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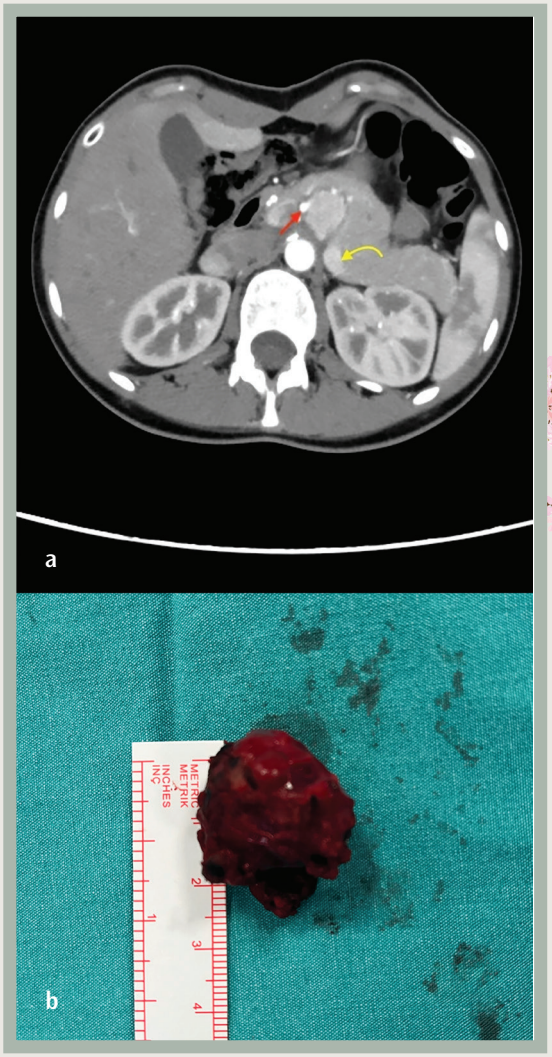

Figure 1. (a) Axial slice from a triphasic computed tomography scan. Red arrow: splenic artery; yellow arrow: splenic vein. (b) Macroscopic specimen

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Preparticipation Cardiac Evaluation in Children and Adolescents: International Guidelines and Practical Considerations

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ABSTRACT

Sudden cardiac death (SCD) in children and adolescents participating in sports, although rare, represents a devastating event with significant clinical and social implications. Preparticipation cardiac screening has been proposed as a preventive strategy to identify individuals at risk before they develop life-threatening arrhythmias or cardiac arrest during exercise. Current evidence demonstrates that the leading causes of SCD in young athletes include hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, anomalous coronary arteries, myocarditis, and inherited channelopathies. International guidelines provide divergent recommendations regarding screening strategies. The American Heart Association and the American College of Cardiology advocate a focused history and physical examination without the routine use of electrocardiography (ECG), whereas the European Society of Cardiology endorses the inclusion of a standard 12-lead ECG. More recent consensus statements, such as those from the International Olympic Committee and Fédération Internationale de Football Association, aim to harmonize approaches across countries. While ECG has been shown to increase sensitivity for detecting silent cardiac conditions, concerns remain about false positives, limited specificity, cost-effectiveness, and the need for experienced interpretation. Emerging strategies, including advanced imaging modalities, genetic testing in selected populations, and artificial intelligence-assisted ECG analysis, may enhance risk stratification in the future. This review summarizes the current evidence, highlights key controversies, and discusses future perspectives on preparticipation cardiac screening in children and adolescents involved in sports.

Keywords: Preparticipation cardiac screening, sudden cardiac death, children, adolescents, electrocardiography, cardiovascular risk assessment

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Introduction

Sudden cardiac death (SCD) in young athletes, though infrequent, remains a devastating clinical and social event that continues to draw attention from physicians, families, and policy makers. The estimated incidence is approximately 1 to 2 per 100,000 athletes annually, with variations across regions depending on population characteristics and methods of ascertainment (1,2). The most common underlying causes in children and adolescents include hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), congenital anomalies of the coronary arteries, myocarditis, and inherited channelopathies such as long QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT). Despite its rarity, the

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psychological impact of sudden death in apparently healthy young athletes is profound, reinforcing the need for effective preventive measures.

Regular sports participation in childhood is associated with improved cardiorespiratory fitness, lower cardiometabolic risk, and better psychological well-being. Accordingly, the primary goal of preparticipation cardiac evaluation is not to exclude children from sports, but to facilitate safe participation by identifying those at increased risk. At the same time, overdiagnosis and unnecessary restriction may lead to avoidable psychosocial and developmental consequences; therefore, a balanced approach is essential.

Preparticipation cardiac screening has emerged as a potential strategy to reduce the risk of exercise-related SCD by identifying occult cardiovascular disease before competitive sports participation. However, the optimal screening approach remains a matter of debate. The American Heart Association (AHA) and the American College of Cardiology (ACC) recommend a targeted 12-element personal and family history and physical examination without routine use of electrocardiography (ECG) (3). In contrast, the European Society of Cardiology (ESC) advocates inclusion of a resting 12-lead ECG based on evidence from the Italian experience showing a reduction in athlete SCD incidence following mandatory ECG screening (2,4). More recently, international governing bodies such as the International Olympic Committee and Fédération Internationale de Football Association have supported harmonized screening approaches that consider regional resources while aiming to maximize sensitivity and specificity (5,6).

This review provides an updated synthesis of the epidemiology, etiology, and current guidelines for preparticipation cardiac screening in children and adolescents participating in sports. In addition, it highlights controversies regarding diagnostic yield, false-positive rates, and cost-effectiveness and discusses emerging strategies, such as genetic testing and artificial intelligence-assisted ECG analysis, that may shape the future of cardiovascular risk assessment in young athletes.

Epidemiology of Sudden Cardiac Death in Young Athletes

The true incidence of SCD in children and adolescents participating in organized sports is difficult to establish due to variations in study methodology, case definitions, and reporting systems. Estimates range from 1 to 2 cases per 100,000 athlete-years, with higher rates reported in competitive athletes compared with the general adolescent population (1,2). Regional differences are also evident: the Italian registry demonstrated a reduction in SCD incidence after the introduction of mandatory ECG-based screening, whereas North American cohorts have reported relatively stable rates when screening is limited to history and physical examination (7,8).

The etiological spectrum of SCD in young athletes is broad, with structural cardiomyopathies and congenital anomalies predominating. HCM remains the most frequent diagnosis in the United States (US), whereas ARVC and anomalous coronary arteries are more prevalent in European series (9,10). Channelopathies, particularly LQTS and CPVT, account for a significant proportion of autopsy-negative cases (11). Myocarditis and premature atherosclerotic coronary artery disease (CAD), though less common, are also recognized causes, especially in older adolescents (12). Table 1 summarizes the most common causes of SCD in child and adolescent athletes.

Etiologies and Risk Factors in Children and Adolescents

As outlined in the epidemiology section, the causes of SCD in young athletes are heterogeneous. A detailed understanding of the associated clinical risk markers is essential for effective preparticipation screening.

Table 1. Common causes of sudden cardiac death in children and adolescent athletes

Category	Examples/notes
Cardiomyopathies	Hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, dilated cardiomyopathy
Congenital anomalies	Anomalous origin of coronary arteries, congenital aortic stenosis, unrecognized congenital heart disease
Primary arrhythmia syndromes (channelopathies)	Long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, Brugada syndrome
Inflammatory/acquired	Myocarditis, Kawasaki disease-related coronary artery lesions
Other causes	Premature atherosclerotic CAD, commotio cordis, undetermined causes at autopsy

CAD: Coronary artery disease

Cardiomyopathies are the most frequent structural cause of SCD. In HCM, risk indicators include a positive family history of premature SCD, exertional syncope, a harsh systolic murmur on examination, and abnormal ECG findings such as deep Q waves or marked repolarization changes. ARVC, more commonly reported in European cohorts, often presents with ventricular arrhythmias, T-wave inversion in right precordial leads, or a history of unexplained palpitations during exercise (9,10).

Congenital coronary anomalies, particularly anomalous origin of the left coronary artery from the right sinus, can precipitate ischemia or malignant arrhythmias during exertion. These conditions often lack objective physical findings, making exertional chest pain or syncope in otherwise healthy athletes an important clinical red flag (10).

Channelopathies such as LQTS, CPVT, and Brugada syndrome frequently underlie autopsy-negative SCD cases. Clinical clues include exertional syncope, unexplained seizures, and a family history of sudden death before the age of 50. Baseline ECG abnormalities -such as prolonged QT interval, bidirectional ventricular tachycardia on exercise testing, or coved-type ST elevations -are key markers when present (1,9).

Acquired causes, such as myocarditis, should be suspected in athletes presenting with recent viral illness, chest pain, or new-onset arrhythmia. Premature CAD, although rare in pediatric patients, may occur in adolescents with significant risk factors, including obesity, smoking, hypertension, and dyslipidemia. Kawasaki disease-related coronary aneurysms represent another important acquired risk in certain populations (13).

Children and adolescents with congenital heart disease (CHD) form another important subgroup that requires careful evaluation before participation in competitive sports. While advances in surgery and interventional cardiology have enabled many patients with repaired CHD to reach adolescence and adulthood with good functional status, residual lesions, arrhythmogenic substrates, and abnormal hemodynamic responses to exercise may persist. The 36th Bethesda Conference Guidelines provide detailed criteria for participation, stratified by the specific lesion, surgical repair status, and arrhythmic risk (14). For example, individuals with mild, repaired ventricular septal defects may be cleared for all sports, whereas those with severe pulmonary hypertension or cyanotic CHD remain restricted. Recognizing these complexities is crucial in tailoring safe and individualized advice for young athletes with CHD.

Risk is also modified by the type and intensity of sport participation. Contemporary AHA/ACC recommendations classify sports according to their dynamic (isotonic) and static (isometric) components, recognizing that high-dynamic and high-static activities impose different hemodynamic loads in specific cardiac conditions (15). This framework is helpful when counselling young athletes with cardiomyopathies or CHD, as both the underlying lesion and the expected cardiovascular demands of the sport must be considered. A simplified overview of this classification, with common examples of pediatric and adolescent sports, is provided in Table 2.

Finally, extrinsic and lifestyle factors may exacerbate the risk in predisposed individuals. The use of stimulant medications or performance-enhancing substances, dehydration, electrolyte imbalance, and extreme endurance

Table 2. Simplified classification of sports according to dynamic and static components in children and adolescents

Category	Hemodynamic profile	Typical sports (children/ adolescents)	Practical considerations in cardiovascular disease
Low dynamic/low static	Minimal increase in heart rate and blood pressure	Bowling, golf, yoga, recreational walking	Usually acceptable in most cardiac conditions if stable
Moderate dynamic/low-moderate static	Moderate volume load, modest pressure load	Recreational cycling, doubles tennis, volleyball	Caution in moderate/severe valvular disease or significant arrhythmias
High dynamic/low static (endurance)	High volume load, marked increase in heart rate and cardiac output	Distance running, competitive swimming, football/soccer, basketball	Potentially problematic in cardiomyopathies, pulmonary hypertension, complex CHD
Low-moderate dynamic/ high static (strength/ power)	Predominantly pressure load, marked BP elevations	Weightlifting, wrestling, gymnastics, judo	Avoid or restrict in severe aortic stenosis, uncontrolled hypertension, aortopathy
High dynamic/high static (mixed/combat)	High volume and pressure load, intense sympathetic activation	Competitive rowing, ice hockey, handball, high-level martial arts	Highest cardiovascular demand; often restricted in high-risk cardiomyopathies and complex CHD

CHD: Congenital heart disease, BP: Blood pressure

training have all been associated with arrhythmic vulnerability in susceptible athletes (13,16,17). Recognizing these risk markers in conjunction with a careful clinical history and examination enhances the diagnostic yield of preparticipation screening. A comprehensive summary of etiologies and their associated clinical red flags is presented in Table 3.

Screening Modalities

Clinical History

A thorough medical history is the cornerstone of preparticipation screening. The AHA/ACC recommends a structured 12-element history, which includes questions on exertional chest pain, syncope, palpitations, unexplained seizures, and family history of premature sudden death or cardiomyopathy (3) (Table 4). Identifying red flags from history alone can help prioritize athletes for further testing. In many reported cases of athlete SCD, symptoms such as exertional syncope or chest discomfort were present but were not adequately investigated (18).

Physical Examination

Physical examination complements the clinical history, though its sensitivity for detecting silent cardiovascular disease is limited. Key elements include auscultation for pathologic murmurs suggestive of HCM or valvular disease, measurement of blood pressure, and assessment for phenotypic features of Marfan syndrome or other connective tissue disorders (9,16). While rarely diagnostic on its own, abnormal findings can guide appropriate use of advanced investigations.

Table 3. Etiologies and key clinical risk markers for sudden cardiac death in children and adolescent athletes

Etiology	Key clinical clues/risk markers
Hypertrophic cardiomyopathy	Family history of SCD, exertional syncope, harsh systolic murmur, abnormal ECG (deep Q waves, repolarization changes)
Arrhythmogenic right ventricular cardiomyopathy	Ventricular arrhythmias, T-wave inversion in V1-V3, unexplained palpitations during exercise
Congenital coronary anomalies	Exertional chest pain or syncope without murmur, ischemic ECG changes during exertion
Long QT syndrome	Prolonged QT interval on ECG, exertional syncope, unexplained seizures, family history of SCD
Catecholaminergic polymorphic VT	Exercise-induced syncope, bidirectional VT on exercise testing, family history of sudden death
Brugada syndrome	Coved-type ST elevation in V1-V3, nocturnal agonal respiration, family history of SCD
Myocarditis	Recent viral illness, chest pain, arrhythmias, elevated troponin
Premature coronary artery disease	Traditional risk factors: obesity, smoking, hypertension, dyslipidemia
Kawasaki disease sequelae	History of Kawasaki disease, coronary aneurysms, ischemia or arrhythmia during exertion
Extrinsic factors	Stimulant/performance-enhancing drug use, dehydration, electrolyte imbalance, extreme endurance training

SCD: Sudden cardiac death, VT: Ventricular tachycardia, ECG: Electrocardiography

Table 4. The 12-element AHA preparticipation cardiovascular screening recommendations (2007 Statement) (3)

Domain	Elements
Personal history	1. Exertional chest pain/discomfort 2. Unexplained syncope/near-syncope 3. Excessive exertional dyspnea/fatigue or palpitations 4. Prior recognition of a heart murmur 5. Elevated systemic blood pressure
Family history	6. Premature death (sudden/unexpected) before 50 years of age due to heart disease 7. Disability from heart disease in a close relative <50 years 8. Knowledge of inherited cardiac conditions (HCM, LQTS, Marfan syndrome, etc.)
Physical examination	9. Heart murmur 10. Abnormal femoral pulses 11. Physical stigmata of Marfan syndrome 12. Brachial artery blood pressure (sitting position)

HCM: Hypertrophic cardiomyopathy, LQTS: Long QT syndrome, AHA: American Heart Association

Red Flags in Pediatric Athletes

Certain clinical features should raise immediate concern for an increased risk of SCD, including exertional syncope, chest pain or palpitations during activity, unexplained seizures, documented arrhythmias, and a family history of sudden death before age 50 (3,10,13). Exertional syncope, chest pain and a positive family history are regarded as particularly high-risk warning signs. Although the positive predictive value of individual symptoms is low in the general population of athletes, their presence is associated with a substantially increased relative risk and should always prompt further cardiovascular assessment.

Special Tests

When history or physical examination raises suspicion, special tests are indicated.

• **Electrocardiography:** The ESC and international consensus guidelines advocate routine ECG, whereas the AHA/ACC recommend its use only in selected cases. Modern athlete-specific interpretation standards, such as the Seattle Criteria and International Criteria, have reduced false-positive rates while maintaining sensitivity (4,6). Echocardiography is valuable for structural evaluation when a murmur or abnormal ECG is detected but is not recommended for universal screening because of cost and limited availability (2,10,19).

• **Exercise Testing (Treadmill/Exercise ECG):** Exercise testing may unmask arrhythmias not evident at rest, particularly in conditions such as CPVT and LQTS. It may also help evaluate exertional chest pain, ischemic ECG changes, and functional capacity in athletes with suspected coronary anomalies or repaired CHD. However, its role in routine population-based screening is limited, and it is best applied in athletes with concerning symptoms or abnormal baseline findings (20,21).

• **Advanced Imaging (Cardiac Magnetic Resonance, Computed Tomography):** Used in selected athletes to clarify suspected cardiomyopathy, anomalous coronary arteries, or myocarditis (22,23). Genetic testing is considered in athletes with a strong family history or features suggestive of inherited arrhythmia syndromes; its role in routine screening remains limited, but may expand with decreasing costs (24).

Challenges and Controversies

Despite its potential benefits, preparticipation cardiac screening in young athletes remains an area of significant debate.

False Positives and False Negatives

The use of ECG as a universal screening tool has improved sensitivity for detecting silent cardiovascular disease, but is associated with considerable rates of false-positive findings, particularly when interpreted without athlete-specific criteria; false negatives also remain a concern for certain conditions. Early ECG screening programs using non-athlete-specific criteria reported false-positive rates as high as 10–20% in some cohorts, largely due to misinterpretation of physiological adaptations of the athlete's heart. With the adoption of contemporary athlete-specific interpretation standards, such as the Seattle and subsequent International criteria, false-positive rates have fallen to approximately 3–5% while maintaining high sensitivity for clinically relevant cardiomyopathies and channelopathies. Nevertheless, false-negative results still occur, particularly in conditions that may have a normal or only subtly abnormal ECG, such as anomalous coronary arteries or very early-stage cardiomyopathies; this remains an inherent limitation of any screening strategy (6,9,16,25,26).

Cost-Effectiveness and Feasibility

Another major controversy is the economic and logistical feasibility of implementing mass screening programs. Studies from the US have raised concerns about the high cost of routine ECG screening relative to its yield, particularly in large populations (17). In contrast, European experiences suggest potential long-term benefits when false positives are reduced using refined interpretation criteria. Nevertheless, disparities in healthcare resources across regions make universal recommendations difficult to establish (13).

