, anxiety, sleep disturbance, and pain may be related to cognitive function in FM patients. Dick et al. [18] investigated these factors in their study and reported that only chronic pain had a significant negative effect on cognitive function. Similar findings were found by Reyes del Paso et al. [30] When considering the results of our study, it should be taken into account that depression, anxiety and sleep disorders were not examined in our study and a separate scale was not used for the pain parameter.

Although cognitive dysfunctions in HT and FM have been investigated separately [13,18], there is no other study examining the effect of blood pressure on cognitive function in FM patients except Kircher et al. [29] and Reyes del Paso et al. [30]. Those with MMSE score <24

were excluded from the study by Kircher et al., and in our study those with cognitive dysfunction according to MMSE score were also examined. Also, Reyes del Paso et al. [30] applied arithmetic task to assess the mental performance of FM patients and healthy controls, but in our study, we preferred to apply MMSE to examine the global cognitive function. In this respect, our study is the first in the literature. This can be considered the strength of our study. The lack of male patients was a limitation, but this was expected due to female gender dominance in FM. FM is generally seen among females [38], and only female patients were included in this study. That's why the conclusions cannot be generalized to males. Although the patients with psychiatric diagnosis are excluded, the lack of investigating depression and anxiety which are generally associated with cognitive functioning is another limitation. Another important limitation of our study was that we did not use a separate scale for the pain parameter, which may negatively affect cognitive function. In addition, although we determined the sample size by power analysis, another limitation of our study was that the sample size was too small. This may lead to such findings. Most of the patients in our study were middle aged and these findings may not be generalized to elderly FM patients. One of the shortcomings of our study was that we did not investigate the HT medications used. Also, we did not consider the severity of HT by following the patients for daily blood pressure. Another limitation of our study was that the study was single-centered. It should be taken into consideration that there may be differences in terms of understanding, comprehension and interpretation of the questions due to regional differences.

Conclusion

In conclusion, in our cohort, which included a group of middle-aged patients, there was no evidence that HT increases cognitive dysfunction in female FM patients. Further studies can be conducted with a larger number of FM patients by including elderly.

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24-26 May 2024 (Available at <https://www.karat.org.tr/wp-content/uploads/2024/06/KARAT-2024-Tam-Metin-Bildiri-Kitabi.pdf>). The study was conducted in accordance with the Declaration of Helsinki and followed the ethical standards of the TÜRKİYE.

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Extraspinal incidental findings on cervical vertebrae magnetic resonance imaging

Gökhan Tonkaz¹

Esra Ibis¹

Duygu Erkal²

Mehmet Tonkaz¹

Tumay Bekci¹

1. Department of Radiology, Faculty of Medicine, Giresun University, Giresun, Turkey.

2. Department of Radiology, Gumushane State Hospital, Gumushane, Turkey.

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Corresponding Author: Dr. Gökhan Tonkaz

Department of Radiology, Faculty of Medicine, Giresun University, Giresun, Turkey

Email: gokhantonkaz@gmail.com

Abstract

Objective: Cervical magnetic resonance (MR) imaging is routinely employed for the assessment of cervical disc pathologies, the evaluation of the cervical spinal canal, and the detection of spinal lesions. The aim of this study was to determine the prevalence of extraspinal incidental findings in patients undergoing cervical MR imaging and to assess the reporting rates of these findings in archived radiologic reports.

Methods: A retrospective review was conducted of digital patient archives between January 2022 and December 2023, comprising 1,000 patients who underwent cervical MR imaging at our institution. Two radiologists jointly identified extraspinal incidental findings. This descriptive study analyzed images obtained using a 1.5 Tesla MR imaging system with standard neck coils, evaluating the prevalence and reporting frequency of incidental findings.

Results: Among 1,000 patients (580 males, 420 females, mean age: 49±31 years), extraspinal incidental findings were observed in 66.4% (n=664) of cases. The most frequent findings were thyroid nodules (13.8%, n=138), goiter (12.2%, n=122), and mucosal thickening of the paranasal sinuses (11.5%, n=115). Incidental findings were more prevalent in women and in the middle-aged group (35–59 years). Only 14.6% of the 664 incidental lesions were documented in radiology reports. These lesions exhibited variability in anatomical location.

Conclusions: This study demonstrates that extraspinal incidental findings are common in routine cervical MR imaging but are often overlooked in radiological reports. Given the potential clinical significance of these findings, their inclusion in reports is important for patient care and management.

Keywords: Incidental findings; cervical spine; extraspinal findings; magnetic resonance imaging; radiological reporting

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Introduction

Cervical vertebral magnetic resonance (MR) imaging is frequently employed in the diagnosis of patients presenting with neck and back complaints. These MR images primarily focus on the evaluation of spinal pathologies, including the vertebral bodies, intervertebral discs, spinal canal, neural elements, and associated ligaments. However, the extent of the evaluation may vary depending on the clinical information provided. Many radiologists limit their assessments to the areas relevant to the clinical query, often excluding the examination of anatomical structures outside the spine.

Incidental findings refer to previously undetected abnormalities that are discovered unexpectedly during imaging and are unrelated to the initial purpose of the examination. In some cases, these findings may even provide insight into the patient's symptoms. The retrospective identification of incidental findings, particularly those with implications for survival, raises significant practical and ethical concerns in clinical management. The literature contains several reports highlighting missed opportunities for the early detection of potentially life-threatening conditions, such as malignancies or aneurysms [1].

Despite the use of signal saturation bands in standard international protocols aimed at reducing artifacts and their negative impact on image quality in cervical vertebra MR imaging scans [2], a wide range of incidental pathologies in the head and neck regions may still be detected, with considerable variability in the types of encountered conditions. The images typically used for reporting are magnified around the vertebra, revealing most of the neck structures. While this approach ensures optimal identification of spinal pathologies, it often results in the exclusion of potentially significant extraspinal pathologies from the final dataset [3]. Additionally, technological advancements such as digital archiving systems and the ability to evaluate regions within the imaging field using high-magnification zoom have substantially improved the detection limits of incidental findings [1].

