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Original Investigations

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Development of Tactical Medicine Knowledge and Awareness Scale: Validity and Reliability Study

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ABSTRACT

Objective: Tactical medicine training is not considered as a part of the curriculum of medical schools or emergency medicine (EM) residency programs. Shifting paradigms of war and conflict natures may require any physician to take a role as a provider in tactical settings. No standardized test or questionnaire study was found in the literature to evaluate physicians' knowledge and awareness levels in tactical emergency medical support. The objective of this study was to develop a scale that can be used to determine the level of awareness and knowledge of EM physicians on tactical medicine.

Methods: This was a cross-sectional study analyzing the validity and reliability of a new scale. An item pool was prepared consisting of 55 questions. Eleven experts evaluated the content validity and the scale was finalized with 28 items.

Results: The study found that the tactical medicine knowledge and awareness scale tool is a valid and reliable measurement for assessing the knowledge and awareness of EM physicians in tactical medicine. The internal consistency of the scale was high, with a Cronbach's α coefficient of 0.808. Confirmatory factor analysis indicated acceptable model fit, and all sub-dimensions positively influenced the total knowledge and awareness score. The results suggest the need for tactical medicine education to be integrated into medical school and EM residency curricula to improve competency in this critical field.

Conclusion: We can conclude that this new scale proved to be a reliable measurement tool to determine the level of knowledge and awareness of EM physicians in tactical medicine.

Keywords: Medical education, military science, questionnaire design, tactical medicine

INTRODUCTION

Tactical medicine provides close medical support to law enforcement officers during their operations and activities, minimizing the potential for additional injury and disease, as well as continuing the care of the sick and wounded until their transfer to a center where they can receive comprehensive care (1,2). Medical support has always been a part of the organizational structure in modern armies. However, the fundamental importance of tactical medicine was understood in the middle of the 20th century due to the experiences gained from the World Wars and civil unrest, and it was observed that the survival rate increased thanks to the rapid care of injured military personnel at the scene and rapid transport to an advanced center (3). In the following years, the concept of tactical emergency medical support (TEMS) became an essential part of tactical medicine due to the increase in multiple injury incidents, including terrorist acts in residential areas where law enforcement officers and the civilian population were harmed (2,4).

TEMS can be considered a natural part of emergency medicine (EM), including prehospital and emergency health care. Today, EM associations emphasize the importance of EM specialization in TEMS and accept it as a sub-specialty of EM (5). However, since the healthcare service to be provided in the conflict area involves several aspects fundamentally distinct from civilian prehospital trauma, it would not be appropriate to use trauma and prehospital care guidelines directly in TEMS or to automatically consider EM physicians as competent in TEMS (4,6).

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The tactical combat casualty care project, first developed in the USA in the mid-1990s, aimed to prevent morbidity and mortality by standardizing trauma care on the battlefield. The data from this project were realized when a section on Military Medicine was added to the Prehospital Trauma Life Support (PHTLS) Guidelines published in 1999. Studies show that employing EM specialists in tactical medicine improves outcomes (7).

tactical medicine training is not a part of the curriculum of medical schools in the USA, Türkiye, or the Turkish EM Core Education Programme (6,8-10). Physicians who lack training in this area may experience deficiencies in TEMS care (6). Therefore, it is important to increase the level of knowledge of EM physicians about tactical medicine. No standardized test or questionnaire study was found in the literature to evaluate physicians' knowledge and awareness levels in TEMS.

This study aimed to develop a scale that can be used to determine the level of awareness and knowledge of EM physicians involved in tactical medicine. Results may provide data that could enable the inclusion of tactical medicine in the local EM residency education curricula.

METHODS

Study Design

This cross-sectional study was conducted between January 1, 2024 and April 1, 2024, after approval from the İzmir Katip Çelebi University Social Research Ethics Committee (decision no: 2023/21-07, date: 20.12.2023). A validity and reliability study was conducted for a scale that measures tactical medicine knowledge and awareness.

Study Protocol

An item pool was prepared for the study by reviewing the relevant literature. Then the item pool (Table 1) was administered to the sample size determined within the scope of content validity. Eleven EM physicians who are experts in their field were asked to choose one of the options of "appropriate", "should be improved", or "not appropriate" for each question. As a result of content validity evaluation, items with item response statistics below 0.5 were eliminated, and the form was finalized. The study started with a question pool of 55 items and was finalized with 28 items.

Table 1. Item pool of the scale

No	Item	Not appropriate	Must be revised	Appropriate	CVR
1	The meaning and scope of tactical medicine can be defined as follows.	0	3	8	0.455
2	I am knowledgeable about the types of equipment used in tactical medicine.	1	2	8	0.455
3	I have received theoretical training in tactical medicine both before and after graduation.	3	2	6	0.091
4	I have received practical training in tactical medicine before or after graduation.	3	3	5	-0.091
5	Being trained in tactical medicine is important for a physician.	0	2	9	0.636
6	I am familiar with the three phases of casualty care in tactical medicine.	4	2	5	-0.091
7	I am knowledgeable about the key points in casualty care in tactical medicine.	4	1	6	0.091
8	I can correctly identify life-threatening bleeding in a battlefield setting.	1	2	8	0.455
9	I can correctly identify tension pneumothorax in a battlefield setting.	1	1	9	0.636
10	I trust my knowledge of applying a tourniquet.	1	2	8	0.455
11	I can effectively intervene in life-threatening bleeding in a battlefield setting.	0	2	9	0.636
12	I can intervene correctly in tension pneumothorax in a battlefield setting.	0	1	10	0.818
13	I can correctly apply a tourniquet in a battlefield setting.	0	1	10	0.818
14	I know the meanings of the MARCH and PAWS treatment acronyms used in tactical medicine.	5	1	5	-0.091
15	I can effectively manage hypothermia in a battlefield setting.	2	2	7	0.273
16	I can perform tactical medicine procedures under low light and high noise conditions.	4	2	5	-0.091
17	I have received theoretical training in tactical medicine procedures under low light and high noise conditions.	6	1	4	-0.273