Ethical and Legal Issues

Ethical dilemmas arise when athletes are disqualified from sports based on screening results, especially in conditions with variable penetrance or uncertain clinical significance. Disqualification may protect the athlete, but it can also cause psychosocial harm and raise legal challenges. Families and clinicians often face a delicate balance between ensuring athlete safety and preserving the athlete's autonomy to participate. Ethical reflections on medical disqualification emphasize that disqualification can carry substantial psychosocial, financial, and identity-related consequences for the athlete and their family (27). Moreover, issues of equity arise, as resource-limited settings may lack the infrastructure for advanced screening, potentially widening disparities in care.

In Türkiye, sports participation and athlete licensing are regulated by national youth and sports legislation and ministerial regulations, which require a medical report documenting fitness to participate when applying for a license. In routine clinical practice, preparticipation evaluations are frequently performed by family physicians, sports medicine

specialists, and cardiologists; the issuance of an athlete license implies medicolegal responsibility for the certifying clinician. These national regulations frame the ethical and legal context in which preparticipation cardiac screening is implemented (28).

Future Perspectives

Future directions in preparticipation cardiac screening focus on integrating novel technologies with traditional approaches. Artificial intelligence-assisted ECG interpretation may reduce false positives and improve accuracy (29). Genetic testing, although currently limited to selected cases, is expected to expand as costs decrease and interpretation frameworks improve (24). Advanced imaging, particularly echocardiography and cardiac magnetic resonance imaging, may play an increasing role in selected high-risk athletes (19,22,23). The future of screening is likely to move toward personalized risk assessment, integrating multimodal data to optimize both sensitivity and feasibility.

Conclusion

In conclusion, SCD in young athletes, though rare, has profound clinical and societal consequences. Preparticipation screening offers an opportunity to identify individuals at risk, but its implementation remains controversial due to variability in guidelines, diagnostic yield, and cost-effectiveness. While the AHA/ACC emphasizes a focused history and physical examination, the ESC and international consensus groups advocate for routine ECG, reflecting different interpretations of available evidence. Key challenges include false positives, limited resources, and ethical dilemmas related to sports disqualification. Nevertheless, ongoing advances in ECG interpretation, imaging, and genetics are expected to refine risk stratification. Future approaches will likely emphasize personalized cardiovascular assessment, balancing athlete safety with the right to participate in sports. A proposed stepwise algorithm, as shown in Figure 1, summarizes how structured history and examination, targeted ECG use, and selective application of further tests can be integrated into

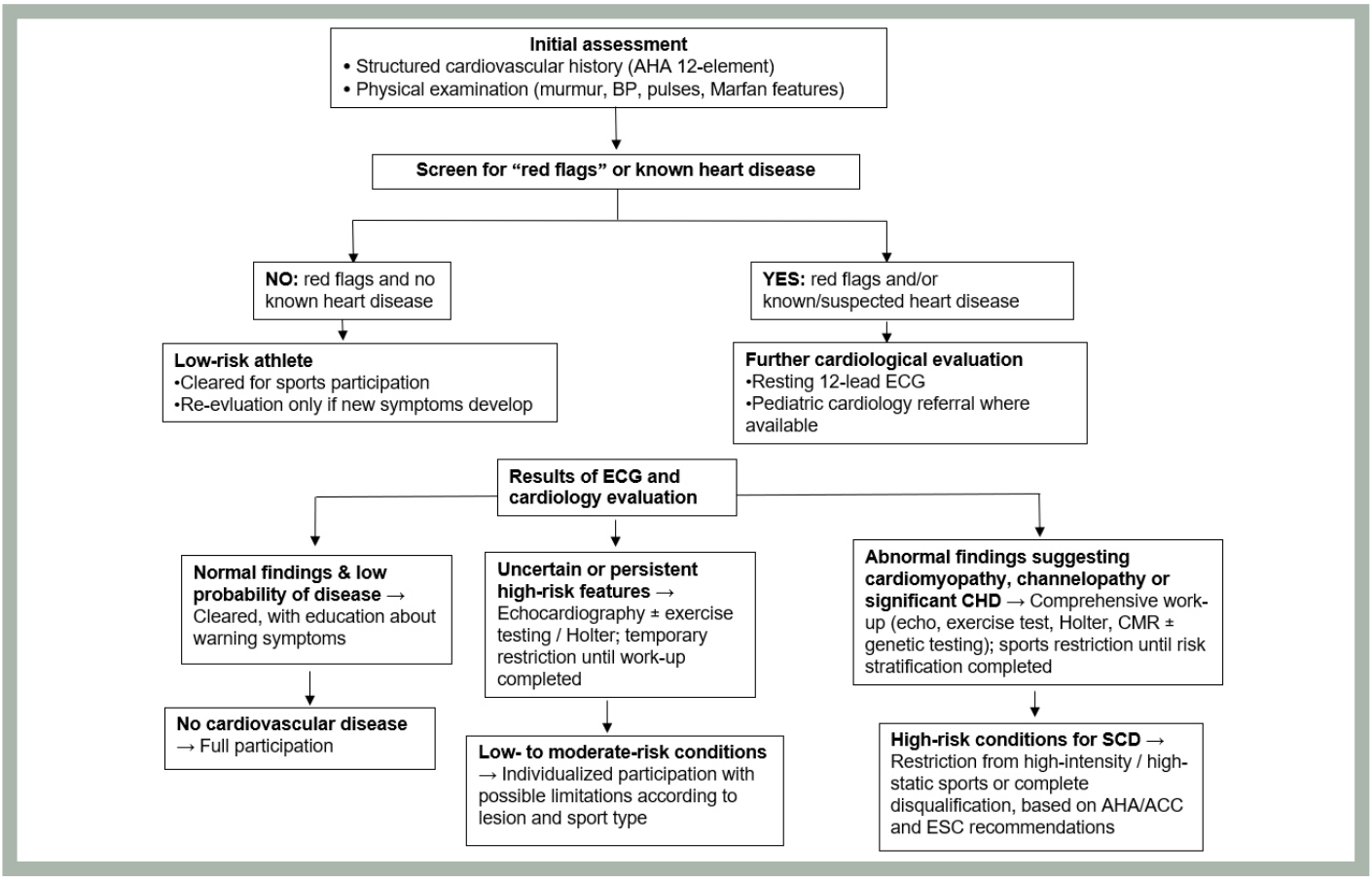

Figure 1. Proposed algorithm for preparticipation cardiac evaluation in children and adolescents

BP: Blood pressure, ECG: Electrocardiography, CHD: Congenital heart disease, CMR: Cardiac magnetic resonance, SCD: Sudden cardiac death, AHA/ACC: American Heart Association/American College of Cardiology, ESC: European Society of Cardiology

a practical preparticipation evaluation pathway. In Türkiye, as in many countries with diverse healthcare resources, adopting a feasible and cost-effective strategy that combines careful clinical evaluation with selective use of ECG and imaging may represent the most practical approach. Efforts to increase awareness among physicians, families, and sports organizations will be critical in implementing effective and equitable screening programs.

Footnotes

Authorship Contributions

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

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The Survival of Relapsed Childhood Leukemia: An 12-year Single-center Experience

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What is known on this subject?

In acute lymphoblastic leukemia, which is the most common type of cancer in childhood, despite a remission rate of up to 85-95%, recurrence and subsequent events are the most common and undesirable situation with a rate of 15-20%.

What this study adds?

To share the outcome of our recurrent cases among acute lymphoblastic leukemia patients who have been treated and followed for 12 years in our hospital, which is at the forefront of newly diagnosed cancer applications every year in our country.

ABSTRACT

Objective: Relapse is still the most important cause of death all over the world, and approximately 15-20% of children experience a recurrence of the disease.

Material and Methods: Among 474 patients who received their first treatment from December 2012 to March 2024 at pediatric hematology oncology clinic, 48 patients who relapsed were included in the study. Diagnosis of initial and relapse acute lymphoblastic leukemia was made by morphological and immunophenotypic evaluation of bone marrow and other samples, and the patients were treated with Berlin-Frankfurt-Munster protocols. The risk of recurrence, T-cell bone marrow relapse, very early relapse, early bone marrow relapse, recurrence after bone marrow transplantation, t(9;22) and t(1;19) positive were defined as "high-risk"; the others as "standard-risk".

Results: Thirty four (71%) of the cases were male, 32 (67%) were bone marrow 4 (8%) were isolated central nervous system (CNS), 5 (10%) were bone marrow + CNS, 7 (17%) were other sites, 27 (44%) were high-risk, and 8 (21%) allogeneic transplants were performed. The calculated 86-month overall survival rate is 51%. The event-free survival (EFS) is 62% at 96 months in standard-risk and 36% at 61 months in high-risk (p=0.037). It is 38% at 37 months after relapse. Furthermore, EFS 53% at 49 months for isolated bone marrow recurrence and 31% at 14 months for recurrence at other sites (p=0.481). Also, it is 25% at 14 months, which is considered very early according to the time of recurrence, 36% in the last 16 months, and 81% EFS at 73 months (p=0.02).

Conclusion: Although follow-up periods are relatively short, our overall and EFS is comparable to that of developed countries. The risk situation and the time of recurrence are the most important factors affecting the outcome. Contrary to expectations, isolated bone marrow recurrences had a better EFS rate, suggesting that the lack of statistical difference is because of the low number of isolated non-bone marrow recurrence cases.

Keywords: Acute lymphoblastic leukemia, child, event-free survival, pediatric hematology, recurrence, survival

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Introduction

Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy, accounting for 25-30% of all childhood cancers. As a result of advances in chemotherapy and supportive care, the 5-year survival rate for childhood ALL has increased from 10% to 86% in the last 50 years (1,2). However, the survival in resource-limited countries is significantly lower compared with high-income countries, with a long-term survival of only 35-80% (3). After two years of treatment that wears out the child and the family, the disease relapses in approximately 15-20% of children, and it is the leading cause of death worldwide from leukemia (4). The present study aimed to evaluate overall survival (OS) and event-free survival (EFS) in children with relapsed ALL.

Material and Methods

The study included 474 ALL patients who were diagnosed and treated at University of Health Sciences Türkiye, Kanuni Sultan Süleyman Training and Research Hospital, Pediatric Hematology Oncology Clinics between December 2012 and June 2020, and at University of Health Sciences Türkiye, Çam and Sakura City Hospital, Pediatric Hematology Oncology Clinics from 2020 to March 2024. Out of 474 patients, the data from 48 ALL patients who relapsed were retrospectively analysed. For newly diagnosed ALL patients ALL-Inter-Continental (IC) Berlin-Frankfurt-Munster (BFM) 2009 trial protocol was used until September 2022, and then ALL European European Standard Clinical Practice 2022 guidance document was used. Relapsed patients were treated according to childhood ALL 1st relapse guidance that was developed by ALL-IC Study Group in 2016, except for 4 patients (5). Diagnosis was made by morphologic and immunophenotypic examination of bone marrow and/or peripheral blood. The flow cytometry analysis for immunophenotyping was performed at İstanbul University Immunology Laboratory until 2018 due to unavailibilty of flow cytometry device, and started to be performed in our hospital since then. Starting from June 2020, an Excel-based software program was used for patients' clinical, laboratory, and follow-up data records. Relapse within 18 months after initial diagnosis is defined as very early relapse; as early relapse if it occurs ≥18 months after initial diagnosis or within <6 months after completion of initial treatment; and late relapse if it occurs ≥6 months after completion of initial treatment. Site of relapse was defined as: bone marrow, central nervous system (CNS), testicular, other sites, bone marrow + CNS, bone marrow + testicular, or bone marrow + other sites. Patients were stratified into "high-risk group" or "standard-risk group" based on immunophenotype, site, and time to relapse. Patients with certain genetic abnormalities, including t(9;22) and t(1;19), T-cell bone marrow relapse, any very early relapse, early bone marrow relapse, and relapse after hematopoietic stem cell transplantation (HSCT), are defined as "high-risk" while those not stratified as high-risk are defined as "standard-risk".

Statistical Analysis

Patient data were analysed retrospectively and evaluated with descriptive statistics. Kaplan-Meier and Cox regression survival analyses were performed using IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY.

Results

Thirty four (71%) patients were male and 14 (29%) were female; median age (interquartile range) at time of diagnosis and at the time of relapses were 6.9 (8.8) and 9 (7.6) years, respectively. The cell types were: 3 proB, 34 preB, and 8 T-cell ALL. The rate of T-cells at the first diagnosis was 17%. According to the time to relapse, 11 (23%) were very early relapse, 19 (40%) early relapse early, and 18 (37%) late relapse. Relapse site was bone marrow in 32 patients (67%); isolated CNS (iCNS) in 4 patients (8%), bone marrow + CNS in 5 patients (10%); and other sites in 9 patients (14%), two of patients with isolated retina involvement, one of whom also subsequently developed CNS relapse (Table 1). There were 27 patients (56%) in the standard-risk group and 21 patients (44%) in

Table 1. Relaps cites of cases

	Frequency	Percent
Bone marrow (BM)	32	66.7
Central nervous system (CNS)	4	8.3
Testis	1	2.1
Other cites	2	4.2
BM + CNS	5	10.4
BM + testis	2	4.2
BM + other cites	2	4.2
Total	48	100

Table 2. Distribution of cases according to risk status at initial diagnosis and relapse

		Relapse		
		Standard	High	Total
Initial diagnosis	Medium	15	12	27
	High	9	12	21
	Total	24	24	48

the high-risk group (Table 2). After the patients experienced relapse, the median follow-up period was 14 months (with an interquartile range of 28 months). Two patients (4%) who were at high-risk due to very early relapse could not achieve remission with induction and subsequent rescue treatments and died of the disease. Another two patients (4%) in the high-risk group, the response to induction therapy was poor, and bone marrow transplantation from a matched unrelated donor was possible for one of them and the other patient died from an infection. In one case in the standard-risk group with inadequate induction response, chemotherapy was continued because a matched donor could not be found, and the patient is currently being followed up in remission in the 15th month of maintenance. A patient with T-ALL who had a relapse at 54 months of follow-up, presented with left retinal involvement. He entered the intensive care unit, due to septic shock that occurred at the third week of induction treatment. He received supportive treatment in the intensive care unit for 1.5 months, and in the meantime, he completely lost his vision in both eyes. The treatment was terminated upon the request of the family; he has been followed in remission without chemotherapy for 20 months.

Ten patients (21%) received allogeneic HSCT; 7 were high-risk and 3 were standard-risk. Four received transplants from matched sibling donors, 1 from a family-matched donor, 4 from matched unrelated donors, and 1 from an HLA-9/10 compatible parent. One of the two patients was lost to follow-up without disease 7 months after transplantation, and the other was lost 1 year later. Three patients died due to disease despite two transplants each, and five patients are being followed up, disease-free, for a median of 15 months.

During the follow-up period, no event occurred in 46% of the cases. The most common events were a second relapse in 24% of the patients, and death due to ALL in 12.5% of the patients (Table 3). Two patients (4%) in their first relapse died during induction from septic shock (unknown source) before response evaluation could be obtained. One patient never achieved remission and was lost to follow-up 6 months later.

Table 3. Events after relapses

	Frequency	Percent
No event	22	45.8
Chemotherapy resistance	1	2.1
Second relapse	11	22.9
Permanent sequelae	3	6.3
Died disease free	4	8.3
Died with disease	7	14.6
Total	48	100

According to the risk status at the time of initial diagnosis, two of the 27 medium-risk patients had non-disease-free deaths and one disease-related death, while two of the 21 high-risk patients had non-disease-free deaths and six disease-related deaths. The rate of T-cells was 17% both at the initial diagnosis and at the time of recurrence. Two of the three permanent sequelae occurred in cases of T-cell relapse (blindness and osteomyelitis). While two of the seven leukemia deaths before remission were due to T-cells, none of the deaths in remission were due to T-cells.

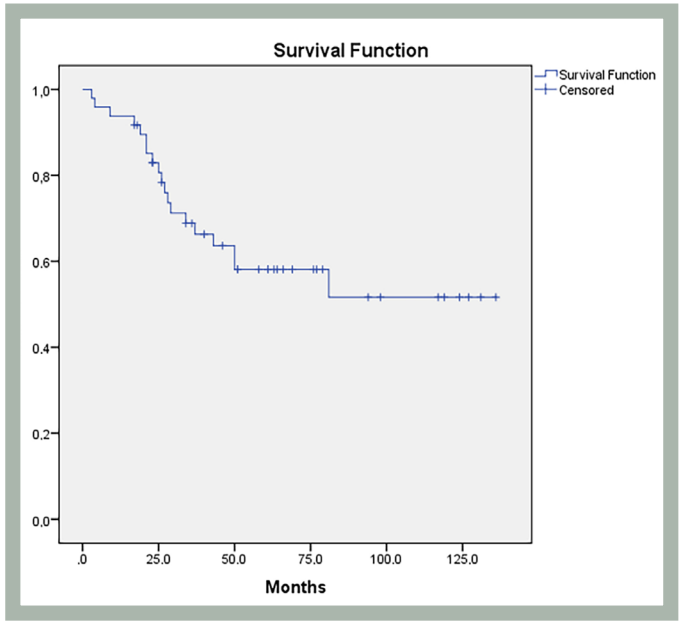

Figure 1. Kaplan-Meier curves of overall survival of all studied patients (n=48)

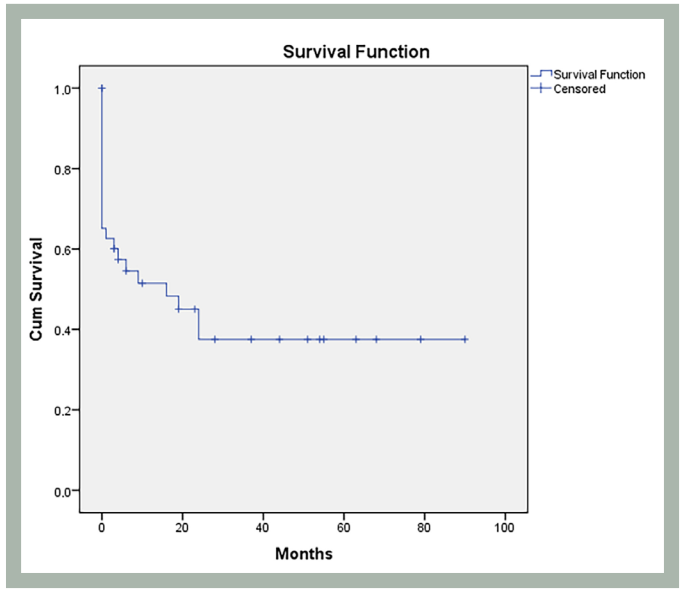

Figure 2. Kaplan-Meier curves of overall survival of all studied patients (n=48)

The estimated OS at 86 [95% confidence interval (CI): 70-104] months was 51% (Figure 1) and EFS at 37 (95% CI: 24-51) months was 38% (Figure 2). According to the risk stratification at the time of relapse, OS was 62% at 96 months (95% CI: 77-115), in the standard-risk group and was 36% at 67 months (95% CI: 42-92) in the high-risk group (p=0.037) (Figure 3). Depending on the site of relapse EFS was 53% at 49 (95% CI: 32-66) months for isolated bone marrow relapse and was 31% at 14 (95% CI: 3-25) months for isolated extramedullary or combined relapse (p=0.481) (Figure 4). According to the time to relapse EFS was 25% at 13 (95% CI: 0-31) months for very early relapse and was 81% at 73 (95% CI: 55-90) months for late relapse, respectively (p=0.02) (Figure 5).