In our study, we aimed to determine the prevalence of incidentally detected extraspinal findings in cervical vertebra MR imaging scans and their reporting rates in radiology reports.

Materials and methods

Patients

Between January 2022 and November 2023, digital patient archives were randomly reviewed, and 1,022 patients aged 18 years and older who had undergone cervical vertebra MR imaging at our hospital were retrospectively re-evaluated. Two patients with a known history of extraspinal pathology (extraspinal malignancy) documented in the hospital system were excluded from the study. Additionally, 18 patients were excluded due to motion artifacts, and 2 patients were excluded due to surgical materials causing significant magnetic susceptibility artifacts. Extraspinal incidental findings in the cervical MR images of 1,000 patients were identified by two radiologists through consensus.

In this descriptive study, the images were acquired using a 1.5 Tesla MR imaging system with standard neck coils, and each image was individually evaluated. The prevalence of the detected findings and the reporting rates were determined. Ethical approval for this study was obtained from our university's ethics committee. Since this was a retrospective study, informed patient consent was not required.

MR Imaging technique:

Examinations were performed on 1.5 Tesla (Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany) at Giresun training and research hospital (GTRH) with a neck coil. All patients were put in supine position. The routine cervical spinal MR imaging protocol in GTRH hospital includes a three-plane localizer series. Sagittal T1-weighted Fast spin-echo (TSE) images (Repetition Time (TR) / Echo Time (TE), 600-700/9-10 ms; slice thickness, 4 mm, field of view (FOV), 25 cm and NEX, 2), sagittal T2-weighted FSE images (TR/TE, 3000/108 ms; slice thickness, 4 mm, field of view (FOV), 25 cm and NEX, 2) and axial T2-weighted GE (TR/TE, 350-400/9-10 ms; slice thickness, 4 mm, field of view (FOV), 20 cm and NEX, 2).

Image Analysis:

The MR images were interpreted by two radiologists with 8 and 2 years of experience, respectively, in consensus. The radiologists evaluated the MR images for the presence of extraspinal incidental findings. The frequency of incidental findings was calculated based on gender and age groups, and the collected data were presented as percentages. Additionally, the radiology reports were re-examined to determine whether these

Table 1. Demographic characteristics and reporting percentages of incidental lesions

Incidental findings	Female	Male	RRF	n (incidence %)
Thyroid nodule	84	54	34 (24.6%)	138 (13.8%)
Goiter	91	31	10 (8.1%)	122 (12.2%)
Mucosal thickening in paranasal sinuses	41	74	13 (11.3%)	115 (11.5%)
Partial empty sella / empty sella	60	32	10 (10.8%)	92 (9.2%)
Mega cisterna magna/arachnoid cyst	38	40	5 (6.4%)	78 (7.8%)
Retention cyst in paranasal sinuses	10	23	10 (30.3%)	33 (3.3%)
Thornwaldt's cyst	14	13	3 (11.1%)	27 (2.7%)
Nasopharyngeal mucosal thickening	10	15	5 (20%)	25 (2.5%)
Cerebellar tonsillar herniation	6	5	2 (18.1%)	11 (1.1%)
Cervical lymphadenopathy	7	3	1 (10%)	10 (1%)
Posterior soft tissue lesion	4	2	1 (16.6%)	6 (0.6%)
Pituitary gland lesion	3	1	2 (50%)	4 (0.4%)
Arteriovenous malformations	1	0	1 (100%)	1 (0.1%)
Calcific meningioma	0	1	0 (0%)	1 (0.1%)
Arachnoid granulation	0	1	0 (0%)	1 (0.1%)
TOTAL			97 (14.6%)	664 (66.4%)

RRF: Reporting rate of findings, n: Number of people

incidental findings were mentioned. The reporting rates for each incidental finding were calculated and presented as percentages. In cases where multiple instances of the same type of lesion were observed, only one was recorded as an incidental finding. The incidental findings were recorded in order of frequency (**Table 1**).

Regions within the thyroid parenchyma with well-defined borders or signal properties distinct from the parenchyma were classified as thyroid nodules (**Figure 1, star**). Enlargement of the thyroid gland, with an anteroposterior diameter exceeding 2 cm, was diagnosed as goiter (**Figure 1, arrows**) [4].

The mucosa lining the paranasal sinuses is respiratory epithelium, typically about 1 mm thick. Mucosal thickening exceeding 3 mm in the maxillary sinuses, 2 mm in the ethmoid sinuses and 1 mm in the sphenoid sinuses is considered pathological. In T2-weighted images, a high signal beyond the aforementioned thicknesses along the periphery of the paranasal sinus was classified as mucosal thickening [5]. In T2-weighted images, when the sella turcica is filled with cerebrospinal

fluid (CSF) and the pituitary gland measures less than 3 mm, it is classified as partial empty sella and less than 2 mm as empty sella [6]. Mega cisterna magna is a focal enlargement of the subarachnoid space filled