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Table 1. Continued

No	Item	Not appropriate	Must be revised	Appropriate	CVR
18	I have received practical training in tactical medicine procedures under low light and high noise conditions.	6	1	4	-0.273
19	I trust my knowledge in emergency trauma resuscitation.	1	0	10	0.818
20	I trust my knowledge of triage.	0	1	10	0.818
21	I am proficient in supraglottic airway placement.	1	1	9	0.636
22	I am proficient in nasopharyngeal airway placement.	3	0	8	0.455
23	I am proficient in endotracheal airway placement.	1	0	10	0.818
24	I am proficient in surgical cricothyroidotomy procedures.	3	2	6	0.091
25	I am proficient in needle decompression procedures.	3	1	7	0.273
26	I am proficient in chest tube procedures.	1	1	9	0.636
27	I am proficient in intraosseous vascular access.	0	1	10	0.818
28	I am proficient in pelvic binder procedures.	0	0	11	1,000
29	I am knowledgeable about emergency burn care.	2	1	8	0.455
30	I am knowledgeable about tranexamic acid administration.	2	0	9	0.636
31	I am knowledgeable about hemostatic wound dressings.	3	2	6	0.091
32	I am competent in using airway suction devices in the field.	3	0	8	0.455
33	I am knowledgeable about sanitation practices.	3	4	4	-0.273
34	I feel confident in providing immediate intervention and splinting for fractures.	3	2	6	0.091
35	I trust my knowledge of medications that can be used in a battlefield setting.	1	1	9	0.636
36	I trust my knowledge in pain management, in a battlefield setting.	2	1	8	0.455
37	I have knowledge of "care under fire" (CUF) procedures.	3	2	6	0.091
38	I feel competent in implementing CUF.	7	1	3	-0.455
39	I am knowledgeable about tactical field care (TFC) procedures.	4	1	6	0.091
40	I feel competent in implementing TFC.	7	1	3	-0.455
41	I feel competent in implementing tactical evacuation care.	6	2	3	-0.455
42	I am proficient in the 10 competencies of NATO's prolonged field care (PFC).	5	0	6	0.091
43	I feel sufficiently capable of working under pressure.	4	1	6	0.091
44	Theoretical training in tactical medicine should receive before graduating from medical school.	0	1	10	0.818
45	The emergency medicine residency program should include theoretical training in tactical medicine.	0	0	11	1,000
46	Medical students should receive practical training in tactical medicine before graduating from medical school.	1	1	9	0.636
47	The emergency medicine residency program should include practical training in tactical medicine.	0	0	11	1,000
48	The presence of specialists trained in tactical medicine in the field during disasters or battles will enhance the success of medical management.	2	0	9	0.636
49	Tactical medicine emphasizes not only on-field intervention but also medical coordination.	1	1	9	0.636
50	Any physician may need knowledge of tactical medicine at any time.	0	1	10	0.818
51	Tactical medicine training should only be provided to emergency medicine specialists.	4	1	6	0.091
52	I understand that I may not use a light source while providing medical intervention in a battlefield setting.	1	1	9	0.636

Table 1. Continued

No	Item	Not appropriate	Must be revised	Appropriate	CVR
53	I understand that there may be a highly noisy environment while providing medical intervention in a battlefield setting.	2	0	9	0.636
54	Even if an emergency physician has not received tactical medicine training, they are competent to perform any necessary interventions in the field.	2	1	8	0.455
55	It is suggested that tactical medicine should be a separate medical specialty.	2	0	9	0.636

CVR: content validity ratio, MARCH: massive bleeding, airway, respiration, circulation, head and hypothermia, PAWS: pain, antibiotics, wounds, and splinting, NATO: North Atlantic Treaty Organization

Then, the survey was administered to all EM physicians working in the Emergency Department of İzmir Katip Çelebi University Ataturk Training and Research Hospital at the time of the study. Written informed consent was obtained from all participants before participation in the study. There were 131 participants involved. Validity and reliability analyses were performed following the application of the survey.

Statistical Analysis

Exploratory factor analysis is used to create measurement instruments (questionnaires, tests, etc.), while confirmatory factor analysis (CFA) tests whether these models are confirmed on the sample studied. The purpose of CFA is to find a small number of latent factors to explain the observed covariance among p observed variables. This analysis enables the model to be tested with all observed and unobserved variables and to reveal the extent to which the result is compatible with the available data. It provides clear results in error calculations. While other traditional methods deal with measurement errors separately, this analysis explicitly takes measurement errors into account in all analyses. A measurement error is associated with each observed variable, and a residual error term is associated with the latent variables. The analysis is also known as structural equation modelling (SEM). SEM can be defined as linear regression models, factor analysis, CFA, path analysis, and structural equation models.

If there is no criterion reference for comparing a test in the analyses, construct validity should be tested. SEM, also known as CFA, is a set of statistical methods used by many branches of science, especially social sciences, behavioral sciences, educational sciences, economics, marketing, and health sciences. It is based on the identification of observable and unobservable variables in a causal and relational model guided by a specific theory, bringing a hypothesis testing approach to the multivariate analysis of the structural theory related to the subject.

SEM is a multivariate analysis method that combines factor analysis and multivariate regression analysis. SEM analysis enables the model to be tested with all observed and unobservable variables and to reveal the extent to which the result is compatible with the available data. Suppose the fit indices obtained by testing the model indicate a good fit between the model and the data. If the fit indices reveal that such a fit does not exist, the hypotheses are rejected; In that case, the structurally generated hypotheses are accepted. Firstly, SEM adopts a confirmatory approach instead of an explanatory approach. While various statistical methods other than SEM try to discover the relationships in the data set, SEM verifies the fit of the theoretically established relationships with the data. SEM reveals clear results in error calculations.

Cronbach's alpha (α) coefficient was used in the reliability analyses to support construct validity. Exploratory and confirmatory factor analyses were applied for validity. Bartlett's test of sphericity assessed the suitability for factor analysis, and Kaiser-Meyer-Olkin (KMO) sampling adequacy statistics assessed the adequacy of the sample size. "Tactical medicine knowledge and awareness scale" (TAMKA) items were determined to have a five-factor structure according to the Varimax rotation method. The summability of the scales was evaluated with the Tukey summability test (11-14), and Statistical Package for the Social Sciences (SPSS) 27 and analysis of moment structures 25 were used using inclusion body myositis (IBM) Corp's statistical package programs (IBM SPSS Statistics for Windows, version 27.0. armonk, NY: IBM Corp). The ($p<0.05$) and ($p<0.01$) levels were considered statistically significant (15,16).

Results

In Table 2, the scale form was prepared using the Lawshe technique, and expert opinions were obtained. Content validity ratios (CVRs) and the content validity index (CVI) were calculated. Whether each item should be included in the scale was decided according to the CVR and CVI criteria.

According to the results of the analyses, the experts generally found the scale content highly appropriate. The determination of the central serous retinopathy critical point as 0.385 and the calculation of the CVI as 0.632 indicate that the scale generally has good content validity. Items with content validity score values above the critical point play an essential role in reflecting the purpose of the scale and indicate that this scale comprehensively addresses the selected subject area.

The KMO test is a measure to determine whether the distribution is suitable for factor analysis. The KMO test is related to the suitability of the sample size, and the value of 0.861 indicates that factor analysis can be used on these data (>0.8 is excellent, 0.7-0.8 is good, 0.5-0.7 is moderate, and at least 0.5 is required). Based on this information, the KMO value in this study is at an excellent level. Bartlett's test result was obtained as 1,973.440

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($p<0.001$). This result means the applied measurement variable is multivariate with respect to the universe parameter. In this study, factors with an eigenvalue greater than 1.50 and those without a limit on number were included in the scale. Cronbach's alpha=0.888 shows excellent reliability, indicating the scale is a reliable measurement tool (Table 3).