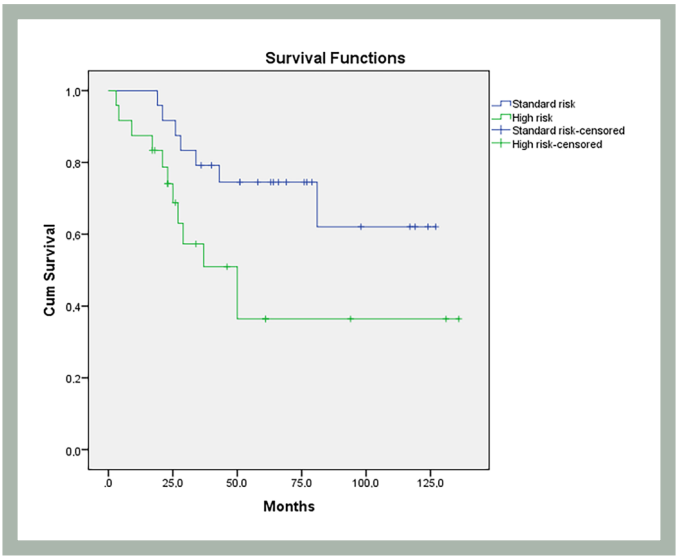

Figure 3. Kaplan-Meier curves of overall survival for standard-risk (n=27) and high-risk (n=21) groups

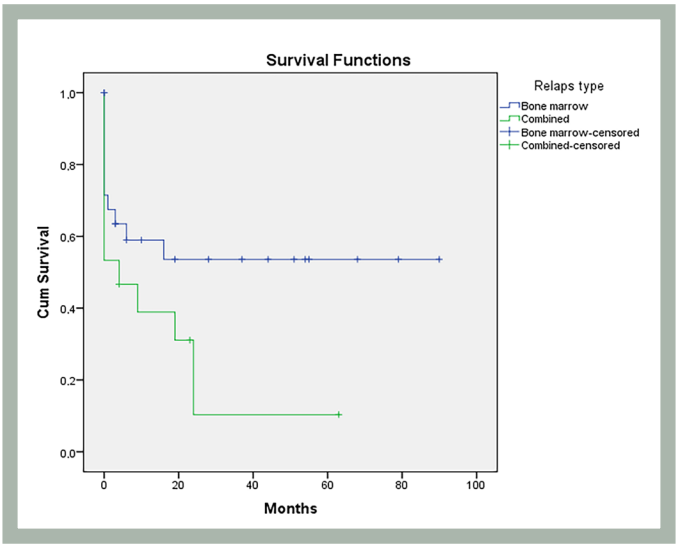

Figure 4. Kaplan-Meier curves of event-free survival for bone marrow (n=32), and combined (n=16) groups

Discussion

Despite the significant survival improvements in newly diagnosed childhood ALL, outcomes for relapsed patients remain poor (2), and only half of patients achieve long-term survival (6). The most important prognostic factors determining survival after relapse are the site of relapse, duration of first complete remission, and disease immunophenotype (7). According to the relapse site, 50-60% of relapses occur in the bone marrow, following relapse CNS in ~20%, isolated testicular relapse in ~5%, and a combination of bone marrow and extramedullary disease in the remainder (8). In our study, relapse rates were similar to those reported in the literature (7,9).

In general, in the treatment of patients at high-risk for the first recurrence of ALL, bone marrow transplantation is performed after several courses of chemotherapy, while in the standard-risk group, several courses of chemotherapy lasting up to 9 months, followed by low-dose chemotherapy, are given orally for up to 2 years (10). Although there have been some improvements in outcomes over the past few decades, only 50% of children with a first relapse of ALL survive long-term, and outcomes are much worse with second or subsequent relapses (11,12). In patients with relapse, chemotherapy-related mortality is approximately three times higher (10%) than in patients with primary treatment, and as with primary treatment, infections are the most common cause of death (9). Relapses that occur within 3 years of diagnosis and any recurrence of T-ALL are particularly difficult to recover from (11). Our results appear to be similar to those in the literature,

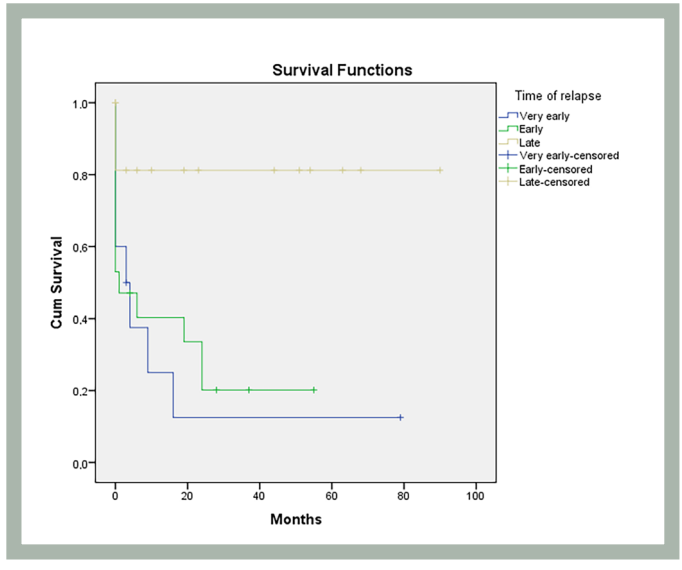

Figure 5. Kaplan-Meier curves of event free survival for very early (n=11), early (n=19), late (n=18) groups

showing a similarity of 54%. We believe that it is valuable not to be left behind as well.

Blinatumomab, a bispecific T-cell-binding antibody that connects CD3+ T-cells to CD19+ B-ALL cells, has become a part of current treatment protocols in high-risk relapsed pediatric ALL cases due to increased disease-free survival with 2 cycles of blinatumomab, lower toxicity, and superior minimal residual disease clearance (13). However, it could not be used in any of our cases. In a subsequent publication by the same researchers, it was stated that there was no statistically significant effect on EFS (14). Although other studies state that it contributes to the short-term effects, it is understood that time is needed to see its long-term effects (10).

In a study from the southeast region of Türkiye, the relapse rate of 93 pediatric ALL patients, who were in remission after induction chemotherapy, was 6.4%. Five patients (4.7%) had a bone marrow relapse, one patient (0.9%) had a retinal relapse, and five patients (4.7%) had a second occurrence of acute myeloid leukemia (15). In this study, the development of second AML was thought to be due to the epipodophyllotoxins that were used in the St. Jude Total XIII protocol during the first treatment (16). By contrast, no ALL patients developed second AML in the current study, despite the fact that the current study's patients' number was four times greater than the latter study, and a total of 500 mg/m^2 etoposide was used in 44% of patients who were stratified into the high-risk arm of the ALL BFM protocols.

In the Children's Cancer Group ALL trial and ALL relapse BFM 90 trial, 5-year OS and 10-year OS rates were 36.3%, and 36%, respectively (11,12). In the recent reports, 5-year OS for first relapse of childhood ALL is around 50% (9,17). Long-term survival was not lagging behind the reported results.

It is known that the presence of T-cell leukemia is one of the most important prognostic factors in general, and in some studies of T-cell leukemia cases, relapse rates of up to 30% have been reported (6,18). However, it is also noteworthy that in our cases, the T-cell rate remained unchanged at 17% both at the time of initial diagnosis and at the time of recurrence. The reason for the low recurrence rate of T-cell cases cannot be an immunophenotyping error. Because they can be easily distinguished from each other in flow cytometric analysis, cells of different types can be efficiently separated. Regional and racial differences remain.

Two of the three permanent sequelae occurred in cases of T-cell relapse. While 2 of the 7 leukemia deaths before remission were caused by T-cells, none of the deaths in remission were due to T-cells. In an analysis of Children's Oncology Group that included 9,585 pediatric ALL patients, patients with iCNS relapse comprised 20.9% of all relapses, and the 5-year OS rates for very early, early, and late iCNS relapse were 44%, 68%, and 78%, respectively (19). In the recent report by Children's Oncology Group, the 3-year EFS and OS rates were 41.4% and 51.7%, respectively, for very early iCNS relapse. The 3-year DFS/OS for transplanted patients was significantly better than those who received chemotherapy/radiotherapy alone among patients with very early iCNS relapse (20,21). In the current study, there were only 4 patients (8.3%) with iCNS relapse, and thus survival comparison could not be carried out. Despite a good prognosis in early and late iCNS relapses, very early iCNS relapses prognosis remains poor. Early initiation of HLA typing and selection of a donor should be performed as soon as possible to shorten the pretransplantation interval, if possible, HSCT from a compatible donor should be performed.

Relapse of childhood ALL presenting as ocular involvement is a rare event, and accounts for only 2.2% of ALL relapses. Although the most common site of involvement in isolated ocular relapse of ALL is the retina, it may involve all parts of one or both eyes with subretinal infiltration; or it may occur as bilateral exudative retinal detachment (22). It is noteworthy that two of our relapsed ALL patients presented with retinal involvement. In the literature, cases of retinal relapse have been treated with the ALL treatment protocol, and radiotherapy, and it has been stated that by this approach, the eye can be saved without surgical removal (23,24). It was remarkable that, in the present study, one patient diagnosed with T-cell ALL who presented with retina relapse received only 3-week induction chemotherapy and has been in remission for 20 months.

Study Limitations

The limitations of the present study were relatively short follow-up time and small number of patients.

Conclusion

Despite the relatively short follow-up period, OS and EFS rates for the the relapsed ALL patients were similar to those in the developed countries. Risk group stratification at the time of relapse (high-risk group vs. standard-risk group) and time to relapse were the most important factors affecting the outcome. Survival rate of patients with recurrences in the first 2.5 years after completion of initial treatment remains below 20%. However, patients with isolated bone marrow relapse had a better EFS, which might have been due to a low number of patients.

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We would like to thank our laboratory technician, Cemile Sak, for doing flow cytometry analysis with fast and reliable results, and thus contributing to the diagnosis and treatment of patients.

Ethics

Ethics Committee Approval: University of Health Sciences Türkiye, Çam and Sakura City Hospital (approval number: 2022/03/82, date: 14/03/2022).

Informed Consent: All participants provided written informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A., S.T., O.Z.Ş., E.A., T.N.T., A.Ö.K., D.Y., G.K., Ö.H., S.E., Ö.Ö., E.P.U., C.B., Concept: A.A., Design: A.A., Data Collection or Processing: A.A., Analysis or Interpretation: A.A., Literature Search: A.A., Writing: A.A.

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

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CSMJ

Pediatric Left Ventricular Non-compaction: A Single-center Experience from Anatolia

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What is known on this subject?

Left ventricular non-compaction (LVNC) is a rare but clinically important cardiomyopathy characterized by the coexistence of compact and noncompact layers, deep intertrabecular recesses, and prominent trabeculations. The phenotypic diversity of LVNC in childhood is remarkable. Dilated, hypertrophic, restrictive forms associated with congenital heart diseases, and isolated LVNC forms have been described, and these phenotypes can occur alone or in combination.

What this study adds?

This pediatric series shows that the isolated form is relatively common in LVNC, but clinical risk varies by phenotype. Arrhythmias are common, and the dilated and mixed-restrictive forms have a poorer prognosis.

ABSTRACT

Objective: To describe the phenotypic diversity, arrhythmia burden, and short-to-medium term clinical outcomes in pediatric left ventricular non-compaction (LVNC) cases, in light of a single-center experience from Anatolia.

Material and Methods: Sixteen children diagnosed with LVNC and followed at the Pediatric Cardiology Department of Ordu University Training and Research Hospital between December 2017 and July 2025 were retrospectively evaluated. Demographic characteristics, presenting symptoms, transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR) findings, 12-lead electrocardiogram and 24-hour Holter results, and treatments were recorded. The diagnosis was made based on TTE criteria and confirmed by CMR in all cases. Genetic analysis results were recorded for the cases.

Results: The median age at diagnosis was 7 years (range: 15 days-16 years), and 68.8% of the patients were male; the median follow-up was 33 months (range: 6-82). At presentation, 62.5% of cases were asymptomatic, whereas heart failure was observed in 37.5% of cases. The phenotypic distribution was predominantly isolated LVNC (n=8, 50%); among the non-isolated forms, the dilated type (n=5) was most common, while hypertrophic (n=1), restrictive (n=1), and mixed types (n=1) were also observed. The overall arrhythmia rate was 37.5% (n=6): ventricular tachycardia (VT) was observed in two cases, Wolff-Parkinson-White associated supra-VT was observed in two cases, and frequent ventricular extrasystoles were observed in two cases. Two cases required intervention: sympathetic denervation in one case (diagnosed with catecholamine-sensitive polymorphic VT) and implantation of an implantable cardioverter-defibrillator in the other. Three patients (18.8%) died during follow-up, and the fatalities were concentrated among the dilated and mixed-restrictive subtypes. Pathogenic variants were detected in two of the three cases that underwent genetic testing: PLEKHM2 in two cases and RYR2 in one. The RYR2 carrier had catecholaminergic polymorphic VT. Acetylsalicylic acid and beta-blockers formed the basis of medical management; antiarrhythmics and advanced interventions were applied in selected cases.

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ABSTRACT

Conclusion: This single-center pediatric series shows that the isolated form is relatively dominant, but clinical risk changes depending on the phenotype. Arrhythmias are common, and dilated and mixed-restrictive forms have a less favorable course. Confirming the TTE-based diagnosis with CMR and closely monitoring pediatric cases based on phenotype-rhythm findings may facilitate accurate classification and risk management.

Keywords: Pediatrics, left ventricular non-compaction, cardiomyopathy, arrhythmia, heart failure

Introduction

Left ventricular non-compaction (LVNC) is a rare but clinically important cardiomyopathy characterized by the coexistence of compact and non-compact layers, deep intertrabecular recesses, and prominent trabeculation (1,2). The American Heart Association classifies LVNC as a genetic cardiomyopathy, attributing it to an arrest of myocardial development during embryogenesis (3). In contrast, the European Society of Cardiology still categorizes it as an "unclassified cardiomyopathy" (4). However, recent studies have shown that acquired mechanisms, such as a physiological increase in trabeculation observed in athletes or pregnant women, can also produce phenotypes that mimic LVNC (5).

The phenotypic diversity of LVNC in childhood is remarkable. Dilated, hypertrophic, and restrictive forms (often associated with congenital heart disease), as well as isolated LVNC forms, have been described; these phenotypes can occur alone or in combination (6,7). While isolated LVNC generally has a better prognosis (8), LVNC accompanied by a dilated phenotype (LVNC-D) is associated with poor short-term outcomes (9). This indicates that the risks of mortality and heart transplantation are particularly high among pediatric patients.

The clinical presentation of LVNC is highly heterogeneous, ranging from asymptomatic cases to heart failure, arrhythmias, and thromboembolic events, which constitute the most common manifestations (3). Although transthoracic echocardiography (TTE) is the most commonly used diagnostic tool (1), cardiac magnetic resonance (CMR) imaging also improves diagnostic sensitivity and provides prognostic information, such as late gadolinium enhancement (10).

With respect to etiopathogenesis, LVNC is associated with a genetic basis. It has been associated with more than 100 genes to date, with sarcomere gene mutations (MYH7, TTN, MYBPC3) being the most frequently detected (11). The overlap between these mutations and genes associated with dilated and hypertrophic cardiomyopathy continues the debate about whether LVNC is a distinct cardiomyopathy or a common phenotype (12).

Although recent developments in symptomatic treatments are promising, there is still no targeted treatment for LVNC in children. Current treatments are primarily aimed at managing complications such as heart failure, arrhythmia, and thromboembolism (13). Therefore, sharing experiences from different centers is of great importance for both understanding the natural history of the disease and developing clinical management strategies. Data on LVNC from centers in Anatolia are particularly limited. Our study aims both to contribute to the literature by presenting pediatric LVNC experiences from a regional center and to guide clinicians in our country regarding the diagnosis and management of this rare cardiomyopathy.

Material and Methods

This retrospective descriptive study included patients diagnosed with LVNC who were followed at the Pediatric Cardiology Outpatient Department of Ordu University Training and Research Hospital between December 2017 and July 2025. A total of 16 pediatric patients with regular follow-ups during this period were included in the study.

Patients' electronic records and files were reviewed retrospectively. Demographic data (age, gender, weight), presenting complaints, family history, and physical examination findings were recorded. Cardiac imaging findings, including TTE and CMR results, were evaluated, and results of genetic tests performed on patients were also recorded.

The presence of heart failure, surface electrocardiogram (ECG) findings, 24-hour Holter ECG findings, arrhythmia detection rates, and treatment approaches were recorded. Additionally, medical treatments (e.g., for heart failure and antiarrhythmic therapies), interventional procedures, mechanical support devices, and advanced treatments (e.g., heart transplantation) were reviewed. Mortality and clinical outcomes during the follow-up period were analyzed.

The diagnosis of LVNC was based on TTE and/or CMR findings. TTE was performed with a Philips EPIQ 7 (Philips Healthcare, Andover, MA, USA). Because CMR images were obtained using various devices across different hospitals, information on device brand and model could not be reported uniformly.