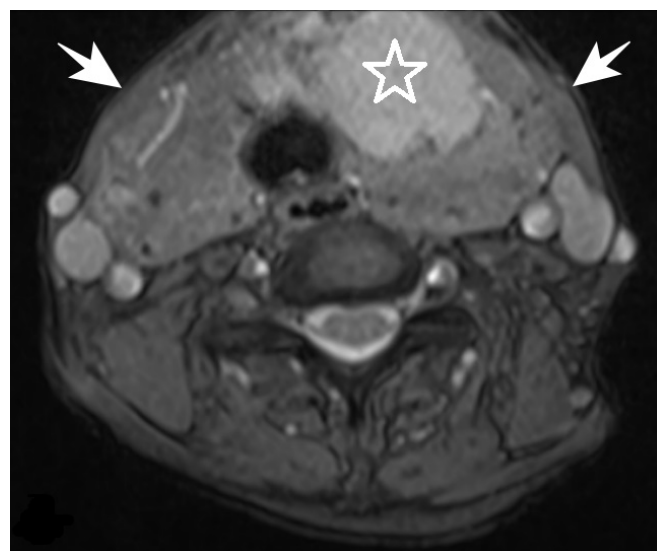


Figure 1. Axial T2-weighted image shows thyroid gland enlargement consistent with goiter (arrows) and a well-circumscribed thyroid nodule (star).

with CSF located in the posterior and lower parts of the posterior cranial fossa. Distinguishing mega cisterna magna from arachnoid cysts, which are also CSF-filled and located similarly, can be challenging on cervical MR images. Therefore, in T2-weighted midsagittal images, a measurement greater than 10 mm was classified as either mega cisterna magna or arachnoid cyst [7]. In T2-weighted images, round or dome-shaped hyperintense lesions in the paranasal sinuses were classified as retention cysts [8]. In T2-weighted images, midline, hyperintense lesions with thin walls located in the nasopharyngeal mucosa were classified as Tornwaldt cysts [9]. In T2-weighted sagittal images, nasopharyngeal mucosa exceeding 3 mm in thickness was classified as nasopharyngeal mucosal thickening [10] (**Figure 2A-B, arrow**).

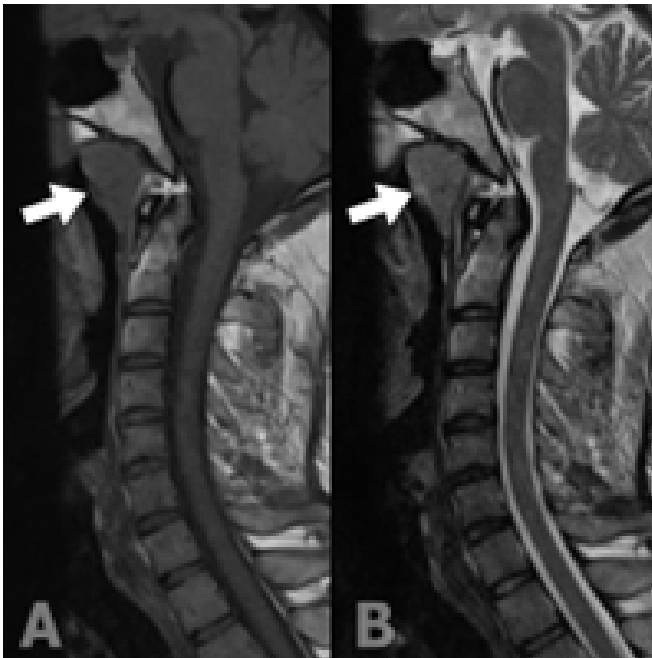


Figure 2. Sagittal T1(A) and T2(B) weighted images show nasopharyngeal mucosal thickening (arrow) in the posterior wall of the nasopharynx.

In T2-weighted images, the descent of the cerebellar tonsils more than 3 mm below the level of the foramen magnum (McRae line) was classified as cerebellar tonsillar herniation [11]. Lymphadenopathy in the cervical chain was defined by a short-axis diameter of 10 mm or greater or a cortical thickness of 3 mm or more. T2-weighted images showing high-signal cystic or necrotic areas were also used to identify lymphadenopathy [12, 13]. Any cervical lymph node with a long-to-short axis ratio of less than two was also classified as lymphadenopathy [14]. In T1 and T2-weighted images of the posterior cervical region, foci



Figure 3. Sagittal T1(A) and T2(B) weighted images show a posterior soft tissue lesion with regular borders (arrow) within the soft tissue in the posterior cervical region.

with different signal characteristics compared to adjacent structures were classified as posterior soft tissue lesions (**Figure 3A-B, arrow**).

Pituitary gland lesions were classified as lesions located in the suprasellar, parasellar, or intrasellar regions with distinct signal characteristics in T1 and T2-weighted sagittal images (**Figure 4A-B, arrow**) [15].

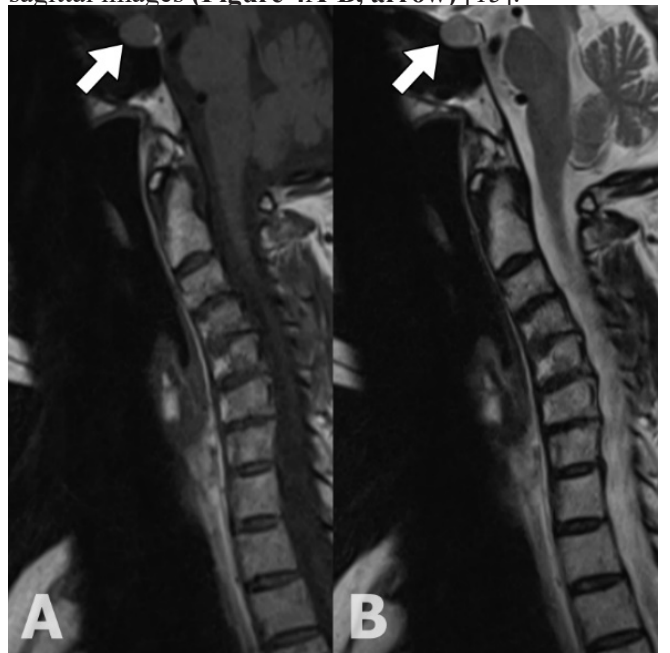


Figure 4. Sagittal T1(A) and T2(B) weighted images show a pituitary gland lesion (arrow) located in the intra-suprasellar region.