Considering that variance ratios ranging between 60% and 80% are accepted as ideal in factor analysis, this study's variance ratios are appropriate. The factor loads of the questions in the first factor (level of knowledge about general medical practices) ranged between 0.541 and 0.842. In the second factor (level of educational awareness), they ranged between 0.435 and 0.905. The third factor (level of general intervention knowledge in the battlefield) had factor loads ranging between 0.687 to 0.798. For the fourth factor (level of awareness of the importance of tactical medicine), they range between 0.686 and 0.888, and for the fifth factor (level of knowledge of medical intervention specific to the battlefield), they range between 0.636 and 0.705.

Root Mean Square Error of Approximation

This index is a measure of the fit of the model to the data. A lower root mean square error of approximation (RMSEA) value indicates that the model fits the data better. Generally, values between 0 and 0.05 indicate good fit, values between 0.05 and 0.08 indicate acceptable fit, and values greater than 0.08 indicate poor fit. As a result of the study, the RMSEA value shows an excellent fit (Table 4).

Incremental Fit Index

This index measures the improved fit of the model. The closer the value is to 1, the better the model fits the data. The incremental fit index (IFI) value should generally be 0.95 or higher. An IFI value of 1 shows an excellent fit.

Comparative Fit Index

This index measures the fit of the model with respect to alternative models. The closer the value is to 1, the better the model fits compared to alternative models. The comparative fit index (CFI) value should generally be 0.97 or higher. The CFI value shows an excellent fit.

Table 2. Scope validity analysis

Item no	Appropriate	Must be revised	Not appropriate	CVR
Item 1	23	2	1	0.77
Item 2	26	0	0	1.00
Item 3	22	3	1	0.69
Item 4	21	5	0	0.62
Item 5	22	4	0	0.69
Item 6	23	3	0	0.77
Item 7	25	1	0	0.92
Item 8	21	5	0	0.62
Item 9	20	6	0	0.54
Item 10	21	5	0	0.62
Item 11	22	3	1	0.69
Item 12	19	7	0	0.46
Item 13	22	4	0	0.69
Item 14	23	3	0	0.77
Item 15	26	0	0	1.00
Item 16	23	3	0	0.77
Item 17	23	3	0	0.77
Item 18	22	4	0	0.69
Item 19	20	5	1	0.54
Item 20	22	4	0	0.69
Item 21	22	4	0	0.69
Item 22	22	4	0	0.69
Item 23	21	5	0	0.62
Item 24	21	5	0	0.62
Item 25	21	4	1	0.62
Total number of experts=26				
CVR critical point=0.385				
CVI=0.632				

CVR: content validity ratio, CVI: Content validity index

Table 3. TAMKA tool factor loadings and factor variances

Factors	Questions	Factor loadings				
		Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Factor 1: level of knowledge about general medical practices	6	0.752				
	8	0.660				
	9	0.818				
	10	0.842				
	11	0.719				
	12	0.774				
	13	0.812				
	15	0.541				

Table 3. Continued

Factors	Questions	Factor loadings				
		Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Factor 2: level of educational awareness	1		0.585			
	16		0.896			
	17		0.903			
	18		0.902			
	19		0.905			
	20		0.435			
	21		0.563			
Factor 3: level of knowledge about general interventions on the battlefield	2			0.695		
	3			0.701		
	4			0.687		
	5			0.798		
Factor 4: level of awareness about the importance of Tactical Medicine	22				0.703	
	24				0.686	
	25				0.888	
Factor 5: level of knowledge about medical interventions specific to the battlefield.	7					0.636
	14					0.705
	23					0.666
Total explained variance ratio=64.543						
Kaiser Meier Olkin=0.861						
Bartlett test result=1,973.440; p<0.001						
Croncbach's alpha (α)=0.808						
TAMKA: Tactical medicine knowledge and awareness scale						

Table 4. Statistical values regarding the fit of structural equation model

Measurement	Good fit	Acceptable fit	Fit index values of the model
(x^2/ standard deviation)	≤3	≤4-5	1,194**
RMSEA	≤0.05	0.06-0.08	0.039**
IFI	≥0.95	0.94-0.90	0.974**
CFI	≥0.97	≥0.95	0.973**
GFI	≥0.90	0.89-0.85	0.858*
TLI	≥0.95	0.94-0.90	0.968**

*Acceptable fit, **Good fit
RMSEA: root mean square error of approximation, IFI: incremental fit index, CFI: comparative fit index, GFI: goodness-of-fit index, TLI: Tucker-Lewis index

Goodness-of-Fit Index

This index measures the model's overall fit. A higher goodness-of-fit index (GFI) value indicates that the model fits the data better. The GFI value should generally be 0.90 or higher. A GFI value of 0.90 or higher shows an acceptable fit.

Tucker-Lewis Index

This index measures the fit of the model and is adjusted for sample size. The closer the value is to 1, the better the model fits the data. The Tucker-Lewis index (TLI) value should generally be 0.95 or higher. A TLI value indicates an excellent fit.

DISCUSSION

Validity and Reliability

Before a measurement tool can be approved for use, it is essential to assess its validity and reliability. Validity refers to the tool's ability to accurately measure the specific subject or field it is designed for, without overlapping with other areas. To ensure construct validity, the factor analysis method should be applied. Construct validity indicates the extent to which the symptoms are measured accurately. For a sample size to be considered adequate, the KMO value prior to factor analysis must exceed 0.50. Values in the range of 0.60-0.69 are deemed acceptable. Furthermore, Bartlett's test

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of sphericity must yield statistically significant results to confirm sample adequacy (17-19). In this study, the KMO test result was 0.861, and Bartlett's test of sphericity yielded a value of 1,973.440. The results were statistically significant ($p<0.05$), indicating that the sample was sufficient for conducting factor analysis.

The literature suggests that items with factor loadings below 0.30 should be excluded from the scale (20). Since all items in this study had factor loadings greater than 0.20, no items were removed. Reliability, which is closely linked to validity, evaluates whether the measurement tool provides consistent results (21). To determine the relationship between the measurement tool and the whole, a reliability coefficient is calculated (22-27). Higher item-total score correlations indicate that the items measure similar characteristics, enhancing internal consistency (27). Consequently, items with strong correlations are considered effective for the intended measurement (20). Typically, items with an item-total score correlation of 0.30 or higher are regarded as having good discriminatory power (28).