The diagnosis of LVNC was established based on TTE and/or CMR findings.

- **TTE Criteria:** The three most commonly used TTE criterion sets in the literature were considered in the study:

Chin Criteria: Defined as a ratio of the distance from the epicardial surface to the trough of the trabeculation (X) to the distance from the epicardial surface to the peak of the trabeculation (Y) of X/Y ≤0.5 at end-diastole (2).

Jenni Criteria: Defined as an end-systolic ratio of non-compacted to compacted (NC/C) myocardium of ≥2 (≥1.4 in children), with a typical location in the apical and lateral/inferior walls, the presence of blood flow communicating with the intertrabecular recesses on Doppler imaging, and the absence of other coexisting structural heart anomalies (1).

Stöllberger Criteria: Defined by the presence of three or more prominent trabeculations located apically, distinct from the compact myocardium but with similar echogenicity and synchronous movement, and blood flow within the intertrabecular recesses visualized on color Doppler. An NC/C ratio of ≥2 at end-diastole was later incorporated as an additional quantitative criterion (14).

• **CMR Criteria:** CMR was used in cases where the diagnosis could not be confirmed by echocardiography or when detailed tissue characterization was required.

Petersen Criteria: Defined as an end-diastolic ratio of NC/C myocardium of >2.3 (10).

Jacquier Criteria: Defined as trabeculated myocardial mass representing >20% of total left ventricular (LV) mass (15).

Grothoff Criteria: Defined by a global NC mass index of >15 g/m² and a ratio of NC mass to total LV mass of >25%, in addition to the presence of an NC/C ratio ≥3:1 in segments 4-6 (16).

The three most commonly used echocardiographic criteria sets were considered in the study (1,2,14). CMR was used to support and confirm diagnoses in patients diagnosed using TTE (10,15,16).

The study was approved by the Ordu University Ethics Committee (decision number: 2025-282, date: 12.09.2025). Due to the retrospective design, informed consent was not obtained. All procedures were conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

All analyses were descriptive and performed using IBM SPSS Statistics for Windows, Version 30.0 (IBM Corp., Armonk, NY, USA). Given the small sample size and the predominantly non-normal distribution of continuous variables, continuous data were summarized as median (minimum-maximum), and categorical variables were presented as frequencies (n) and percentages (%).

Results

A total of 16 pediatric LVNC cases were included in the study. The median age at diagnosis was 7 years (range: 15 days-16 years); 68.8% (n=11) of patients were male. The median body weight was 19.5 kg (range: 3.8-58 kg), and the median follow-up duration was 33 months (range: 6-82 months). Most cases were asymptomatic at presentation (n=10; 62.5%). In symptomatic patients, easy fatigability (n=5) and palpitations (n=3) were most frequently observed; shortness of breath (n=2), chest pain (n=2), and syncope (n=1) were recorded less frequently. Some cases presented with multiple complaints concurrently. Family history was positive in four patients (25%). One case had genetically confirmed (PLEKHM2-positive) LVNC in their mother; two cases had asymptomatic LVNC in their siblings; and one case had LVNC in their father accompanied by dilated cardiomyopathy and heart failure. Phenotypic distribution analysis revealed that the most common type was isolated LVNC (n=8, 50%); the dilated type was observed in five patients, the hypertrophic type in one patient, the restrictive type in one patient, and the mixed type in one patient. Heart failure was detected clinically in six cases (37.5%). The demographic and clinical characteristics of the patients are presented in Table 1.

Table 1. Demographic and clinical characteristics of the patients

Parameters	
Age (years), median (min-max)	7 years (15 days-16 years)
Sex, n (%)	Male: 11 (68.8%) Female: 5 (31.2%)
Weight (kg) Median (min-max)	19.5 (3.8-58)
Follow-up duration (months) Median (min-max)	33 (6-82)
Presenting symptoms*, n	None: 10 Fatigue: 5 Palpitation: 3 Dyspnea: 2 Chest pain: 2 Syncope: 1

Table 1. Continued

Parameters	
Family history, n (%)	Absent: 12 (75) Present: 4 (25)
LVNC type, n (%)	Isolated: 8 (50) Dilated: 5 (31.2) Hypertrophic: 1 (6.2) Restrictive: 1 (6.2) Mixed type (H+R):1 (6.2)
Heart failure, n (%)	6 (37.5)
Arrhythmia, n (%)	Absent: 10 (62.5) Present: 6 (37.5)
Thrombus, n (%)	Absent: 15 (93.8) Present: 1 (6.2)
Death, n (%)	3 (18.8)

**Some patients presented with multiple complaints. LVNC: Left ventricular non-compaction cardiomyopathy, H: Hypertrophic, R: Restrictive, min: Minimum, max: Maximum*

All patients were diagnosed with LVNC by TTE, and CMR confirmed the diagnosis in all patients. Pathogenic mutations were detected in three cases by genetic testing; PLEKHM2 variants were found in two cases, and an RYR2 variant in one case. The case harboring the RYR2 mutation was also diagnosed with CPVT (Table 2).

Arrhythmia was observed in six patients (37.5%). Ventricular tachycardia (VT) was detected in two cases, one of whom was a patient diagnosed with CPVT. Wolff-Parkinson-White (WPW) syndrome-associated supra-VT was observed in two cases, and frequent ventricular extrasystoles were observed in two cases. On 12-lead surface ECG and 24-hour Holter ECG assessments, sinus tachycardia, left bundle branch block, and biatrial dilatation were also recorded in two patients each (Table 2).

Two patients underwent interventional procedures. Sympathetic blockade (sympathectomy) was performed in one patient diagnosed with catecholaminergic polymorphic VT, and an implantable cardioverter-defibrillator (ICD) was implanted in another patient. The patient who received an ICD also underwent heart transplantation and died on the third postoperative day. Three patients (18.8%) died during the follow-up period: the first, a 14-year-old male, had dilated-type LVNC, congestive heart failure, and a PLEKHM2 mutation; the second, a four-year-old patient, had mixed-type LVNC (dilated-restrictive); and the third, a three-year-old child, had restrictive-type LVNC (Table 2).

As medical treatment, acetylsalicylic acid was initiated in all patients, and beta-blockers were added in most patients. Antiarrhythmic agents such as flecainide and amiodarone, as well as anticongestive treatments, were used when clinically necessary. Multiple-drug combinations were preferred, especially in patients with arrhythmia or who had developed heart failure.

Discussion

In this single-center pediatric series, we presented the phenotypic diversity, arrhythmia burden, and short- to medium-term outcomes of LVNC based solely on our data, and compared our findings with the current literature.

Phenotypic heterogeneity in pediatric LVNC and its impact on prognosis are well known (a relatively better course in the isolated form and a worse course in the dilated form) (1,7). The predominance of isolated LVNC in our series (50%) was consistent with the phenotype distributions reported in the literature for pediatric patients; however, the clustering of death and the need for advanced intervention in the dilated/mixed-restrictive subtypes support the view that phenotype-based risk distinction may be determinative in clinical management (7,9). The higher symptom burden and more advanced stage of disease among cases presenting to our clinic, compared with the general population, may have contributed to the high observed rate of heart failure (37.5%) (9,17).

Our total arrhythmia rate is 37.5%. Our VT frequency was 12.5% (2/16), close to rates reported in pediatric series: Stanton et al. (18) reported 13.3%, Brescia et al. (9) reported 17%, and Chin et al. (2) reported VT rates up to 38%. Our WPW association rate was 12.5% (2/16), which is highly consistent with the findings of Howard et al. (19), who reported a WPW association of approximately 10% in the pediatric LVNC population. These findings support the need for close rhythm monitoring in pediatric LVNC and for early rhythm-

Table 2. Diagnosis, follow-up, and outcomes of pediatric LVNC patients

Case	Age (year)	Echo findings	MRI confirmation	Genetics confirmation	ECG-Holter findings	Thrombus	Medical treatment	Interventional procedure	Transplantation	Death
1	4 y	LVNC, RCM-LVH, MR (moderate)	+	-	LBBB, BAD, sinus tachycardia	+	ASA, β1-BB, AC	-	-	+
2	14 y	LVNC+D	+	PLEKHM2	VT	-	ASA , β1-BB, FLEC, AC	ICD	Yes	+
3	15 day	LVNC+D, Ebstein anomalisi	+	-	SVT, WPW	-	ASA, AMIO, β1-BB, AC	Sympathectomy	-	-
4	8 y	LVNC	+	-	Normal	-	ASA	-	-	-
5	12 y	LVNC+H	+	RYR2	VT	-	ASA, β1-BB, FLEC	-	-	-
6	2 y	LVNC+D	+	-	Normal	-	ASA	-	-	-
7	4 y	LVNC	+	-	Normal	-	ASA	-	-	-
8	13 y	LVNC	+	-	Normal	-	ASA	-	-	-
9	5 y	LVNC+D, MR (mild)	+	-	Frequent VES	-	ASA, β1-BB, AC	-	-	-
10	1 y	LVNC	+	-	Normal	-	ASA	-	-	-
11	6 y	LVNC	+	-	Normal	-	ASA	-	-	-
12	16 y	LVNC+D	+	-	Frequent VES, LBBB	-	ASA, β1-BB, AC	-	-	-
13	14 y	LVNC	+	PLEKHM2	Normal	-	ASA	-	-	-
14	6 y	LVNC	+	-	SVT, WPW	-	ASA	-	-	-
15	3 y	LVNC+R	+	-	Sinus tachycardia, BAD	-	ASA, β1-BB, AC	-	-	+
16	4 y	LVNC	+	-	Normal	-	ASA	-	-	-

MRI: Magnetic resonance imaging, ECG: Electrocardiogram, LVNC: Left ventricular non-compaction, LVH: Left ventricular hypertrophy, D: Dilated, H: Hypertrophic, R: Restrictive MR: Mitral regurgitation, LBBB: Left bundle branch block, BAD: Biatrial dila, VT: Ventricular tachycardia, SVT: Supraventricular tachycardia, WPW: Wolff-Parkinson-White syndrome, VES: Ventricular extrasystole, ASA: Acetylsalicylic acid, β1-BB: Beta-blocker, AMIO: Amiodarone, FLEC: Flecainide, AC: Anticongestive, ICD: Implantable cardioverter-defibrillator, RCM: Restrictive cardiomyopathy

management strategies in patients with conduction defects or accessory pathways (19,20).

In our study, TTE criteria (1,2,14) were systematically applied; given the interpretive differences of the criteria in pediatric cases and the controversial nature of NC/C, confirmation with CMR was performed in all patients (1,2,10,14). The structural and confirmatory power of CMR [e.g., Petersen et al. (10) NC/C >2.3; trabeculated mass ratio as described by Jacquier et al. (15); global NC mass criteria proposed by Grothoff et al. (16)] is particularly valuable in reducing the risk of overdiagnosis or missed diagnoses, especially in childhood. Furthermore, since increased physiological trabeculation in athletes has been shown to mimic LVNC, it is prudent to avoid making a diagnosis based solely on morphology and to adopt a multiparametric TTE + CMR + ECG + family history ± genetic) approach (3,4,5).

In our series, two PLEKHM2 variants and one RYR2 variant were detected, and the RYR2 carrier presented with CPVT. Although sarcomere gene variants (MYH7, TTN, MYBPC3) are most frequently reported in LVNC, genetic heterogeneity is substantial, and the same genes can be associated with different cardiomyopathy phenotypes; these findings support individualized screening and family investigation in pediatric cases (1,3,11). Our small sample size is insufficient for statistical testing of genotype-outcome relationships; however, the VT event in the case of CPVT underscores the arrhythmic risk among channelopathy-related phenotypes (20).

In our series, with a median follow-up of 33 months, mortality was 18.8%, a rate consistent with the 12.8-22% range reported in the pediatric literature, and fatalities were concentrated in the dilated/mixed-restrictive subtypes, an expected pattern (9,17). Our experience yields three clinical

messages: 1) Phenotype-focused monitoring, particularly close clinical follow-up for the dilated and mixed-restrictive subtypes. 2) Rhythm strategies, pathways for early intervention in the presence of WPW/conduction defects and VT. 3) Diagnostic assurance, confirmation of TTE criteria with CMR in pediatric patients (10,19,20). Treatment in pediatric LVNC is focused on the management of heart failure, arrhythmias, and thromboembolism rather than on targeted therapy; in our practice, treatment with acetylsalicylic acid and beta-blockers was emphasized, with antiarrhythmics and interventions applied in selected cases (3,13).

Study Limitations

This study has several limitations that should be considered. The retrospective and single-center design with a small sample size limits the statistical power, particularly for phenotype-outcome and genotype-outcome relationships. Rhythm assessment is based on ECG/Holter; invasive electrophysiological data and long-term device outcomes are not available for all patients.

Conclusion

This pediatric series reported from Anatolia shows that the isolated form predominates in LVNC, but clinical risk varies in a phenotype-dependent manner. The burden of arrhythmia and heart failure is notable; fatalities were concentrated in the dilated and mixed-restrictive subtypes. In pediatric patients, confirming TTE criteria with CMR and implementing close monitoring based on phenotype-rhythm findings may facilitate accurate classification and risk management. Larger, multicenter, and genetically integrated pediatric cohorts will contribute to the development of phenotype-focused risk models.

Ethics

Ethics Committee Approval: The study was approved by the Ordu University Ethics Committee (decision number: 2025-282, date: 12.09.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

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

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

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ORIGINAL ARTICLE

93

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Clinical and Laboratory Impact of Postpartum Enoxaparin Prophylaxis After Vaginal Delivery: A Retrospective Cohort Study

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What is known on this subject?

Venous thromboembolism is a leading cause of maternal morbidity and mortality postpartum. Low molecular weight heparin is recommended for prophylaxis in moderate- to high-risk women. Limited data exist on the effects of enoxaparin on wound healing and laboratory parameters.

What this study adds?

This study demonstrates that prophylactic enoxaparin after vaginal delivery is not associated with significant bleeding, wound complications, or changes in routine hematological parameters. Risk-based enoxaparin prophylaxis appears feasible and safe, but large-scale prospective studies are needed to confirm these findings and determine the optimal dose and treatment duration.

ABSTRACT

Objective: To assess the clinical and laboratory effects of prophylactic enoxaparin use after vaginal delivery on bleeding, wound complications, and hematological parameters.

Material and Methods: This retrospective cohort study included 36 postpartum women who received enoxaparin prophylaxis for deep vein thrombosis and 95 who did not; all delivered at 37-41 weeks of gestation. Maternal demographic characteristics, delivery-related data, bleeding- and wound-related complications, as well as hemoglobin, hematocrit, and platelet counts before delivery, at 6 hours postpartum, and on the 10th postpartum day were retrieved from the hospital database. Changes in laboratory values between 6 hours and 10 days postpartum were calculated. All variables were compared between the enoxaparin and non-enoxaparin groups.

Results: Women who received enoxaparin were older, had higher body mass index and greater parity, and had significantly lower episiotomy rates ($p<0.001$), compared with those who did not receive enoxaparin. No significant differences were observed between the groups in rates of labor induction or in bleeding- or wound-related complications. The differences in hemoglobin (1.90±0.67 vs. 1.57±0.67 g/dL, $p=0.115$), hematocrit (6.84±2.40 vs. 5.76±2.21%, $p=0.127$), and platelet counts (113.94±62.70 vs. 125.10±70.89×10^3/μL, $p=0.592$) between the 10th day and 6 hours postpartum were also not significantly different between groups.

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ABSTRACT

Conclusion: Prophylactic enoxaparin use after vaginal delivery was not associated with significant adverse effects on bleeding, wound complications, hemoglobin, hematocrit, or platelet counts. Risk-based enoxaparin prophylaxis appears safe and feasible for women after vaginal delivery. Our findings need to be confirmed by large-scale prospective studies.

Keywords: Enoxaparin, hemoglobin, low molecular weight heparin, postpartum prophylaxis, thromboprophylaxis, vaginal delivery, venous thromboembolism

Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis and pulmonary embolism, is a major vascular disorder and a significant cause of morbidity and mortality worldwide (1). Risk factors include surgery, trauma, malignancy, and pregnancy, among others, with events often remaining unprovoked in the absence of clear triggers (2). Pregnancy and the postpartum period are important risk factors for VTE. The incidence of pregnancy-related VTE was approximately 1.2 per 1.000 deliveries (3). Since VTE is one of the leading causes of maternal morbidity and mortality (4), identifying women at high risk is crucial. The incidence of VTE is higher in the postpartum period than at any time during pregnancy, with the risk peaking particularly within the first 6 weeks after delivery (5). The Royal College of Obstetricians and Gynaecologists (RCOG) has proposed a risk assessment scoring system for VTE in the postpartum period (6). According to this protocol, women in the low-risk group are recommended early mobilization and avoidance of dehydration; those in the intermediate-risk group are recommended at least 10 days of low molecular weight heparin (LMWH) therapy; and those in the high-risk group are recommended at least 6 weeks of LMWH therapy (6).

The current literature provides insufficient data regarding the efficacy and potential adverse effects of LMWH in the prevention of postpartum VTE. A randomized controlled trial (RCT) evaluated the efficacy of short-term enoxaparin prophylaxis; participation was feasible, but the number of events was very low, highlighting the need for large, multicenter trials (7). A large prospective study compared bemiparin with enoxaparin and reported that both agents reduced the incidence of VTE compared with the control group, with bemiparin showing more favorable outcomes regarding both efficacy and wound complications (8). In contrast, retrospective observational studies indicated that enoxaparin use may increase the risk of wound dehiscence and hematoma following cesarean delivery (9,10). Pilot studies using risk-score models have demonstrated that prophylaxis can effectively prevent VTE in appropriately selected patients while reducing unnecessary drug exposure (11).

Although the use of LMWH is recommended, studies investigating its potential adverse effects in the postpartum period are limited. Moreover, most existing studies focus on cesarean deliveries, whereas studies on vaginal deliveries are considerably fewer. The aim of our study is to systematically evaluate the clinical effects and laboratory parameters of enoxaparin in women undergoing vaginal delivery, focusing on wound complications and laboratory outcomes.