A lesion located in the cranial extra-axial region, containing calcified foci and having different signal characteristics compared to adjacent tissues was classified as calcific meningioma (**Figure 5A-B, arrow**) [16].

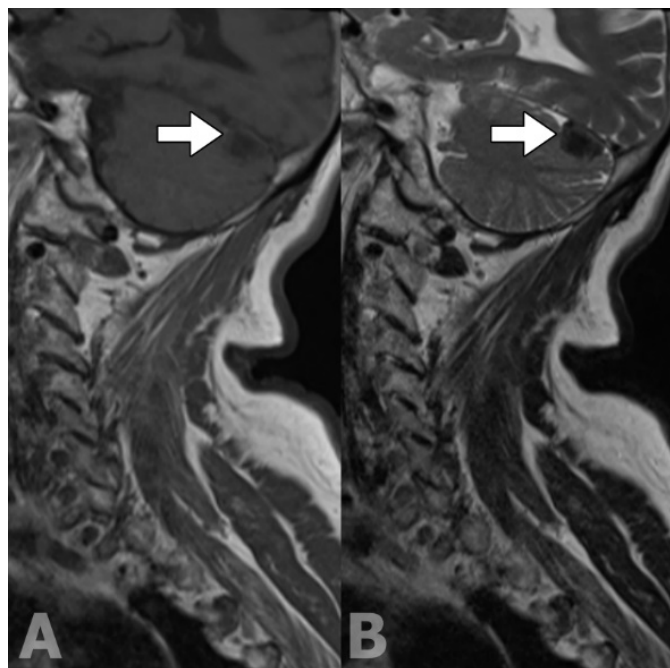


Figure 5. Sagittal T1(A) and T2(B) weighted images show a calcific meningioma (arrow) with calcified foci located extra-axially and with different signal characteristics compared to adjacent tissues.

Brain arteriovenous malformation (AVM) was identified by observing enlarged feeding arteries, nidus closely associated with brain parenchyma, and draining veins with flow voids on T2-weighted sagittal images [17]. Foci with different signal characteristics forming a filling defect at the calvarium or dural venous sinus in T1 and T2-weighted sagittal images were classified as arachnoid granulations [18].

Results

This study included 1,000 patients, comprising 580 males and 420 females, who underwent cervical vertebra MR imaging for the evaluation of spinal pathologies. The percentage of extraspinal incidental findings was

66.4% (n=664). The mean age of the study population was 58.7 years (49±31). The distribution of incidental findings by age group and gender is listed in Table 1. The most common incidental findings were thyroid nodules, goiter, and mucosal thickening in the paranasal sinuses. Other incidental findings and their demographic characteristics are also provided in Table 1. Incidental findings were identified in 36.9% of females (n=664) and 29.5% of males (n=295). In our study, we observed that the prevalence of incidental findings was higher in the middle-aged group (35-59 years) compared to other age groups (**Table 1**). It was determined that only 14.6% (n=97) of the extraspinal incidental findings were mentioned in the radiology reports (**Table 1**). Additionally, no lesions were detected in categories such as thyroglossal duct cysts, other vascular lesions such as aneurysms, esophageal lesions, or cerebral and cerebellar mass lesions.

Size and location characteristics of thyroid nodules are shown in **Table 2**.

Discussion

Incidental findings, which are a part of medical practice, are abnormalities detected during investigations performed for reasons unrelated to the primary examination. The impact of detecting incidental findings on patient health is uncertain [19], but identifying such findings may lead to the discovery of more serious conditions requiring treatment [20]. In this study, 1,000 patients were evaluated, and incidental findings were identified in 664 patients, as shown in Table 1. The most common incidental findings were observed in the thyroid gland and paranasal sinuses.

In our study, the prevalence of thyroid nodules was 13.8% (n=138), with 68.1% (n=94) of these nodules measuring larger than 1 cm (Table 2).

It was noted that only 24.6% (n=34) of patients with thyroid nodules were noted in radiology reports. In a study by Ottonello et al., thyroid nodules were detected in 33% of adults undergoing ultrasound screening [21].

Table 2. Size and location characteristics of thyroid nodules

Incidental findings	RL (F / M)	LL (F / M)	I (F / M)	SIZE >1CM	n (incidence %)
Thyroid nodule	82 (52/30)	43 (23/20)	13 (9/4)	94	138 (13.8%)

RL: Right thyroid lobe, LL: Left thyroid lobe, I: Isthmus lobe, F: Female, M: Male, n: Number of people

In another study, multiple thyroid nodules were detected in 37.3% of those who underwent random autopsies [4]. The lower prevalence of thyroid nodules in our study compared to the literature may be due to undetected nodules located outside the imaging field. In addition, incidental thyroid nodules may sometimes represent thyroid cancer, a clinically significant condition [22]. It is very important that this condition is noted in radiology reports as it will affect the patient's life.

In our study, the prevalence of goiter was found to be 12.2% (n=122). The prevalence of goiter was significantly higher in the female population ($p < 0.005$), with a female-to-male ratio of 3:1, and its occurrence decreased with age. Goiter was mentioned in 8.1% (n=10) of the radiology reports of patients with goiter. A study by Ottonello et al. similarly reported a decrease in the prevalence of goiter with age, with a female-to-male ratio of at least 4:1, and the highest prevalence observed in premenopausal women [21]. The findings of our study regarding goiter are consistent with the literature.

In our study, the prevalence of mucosal thickening in the paranasal sinuses was 11.5% (n=115). It was observed more frequently in males than in females, and its prevalence increased with age. Mucosal thickening was mentioned in 11.3% (n=13) of the radiology reports. The data on paranasal sinus mucosal thickening in our study are in line with the existing literature [23].