For scale validity and reliability, item-total score analysis is a key method (27). One of the reliability measures, the split-half reliability test, assesses the consistency of test scores by splitting the items into two groups (odd-even, first-half-second-half, or neutral) and calculating a reliability coefficient using the Spearman-Brown formula (24-26). This method evaluates the consistency between the scores of the two halves. Adequate reliability coefficients, such as Spearman-Brown, Guttman split-half, and Cronbach's α, are utilized for these calculations. Cronbach's α is specifically recommended for Likert-type scales, as it measures the internal consistency of the items (27). For a tool to be deemed reliable, its reliability coefficient should approach one. A Cronbach's α below 0.40 indicates unreliability, values between 0.40-0.59 indicate low reliability, 0.60-0.79 indicate high reliability, and 0.80-1.00 indicate very high reliability (21). In this study, Cronbach's α was calculated to evaluate internal consistency, and found to be 0.808, demonstrating that the scale's internal consistency was highly reliable.

The research findings reveal that the TAMKA tool met the requirements for validity and reliability. The explanatory factor analysis results indicated adequate sample distribution based on the KMO test. The factor loadings for the scale items, organized into five sub-dimensions, ranged from 0.435 to 0.905. While the variance ratios were satisfactory, Cronbach's α was above 0.70. These results confirm that TAMKA is a reliable measurement tool.

Based on CFA, the model fit indices revealed that the TAMKA exhibited acceptable goodness of fit according to the first-order CFA structural equation model. All items significantly contributed to the model.

The 1st order CFA structural equation model further demonstrated that TAMKA's sub-dimensions positively influenced the total knowledge and awareness score. Consequently, TAMKA was validated and found reliable for use among young individuals undergoing EM Specialty training. The tool comprises 25 questions grouped into five factors: factor 1 (level of knowledge about general medical practices) includes questions 6, 8, 9, 10, 11, 12, 13, and 15; Factor 2 (level of educational awareness) includes questions 1, 16, 17, 18, 19, 20, and 21; Factor 3 (level of knowledge about general interventions on the battlefield) includes questions 2, 3, 4, and 5; Factor 4 (level of awareness about the importance of tactical medicine) includes questions 22, 24, and 25; And factor 5 (level of knowledge about medical intervention specific to the battlefield) includes questions 7, 14, and 23 (Figure 1).

Despite the promising results regarding the scale's validity and reliability, certain limitations warrant consideration. The single-center design and relatively small sample size may restrict the generalizability of the findings. Future multi-center studies with larger cohorts are essential to validate the scale in diverse

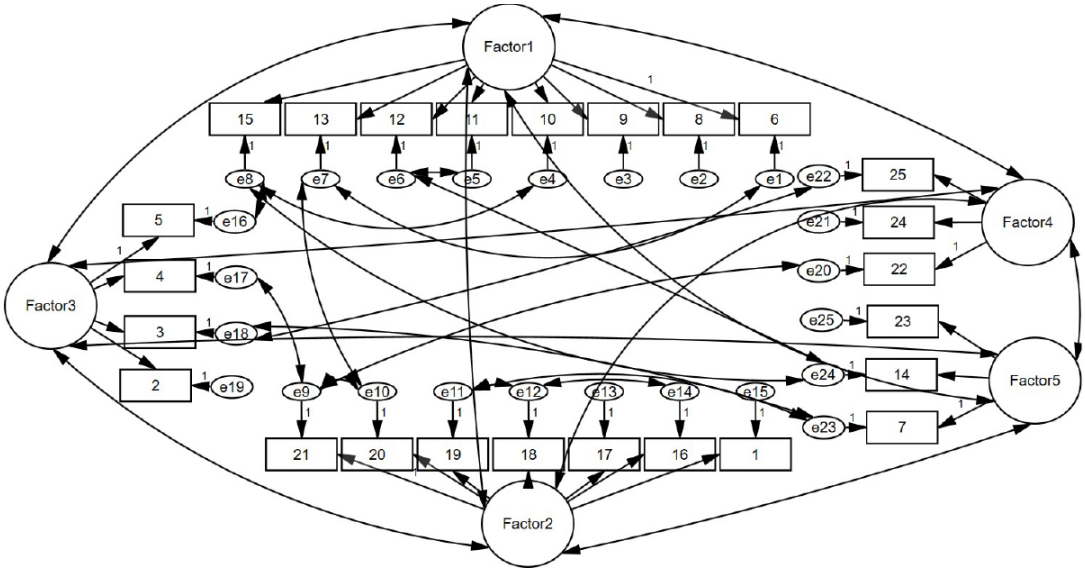

Figure 1. Confirmatory factor analysis scheme

settings. Additionally, while CFA demonstrated a good model fit, comparative evaluations with alternative models could provide further insights into the scale's structure. Some items showed lower factor loadings, highlighting the need for ongoing refinement to enhance construct validity. Furthermore, the absence of discriminant and convergent validity testing represents a limitation that future research should address to solidify the scale's psychometric properties.

Application of the Survey

The "conventional warfare" era, in which the wars typically took place between regular armies and civilian involvement was collateral, was replaced by the "unconventional warfare" era in the 21st century, where the conflicts often involved civilians and non-state actors (29). Battle-related deaths have increased in recent years, with a calculated number of 225,000 people dying in 2022 (30). The current situation has led to a re-evaluation of the traditional view of tactical medicine (6,7,29), and TEMS has become a field of expected demand and growth (4). While EM specialists may be familiar with algorithms and procedures included in tactical EM, there are fundamental differences between emergency care and TEMS (1,6). While it is not a requirement mandated by the Accreditation Council for Graduate Medical Education, Petit et al. (10) showed that EM residencies in the USA, including tactical medicine training in their curriculum, have grown from 18% to 53% between 2005 and 2018. As is true across the globe, there is no formal training on tactical medicine in the curricula of the faculty of medicine and EM residency training in Türkiye (8,9).

A literature review showed that no standard questionnaire evaluates the level of knowledge and awareness of EM physicians in the tactical medicine field. Our study concluded that 25 of the 55 questions defined by the researchers according to the literature review were appropriate for the TAMKA tool.

It was observed that EM physicians did not feel competent in the essential tactical medicine components such as the meaning and scope of tactical medicine; The necessary equipment and algorithms; Recognition of hemorrhage, tourniquet application, and hypothermia management; Nasopharyngeal airway, surgical cricothyroidotomy, and needle decompression; Burns and wound care; And pain control. Heiskell and Carmona (3) reminded us that EM specialists and surgeons typically see and treat blunt trauma in the civilian setting and may not be experts on managing multiple blast injuries and penetrating trauma. Like any other specialist, an EM physician who did not receive tactical medical education may need to improve their competence. Today, specific guidelines and courses are available for tactical medicine, reminding us that tactical medicine is not equal to "trauma medicine" (31).

In our study, participants did not think the EM residency training should be unique, in including tactical medicine education. Indeed, tactical medicine is a multidisciplinary field and may need the expertise of several specialties including trauma surgery, cardiothoracic surgery, EM, critical care, operational medicine, and medical education (1,6,7).

Including physicians in tactical teams seems to be an increasing trend (1). Gildea and Janssen (32) survey showed that the rate of tactical teams with a physician on the team increased from 9% to 48% in ten years, and 97% of the participants felt physician involvement was beneficial.