Material and Methods

This retrospective cohort study was conducted at a tertiary care center after approval from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Ethics Committee (approval number: KAEK/11.09.2024.222, protocol code: 2024-222, date: 17.09.2024). Data were obtained from the electronic hospital information system, which included clinical, laboratory, and treatment records of eligible patients. Women who delivered vaginally between 37 and 41 weeks of gestation were screened for eligibility. The inclusion criteria were maternal age between 18 and 40 years, singleton pregnancy, and vertex presentation. Women were excluded if they had non-vertex presentation, multiple pregnancy, body mass index (BMI) greater than 40 kg/m², acute chorioamnionitis, known coagulopathies, prior uterine or cervical surgery, cervical or high-grade perineal lacerations, uterine rupture, uterine atony, placental invasion anomalies, placenta previa, vasa previa, placental or cord anomalies, history of postpartum hemorrhage, major or massive intrapartum hemorrhage, thalassemia, sickle cell anemia, sideroblastic anemia, intravenous iron therapy, use of antiplatelet medications, or blood transfusion.

The primary maternal characteristics analyzed were age, BMI, gravidity, parity, gestational age, fetal weight, and ethnicity. Delivery-related data included induction of labor, episiotomy, and the presence of bleeding-related or wound complications. Laboratory values included hemoglobin, hematocrit, and platelet count, which were measured before delivery, at six hours postpartum, and on the tenth postpartum day. Treatment-related data focused on the administration of enoxaparin -including dosage

and duration- and on other prophylactic or therapeutic postpartum interventions. For women with hemogram results available on the 10th postpartum day, changes in hemoglobin, hematocrit, and platelet counts from the 6th postpartum hour to the 10th postpartum day were calculated and compared between groups. In our clinic, postpartum prophylaxis with enoxaparin is administered in accordance with the Turkish Ministry of Health Guideline on the Management of High-Risk Pregnancies and the RCOG recommendations. Under this protocol, early mobilization and prevention of dehydration are advised for women in the low-risk category; a minimum of 10 days (or longer, if indicated) of LMWH therapy is recommended for those in the intermediate-risk category; and at least 6 weeks of LMWH therapy is recommended for those classified as high-risk (6). The first dose of enoxaparin was administered after ensuring hemostasis and the absence of contraindications, particularly active bleeding or complications related to regional anesthesia. Treatment duration and dose adjustments were tailored according to the clinical status, and hematology consultation was requested in complex cases.

Statistical Analysis

All analyses were performed using SPSS version 26.0.1 (SPSS Inc., Chicago, IL, USA). The distribution of continuous variables was assessed with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed variables were presented as mean ± standard deviation and compared using the Student's t-test. Non-normally distributed variables were expressed as median (minimum-maximum) and analyzed with the Mann-Whitney U test. Categorical variables were summarized as frequencies and percentages and compared using the chi-square test. A two-tailed p value less than 0.05 was considered statistically significant.

Results

A total of 131 women who met the eligibility criteria were included in the analysis. Of these, 36 women received enoxaparin prophylaxis for 10 days following vaginal delivery, while 95 did not receive prophylaxis. A total of 28 women received 40 mg/day, seven received 60 mg/day, and one received 80 mg/day of enoxaparin prophylaxis for ten days. Baseline demographic and clinical characteristics are summarized in Table 1. Women who received enoxaparin were significantly older (30.14±6.69 vs. 25.21±4.15 years, p<0.001) and had a higher BMI (31.54±4.75 vs. 27.81±3.92 kg/m², p<0.001). Gravidity and parity were higher in the enoxaparin group (p<0.001 for both). Gestational age at delivery and fetal birth weight were comparable between groups. Ethnic distribution did not differ significantly. The frequency of episiotomy was lower among enoxaparin users (22% vs. 66%, p<0.001). Rates of labor induction and bleeding-related or wound-related complications did not differ significantly between groups.

The hematological changes between the 6th postpartum hour and the 10th postpartum day are presented in Table 2. No statistically significant differences were observed between the groups. The mean reductions in hemoglobin (1.90±0.67 vs. 1.57±0.67 g/dL; p=0.115) and hematocrit (6.84±2.40% vs. 5.76±2.21%; p=0.127) were greater in the enoxaparin group, although these differences were not statistically significant. Changes in platelet count were also similar (113.94±62.70 vs. 125.10±70.89)×10³/µL (p=0.592).

Table 1. Demographic and obstetric characteristics of the study groups

Parameter	Enoxaparin non-users (n=95)	Enoxaparin users (n=36)	p value
Age[a] (years)	25.21±4.15	30.14±6.69	<0.001
BMI[a] (kg/m²)	27.81±3.92	31.54±4.75	<0.001
Gestational age[b] (days)	275 (259-287)	276 (259-287)	0.816
Gravidity[b]	1 (1-5)	3 (1-6)	<0.001
Parity[b]	1 (1-5)	3 (1-5)	<0.001
Fetal weight[a] (g)	3210.45±389.28	3322.92±416.91	0.150
Turkish ethnicity[c] (n)	73 (77%)	29 (81%)	0.814
Episiotomy[c] (n)	63 (66%)	8 (22%)	<0.001
Labor induction[c] (n)	20 (21%)	11 (31%)	0.253
Bleeding-related and wound complications[c] (n)	14 (15%)	1 (3%)	0.067

[a]: Normally distributed data; presented as mean ± standard deviation, compared using t-test, [b]: Non-normally distributed data; presented as median (min-max), compared using Mann–Whitney U test, [c]: Categorical data; presented as n (%), compared using chi-square test. BMI: Body mass index

Table 2. Comparison of the difference between 10th postpartum day and 6th postpartum hour laboratory values in the study groups

Difference	Enoxaparin non-users (n=30)	Enoxaparin users (n=17)	p value
HB[a] (g/dL)	1.57±0.67	1.90±0.67	p=0.115
HCT[a] (%)	5.76±2.21	6.84±2.40	p=0.127
PLT[a] (10^3/μL)	125.10±70.89	113.94±62.70	p=0.592

[a]: Normally distributed data; presented as mean ± standard deviation, compared using t-test. HB: Hemoglobin; HCT: Hematocrit; PLT: Platelet count

Discussion

Rates of bleeding and wound complications were similar in women who received enoxaparin prophylaxis and in those who did not. Changes in hemoglobin, hematocrit, and platelet counts between the 6th postpartum hour and the 10th postpartum day did not differ significantly between groups. Compared with non-users, enoxaparin users were older, had higher BMI and parity, underwent episiotomy less frequently, and had similar rates of labor induction.

Pregnancy and the postpartum period represent physiologic states in which all three components of Virchow's triad (venous stasis, endothelial injury, and hypercoagulability) are present and collectively contribute to an elevated risk of VTE (12). Venous stasis occurs primarily due to pregnancy-related alterations in the venous system. Although total blood volume and venous return increase during gestation, linear flow velocity in the lower extremity veins decreases because of hormonally mediated dilation of capacitance veins, promoting venous pooling and valvular incompetence (13). This effect is further amplified by compression of the inferior vena cava and the iliac veins by the gravid uterus, particularly in late pregnancy, and may be accentuated in the supine position (13,14). Additionally, compression of the left iliac vein by the right iliac artery contributes to the observed predominance of left-sided deep vein thrombosis in pregnancy (15,16). Endothelial injury is another important factor, as delivery involves vascular disruption at the uteroplacental interface. Instrumental deliveries (forceps or vacuum extraction) and cesarean section can exacerbate vascular intimal damage, thereby increasing immediate postpartum VTE risk (16). Hypercoagulability during pregnancy is characterized by progressive increases in several coagulation factors (I, II, VII, VIII, IX, X) alongside decreased protein S activity (16,17,18). Resistance to activated protein C increases during the second and third trimesters and correlates with increased thrombotic risk (19). Fibrinolytic inhibitors, such as plasminogen activator inhibitor-1 and -2, also increase, although total fibrinolytic capacity may remain unchanged (20). The postpartum period carries the highest VTE risk, particularly within the first six weeks following delivery, after which the risk gradually declines to approximate baseline levels by 13-18 weeks (5). Pregnancy itself is a recognized VTE risk factor, and this risk is further magnified in the presence of inherited thrombophilias, such as factor V Leiden, the prothrombin G20210A mutation, antithrombin III deficiency, protein C or protein S deficiency, and antiphospholipid syndrome (17,21,22,23). Patients with these conditions, particularly those with a personal or family history of VTE, may experience a several-fold increase in thrombotic risk during the antepartum and postpartum periods (23,24). In our study, enoxaparin users were older and had higher BMI and parity than non-users. These findings are consistent with the risk factors outlined in the RCOG protocol (6). The episiotomy rate was significantly lower among patients who received enoxaparin. We attribute this finding to episiotomy being more commonly performed during first deliveries and to parity being scored as a risk factor according to the RCOG protocol.

Only a limited number of studies have investigated the association between enoxaparin and bleeding and surgical-site complications in the postpartum period, and their results are inconsistent. In a prospective pilot study, Cavazza et al. (11) reported that postpartum LMWH prophylaxis after cesarean delivery was not associated with hemorrhagic events. Similarly, in a pilot RCT, Blondon et al. (7) evaluated enoxaparin in women undergoing cesarean or vaginal delivery and demonstrated that it had no significant effect on surgical wound complications. In the study by Ferres et al. (9), wound complications were reported more frequently among women receiving enoxaparin after cesarean delivery, with the risk particularly pronounced among morbidly obese women (BMI >35). In contrast, rates of deep vein thrombosis and pulmonary embolism remained low and did not differ significantly between groups. In our study, however, enoxaparin use among women who delivered vaginally was not associated with any significant effect on bleeding, wound complications, or hematological parameters. This discrepancy may largely stem from differences in the characteristics of the studied populations. The cohort in the study by Ferres et al. (9) consisted of women with a higher maternal risk profile who

underwent a surgical procedure (cesarean delivery), whereas our study focused on women who delivered vaginally, a population at lower surgical risk. Therefore, postoperative recovery and additional comorbidities among cesarean patients may have contributed to the increased wound complication rates, whereas the lower surgical risk associated with vaginal delivery could explain the absence of such complications in our study. To our knowledge, this is the first study in Türkiye to specifically investigate the prophylactic use of enoxaparin after vaginal delivery at a tertiary-care center. Previous research in Türkiye has largely focused on prophylaxis following cesarean section (25). Şahin and Şahin (25) evaluated 41 women who received enoxaparin after cesarean delivery, comparing doses of 40 mg/day and 60 mg/day. Although there were no significant differences between the two dosing groups in age, gravidity, gestational age, or hematological parameters, higher-dose enoxaparin was associated with a marked increase in surgical site complications, including wound infections and hematomas. Reductions in platelet counts were also more pronounced in the 60-mg/day group. These findings highlight a potential dose-dependent increase in the risk of surgical-site complications without conferring additional hematological benefit. In contrast, our study focused on women delivering vaginally, a population in which surgical-site complications are less frequent. Accordingly, we observed no significant increase in bleeding-related or wound-related complications among enoxaparin users; the hematological parameters remained stable. Taken together, these data suggest that prophylactic enoxaparin may be safely administered after vaginal delivery and may support risk-stratified prophylaxis based on maternal characteristics.

Our study demonstrated that prophylactic use of enoxaparin after vaginal delivery did not have a significant adverse effect on bleeding, surgical site complications, or routine hematological parameters (hemoglobin, hematocrit, and platelet count). These preliminary findings suggest that applying risk-based prophylaxis in low-surgical-risk vaginal deliveries may be feasible without undue concern regarding the hematological side effects of enoxaparin. However, due to the limited sample size and the retrospective design of our study, further confirmation in larger cohorts and prospective RCTs is required before more definitive and reliable recommendations can be made for clinical practice. We propose several directions for future research. Dose-response studies comparing different doses and durations (e.g., 10 days vs. 6 weeks; 20/40/60 mg regimens) may address an important gap in clinical practice. In addition, studies that incorporate measures of treatment adherence, treatment burden, patient satisfaction, and cost-effectiveness may provide valuable insights into the feasibility of prophylactic use of enoxaparin. Furthermore, large-scale prospective studies to capture rare VTE events and investigations evaluating the short-term effects of enoxaparin on hemostasis through biomarkers such as thrombin generation, D-dimer, and fibrinogen may be conducted.

The strengths of our study include that it is the first dataset obtained from a tertiary care center that specifically focuses on the vaginal-delivery population. This provides insight into a distinct clinical group, in contrast to previous studies that largely focused on prophylaxis following cesarean delivery. In addition, the careful application of well-defined exclusion criteria (such as coagulopathies, severe anemia, and major intrapartum hemorrhage) ensured that the analyzed patient group was more homogeneous and targeted.

Study Limitations

The limitations of our study include its retrospective design, small sample size, and the limited number of patients with 10th-day laboratory data. This limited sample size substantially reduces the study's power to detect small effect sizes and rare events, such as VTE. Additionally, patients in the enoxaparin group had a higher baseline risk for VTE, characterized by older age, higher BMI, and greater parity. This may have influenced both event rates and bleeding profiles, potentially masking or exaggerating the true effect of the drug. Limitations in follow-up duration and methodology may have led to under-detection of late or asymptomatic VTE events. The study did not systematically assess dose-response relationships or the impact of treatment duration, which limits the ability to draw definitive conclusions regarding optimal dosing and therapy length.

Conclusion

In this retrospective cohort study, prophylactic enoxaparin use after vaginal delivery was not associated with significant adverse effects on bleeding, wound complications, or routine hematological parameters. These findings suggest that risk-based enoxaparin prophylaxis may be feasible and safe in women following vaginal birth. However, due to the retrospective design and limited sample size, definitive conclusions cannot be drawn. Large-scale prospective RCTs are needed to validate these preliminary findings and to investigate dose–response relationships and optimal treatment durations.

Ethics

Ethics Committee Approval: Approval for the study was received from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Ethics Committee (approval number: KAEK/11.09.2024.222, protocol code: 2024-222, date: 17.09.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

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

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ORIGINAL ARTICLE

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Remote vs. In-person Anatomy Education: A Comparative Study Among Health Vocational Students

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What is known on this subject?

Anatomy is a fundamental course for health vocational students, yet teaching applied content through remote instruction has been shown to reduce engagement and learning efficiency. Previous studies have reported that online anatomy education may limit interaction, practical skill development, and students' sense of professional identity.

What this study adds?

This study directly compares remote and in-person anatomy education within the same curriculum, instructor, and content framework. It identifies specific barriers such as inequalities in access and a reduced sense of professional identity, emphasizing the importance of infrastructure and interactivity in remote anatomy teaching.

ABSTRACT

Objective: This study aimed to compare the educational effectiveness of students who continued their anatomy education remotely with that of students who had taken the same course in person the previous year.

Material and Methods: This cross-sectional study included 116 first-year students who took the anatomy course via remote education and 138 second-year students who took the same course in person during the previous academic year. Data collected via an online survey included socio-demographic characteristics, the comprehensibility of the course, participants' understanding of its importance, and problems encountered. Descriptive statistics are presented as numbers and percentages, and the chi-square test is used to compare categorical variables.

Results: Although the course was taught using the same syllabus, presentation materials, and instructor, the perceived difficulty was 59.4% in the in-person education group and 82.8% in the remote education group ($p<0.05$). It was determined that 37.1% of students in remote education lacked a personal device (computer or tablet) to access education, 19.8% experienced internet connection problems, and 12.1% lacked a suitable working environment.

Conclusion: Remote education complicates learning in applied courses such as anatomy. The absence of in-person interaction reduced participation, diminished course effectiveness, and hindered the development of professional identity. Infrastructural deficiencies and technological inequalities were also identified as significant barriers. These findings can guide the development of sustainable and inclusive remote education policies.

Keywords: Anatomy education, remote education, health education, in-person education

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Introduction

Synchronous (real-time) education refers to instruction conducted online via internet technologies, bringing together students and instructors in different locations. It is a virtual classroom environment. In these virtual classrooms, students can ask the instructor questions and participate in lessons in real time. Asynchronous (non-simultaneous) education refers to students accessing pre-prepared or recorded course materials at their convenience (1,2).

Remote education is known to offer numerous benefits, such as allowing students to learn outside the classroom and instilling in them a sense of responsibility for independent learning (3,4). The ability to continuously replay recorded lessons and the opportunity to provide a learning environment where everyone can hear equally well and watch from the same distance, compared with the difficulties experienced in crowded classrooms, are some of the advantages of remote education (1,4). Moreover, the best-known limitations of remote education are increased failure rates among students who have not acquired responsibility for their learning, greater difficulty communicating with instructors compared with in-person education, and reduced student socialization. The most serious limitation encountered is that students can observe but cannot practice in application-based courses (2,5). The absence, in remote education, of activities such as collaborative learning experiences, real-time feedback, individual participation in class, and instant information exchange, which are common in classroom and school settings, has the potential to harm educational outcomes (6). These conditions have also required instructors to prepare new course content and develop new teaching methods for practical courses, rather than rely on existing methods (7). Recent global developments have compelled higher education institutions to transition rapidly to mass remote learning models. This sudden and comprehensive transition has made the educational effectiveness and student gains in practice-based courses, such as anatomy, a significant topic of discussion.

Anatomy is the scientific discipline that studies the standard shape and structure of the human body, including the organs that compose it, and the structural and functional relationships among these organs (8,9). Anatomy education, the foundation of medicine and the health sciences, has been described in numerous studies as a challenging subject to learn (10,11). Anatomy courses are among the most challenging subjects for students, partly because they are easily forgotten if not reviewed frequently and partly because of the Latin terminology they contain (8).

Therefore, the primary objective of this study is to compare the learning experiences and perceived levels of effectiveness and efficiency of students taking anatomy courses taught by the same instructor using the same curriculum but delivered in person rather than online. The secondary objective is to examine how the teaching method (online or in-person) affects students' perceptions of their professional identity as future healthcare professionals. It also aims to identify the problems, limitations, and opportunities encountered in online education.

Material and Methods

This cross-sectional study was conducted at Istanbul University-Cerrahpaşa, Vocational School of Health Services between May and June 2021. The study included 254 students who voluntarily participated. Data were collected using a structured online questionnaire. The study population consisted of first-year students who took anatomy remotely during the 2020-2021 academic year, and second-year students who had taken the course in person during the previous year. Although students were enrolled in different associate-degree programs and their distribution was unequal, they all took the anatomy course from the same instructor. Furthermore, the course syllabi and presentations used in both online and in-person education were identical. One hundred and sixteen first-year students took an anatomy course for the first time and attended it online. In contrast, 138 second-year students took the anatomy course in person during their first year (the previous academic year), with the same content and instruction.