The prevalence of empty sella in our study was 9.2% (n=92). It was more commonly observed in females compared to males, and its prevalence increased with age. Empty sella was noted in 10.8% (n=10) of the radiology reports of patients with this finding. A study by Foresti et al. identified incidental empty sella in 38% (n=140) of 500 patients who underwent brain MR images. In that study, empty sella was more frequently observed in females (72/68) and was detected in 39.9% of individuals aged 40 years and older [24]. Apart from the lower prevalence of incidental empty sella in our study, the other findings are consistent with the literature. The lower prevalence in our study may be attributed to the fact that incidental findings are more frequently identified in cranial MR scans performed for intracranial pathologies, and empty sella is more commonly associated with such pathologies. Apart from this, empty sella, which refers to the filling of the sella turcica with CSF, is usually an incidental finding with no clinical significance. However, although rare, it may be associated with idiopathic intracranial hypertension. Noting this condition in the radiology report may allow patients with headaches to be guided

and receive the correct diagnosis and treatment.

In our study, the prevalence of mega cisterna magna/arachnoid cyst was found to be 7.8% (n=78). It was noted that only 6.4% (n=5) of patients with mega cisterna magna/arachnoid cyst had this finding mentioned in their radiology reports. It is estimated that mega cisterna magna is present in approximately 1% of brains imaged postnatally [25]. In a study of 48,417 patients who underwent neuroimaging, 1.4% (n=661) were diagnosed with arachnoid cysts [26]. The higher prevalence of mega cisterna magna/arachnoid cyst in our study compared to the literature may be due to the diagnosis being made solely based on sagittal slices, without axial images, leading to potential misdiagnosis as a result of partial volume effects.

In our study, the prevalence of retention cysts was 3.3% (n=33), with a higher frequency in males compared to females. Retention cysts were mentioned in 30.3% (n=10) of the radiology reports. Retention cysts are found in 1.4–9.6% of the general population, with most being asymptomatic [27]. In contrast, a study by Tarp et al. reported a slightly higher prevalence of 15% [28]. The lower prevalence in our study may be due to the fact that the imaging was not specifically targeted at the paranasal sinuses, and only partial sections of the paranasal sinuses were included in the imaging field.

In our study, the prevalence of tornwaldt cysts was 2.7% (n=27). A study by Alper Dilli et al. reported a tornwaldt cyst prevalence of 3% [29]. Our findings are consistent with the literature, and tornwaldt cysts were mentioned in 11.1% (n=3) of the radiology reports.

In our study, the prevalence of nasopharyngeal mucosal thickening was 2.5% (n=25). Nasopharyngeal mucosal thickening was mentioned in 20% (n=5) of the radiology reports. In a study in the literature, nasopharyngeal mucosal thickening was detected in 44.2% (n=442) of 1000 patients who underwent cervical MR imaging [30]. The lower prevalence of nasopharyngeal mucosal thickening in our study may be attributed to a lower prevalence of diseases causing such thickening in our region compared to other areas.

In our study, the prevalence of cerebellar tonsillar herniation was 1.1% (n=11), consistent with the literature [30]. It was noted that 18.1% (n=2) of the patients with cerebellar tonsillar herniation had this finding mentioned in their radiology reports.

In our study, the prevalence of lymphadenopathy was 1%

(n=10). Lymphadenopathy was mentioned in 10% (n=1) of the radiology reports in our study. In a retrospective study by Frager et al., lymphadenopathy was identified in 1.45% (n=22) of cases with extraspinal pathology found in CT scans [31]. The prevalence of lymphadenopathy in our study was close to the reported rates in the literature.

Posterior neck soft tissue lesions include all outgrowths, both benign and malignant, originating from tendons, muscles, ligaments, cartilage, nerves, blood vessels, fat, and other tissues [15, 16]. The exact prevalence of posterior neck soft tissue lesions is unknown, but the majority of these lesions are benign pathologies [32]. In our study, the prevalence of posterior neck soft tissue lesions was 0.6% (n=6). It was mentioned in 16.6% (n=1) of the radiology reports.

The prevalence of pituitary gland lesions in our study was 0.4% (n=4). The prevalence of pituitary tumors is approximately 1 in 1,000 [33]. Pituitary gland lesions were mentioned in 50% (n=2) of the radiology reports.

The prevalence of calcific meningioma, AVM, and arachnoid granulation in our study was 0.1% (n=1). AVM was mentioned in the radiology report, whereas calcific meningioma and arachnoid granulation were not reported.

There are few studies that examine incidental lesions in cervical MR imaging and discuss the reporting rates in radiology reports. A study conducted in 2018 found that 29.1% of 192 cervical MR images contained incidental findings, with lesions in the paranasal region being the most frequently encountered, followed by thyroid lesions. The study also reported that the reporting rate for incidental findings in cervical MR image was 29.5% [34]. In a study by Zidan et al., 266 cervical MR images were re-evaluated, and incidental findings were detected in 16.9% of cases. The most common incidental findings were thyroid nodules (6.3%), goiter (4.6%), and mucosal thickening in the paranasal sinuses (2.68%). This study also examined the distribution of incidental findings by age group, with the highest prevalence of incidental lesions observed in patients aged 41-60 years [25]. In a study by Kaya et al., 300 cervical MR images were re-evaluated, and incidental findings were detected in 13.7% of cases, with thyroid nodules being the most common incidental finding [35]. In a 2024 study by Kızılgöz et al., at least one incidental finding was present in 72.6% of the cervical MR images reviewed, with the nasopharyngeal and thyroid regions being the most frequently affected areas. Additionally, the reporting rate for incidental findings in this study was recorded at

5.29% [30]. In a study by Kamath et al., meningiomas, thyroid, salivary gland lesions, and nasopharyngeal tumors were frequently encountered incidental findings in cervical MR imaging [20].