It is challenging to conduct studies on tactical medicine due to the inherent difficulties in the tactical field (6). Gerhardt (7) demonstrated a 44% increase in survival rates (odds ratio 0.56; 95% confidence interval, 0.37-0.86; $p<0.01$) by including EM providers in tactical care. EM associations see TEMS as an essential component of tactical teams and encourage TEMS programs to include EM presence (5). Our study observed that EM physicians believe that medical schools and EM residency programs should include theoretical and practical education in the tactical medicine field. Physicians trained in tactical medicine will improve the results in the tactical field.

Since the questionnaire is short, it is likely functional in terms of being usable in emergency departments and situations requiring rapid intervention. The validity and reliability study with EM physicians should be conducted on different groups and tested with different variables.

Study Limitations

This study's main limitations include its single-center design, relatively small sample size, and cross-sectional nature, which may limit generalizability and preclude assessment of changes over time. Additionally, reliance on expert opinions for content validity may introduce subjective bias. Multi-center and longitudinal studies are recommended for further validation to enhance the scale's applicability in different settings.

Although the CFA demonstrated excellent fit indices (RMSEA, CFI, IFI), the model's robustness would benefit from further evaluation by comparing it with alternative models. Such comparative analyses would provide deeper insights into the factor structure and overall validity of the scale.

CONCLUSION

The changing paradigms of war and conflicts require that all physicians, and especially the EM specialists, gain more knowledge in the tactical medicine field. This new scale, TAMKA, proved to be a reliable measurement tool, for determining the level of knowledge and awareness of EM physicians in tactical medicine. We believe that TEMS should be included in the curricula of medical school and EM residency programs.

Ethics

Ethics Committee Approval: This cross-sectional study was conducted between January 1, 2024 and April 1, 2024, after approval from the İzmir Katip Çelebi University Social Research Ethics Committee (decision no: 2023/21-07, date: 20.12.2023).

Informed Consent: Written informed consent was obtained from all participants before participation in the study.

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Footnotes

Author Contributions: Concept - İ.S., M.G.E., M.A.T.; Design - İ.S., E.K., M.G.E., M.A.T.; Z.P; Data Collection and/or Processing - İ.S., E.K., M.G.E., El.K., Z.Ö.; C.K.; Analysis and/or Interpretation - M.G.E., El.K., Z.Ö., M.A.T.; Literature Search - E.K., M.G.E.; C.K.; Writing - İ.S., E.K., M.G.E., M.A.T.

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Objective Evaluation of Auditory Function of Axolotls Pre- and Post-metamorphosis and its Comparison with Rats

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ABSTRACT

Objective: Axolotls possess remarkable regenerative capabilities, including the ability to regenerate the brain, spinal cord, internal organs, lateral line system cells, and inner ear hair cells. However, following metamorphosis, their regenerative capacity diminishes, accompanied by changes in auditory function. This study aimed to objectively assess these changes to enhance understanding of the relationship between metamorphosis, regeneration, and auditory function, with potential implications for regenerative biology and auditory research. Additionally, 3-month-old rats were included as a comparative model for evaluating auditory function.

Methods: Auditory function in axolotls (maximum length: 20 cm) and 3-month-old rats was evaluated using auditory brainstem response (ABR) testing. ABR measurements were conducted on axolotls both pre- and post-metamorphosis using tone burst stimuli at 250 Hz, 500 Hz, 600 Hz, and 800 Hz. In rats, measurements were taken at 8, 12, 16, and 20 kHz frequencies.

Results: ABR recordings in axolotls pre- and post-metamorphosis revealed that 600 Hz produced the most consistent wave morphology. Wave II latencies were significantly longer before metamorphosis compared to after metamorphosis, indicating alterations in auditory processing. In contrast, 3-month-old rats exhibited stable auditory thresholds across all tested frequencies, demonstrating consistent auditory function.

Conclusion: This study presents the first successful application of ABR methodology for evaluating auditory function in axolotls, providing a comparative analysis with auditory function in 3-month-old rats. Significant changes in auditory function were observed in axolotls following metamorphosis, indicating a decline in auditory capabilities concurrent with the reduction in regenerative capacity. These findings underscore the feasibility of using ABR testing in axolotls and highlight important implications for auditory function research across different species.

Keywords: Ambystoma mexicanum, axolotl hearing, regeneration, rat hearing, animal experimentation

INTRODUCTION

Rats have become a fundamental model in auditory research due to their anatomical and physiological similarities to the human auditory system, as well as their suitability for behavioral and electrophysiological studies. As the second most commonly used laboratory animal after mice, rats have proven essential in understanding auditory processing, hearing loss mechanisms, and neuroplasticity within the auditory pathway (1,2). Their ability to perform complex auditory tasks and adapt to both naturalistic and controlled experimental settings makes them invaluable for investigating sensory processing and auditory cognition (3). The application of advanced imaging techniques, such as functional magnetic resonance imaging and auditory brainstem response (ABR) measurements, has further expanded insights into rat auditory function, enabling researchers to study neural activity patterns linked to auditory perception and disorders (4-6). These approaches have provided significant contributions to our understanding of auditory networks and their relevance to human hearing and auditory-related diseases (5,6).

The use of rats in hearing research has also been instrumental in the development of therapeutic strategies for hearing loss and auditory neuropathies, especially in exploring treatments for noise-induced hearing loss, age-related hearing decline, and ototoxicity (7). The larger brain and auditory structures of rats, compared to those of mice, offer enhanced precision for surgical and imaging techniques, facilitating a more comprehensive investigation of auditory anatomy and neural pathways (8).

In some invertebrates, such as sponges and cephalopods, the potential for regeneration is markedly higher, but it decreases progressively from fish to mammals (9,10). In most mammals, however, the hair cells responsible for hearing, located in the inner ear, have lost their ability to regenerate, resulting in

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permanent hearing loss and disturbances of balance. In contrast, certain organisms, such as the axolotl and the zebrafish, retain the ability to regenerate hair cells throughout their lives (11-14). While mammalian regeneration typically remains at the tissue level, salamanders are more remarkable because they have the ability to regenerate entire organs, a feature that distinguishes them from other amphibians. Salamanders are of great interest in regenerative biology because they can regenerate amputated or severely damaged organs (15).

Among salamanders, Ambystoma mexicanum (commonly known as the axolotl), a species within the family Ambystomatidae, has received considerable attention from regenerative researchers. Studies show that axolotls are able to regenerate not only their amputated limbs, but also their hearts, brains, spinal cords, and several other internal organs (9). Studies in axolotls often focus on the regeneration of the tail. This is because the tail contains a range of tissues, muscle, connective tissue, and nerves, making it an ideal model for studying regeneration.