In this study, two separate survey forms were used. These were sent electronically via Google Forms. Each form had multiple-choice questions that were the same for all participants within a group but different across groups. Everyone taking part was informed about the study on the first page. This information emphasised that responses would be kept anonymous and that the data would be used only for research purposes. Completion and submission of the survey constituted informed consent. To ensure the reliability of the feedback, students were asked not to provide their names. The survey questions were designed to compare remote and in-person anatomy education, measure how well students understood the course and how important they perceived it to be, and identify problems students experienced. The questionnaire used in this study was developed by adapting items from previously published questionnaires related to remote learning and anatomy education and by incorporating our students' feedback on remote learning courses. The questionnaire contains items related to the perceived effectiveness and adequacy of the

anatomy course, students' perceptions of their professional identity as future health professionals, and the problems they experience during distance learning.

This study was approved by the Clinical Research Ethics Committee of University of Health Sciences Türkiye, İstanbul Training and Research Hospital (decision number: 2842, date: 21.05.2021).

Statistical Analysis

IBM SPSS Statistics software (version 21.2; Armonk, NY: IBM Corp.) was used for data analysis. The distribution of responses to Likert-type questions was evaluated using descriptive statistics (frequency and percentage) and multiple-choice questions were analyzed using frequency analysis. The chi-square (χ^2) test was applied to evaluate the relationship between categorical variables. The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to assess whether the data were normally distributed. The statistical significance level was set at $p<0.05$.

Results

Demographic and academic characteristics of the students included in the study are summarized in Table 1. These data were analyzed to ensure the comparability of the two groups in terms of gender, department, and employment status.

The majority of the participants were female (79.9%), and most were enrolled in programs related to dental health, radiotherapy, and medical imaging. In addition, approximately half of the students were working either full-time or part-time while pursuing their education.

Findings comparing the opinions of students who received anatomy education remotely and in person are presented in Table 2.

Statistically significant differences were found between the two groups with respect to perceptions of course sufficiency, the necessity of including anatomy in the second-year curriculum, and feelings of professional identity ($p<0.05$).

For instance, 60.1% of second-year students (in-person) considered the first-year anatomy course sufficient, whereas this rate was 46.6% among first-year students (remote). Similarly, nearly half of the in-person students (47.1%) believed anatomy should continue in the second year, compared with only 23.3% of the remote learners. Moreover, while 89.9% of students who received in-person education stated that anatomy made them feel like healthcare professionals, this rate dropped to 64.7% among those who received remote education.

In addition to the overall comparisons, the specific views of second-year students who previously received in-person anatomy education are summarized in Table 3. For example, 53.6% of these students reported that the information learned in anatomy classes is easily forgotten, and 49.3% indicated that the main reason for this is the subject's memorization-based nature. Furthermore, 63.0% of the students believed that the anatomy classes they attended would be beneficial for their professional practice after graduation.

Table 4 details the perceptions and experiences of first-year students who received remote anatomy education, including their communication with instructors, class participation, and technological access. For example, 68.1%

Table 1. Descriptive information about the students participating in the study

Variables		1st year n (%)	2nd year n (%)	Total n (%)
Gender	Female	96 (82.8)	107 (77.5)	203 (79.9)
	Male	20 (17.2)	31 (22.5)	51 (20.1)
Department of study	Oral and dental health program	13 (11.2)	59 (42.8)	72 (28.3)
	Dental prosthetics technology program	25 (21.6)	24 (17.4)	49 (19.3)
	Nuclear medicine techniques program	4 (3.4)	22 (15.9)	26 (10.2)
	Radiotherapy program	38 (32.8)	6 (4.3)	44 (17.3)
	Medical documentation and secretarial program	10 (8.6)	1 (0.7)	11 (4.3)
	Medical imaging techniques program	7 (6.0)	26 (18.8)	33 (13.0)
	Medical laboratory techniques program	19 (16.4)	0 (0.0)	19 (7.5)
Are you working at the same time as being a student?	Yes, I am in permanent employment	37 (31.9)	37 (26.8)	74 (29.1)
	Yes, I am sometimes employed	16 (13.8)	35 (25.4)	51 (20.1)
	No, I am not employed	63 (54.3)	66 (47.8)	129 (50.8)
Total		**116 (100.0)**	**138 (100.0)**	**254 (100.0)**

Table 2. **Students' opinions on anatomy education by mode of delivery (remote vs. in-person)**

Questions	Response options	1st year n (%)	2nd year n (%)	Total n (%)	p-value
Do you think the 1st-year anatomy course is sufficient?	Yes	54 (46.6)	83 (60.1)	137 (53.9)	**0.016***
	No	44 (37.9)	47 (34.1)	91 (35.8)	
	I don't know	18 (15.5)	8 (5.8)	26 (10.2)	
Should anatomy be included in the 2nd-year curriculum?	Yes	27 (23.3)	65 (47.1)	92 (36.2)	**0.000***
	No	58 (50.0)	56 (40.6)	114 (44.9)	
	I don't know	31 (26.7)	17 (12.3)	48 (18.9)	
Is a practical component essential in anatomy courses?	Yes	86 (74.1)	96 (69.6)	182 (71.7)	**0.284**
	No	20 (17.2)	34 (24.6)	54 (21.3)	
	I don't know	10 (8.6)	8 (5.8)	18 (7.1)	
Should clinical examples be included in anatomy courses?	Yes	94 (81.0)	113 (81.9)	207 (81.5)	**0.005***
	No	3 (2.6)	15 (10.9)	18 (7.1)	
	I don't know	19 (16.4)	10 (7.2)	29 (11.4)	
Should cadaver or lab-based anatomy be part of associate degree education?	Yes	91 (78.4)	112 (81.2)	203 (79.9)	**0.381**
	No	14 (12.1)	19 (13.8)	33 (13.0)	
	I don't know	11 (9.5)	7 (5.1)	18 (7.1)	
Does anatomy education make you feel like a healthcare professional?	Yes	75 (64.7)	124 (89.9)	199 (78.3)	**0.000***
	No	33 (28.4)	10 (7.2)	43 (16.9)	
	I don't know	8 (6.9)	4 (2.9)	12 (4.7)	
Should anatomy be offered as an elective course?	Yes	35 (30.2)	21 (15.2)	56 (22.0)	**0.000***
	No	60 (51.7)	112 (81.2)	172 (67.7)	
	I don't know	21 (18.1)	5 (3.6)	26 (10.2)	
Would you take anatomy if it were an elective?	Yes	63 (54.3)	102 (73.9)	165 (65.0)	**0.004***
	No	32 (27.6)	24 (17.4)	56 (22.0)	
	I don't know	21 (18.1)	12 (8.7)	33 (13.0)	
Did you experience difficulty in learning anatomy?	Yes	96 (82.8)	82 (59.4)	178 (70.1)	**0.000***
	No	17 (14.7)	53 (38.4)	70 (27.6)	
	I don't know	3 (2.6)	3 (2.2)	6 (2.4)	
Is it necessary to provide lecture notes before anatomy class?	Yes	116 (100.0)	135 (97.8)	251 (98.8)	0.279
	No	0 (0.0)	2 (1.4)	2 (0.8)	
	I don't know	0 (0.0)	1 (0.7)	1 (0.4)	
Do anatomy exams adequately assess your knowledge?	Yes	79 (68.1)	101 (73.2)	180 (70.9)	0.600
	No	22 (19.0)	24 (17.4)	46 (18.1)	
	I don't know	15 (12.9)	13 (9.4)	28 (11.0)	
Could you ask questions freely in anatomy classes?	Yes	85 (73.3)	85 (61.6)	170 (66.9)	0.116
	No	21 (18.1)	32 (23.2)	53 (20.9)	
	I don't know	10 (8.6)	21 (15.2)	31 (12.2)	
Do you think this survey will be beneficial?	Yes	79 (68.1)	86 (62.3)	165 (65.0)	0.507
	No	18 (15.5)	29 (21.0)	47 (18.5)	
	I don't know	19 (16.4)	23 (16.7)	42 (16.5)	
Is remote anatomy education an alternative solution?	Yes	49 (42.2)	46 (33.3)	95 (37.4)	**0.011***
	No	42 (36.2)	75 (54.3)	117 (46.1)	
	I don't know	25 (21.6)	17 (12.3)	42 (16.5)	

Table 2. **Continued**

Questions	Response options	1st year n (%)	2nd year n (%)	Total n (%)	p-value
Should remote anatomy education be expanded?	Yes	26 (22.4)	26 (18.8)	52 (20.5)	0.116
	No	56 (48.3)	84 (60.9)	140 (55.1)	
	I don't know	34 (29.3)	28 (20.3)	62 (24.4)	
Can remote anatomy education be avoided in the future?	Yes	32 (27.6)	43 (31.2)	75 (29.5)	0.799
	No	44 (37.9)	48 (34.8)	92 (36.2)	
	I don't know	40 (34.5)	47 (34.1)	87 (34.3)	
Is remote education an effective learning model for anatomy?	Yes	17 (14.7)	31 (22.5)	48 (18.9)	**0.042***
	No	87 (75.0)	83 (60.1)	170 (66.9)	
	I don't know	12 (10.3)	24 (17.4)	36 (14.2)	
Total		**116 (100.0)**	**138 (100.0)**	**254 (100.0)**	

**p<0.05 indicates statistical significance*

of the students reported that they could easily communicate with the instructor during remote learning, and 69.0% stated that they were able to express their thoughts freely. However, 47.4% believed that remote learning reduced the effectiveness of teamwork.

The 35.3% of students regularly attended courses, whereas 6.0% reported that they were unable to attend them at all. The most common reasons cited for inability to attend were lack of a personal device (37.1%) and lack of an internet connection (25.0%); other reasons included an unsuitable study environment (12.1%), connection problems (19.8%), and employment outside the home (6.0%).

In general, most students (84.5%) attended anatomy classes at home; the proportion who considered the remote learning environment suitable was equal to the proportion who did not (44.8%). The most common reasons cited for the learning environment being unsuitable for listening to lectures were environmental noise (48.6%) and the presence of other people (36.9%). Furthermore, 73.3% of the first-year students participating in the study believed that remote learning was less effective than in-person education.

Table 3. **Perceptions of second-year students who received in-person anatomy education**

Questions	Response options	n (%)
Is the information learned in anatomy education forgotten quickly/easily?	Yes	74 (53.6)
	No	48 (34.8)
	I don't know	16 (11.6)
If anatomy knowledge is forgotten, what do you think is the reason?	Rote memorization	68 (49.3)
	Insufficient prior knowledge	32 (23.2)
	Latin terms	38 (27.5)
Is anatomy education absolutely necessary for your current academic program?	Yes	100 (72.5)
	No	26 (18.8)
	I don't know	12 (8.7)
Was the anatomy education you received beneficial for your other courses?	Yes	100 (72.5)
	No	27 (19.6)
	I don't know	11 (8.0)
Do you believe the anatomy course will be beneficial in your professional life after graduation?	Yes	87 (63.0)
	No	33 (23.9)
	I don't know	18 (13.0)

Table 4. **Perceptions of first-year students who received remote anatomy education**

Questions	Response options	n (%)
I can easily communicate with the instructor in online anatomy classes	Yes	79 (68.1)
	No	20 (17.2)
	I don't know	17 (14.7)
I can easily express my thoughts in online anatomy classes	Yes	80 (69.0)
	No	19 (16.4)
	I don't know	17 (14.7)
Remote anatomy education increases independent work but reduces opportunities for teamwork	Yes	55 (47.4)
	No	22 (19.0)
	I don't know	39 (33.6)
How often do you attend online anatomy classes?	Regularly	41 (35.3)
	Often but sometimes miss	54 (46.6)
	Rarely	14 (12.1)
	Do not attend	7 (6.0)
What is the most common reason you cannot follow the online anatomy lessons?	Lack of device	43 (37.1)
	No internet package	29 (25.0)
	Connection problem	23 (19.8)
	Inadequate environment	14 (12.1)
	Working outside the home	7 (6.0)
Which device do you use to attend online anatomy classes?	Laptop	54 (46.6)
	Desktop	10 (8.6)
	Tablet	3 (2.6)
	Smartphone	49 (42.2)
When you follow the lesson via smartphone, does it reduce learning efficiency?	Yes	52 (44.8)
	No	29 (25.0)
	I don't know	35 (30.2)
What is the most effective online teaching method in anatomy, in your opinion?	Live class	51 (44.0)
	Recorded lecture	48 (41.4)
	Shared video links	10 (8.6)
	Homework delivery	7 (6.0)
Where do you most frequently attend your online anatomy classes?	Home	98 (84.5)
	Workplace	18 (15.5)
Do you think your learning environment is suitable while attending online anatomy classes?	Yes	52 (44.8)
	No	52 (44.8)
	I don't know	12 (10.3)
If not, what is the most common reason your environment is not suitable for online anatomy education?	Noisy environment	54 (48.6)
	Presence of other people	41 (36.9)
	Being at the workplace	16 (14.4)
Is remote anatomy education as effective as in-person education?	Yes	13 (11.2)
	No	85 (73.3)
	I don't know	18 (15.5)

Discussion

The use of remote education models in higher education has made educational effectiveness, particularly in applied health sciences courses such as anatomy, a fundamental research issue. This study differs from many previous reports on anatomy education in several respects. Both remote and in-person groups received the same curriculum and materials from the same instructor, minimizing differences attributable to teachers or course designs. Furthermore, the sample consisted of students enrolled in vocational health services programs, who play an important role in routine health services but are infrequently mentioned in the literature. Finally, our study evaluates the advantages and challenges of online anatomy education from a broad perspective, not only regarding the effectiveness of the course but also regarding students' perceptions of professional identity and their access to devices, internet connectivity, and suitable working environments. The most significant finding of our study is that, despite sharing the same course, subject, instructor, and materials, the rate of learning difficulties was 59.4% among second-year students who received in-person education, compared with 82.8% among first-year students who received remote education ($p<0.001$).

A study on anatomy and physiology education supports our findings (12). In this study, even with in-person education, 59.6% of students reported difficulty learning the course, which closely matches the 59.4% observed in our study's formal education group. In the same study, 48.8% of students reported that they did not consider anatomy lessons necessary, and 67.4% that they would not choose them as an elective course (12).

According to a study by Kürtüncü and Aylin (13), 76.4% of students believe that remote learning is insufficient for practice-based courses. The 79.9% of the students participating in our study believe that associate-degree education should include cadaveric anatomy or laboratory training. Studies by Sahu (14) and Wang et al. (15) report that it is not appropriate to deliver practical courses through remote education. Other studies suggest that remote education can contribute to theoretical knowledge, whereas in-person education is necessary for practical skills. It is important for students to practice analyzing and integrating the information obtained (16,17). These findings indicate that students recognize the importance of practical courses, which are essential to education, and that they have concerns about the practical aspects of remote learning.

Among participants in our study, 60.1% of second-year students and 46.6% of first-year students considered the anatomy course sufficient in their first year; however, the proportion of undecided respondents was higher among first-year students. A statistically significant difference was found between the responses of the two groups ($p=0.016$). This indicates that students who took the course remotely did not fully grasp the importance of the anatomy course, did not consider the information available to them adequate, and did not master the subject matter. Responses to the question "Is remote anatomy education an alternative solution?" also support this finding ($p=0.011$). Indeed, the percentage of first-year students with no experience comparing remote and formal education who responded "I don't know" (21.6%) was higher than the percentage of second-year students with formal education experience who responded "I don't know" (12.3%) confirming this lack of experience and indecision.

In work environments, schools, and universities, individuals socialize and interact constantly with their colleagues and friends. In group settings, individuals exchange ideas more frequently and actively attempt to understand others' thoughts and teachings (18,19). Bernard et al. (20) examined the effect of three types of interaction (student-student, student-instructor, and student-material) on student achievement using meta-analytic methods. The study found that all three types of interaction had positive effects; student-instructor interaction, in particular, had stronger effects than the other two. Cheng and Chau's (18) study reported that the lack of social communication among students in remote education and the reduced sense of community could contribute to poorer academic performance by diminishing students' social interactions. In the study by Keskin and Kaya (17), 36.0% of students reported that remote education reduced teamwork by directing them toward individual work. Similar to these studies, 68.1% of first-year students in our study stated that they could easily communicate with the instructor in remote anatomy education; 69.0% stated that they could easily express their thoughts; and 47.4% believed that remote anatomy education increased individual work and reduced teamwork.

Our study revealed the decisive role of formal and remote education in students' awareness of the professional necessity of the course. The clearest evidence of this lack of awareness is the responses to the question: "Should the anatomy course be included in the second-year curriculum?" Second-year students with formal educational experience who understand the importance of the course support this idea at a rate of 47.1%. By comparison, 50.0% of first-year students who take the course remotely and struggle to develop this awareness

answered "No". This difference in perception between the two groups is statistically significant ($p<0.001$) and parallels findings in the literature (12). These findings strongly support the notion that remote learning leads not only to a deficiency in students' learning of the course content but also to a deficiency in their understanding of why that course is essential for their profession.

The 67.7% of the students in our study believed that anatomy should not be an elective course, and 65.0% stated that they would take the course if it were an elective. Again, there were statistically significant differences between first- and second-year students for these responses ($p<0.001$ and $p=0.004$). Moreover, in these responses, we observe that second-year students who received in-person education in their first year make more accurate judgments.

One of the most striking findings of our study emerged in relation to students' perception of professional identity. When asked, "Does anatomy education make you feel like a healthcare professional?", 64.7% (n=75) of first-year students enrolled in remote education answered "Yes". In comparison, this rate rose to 89.9% (n=124) among second-year students with formal educational experience. This difference is statistically significant. Similarly, 63% of second-year students answered "Yes" to the question: "Do you believe that the anatomy course you are taking will be useful in your professional life after graduation?". In light of these data, remote anatomy education appears to provide less support than formal education for students' development of their health professional identity and professional self-confidence. This finding is consistent with a study conducted in Brazil that showed that over 70.0% of students were concerned about the future of their professional education and only 24.1% found remote learning effective (21).