There are several limitations in interpreting the results of this study that must be considered. First, this study relied on radiological findings for the detection of incidental lesions, without histopathological correlation. Second, as the patients were not followed up, the radiological findings were not correlated with clinical data, which could lead to incomplete or inaccurate interpretations. Third, the clinical significance of these incidental findings was not assessed. Fourth, there was no evaluation of the incidental findings from the perspectives of patients, radiologists, healthcare economics, or medicolegal aspects. Fifth and finally, to determine more accurate prevalence numbers and reporting rates, larger populations must be studied, and additional research is required to contribute to the body of literature.

This study highlights the high prevalence and variability of incidental lesions encountered in cervical MR imaging, despite the low reporting rates in daily radiology practice. The omission of these lesions from radiology reports may be a result of the focus on the primary purpose of the imaging technique.

Conclusion

In conclusion, extraspinal incidental findings detected in cervical vertebra MR imaging are more common than expected, yet they are rarely reported in radiology reports. These incidental findings are important because they may affect the patient's treatment or life. Therefore, incidental findings should be included in radiology reports, as they provide valuable additional information.

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Improvement after tattoo eradication with acupuncture in a case of fibromyalgia

Levent Tekci¹ 
Sule Sahin Onat² 

1. Private practice, The Academy of Acupuncture, Ankara, Türkiye

2. Private practice, Ankara, Türkiye

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Corresponding Author: : Şule Şahin Onat,
M.D., Associated professor

Private practice, Ankara, Türkiye

Email: sahinonatsulester@gmail.com

Abstract

The disruptive area is the problem areas of the body that create effects far from where it is located. Scars, tattoos, dental problems, paranasal sinuses are the most common disruptive areas. In the treatment of disruptive areas is neuropsychopathogen elimination acupuncture method and neural therapy. In this article, the improvement with neuropsychopathogen elimination acupuncture method that we applied to our patient with fibromyalgia and depression is discussed.

Key words: Fibromiyalgiya; disruptive area; acupuncture

Introduction

Fibromyalgia is a chronic disease characterized by pain and stiffness in the muscles, tendons, and joints. Its prevalence is between 2-4%. In medical treatment, duloxetine hydrochloride and pregabalin are used. Complementary treatments include acupuncture, moxibustion, electroacupuncture, herbal extracts, and massage. The 2017 EULAR treatment guidelines specifically recommend the use of acupuncture [1].

In patients who do not respond to classical acupuncture practices, disruptive fields that block the flow of stimuli in the fascia should be suspected. Disruptive fields are problematic areas of the body that create effects distant from their location [2]. These areas are chronic, nonspecific, have few symptoms, or are asymptomatic. Scars, tattoos, dental problems, and paranasal sinuses are the most common disruptive fields [2]. In addition to neural therapy, the Neuropsychopathogen Elimination (NPPE) acupuncture method is used for treating disruptive fields. Neuropsychopathogen elimination is an acupuncture method that optimizes the primo vascular channel systems of consciousness [3,4]. The primo vascular channel system ensures the transmission of biophotonic

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activity (Qi) to all anatomical compartments of the body within the fascial network through acupuncture meridians. NPPE aims to eliminate the pathology by optimizing these channel systems [3].

This case report discusses the dramatic clinical improvement and neutralization of the disruptive field with the application of neuropsychopathogen elimination acupuncture.

Case

A 26-year-old female patient presented to our clinic with complaints of widespread body pain starting in the right arm, insomnia, and depression, progressively increasing over the past eight months. On examination of the patient, Adler-Langer points were found to be bilaterally positive at C3, and the Kibler skin sliding test was normal. According to the ACR 1990 criteria, 11 of the fibromyalgia tender points were positive on palpation [5]. The widespread pain index score was 14, and the symptom severity scale was 8 according to the ACR 2010 criteria [5]. Her pain level was 8 on the visual analog

scale. The patient's Beck depression inventory score was 60 at the initial evaluation, and she had a history of a previous suicide attempt. The fibromyalgia impact questionnaire score was 70 [5]. The patient had a large tattoo covering the entire brachial area of her right arm. Diagnosed with fibromyalgia and severe depression, the patient underwent 5 sessions of acupuncture, each lasting 50 minutes, twice a week. Since her pain did not subside, 5 sessions of neuropsychopathogen elimination and disruptive field therapy were performed (Figures 1A,B). After 10 sessions, the patient had no pain, the number of tender points was 0, the widespread pain index score was 3, the symptom severity scale was 2, the Beck depression inventory score was 8, and the fibromyalgia impact questionnaire score was 16. During the clinical follow-up, a significant lightening of the tattoo color was observed in the areas where the disruptive field therapy was applied (Figures 1A,B).

Discussion

There is a considerable amount of research on the effectiveness of acupuncture in fibromyalgia [6-8]. In

fibromyalgia patients where clinical outcomes with classical acupuncture are unsuccessful, it is necessary to reevaluate the patient in terms of disruptive fields. In this patient, dramatic improvement in treatment process was observed with the eradication of disruptive fields.

Disruptive fields are formed by the chronic stimulation of afferent sympathetic fibers. With the NPPE acupuncture application used in our patient, resynchronization is achieved through the retransport of dielectric abnormal transmissions in the fascia system and primo vascular optical channels.

There is a magnetoinformational transformation between the primo vascular channel system and connective tissue. In the presence of tattoos, burns, or scar surfaces, stagnation areas with signal-disruptive properties develop in all dermatomuscular



Figure 1A: The needled version of tattoo before treatment

Figure 1B: The needled version of tattoo after treatment

surfaces, including collagen fibers, and the transmission of the primo vascular channels is blocked. As a result, signal-disruptive properties develop in the tissue compartments where the primo vascular channels pass, and the integrated neuronal communication of the central and peripheral nervous systems is disrupted.