The axolotl begins to grow limb buds, which later elongate and differentiate into fully functional limbs, after the development of their external gills. As these developmental changes occur, axolotls typically reach a length of 20-28 cm (16). Although the regenerative capacity of axolotls is well known, to our knowledge very few studies have assessed axolotl auditory function in relation to their regenerative capacity. The present study therefore represents the first objective documentation of the auditory function of the salamander.

The tissue impedance of axolotls is higher than that of air. Therefore, a significant amount of incoming sound energy is reflected, especially when axolotls emerge from water post-metamorphosis. This challenge is met by the development of a tympanic middle ear, which transforms sound pressure in the air into particle motion in the inner ear fluid. In addition, the post-metamorphic middle ear contains an operculum. The opercularis muscle connecting scapulae and operculum was easily recognized in iodine-stained specimens of tiger salamanders and adult axolotls, but could not be found in the juvenile axolotls (17). Additionally, the urodele middle ear also contains the operculum, which is connected to the scapula of the shoulder girdle through the opercularis muscle and has been proposed to aid the transmission of substrate vibrations into the inner ear via the forelegs, plays a role in airborne hearing by bone conduction, or functions as a protective mechanism against loud sound exposures (18).

Bullock (19) first introduced non-invasive ABR recordings in fish. The ABR technique has since become widely used in auditory research. It has been applied to several vertebrate species, including fish and amphibians. ABR testing is particularly suitable for developmental studies in fish and salamanders due to its non-invasive nature and the lack of need for animal training (20).

Comparative studies of amphibian auditory systems can provide valuable insights into how terrestrial hearing evolved and how neural models have adapted to the selective pressures associated with communication. A key model for understanding vertebrate hearing (21) is the amphibian auditory system. The regeneration of hair cells that has been observed in amphibians, such as the axolotl, holds great promise for the development of therapeutic strategies aimed at restoring hearing health in humans.

METHODS

This study is an experimental research of auditory function in axolotls, before and after metamorphosis, and compares it with rats using electrophysiological measurements through ABR testing. A total of 10 3-month-old rats were obtained from the Medical Research Centre of the University of Medipol. For auditory evaluations, rats were anesthetized with ketamine (40 mg/kg, i.p.) and xylazine (Rompun, 10 mg/kg, i.p.). If needed, additional doses of ketamine (20 mg/kg, i.p.) and xylazine (5 mg/kg, i.p.) were administered to maintain anesthesia.

In the ABR test for rats, during the recordings, the active electrode was placed subcutaneously at the midline of the skull, the reference electrode beneath the pinna on the side where the hearing threshold was being determined, and the ground electrode under the contralateral pinna. The needle electrodes used (Ambu, Malaysia) were 0.40 mm in diameter and 12 mm in length. Testing began when electrode impedances were between 0 and 3 kΩ. Stimulus presentation and recordings were performed using an intelligent hearing systems (Miami, FL, USA) device, which was calibrated according to American National Standards Institute standards prior to the experiments. The stimuli used were 4 ms (rise time: 2 ms, plateau: 0 ms, fall time: 2 ms) tone bursts. The tone burst stimuli were presented at 8, 12, 16, and 20 kHz, using a Blackman envelope. The stimuli were delivered via high-frequency earphones designed for animal use. In all tests, a neonatal probe was used. The stimulus presentation rate was set at 19.3 stimuli per second, and 750 waveforms were averaged after amplification. A band-pass filter between 100 and 3,000 Hz was applied to the recordings, and the recording window was set to a total of 14 ms. At the end of the experiments, euthanasia was performed using a high-dose anesthesia protocol.

The axolotl specimens were obtained from the Medical Research Centre of the University of Medipol. In the present study, three axolotls were used for the recordings pre- and post-metamorphosis. We observed morphological and histological changes that are consistent with thyroid hormone-induced metamorphosis. The axolotls were given thyroid hormones and their metamorphoses were induced regardless of limb regeneration. The first Stage 1 animal was observed at day 8, and individuals completed metamorphosis (Stage 4) between day 28 and day 32 (22). The animals were housed in 5-liter containers. Their maximum length was recorded at 20 cm. Electrophysiological assessments were performed using ABR testing. This technique is widely used in humans and other animal models. Prior to testing, the axolotls were anaesthetized with a 0.025% benzocaine solution. Once anaesthetized, they were transferred to a test chamber. The test chamber was designed to minimize environmental and electromagnetic noise.

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During the test, the axolotls were placed on a hollow platform, and a wet towel was placed above and below them to maintain their viability before metamorphosis and facilitate skin respiration. The towels were re-moistened with fresh water every two minutes during the experiment to maintain optimal conditions for skin respiration, ensuring that the axolotls remained viable throughout the procedure. Electrophysiological responses were recorded using three stainless steel subdermal needle electrodes placed on the vertex (-), the ipsilateral mastoid (+), and the forehead (ground) (Figure 1). The ground electrode was placed on the animal's tail, the reference electrode on the nose tip, and the recording electrode on the forehead. The impedance values were measured between 0 and 1 kΩ but never reached 0 kΩ.

Responses were recorded using the Intelligent Hearing System with a gain of 100,000, a band-pass filter set between 100 and 3000 Hz, and a sweep count of 500. The rate was 11.1 Hz with an analysis time of 12 ms. Two trials were performed for each intensity level. An average response was calculated based on 1000 sweeps. Auditory stimuli consisted of tone bursts delivered through a bone vibrator at frequencies of 250 Hz, 320 Hz, 500 Hz, 600 Hz, 800 Hz, and 1000 Hz. In the earlier studies, the hearing was generally evaluated at low frequencies (17,23). The stimuli were monaural tone bursts with alternating onset phases and 4-8-4 ms rise-plateau-fall times. The Blackman envelope was used. The frequencies tested in axolotls and rats were selected based on their known auditory sensitivities and biological differences in hearing mechanisms. Axolotls are primarily sensitive to low-frequency sounds, as their hearing relies on bone conduction and particle motion detection rather than airborne sound waves. In contrast, rats have a well-established auditory range that extends into the high-frequency spectrum, typically between 1 kHz and 40 kHz, with most auditory studies focusing on mid-to-high frequencies (8 kHz-20 kHz), due to their natural sensitivity in these ranges. Therefore, the chosen frequencies for each species align with their natural auditory capabilities, ensuring a more accurate evaluation of their hearing function. The level of the stimulus was reduced step by step until the threshold was found. The axolotls were humanely euthanized with a highly concentrated benzocaine solution at the end of the experiments.