In a study by Rizun and Strzelecki (22), university students reported wanting to return to in-person education. In a study by Uzun et al. (23) examining the attitudes of 128 university students toward distance learning, only 15 (11.72%) considered it practical. Similarly, 73.3% of first-year students in our study reported that distance anatomy education was less effective than in-person instruction, whereas 55.1% of students in both classes opposed expansion of distance anatomy education. In the studies conducted by Başer et al. (7) during the pandemic, 46.4% of students reported having a suitable home environment for studying. Additionally, 55.1% of students were unable to attend their lessons regularly due to problems with internet infrastructure and access. In our study, 44.8% of students considered the learning environment was suitable. According to a study by Kürtüncü and Aylin (13) among nursing department students (n=824), only 105 of 516 participants reported that they could follow their classes without problems related to internet access or computers. In a study by Karadağ and Yücel (24) involving 17,939 students from various classes at 163 universities, 37.0% lacked internet access at home, 34.0% lacked a computer or tablet, and 23.0% reported that they could not continue their remote education. According to a report published by Kırşehir Ahi Evran University in 2020 (25), 23.0% of the 2,781 students were unable to attend online classes, and 75.0% of those unable to attend online classes reported internet connection issues. According to the data from our study, 37.1% of the 116 students did not have access to a computer, tablet, or smartphone; 25.0% did not have an internet package; and 19.8% experienced internet connection problems. Based on the studies conducted and our findings, it is evident that internet connectivity and infrastructure problems have not yet been completely resolved in our country, and that the percentage of students without access to a computer, tablet, or smartphone remains high. When equal opportunities in education cannot be fully ensured, courses may not reach their full potential, and instructors may have fewer opportunities to effectively support students. Many studies comparing online and in-person education found no difference in participants' success at the end of training (26,27,28). In fact, according to some studies, remote education is more effective than formal education in terms of participants' academic success (26,29,30). Considering these data, we believe that remote education in our country will again become a debatable issue once the learning environment is more suitable, internet infrastructure and access problems are resolved, and access to technology (e.g., phones, tablets, and computers) is ensured.

Study Limitations

The first major limitation of the study is that the sample consisted exclusively of students from the Health Services Vocational School of a single university, drawn from multiple health-related associate degree programs with unequal group sizes. Consequently, the findings may not be generalizable to other institutions or programs, and unmeasured program-level differences (e.g., baseline academic preparation or career orientation) may have confounded the comparative results. Furthermore, since the data obtained through the questionnaire are based on the students' subjective statements, the accuracy of the responses may have been affected by individual differences. Another important

limitation is that although the survey is based on existing surveys and student feedback, no separate pilot test or formal psychometric analyses (e.g., Cronbach's alpha or KR-20 for internal consistency) were conducted on the current version of the instrument. Therefore, measurement error and limited generalizability of survey scores cannot be completely disregarded.

Conclusion

This study has revealed that distance learning models used in practical health courses, such as anatomy, may significantly complicate the learning process and negatively impact educational efficiency. Limited in-person interaction and active participation have prevented students from fully grasping the professional importance of the course. Furthermore, infrastructural deficiencies, technological limitations, and educational inequality experienced during this process have been identified as key factors reinforcing these negative outcomes. These digital education models, whose use is expected to increase in the near future, need to be reevaluated and improved in light of the current findings, to make them sustainable and inclusive.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of University of Health Sciences Türkiye, İstanbul Training and Research Hospital (decision number: 2842, date: 21.05.2021).

Informed Consent: Completion and submission of the survey constituted informed consent.

Footnotes

Authorship Contributions

Concept: Ö.C.S., Ö.K., F.F.K., Design: Ö.C.S., F.F.K., Data Collection or Processing: Ö.C.S., Ö.K., F.F.K., Analysis or Interpretation: Ö.K., Literature Search: Ö.C.S., Ö.K., Writing: Ö.C.S., Ö.K., F.F.K.

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Impact of Pre-procedural Information Videos on Anxiety in Patients Undergoing Colonoscopy

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What is known on this subject?

Colonoscopy is widely utilized in clinical practice; however, the invasive nature of the procedure may still elicit notable anxiety in patients despite conventional pre-procedural counseling. Although several studies have investigated multimedia-supported education prior to colonoscopy, the results are varied and do not allow for a firm consensus.

What this study adds?

As one of the largest randomized controlled investigations in this field, our study confirmed that video-based education effectively decreases state anxiety and enhances satisfaction among patients awaiting colonoscopy. These results endorse animated video education as an accessible and efficient strategy for improving the patient experience and cooperation during colonoscopy.

ABSTRACT

Objective: Colonoscopy is a complex procedure whose optimal outcome depends largely on the patient's active cooperation. This study sought to evaluate whether providing an informative video could reduce anxiety levels in patients awaiting colonoscopy.

Material and Methods: This prospective randomized controlled trial assigned participants to two groups by sequential randomization. One group received standard verbal and written explanations before the colonoscopy, while the other group received an additional video-based educational intervention. Demographic characteristics, satisfaction scores, and State-Trait Anxiety Inventory- State (STAI-S) and State-Trait Anxiety Inventory-Trait (STAI-T) anxiety scores were compared between groups.

Results: A total of 347 patients were assessed prospectively. Following the application of exclusion criteria, the final study population consisted of 300 individuals. Participants were equally distributed, with 150 allocated to the video group and 150 to the control group. The two groups had comparable STAI-T scores; the difference was not statistically significant. In the video group, the mean STAI-S score decreased from 42.3±8.3 pre-intervention to 39.1±8.2 post-intervention, indicating a statistically significant reduction ($p<0.001$). Conversely, in the control group, STAI-S scores remained essentially unchanged (41.1±10.1 vs. 41.2±9.6; $p=0.581$). Post-procedural satisfaction levels were significantly higher in the video group than in the control group (4.3±0.8 vs. 2.8±1.0, $p<0.001$).

Conclusion: Providing video-animated information, in addition to written and verbal information, before colonoscopy reduces patients' preoperative anxiety. Furthermore, incorporating video-based education leads to improved patient satisfaction with the procedure.

Keywords: Anxiety, colonoscopy, satisfaction, STAI-S, STAI-T

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Introduction

Colonoscopy enables endoscopic visualization of the rectum, colon, and terminal ileum. This invasive technique is commonly used to evaluate unexplained weight loss, rectal bleeding, or persistent constipation, and to screen for colorectal cancer, particularly in adults over the age of 50 (1,2).

Anticipating possible discomfort or harm prior to an invasive procedure can trigger a natural emotional reaction characterized by heightened anxiety (3). Sedation and analgesia are typically administered during colonoscopy, rather than full general anesthesia. Many patients express concerns regarding the sufficiency of sedation, the details of the intervention, its length, and the potential complexity of the procedure. Such heightened anxiety can impair patient tolerance, cause physiological instability, increase postoperative medication requirements, and raise the likelihood of further medical interventions (4,5,6). Therefore, providing patients with adequate and effective pre-procedural information is essential.

Standard pre-colonoscopy preparation typically includes written and verbal counselling about the procedure. Nevertheless, misinterpretation or inadequacy of this information may persist, with anxiety remaining a common challenge. Several studies have explored whether supplementing conventional instructions with animated video content can help reduce anxiety in patients undergoing colonoscopy (7,8). Yet, the findings remain inconsistent, and no definitive conclusion has been established. Therefore, we sought to determine whether adding a brief informational video to standard counselling could impact both anxiety and satisfaction among patients undergoing colonoscopy.

Material and Methods

We designed a prospective randomized controlled trial involving individuals scheduled for elective colonoscopy. The Institutional Ethics Committee of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital granted approval for the study protocol, and the study adhered to the principles of the Declaration of Helsinki (approval number: KAEK-11/25.09.2024.178, approval date: 30.09.2024). This study was conducted at City Hospital, a tertiary healthcare centre with a high patient volume and a focus on education and research. The prospective cohort consisted of patients who underwent colonoscopy between December 2024 and June 2025. Written informed consent was obtained from all participants prior to enrolment.

Individuals aged 18-75 years who were referred for colonoscopy after evaluation in the internal medicine outpatient clinic were eligible for inclusion. Patients who were illiterate or who had previously undergone a colonoscopy were excluded. Additional exclusions were applied to individuals with documented psychiatric disorders or those receiving psychiatric or anxiolytic treatment. Baseline characteristics, including age, sex, body mass index (BMI), educational status, and relevant comorbidities, were collected for each participant.

Sequential randomization was implemented to minimize allocation bias. Patients who met the inclusion criteria were allocated to the video or control group in a 1:1 ratio using sequential assignment based on the order of admission. This approach ensured an even distribution of participants across the two groups. All subjects received routine written and verbal explanations before colonoscopy. The intervention group was also shown an animated educational video. All patients underwent conscious sedation during the procedure.

Anxiety was assessed using the State-Trait Anxiety Inventory (STAI), which includes two separate 20-item scales to measure temporary state anxiety [STAI-State (STAI-S)] and long-standing trait anxiety [STAI-Trait (STAI-T)]. The Turkish adaptation of the STAI, previously validated for clinical use, was utilized in the assessment (9). The STAI-S component captures temporary emotional reactions to the immediate situation, whereas the STAI-T evaluates more persistent anxiety tendencies. Baseline STAI-T scores were collected in both groups to allow comparison of trait anxiety. In both study arms, STAI-S scores were recorded prior to and following the informational intervention to evaluate changes in state anxiety. The enrolment and allocation process is illustrated in Figure 1.

Post-procedure satisfaction was quantified on a 1-to-5 Likert scale, with higher values indicating a more favourable experience (5: very satisfied; 1: very dissatisfied).

Video Information

In the intervention group, the animation was shown on a computer within a separate area adjacent to the endoscopy department, with a physician present to provide support if needed. The educational material consisted of an animated video explaining the steps and purpose of colonoscopy. (https://www.youtube.com/watch?v=mh90RPA-C10&list=PPSV) To ensure comprehension, the video was simultaneously translated into the patient's language by a physician. Patients were encouraged to ask questions about the intervention at any time.

Data analysis was conducted using SPSS 24 (IBM Corp., Armonk, NY, USA). Results for continuous variables are presented as mean values with standard deviations. Group differences were examined using independent-samples t-tests for numerical outcomes and Pearson's chi-square tests for categorical outcomes. Alterations in STAI-S scores were evaluated using paired samples t-tests.

To account for potential confounding factors, univariate analyses were first performed to identify variables associated with changes in state anxiety (ΔSTAI-S), calculated as the difference between pre- and post-intervention STAI-S scores. Variables that were significant or borderline significant ($p<0.10$) in univariate analyses, along with clinically relevant factors, were subsequently included in a multivariate linear regression model. The change in state anxiety (ΔSTAI-S) was used as the dependent variable. Statistical significance was defined as a two-tailed p value <0.05.

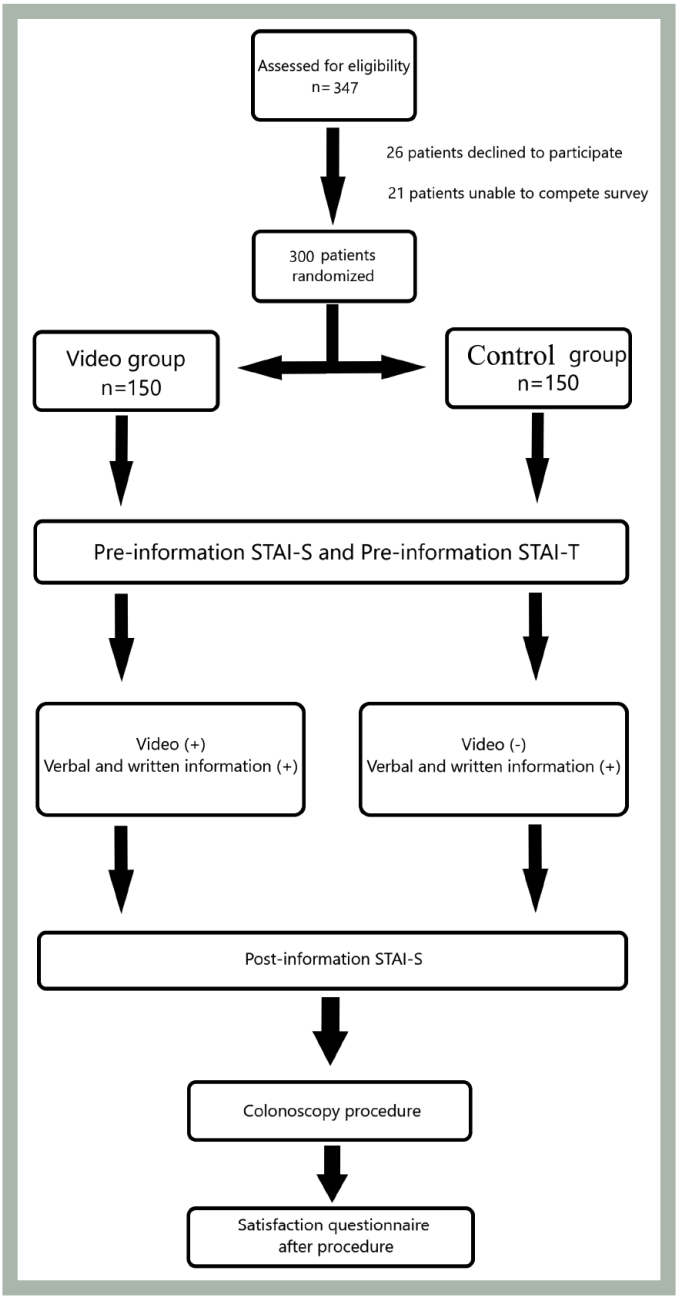

Figure 1. Participant flow diagram.
STAI-T: State-Trait Anxiety Inventory-Trait, STAI-S:State-Trait Anxiety Inventory-State

Results

During the initial assessment phase, 347 patients were prospectively assessed to determine their suitability for inclusion. Of these, 26 individuals declined participation and 21 could not complete the questionnaires. Randomization resulted in two balanced groups of 150 patients each: one group received the video intervention and the other received standard information. Baseline demographic variables, pre-intervention STAI-T scores, and satisfaction results are presented in Table 1.

Participants in the intervention group had a mean age of 39.8±12.5 years, compared with 39.6±12.8 years in the control group (p=0.881). The video group included 72 males and 78 females, whereas the control group consisted of 57 males and 93 females (p=0.102). The mean BMI was similar between the groups: 30.3±5.0 kg/m² in the video group and 29.1±5.4 kg/m² in the control group (p=0.134). Hypertension, diabetes mellitus, and other comorbidities did not differ significantly between groups (p=0.280, p=0.105, and p=0.375, respectively). Educational status distributions were also comparable (p=0.495). Long-term anxiety did not differ significantly between the groups, as reflected by baseline STAI-T means of 47.2±8.1 in the video arm and 46.2±9.0 in the control arm (p=0.307). In contrast, satisfaction scores after the procedure were higher in the video group (4.3±0.8) than in the control cohort (2.8±1.0); $p<0.001$.

As shown in Table 2, state anxiety decreased significantly in the video-based education arm (42.3±8.3 before the intervention vs. 39.1±8.2 after; $p<0.001$). Conversely, STAI-S scores in the control group remained nearly unchanged (41.1±10.1 vs. 41.2±9.6; p=0.581).

Additionally, we compared the change in state anxiety (ΔSTAI-S) between groups. Patients in the video group showed a significant reduction in anxiety (-3.2±1.7, $p<0.001$), whereas no significant change was observed in the control group (0.1±1.9, p=0.742). The between-group difference in ΔSTAI-S was statistically significant ($p<0.001$), further supporting the anxiolytic effect of the video intervention. This analysis is presented in Table 3.

Univariate and multivariate analyses of factors associated with ΔSTAI-S are presented in Table 4. In univariate analyses, group allocation, sex, and baseline trait anxiety (STAI-T) were associated with changes in state anxiety (ΔSTAI-S), while BMI showed a borderline association. These variables were included in a multivariate linear regression model.

The multivariate model was statistically significant (R^2: 0.11, adjusted R^2: 0.098; F: 9.14, p<0.001). Importantly, after adjustment for baseline STAI-T, sex, and BMI, group allocation remained a statistically significant independent predictor of change in state anxiety. Patients in the video group exhibited a significantly greater reduction in state anxiety than those in the non-video group [B: 3.17, 95% confidence interval (CI): 1.81-4.54, p<0.001]. Male sex was also independently associated with ΔSTAI-S (B: 1.62, 95% CI: 0.24-3.00, p=0.022); whereas baseline STAI-T and BMI were not significant in the adjusted model.