The NPPE technique was developed within the scope of the Tekci Diagonal Acupuncture Systems (TDAS) and offers interaction diagonally (crosswise). In the TDAS microacupuncture system, the micro and macro holographic images of the organism are projected onto the head, face, nose, back, abdomen, feet, wrists, knees, and thigh zones [3]. The neurocranial zone in the medial thigh depicts anatomical components belonging to the prefrontal cortex, temporal, parietal, occipital brain surfaces, and subcranial cortex [3]. In NPPE, the optimization of physical, cognitive, and mental pathological conditions in humans is achieved through the activation of somatotopic points of the amygdala, nucleus raphe, and hippocampus, which are members of the limbic system. This system was developed based on Benoit Mandelbrot's Fractal Field Model on a fasciology basis, and it operates through the interaction of quantum-holographic Hopfield-like integrative neural networks via the primo vascular system using Feynman's propagator version [9,10,11].

In our case, the application of the NPPE acupuncture technique resulted in both the complete regression of the patient's fibromyalgia and depression and the simultaneous lightening of the tattoo colors, demonstrating the correlation between the two. The localized superficial fascial network on the dermatomal surface of the tattoos caused distransportation of the magnetoinformational field between the primo vascular channels and the superficial fascial structure due to stagnation areas on collagen surfaces, leading to the clinical presentation of fibromyalgia and depression. Further studies are needed regarding the effectiveness of the NPPE microacupuncture method in this area.

Conflict of interest

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Confusing processes leading to diagnosis of infective endocarditis

Aysegul Okur¹ 
Emsal Aydin¹ 
Sinan Cetin¹ 
Ahmet Melih Sahin¹ 
İlknur Senel¹ 
Meltem Arzu Yetkin¹ 

1. Giresun University Faculty of Medicine,
Department of Infectious Diseases and
Clinical Microbiology, Giresun, Türkiye

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Corresponding Author: Ayşegül OKUR,
Giresun University Faculty of Medicine,
Küçükköy, Mehmet İzmen Road, 28100
Giresun

Email: aysegullokur@live.com

Abstract

Infective endocarditis (IE) is a life-threatening condition caused by infections of the heart valves or walls. Diagnosis can be challenging due to varied clinical presentations, often leading to delayed recognition and severe complications. Chronic kidney disease (CKD) patients, especially those on hemodialysis, are at increased risk of bacteremia from catheter-related infections. With the rising prevalence of CKD, associated comorbidities like diabetes and hypertension have also become more common. This case report highlights the diagnostic process of IE in a 78-year-old CKD patient initially misdiagnosed and treated for a urinary tract infection, emphasizing the need for vigilance in such cases.

Keywords: infective endocarditis; catheter; hemodialysis; renal failure

Introduction

Infective endocarditis (IE) is a serious condition that occurs when the valves or walls of the heart are infected by bacteria, fungi or viruses. The diagnosis of IE patients who present to health institutions with different clinical presentations may be overlooked and patients may encounter irreversible complications until they are diagnosed. Despite all the advances in the medical world, diagnosis and treatment are still challenging. Cardiac problems are common in patients with chronic kidney disease (CKD). Many patients with end-stage renal disease require hemodialysis to survive. These patients carry a risk of morbidity and mortality due to bacteremia developing due to infection in indwelling catheters. [1,2,3]. Recently, CKD has been seen at an increasing rate (the rate in our country is 15.7% [4]) and leads to an increase in the incidence of comorbid diseases such as DM and HT. In this case report, it is aimed to emphasize this issue by presenting the process of receiving the diagnosis

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of infective endocarditis in a 78-year-old chronic renal failure patient who was followed up and treated with the diagnosis of urinary tract infection.

Case

A 78-year-old female patient who applied to the emergency department with complaints of chills, shivering, weakness, nausea, vomiting and dysuria was undergoing dialysis three times a week due to chronic renal failure. A permanent dialysis catheter was inserted into the subclavian vein 3 months ago. It was learned that the patient's complaints on admission were during dialysis. Her additional diseases were multiple myeloma, diabetes mellitus, hypertension and coronary artery disease and she had medications for these diseases. In her physical examination, fever was 36°C, arterial blood pressure was 120/80 mm/Hg, pulse was 78/minute, suprapubic tenderness on abdominal palpation and pain on stimulation in the right costovertebral region. The patient had bilateral pretibial edema and no acute pathological findings were detected in other system examinations. The laboratory parameters on admission were leukocyte count 12,710 /mm³, neutrophil count 86.9%, hemoglobin 10.6 g/dL, platelet count 230,000 hours/mm³, sedimentation rate 62 mm/hour, C-reactive protein 119.97 mg/L (normal 0-5 mg/L), urea 21 mg/dL, creatinine 1.23 mg/dL. The patient had been hospitalized for 21 days due to myocardial infarction four months ago, and also three months ago due to pulmonary edema and catheter infection due to *Enterococcus faecium*, and parenteral vancomycin treatment was applied. Multiple myeloma was diagnosed two weeks before admission and two cycles of chemotherapy were applied. The patient, who was hospitalized with a preliminary diagnosis of urinary system infection, was started on ertapenem treatment due to a recent hospitalization history. Since the urine culture taken before the treatment yielded *E. coli* that was sensitive to the treatment applied, the current treatment was continued. *Enterococcus faecalis* grew in the blood culture. The treatment was adjusted to parenteral ampicillin. Vancomycin lock therapy was added for catheter infection. There was no growth in the control blood culture taken after the treatment was started, but since growth continued in the catheter cultures despite the lock therapy, the catheter was removed. The new catheter was inserted into the right femoral vein. Since there was a history of catheter infection before, cardiology was consulted for infective endocarditis. Transesophageal echography revealed an 18x8 mm vegetation on the posterior mitral valve and severe exenteric mitral valve insufficiency, as well as

a suspected posterior mitral valve fistula. The patient's treatment was changed to parenteral vancomycin, and after two weeks of parenteral treatment, he was transferred to the cardiovascular surgery unit for cardiac surgery.