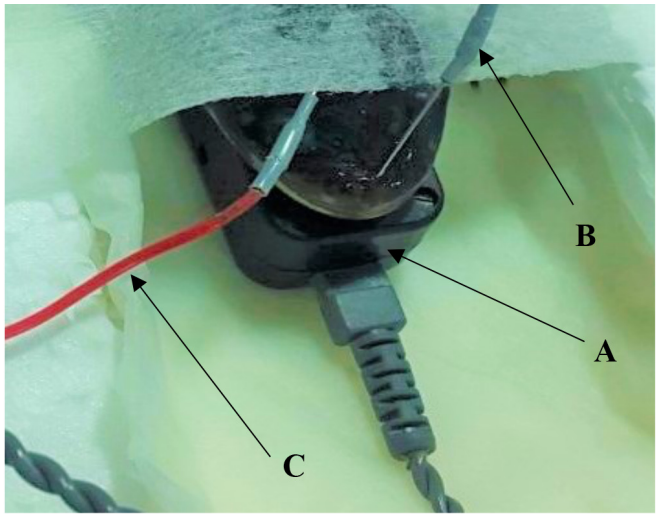

Figure 1. The experiment setup
A: Bone vibrator, B: Positive electrode, C: Negative electrode

For the first time, a bone vibrator (Radio Ear B71) was used as a transducer for an electrophysiological test system in axolotls in this study. The bone vibrator was carefully calibrated and positioned on the jaw bone of the axolotls to ensure that the same pressure was applied during all the recordings. To obtain reliable ABRs, it was essential to maintain constant pressure on the bone vibrator. To ensure this, a belt-like system was created and in each test the belt-like system was tightened the same amount. As the axolotls were all about the same size, the pressure applied to the test objects was consistent. The stimulus intensity was decreased in 5 dB SPL steps until the lowest detectable sound pressure level was reached. At this point, the auditory waveform became undetectable.

The difference in the methods of conduction used for the rats and the axolotls was because axolotls do not have conventional ears where classic transducers can be used for testing. To combat this, we had to use bone conduction. Because we wanted to compare the results of rats and axolotls, we aimed to standardize the results. We used air conduction for the rats as it is the accepted way of testing for these animals. The reason for this comparison is that we are familiar with the results of rats. We wanted to get an idea of the results of axolotls similarly by comparing the threshold morphologies.

Statistical Analysis

Due to the limited number of axolotl specimens used in this study, direct statistical comparisons between pre- and post-metamorphosis conditions could not be performed. Additionally, the different ABR testing methodologies used for rats prevented a direct comparison between rats and axolotls. As a result, only descriptive statistical analyses were conducted, including the calculation of mean and standard deviation for ABR thresholds and latencies. No formal inferential statistical tests, such as t-tests or one-way ANOVA, were employed in this study.

Informed Consent

This study did not involve human participants; therefore, informed consent was not required.

Ethical Statements

Approval for this study was obtained from the İstanbul Medipol University Animal Experiments Local Ethics Committee (decision no: 17, date: 10.02.2025).

RESULTS

All data presented in this study were collected using the Smart EPdevice from Intelligent Hearing Systems. In the auditory evaluations conducted on rats, ABR testing yielded distinct and reliable waveforms across all tested frequencies, thus demonstrating the efficacy of this methodology. The auditory

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thresholds for each frequency were determined, and clear ABR waveforms were recorded in response to tone bursts at 8, 12, 16, and 20 kHz. The lowest sound pressure level (dB SPL) at which a recognizable ABR waveform could be identified was defined as the threshold. Figure 2 illustrates a representative ABR waveform for one of the frequencies, while Table 1 presents the threshold values for each frequency. Additionally, Figure 3 illustrates the comparison of ABR thresholds between the right and left ears across the tested frequency spectrum. These results provide a baseline understanding of auditory function in rats, facilitating a comparative analysis with other species. The observed waveforms were consistent and demonstrated typical auditory processing patterns across the frequency spectrum.

The use of a bone vibrator for evoked ABR testing in axolotls is the first of its kind in the literature. As a result, we have been able to test this novel technique in this rare species. Recognizable responses were obtained for all of the stimulus frequencies that were tested. Among the bursts used, the 600 Hz burst elicited the best waveform morphology (Figure 4).

The thresholds for the 600 Hz tone bursts pre- and post-metamorphosis were 55 dB SPL and 58 dB SPL, respectively. These thresholds are indicated by an asterisk (Figures 3,4). To ensure consistency of the waveforms, multiple traces were recorded. The mean hearing threshold for the axolotl was found to be 55 dB SPL. One of the most critical findings was the longer ABR latencies recorded pre-metamorphosis, averaging 1.5 ms, compared to post-metamorphosis (Figure 4).

Figure 5 shows the effect of decreasing stimulus intensity (from 70 to 40 dB SPL). As intensity decreases, wave amplitudes decrease and wave latencies increase. In this recording, the threshold of hearing at 250 Hz was found to be 50 dB SPL. The neurogenic characteristics of the auditory responses are reflected in these results. Another significant finding is that the prolongation of wave latencies, compared to humans and rats, is less pronounced in axolotls. Figures 6 and 7 show the objective ABR thresholds.

Figure 2. Comparison of ABR thresholds between the right and left ears in rats across different frequencies (8, 12, 16, and 20 kHz)
ABR: Auditory brainstem response

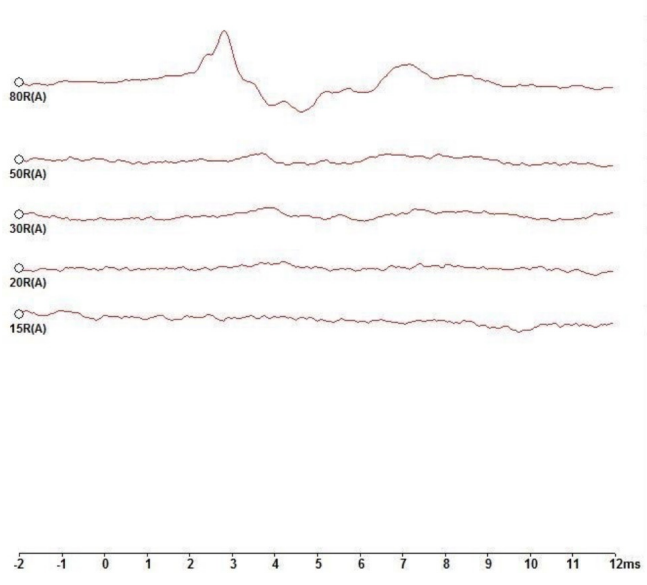

Figure 3. Representative ABR waveform in a rat at 8 kHz. The waveform shows the distinct peaks used to determine the hearing threshold. The threshold is marked with an asterisk
ABR: Auditory brainstem response

Table 1. ABR thresholds (dB SPL) for each frequency tested in rats. The table summarizes the minimum sound pressure levels at which ABR waveforms were identifiable

	Mean	Standard deviation	Minimum	Maximum
8 kHz Left	21.0	±5.67	10	25
12 kHz Left	17.0	±4.21	10	25
16 kHz Left	21.5	±3.37	15	25
20 kHz Left	5.5	±6.43	0	20
8 kHz Right	20.5	±3,68	15	25
12 kHz Right	15.5	±2.83	10	20
16 kHz Right	22.0	±2.58	20	25
20 kHz Right	5.5	±4.97	0	15