Discussion

Preoperative anxiety is highly prevalent, with reported rates ranging from 25% to 80% among surgical patients (10). Such anxiety can manifest as physiological responses,

Table 1. Demographic features and questionnaire scores

	Video group n=150	Control group n=150	p value
Age (mean ± SD)	39.8±12.5	39.6±12	0.881
Gender (Male/female)	72/78	57/93	0.102
BMI (kg/m²) (Mean ± SD)	30.3±5	29.1±5.4	0.134
Hypertension (Yes/no)	14/136	21/129	0.280
Diabetes mellitus (Yes/no)	9/141	18/132	0.105
Other comorbidities (Yes/no)	15/135	21/129	0.375
Educational level Primary education qualified Highly qualified	24 93 33	18 102 30	0.495
STAI-T score (mean ± SD)	47.2±8.1	46.2±9	0.307
Satisfaction score (Mean ± SD)	4.3±0.8	2.8±1	<0.001

BMI: Body mass index, STAI-T: State-Trait Anxiety Inventory-Trait, SD: Standard deviation

Table 2. Change in STAI-S scores after video-information between groups

	STAI-S (mean ± SD) (Pre-information)	STAI-S (mean ± SD) (Post-information)	p value
Video group	42.3±8.3	39.1±8.2	<0.001
Control group	41.1±10.1	41.2±9.6	0.581

STAI-T: State-Trait Anxiety Inventory-Trait, STAI-S: State-Trait Anxiety Inventory-State, SD: Standard deviation

Table 3. Comparison of pre- and post-procedure STAI-S scores and change in anxiety levels between groups

	ΔSTAI-S (post-pre) mean ± SD	p value*
Video group	-3.2±1.7	<0.001
Control group	+0.1±1.9	0.742
Between-group comparison	-	<0.001

**: Between-group comparison: independent samples t-test. ΔSTAI-S: State-Trait Anxiety Inventory-State change, SD: Standard deviation*

Table 4. Univariate and multivariate analysis of factors associated with change in state anxiety (ΔSTAI-S)

Univariate analyses				Multivariate analyses			
Variable	**Comparison/r**	**Effect estimates**	**p value**	**Variable**	**β (B)**	**95% CI**	**p value**
Group	Video vs. non-video	Mean difference: 3.50 (95% CI: 2.13-4.87)	**<0.001**	Video group	3.17	1.81-4.54	**<0.001**
Sex	Male vs. female	Mean difference: 1.91 (95% CI: 0.49-3.33)	**0.009**	Sex (male)	1.62	0.24-3.00	**0.022**
STAI-T	Pearson r	r: 0.116	**0.044**	STAI-T	0.07	−0.01-0.15	0.093
BMI	Pearson r	r: 0.102	**0.077**	BMI	0.11	−0.02-0.24	0.106
Age	Pearson r	r: 0.040	0.494				
Diabetes mellitus	Yes vs. no	Mean difference: -0.06	0.961				
Hypertension	Yes vs. no	Mean difference: -0.89	0.428				
Educational level	ANOVA	–	0.487				

Δ*STAI-S: State-Trait Anxiety Inventory-State change, CI: confidence interval, BMI: Body mass index, STAI-T: State-Trait Anxiety Inventory-Trait, ANOVA: Analysis of variance*

including hypertension and cardiac rhythm disturbances (11). These effects may compromise not only patient well-being but also procedural performance. Conventional written and verbal counselling often remains insufficient to alleviate this anxiety completely. Therefore, we conducted the largest randomized controlled trial to date to investigate whether supplementing standard counselling with video-based education more effectively reduces colonoscopy-related anxiety.

Even with routine sedation and analgesia, colonoscopy can still be associated with pain and discomfort. Previous studies have shown that heightened anxiety increases sedative and analgesic requirements (12). Thus, strategies aimed at reducing anxiety represent a logical means to improve procedural tolerance. Multimedia-supported educational approaches have been evaluated in different branches of medicine. Research in urology and anesthesia has demonstrated that video-assisted preoperative information can effectively reduce anxiety (13,14). Conversely, a study in gynecology reported no significant anxiolytic effect of video education prior to intrauterine device insertion (15).

Although available evidence on colonoscopy-specific video education remains limited, findings have similarly been inconsistent. Arabul et al. (8) reported reduced anxiety and improved procedural outcomes with video education, whereas Bytzer and Lindeberg (16) observed no significant improvements in tolerability or anxiety.

Arabul et al. (8) also noted decreased pain levels among patients receiving video-assisted information. Given the potential confounding effects of sedation and analgesia on pain perception, we did not include pain scoring in our methodology. Instead, patient-reported satisfaction was analysed and found to be significantly higher in the video group.

Some previous studies have suggested that female patients may experience greater anxiety during colonoscopy (8,16). Accordingly, gender-tailored educational strategies have been proposed. In contrast, our larger cohort did not reveal significant gender-related differences in anxiety scores. We believe that the impact of gender differences on anxiety remains a topic of debate. Therefore, the influence of sex on procedural anxiety remains open to interpretation.

The psychological determinants of anxiety are multifaceted and highly individualized. Patients may also differ in their desire for procedural information, with some seeking extensive details and others preferring limited disclosure (17). For this reason, ensuring comparable baseline anxiety characteristics between groups was prioritized. We confirmed measurement equivalence for trait anxiety using the validated STAI-T. This methodological consistency strengthens the validity of our group comparisons. Despite existing evidence, the optimal format for patient education continues to be debated in the literature.

In the present study, anxiety levels decreased significantly in the video group, whereas no significant change was observed in the control group. Additionally, the between-group comparison of ΔSTAI-S confirmed a greater reduction in anxiety among patients who received video-based education. These findings support the hypothesis that visual information may reduce the fear of the unknown by enhancing cognitive preparedness and procedural predictability. Increased

familiarity with the upcoming steps of colonoscopy may also strengthen the patient-provider relationship and provide a sense of control, thereby reducing situational anxiety.

Study Limitations

One notable advantage of this study is the relatively large number of participants included, making it the largest randomized trial to investigate video-assisted education prior to colonoscopy. We did not evaluate certain procedure- or anesthesia-related factors that may influence patient stress, including pre-procedural complications, colonoscopy duration, or variability in sedation quality. Therefore, the potential impact of these factors on anxiety levels could not be assessed

Conclusion

Colonoscopy may be a challenging experience for patients, and anxiety can adversely influence procedural success. Effective pre-procedural education aims to improve understanding of the procedure and to alleviate anxiety. Video-based education was independently associated with a greater reduction in pre-procedural anxiety after adjustment for potential confounders. Our findings demonstrate that incorporating animated video-based information not only reduces pre-procedural anxiety but also enhances patient satisfaction with the colonoscopy experience.

Ethics

Ethics Committee Approval: The Institutional Ethics Committee of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital granted approval for the study protocol, and the study adhered to the principles of the Declaration of Helsinki (approval number: KAEK-11/25.09.2024.178, approval date: 30.09.2024).

Informed Consent: Written informed consent was obtained from all participants prior to enrolment.

Footnotes

Authorship Contributions

Concept: B.C., Design: B.C., E.D.K., Data Collection or Processing: B.C., E.D.K., Analysis or Interpretation: B.C., Literature Search: B.C., E.D.K., Writing: B.C.

Conflict of Interest: The authors declare that there is no conflict of interest with any financial organization, corporation, or individual that can inappropriately influence this work.

Financial Disclosure: The author declared that this study received no financial support.

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GalvanoRegeneration: A New Term and a New Page in Regenerative Therapy with Percutaneous Needle Electrolysis

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Keywords: Percutaneous needle electrolysis, regeneration, galvanic current, pain, musculoskeletal

Dear Editor,

Percutaneous needle electrolysis (PNE) is a treatment modality that uses an acupuncture needle to apply galvanic current to injured tissue, mechanically and electrically stimulating the tissue. PNE produces a non-thermal, electrolytic ablation that activates cellular systems involved in phagocytosis and soft tissue repair, thereby inducing a regulated inflammatory response (1). While PNE is not a technically new intervention the term "galvanoregeneration" is proposed here as a conceptual framework to re-define its regenerative impact with a modern perspective.

Both *in vivo* and *in vitro* studies have shown that cells move directionally in response to electric current. This response is known as electrotaxis or galvanotaxis (1). This cell migration is important in initiating the inflammatory response. Galvanic current application also affects cell adhesion, alignment, proliferation, differentiation, and apoptosis. Evidence suggests that the migration of inflammatory cells towards injured tissue can lead to morphological alterations and promote healing. Concurrently, vascular endothelial cells also exhibit responses to galvanotaxis, which is associated with an increase in angiogenesis (2).

Histological analysis has revealed that the application of galvanic current to injured tissues results in a reduction of pro-inflammatory cytokines, specifically tumor necrosis factor-α and interleukin-1β. Concurrently, there's an upregulation of anti-inflammatory proteins like PPAR-γ, alongside a marked upregulation of in vascular endothelial growth factor (VEGF) and its receptor VEGF-R1. Additionally, the activity of NF-κB, which is instrumental in phagocytosis and tendon regeneration, is notably suppressed. Collectively, these observations suggest that galvanic current, as administered through PNE therapy, plays a significant role in promoting the repair of tissues (2).

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Galvanic current applied with PNE has also been shown to increase the expression of some genes associated with collagen regeneration and tissue remodeling in the extracellular matrix. Changes in the expression of COX-2, MMP-9, and VEGF are more pronounced than in other genes (3). Galvanic current enhances the proinflammatory M_1 phenotype of macrophages, activates the $NLRP_3$ inflammasome, does not induce inflammasome-mediated pyroptosis, increases *in vivo* inflammation, and induces a tissue regenerative response. Therefore, it has been reported that galvanic current is a viable technique for tendon regeneration and PNE is effective for the treatment of chronic lesions (4).

Several case studies have suggested that PNE is effective in the treatment of various musculoskeletal conditions. PNE has been found to have a significant effect on reducing musculoskeletal pain and improving pain-related disability in both the short and long term. However, it is considered safe in terms of its favorable application side effect profile of PNE. Ultrasound-guided application further enhances safety. Ultrasound-guided application of PNE not only enhances targeting accuracy but also ensures safety and reproducibility in clinical settings (5).

In conclusion, PNE appears to contribute positively to the healing of muscle and tendon injuries. PNE therapy is still in its infancy. It has a history of only 10 years. Nevertheless, based on these promising results, we believe that PNE will be a modern weapon for physicians in regenerative medicine. Therefore, we use the term "galvanoregeneration" to describe the treatment of PNE. It is important to increase scientists' awareness of PNE.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.A., F.B., M.T.Y., Concept: B.A., F.B., M.T.Y., B.T.D., Data Collection or Processing: B.A., F.B., M.T.Y., Analysis or Interpretation: B.A., F.B, M.T.Y., B.T.D., Literature Search: B.A., F.B., M.T.Y., B.T.D., Writing: B.A., F.B., M.T.Y.

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Surgical Management of Recurrent Retroperitoneal Paraganglioma: Anatomical Challenges in Surgical Dissection

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Keywords: Retroperitoneal paraganglioma, recurrent tumor, surgical anatomy

Paragangliomas (PGL) are rare neuroendocrine tumors that arise from sympathetic or parasympathetic ganglia of the autonomic nervous system (1). PGLs of sympathetic origin are predominantly located in the retroperitoneum, particularly at the aortic bifurcation and the organ of Zuckerkandl, and are associated with high catecholamine secretion (1,2). Approximately one-third of PGL are hereditary; succinate dehydrogenase complex iron sulfur subunit B (SDHB) mutations and other germline mutations are associated with recurrence and metastasis (3). Since a histopathological distinction between benign and malignant lesions cannot be made, metastasis is the main indicator of malignancy (3). The main approach for curative treatment is complete surgical resection. However, in cases of recurrence with retroperitoneal involvement, surgical dissection can be challenging because of dense fibrosis, anatomical distortion, and proximity to major vessels (1).

This letter discusses the surgical strategy and anatomical challenges encountered in managing a recurrent retroperitoneal PGL, with reference to current literature.

A 21-year-old woman presented three years ago with persistent vomiting, headache, and hypertension. Abdominal imaging revealed a 6×5-cm mass in the left preaortic area adjacent to the celiac trunk, pushing the pancreas anteriorly. The mass, which was evaluated for pheochromocytoma and PGL spectrum, was completely excised; pathology revealed PGL, a Ki-67 proliferation index of 5%, vascular-lymphatic-capsular invasion, and a heterozygous SDHB mutation. The patient, who was hormonally inactive in the postoperative period, was followed annually with radiological and biochemical assessments.

On follow-up magnetic resonance imaging (MRI) and Ga-68 DOTATATE positron emission tomography-computed tomography (CT), a recurrent lesion measuring 2-2.5 cm and exhibiting intense receptor uptake was observed posterior to the pancreas and anterior to the aorta. Preoperative imaging demonstrated that the mass was in close proximity to the superior mesenteric artery, splenic artery, and renal artery and vein (Figure 1). Accordingly, patients were routinely

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informed about the potential risk of vascular injury and the need for additional surgical procedures, and written informed consent was obtained prior to surgery. For 1 week prior to surgery, the patient underwent preoperative fluid replacement for volume expansion at a rate of 1,000 mL/day with a crystalloid-to-colloid ratio of 1:1.

A subcostal incision was made, the gastrocolic ligament was released, and a partial Mattox maneuver was performed. The bilobed recurrent mass extending beneath the pancreas into the retroperitoneal space caused severe difficulty during dissection because of dense perivascular fibrosis resulting from prior surgery and significant anatomical distortion surrounding the superior mesenteric artery and the renal hilum. The patient's blood pressure remained stable throughout the intraoperative tumor excision, and the mass was excised en bloc without vascular injury. No postoperative complications developed, and the patient was discharged on the seventh postoperative day.

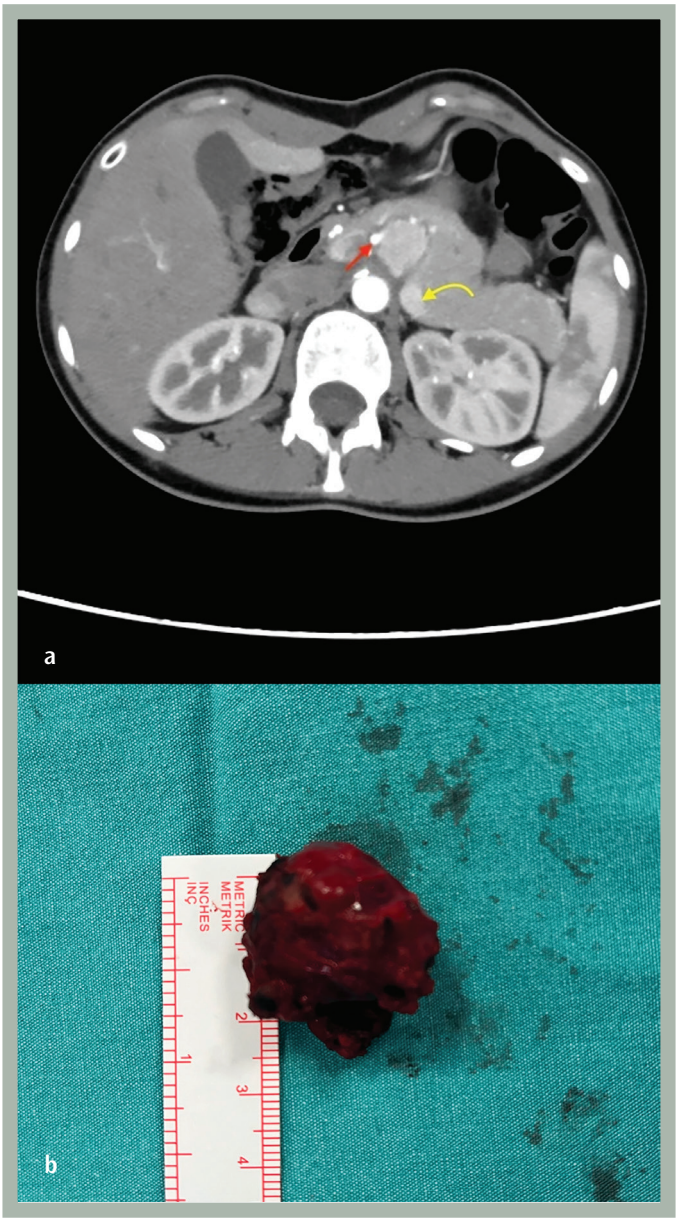

Figure 1. (a) Axial slice from a triphasic computed tomography scan. Red arrow: splenic artery; yellow arrow: splenic vein. (b) Macroscopic specimen

Histopathological examination revealed two foci of PGL measuring 3 cm and 1.5 cm, respectively. Mitotic activity was low (1 mitosis/2 mm^2); no atypical mitoses, vascular invasion, or lymphovascular invasion were observed, and surgical margins were reported as negative. Since the surgical margins were negative and the patient remained asymptomatic, no adjuvant therapy was administered and follow-up was planned with clinical and biochemical evaluations every 6 months and cross-sectional imaging (CT or MRI) annually during the first five years. At the 6-month postoperative follow-up, the patient remains disease-free.

Surgery for recurrent retroperitoneal PGL is a high-risk procedure due to anatomic proximity and fibrotic scarring. In addition, since recurrence rates are higher in patients with SDHB mutations, long-term, close follow-up is recommended (2). Visceral rotation techniques (e.g., the Mattox maneuver) increase the likelihood of successful resection by facilitating safe exposure of major vascular structures (4). In addition, ensuring intraoperative hemodynamic stability during PGL surgery requires close coordination between the surgical and anesthesia teams, and is critical for operative safety (1).

In conclusion, retroperitoneal PGLs are rare tumors whose surgical management requires advanced expertise because of their anatomical location. Successful surgical treatment in recurrent cases is possible with detailed preoperative planning, appropriate hemodynamic preparation, precise dissection to preserve vascular structures, and multidisciplinary teamwork. Long-term radiological and biochemical follow-up is of great importance, especially in patients with an SDHB mutation.

Footnotes

Informed Consent: The written informed consent was obtained prior to surgery.

Authorship Contributions

Surgical and Medical Practices: F.G., Y.Y.K., N.A., E.K., Concept: F.G., Y.Y.K., N.A., E.K., Design: F.G., Y.Y.K., N.A., E.K., Data Collection or Processing: F.G., Y.Y.K., N.A., E.K., Analysis or Interpretation: F.G., Y.Y.K., N.A., E.K., Literature Search: F.G., Y.Y.K., N.A., E.K., Writing: F.G., Y.Y.K., N.A., E.K.

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The article titled **"The Role of Fascia in Myofascial Pain Syndrome: A Look at Cinderella Tissue"**, published in *Cam and Sakura Medical Journal*, Volume 4, Issue 1, 2024, pages 1–8, DOI: 10.4274/csmedj.galenos.2024.2024-3-1, has been retracted due to the identification of an ethical violation concerning image use. The authors combined images from different sources included in Articles 1 and 6 to create a single figure but did not provide appropriate attribution. This issue was not detected during the evaluation and publication process.

Additionally, the same figure was used as the cover image of **Volume 4, Issue 1 (2024)**. In accordance with the retraction decision, this cover will be corrected and the figure will be removed **simultaneously with the publication of the issue in which this retraction notice appears**. The corrected cover will replace the previous online version to maintain editorial accuracy and ethical compliance.

Although an erratum was published in Volume 4, Issue 2 (2024) to add the missing source, the act was determined to constitute clear plagiarism, even if unintentional. To ensure compliance with international publication ethics standards (COPE, ICMJE, WAME, TR Dizin Ethical Principles) and to maintain the integrity of the scientific record, the article has been retracted by the Editorial Board.

CAM & SAKURA MEDICAL JOURNAL

2025 Referee Index