Discussion

Infective endocarditis is a significant cause of morbidity and mortality. There are several risk factors for infective endocarditis. Any pre-existing heart condition, such as pre-existing valve disease, congenital heart defects, mitral prolapse, or degenerated heart valves, increases the risk of developing infective endocarditis. Procedures performed on the vessels, such as hemodialysis, intravenous drug use, and intravenous catheterization, can cause bacteria to mix with the blood and settle on the heart valves. The increase in intravenous devices used over the years has also caused an increase in the rate of infective endocarditis [5,6]. In our case, there was a permanent catheter due to chronic renal failure requiring dialysis and the risk of infection was high. The risk of bacteremia should be kept in mind in these patients and attention should be paid to infective endocarditis. *Staphylococcus aureus* is the most common cause, followed by streptococci and enterococci [5]. In the case report, there was enterococcus growth in the blood and catheter cultures and she had recently received treatment for another catheter infection. Despite receiving treatment for 21 days, the catheter infection had recurred. In cases where the focus of the infection is not removed in terms of treatment, there is a risk of recurrence, as seen in the case report. Various symptoms can be seen in infective endocarditis. Among the main symptoms, general signs of infection such as fever, chills, weakness, fatigue, loss of appetite, weight loss, sweating, high fever and chills are frequently seen. Cardiac findings include new heart murmur, heart failure symptoms and changes in cardiac rhythm, which are important signs suggesting infective endocarditis. Sometimes, headache, muscle-joint pain, rash, skin lesions on the hands and feet, renal failure, spleen enlargement and findings related to central nervous system involvement may occur. These various symptoms may vary depending on the patient and may make diagnosis difficult. Therefore, especially in risky patients, infective endocarditis should be suspected and appropriate diagnostic evaluations should be made without delay. [7] In the case, there were signs of infection at the time of admission, urinary symptoms were prominent, and there were no findings in the cardiac examination that would lead to suspicion of infective endocarditis. Therefore, treatment for urinary

infection was planned and there was also growth in the urine culture. Enterococcus growth in the catheter and blood cultures and due to the previous catheter infection, infective endocarditis diagnosis was made. Symptoms vary according to the severity and spread of the infection. While acute cases usually have a more severe and rapid onset, subacute cases may have symptoms that develop more slowly and insidiously. The course of the disease and the general condition of the patient are also reflected in the symptoms. In advanced cases, more severe findings such as heart valve damage, bacteremia, and brain complications may occur. In our case report, it was thought that it may have been suppressed and chronic during the treatment applied due to catheter infection and therefore may have caused the clinical course to be more vague.

More than one diagnostic method is used to diagnose infective endocarditis. The most basic step is to evaluate the patient's history and physical examination findings. Infective endocarditis is suspected when the patient's complaints and symptoms are carefully evaluated and changes in heart sounds are detected. In addition, some laboratory tests are also important in the diagnostic process. Blood culture is the most important diagnostic method in infective endocarditis. [8] The growth of the causative microorganism in the blood samples taken from the patient helps to determine the source of the infection and to plan effective treatment. At least three consecutive blood cultures should be taken from the patient. The cardiac examination was unremarkable at the time of the case's application and a blood culture was taken due to his clinical condition. Infective endocarditis was diagnosed due to the enterococcus bacteria that grew after the treatment was started.

Imaging methods play an important role in diagnosis. Echocardiography is the most basic examination in the evaluation of infective endocarditis. Vegetation located on the heart valves or endocardium, damage to the valves, and intracardiac abscess formations can be visualized with transthoracic or transesophageal echocardiography. In addition, computerized tomography and magnetic resonance imaging are also used to evaluate the extent of the disease and its complications. In the case report, vegetation was detected in echocardiography. Infective endocarditis is a serious infection that can result in death in 24% of patients if not treated promptly and appropriately [9]. The treatment approach in infective endocarditis is customized according to the patient's clinical condition, underlying risk factors, severity of infection and causative microorganisms. The first step

is to start appropriate antibiotic therapy. However, blood culture must be taken before treatment to identify the causative agent. Antibiotics are usually administered intravenously. During appropriate antibiotic therapy, the patient's clinical, biochemical and microbiological responses are closely monitored. In the case report, lock therapy was first applied for catheter infection due to the catheter growth and since growth continued despite treatment directed at the catheter, the catheter was removed to eliminate the focus. Surgical intervention may be required in patients who develop complications despite antibiotic therapy. Heart valve replacement is important to reduce the progression of tissue destruction and the risk of embolism. It is also critical to preserve the functionality of the remaining heart structure. Surgical treatment should be planned considering the patient's general condition, severity of the valve lesion and risk of embolism. In this case, there was a vegetation larger than one centimeter and surgery was indicated according to the guidelines. After 2 weeks of parenteral treatment, the patient was transferred to the cardiovascular surgery service for surgical intervention.

Conclusion

Infective endocarditis is a very serious health problem and early diagnosis and correct treatment are vital. A multidisciplinary approach is required for the correct management of the disease. It should be addressed multidisciplinary with a team work including a cardiologist, infectious disease specialist, cardiac surgeon and other relevant specialists.

Keywords: infective endocarditis, catheter, hemodialysis, renal failure

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