ABR: Auditory brainstem response

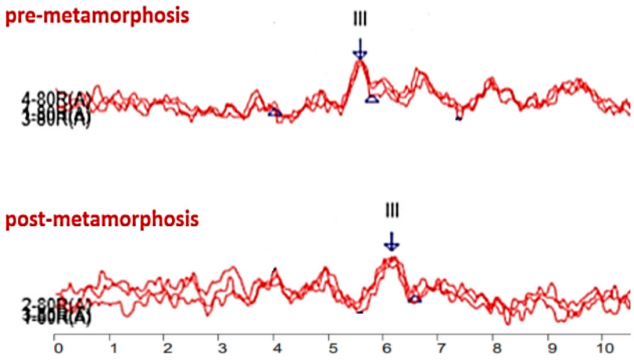

Figure 4. ABR result made at a frequency of 600 Hz. Recordings were performed for 3 times to prove the reliability of the ABR waveforms
ABR: Auditory brainstem response

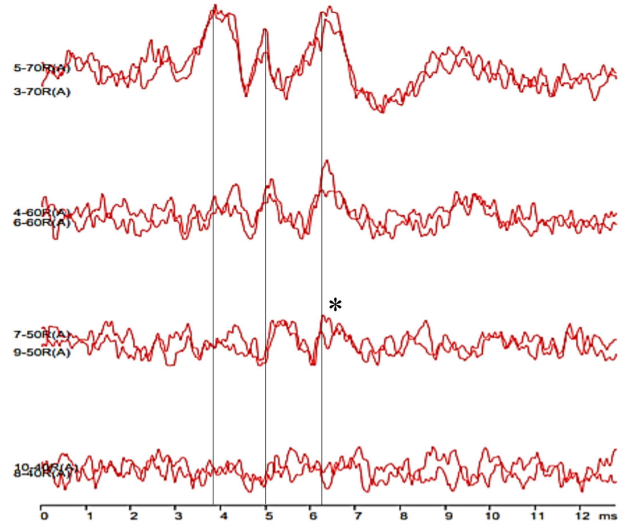

Figure 5. ABR waveforms recorded at a frequency of 250 Hz of Axolotl post-metamorphosis. The threshold is marked with an asterisk
ABR: Auditory brainstem response

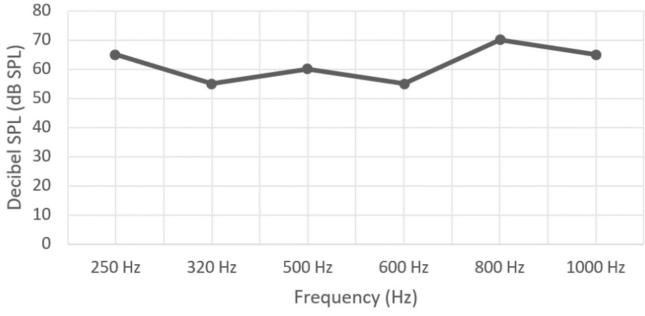

Figure 6. Estimated objective thresholds of an Axolotl pre-metamorphosis

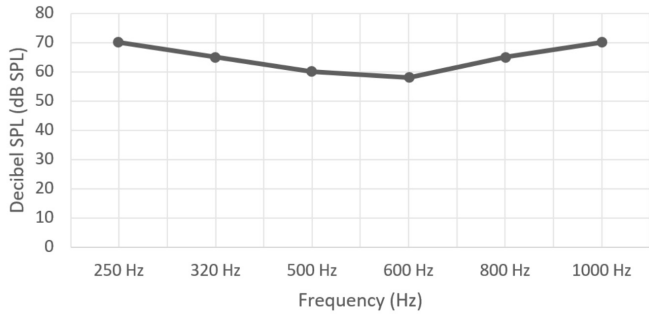

Figure 7. Estimated objective thresholds of an Axolotl post-metamorphosis

DISCUSSION

The primary aim of this study was to investigate the effects of metamorphosis on the auditory system in axolotls. Auditory evoked potentials (AEPs) were used to assess the animals' ability to perceive vibrating sounds. Metamorphosis induces several changes in the axolotl body. One of the systems that undergoes changes is the auditory system. For example, the columella auris is free pre-metamorphosis. Post-metamorphosis, it fuses with the otic capsule (17).

Pre-metamorphosis, the latencies of AEPs were longer than those recorded post-metamorphosis. While the precise mechanisms underlying this observation remain unclear, it is likely that both anatomical and physiological changes during metamorphosis contribute to this shift. One hypothesis is that the fusion of the columella auris with the otic capsule post-metamorphosis may alter the conduction pathway for sound waves, leading to changes in latency and threshold values. Additionally, the development of the tympanic middle ear could introduce structural changes that modify how sound pressure is transformed into particle motion within the inner ear fluid.

At the cellular level, metamorphosis could impact the density and arrangement of hair cells within the inner ear, potentially influencing how auditory signals are transmitted to the brainstem. Research on other amphibians and vertebrates has shown that changes in the mechanical properties of auditory structures, such as the ossicles or tympanic membrane, can affect auditory sensitivity and latency. Further histological and molecular studies on the inner ear structures pre- and post-metamorphosis would be necessary to identify the specific alterations driving these functional changes in axolotls.

Furthermore, the amplitudes were higher post-metamorphosis. However, the amplitude might be partly dependent on the pressure exerted on the animal by the bone vibrator. Metamorphosis is a process of many changes in AER characteristics would be expected. Factors such as cranial bone density, tissue density and skin permeability may all have an effect.

Following metamorphosis, sound has more difficulty reaching the inner ear because of the increased impedance mismatch between air and body skin. The delay in auditory evoked responses

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observed post-metamorphosis (16) may be partly explained by this. However, more detailed research is needed in this field.

This study has successfully demonstrated the feasibility of conducting objective auditory testing in axolotls using ABR testing for the first time in this species, employing a bone vibrator as a transducer. The findings show that metamorphosis induces significant changes in the axolotl auditory system, as evidenced by increased ABR thresholds and altered latencies. Specifically, the longer latencies observed pre-metamorphosis suggest fundamental physiological changes that affect auditory processing post-metamorphosis. These results indicate that metamorphosis leads to increased impedance and modifications to the middle ear structure, contributing to changes in sound transmission.

The successful use of a bone vibrator to measure auditory responses in axolotls is a noteworthy outcome of this study, providing a reliable method for assessing auditory function in amphibians. Additionally, the identification of 600 Hz as the most effective frequency for ABR recordings both pre- and post-metamorphosis further solidifies this technique's potential utility in future research on auditory systems in regenerating species.

The findings from this study offer promising insights not only for amphibian auditory research but also for broader applications in regenerative medicine and auditory system repair. Axolotls' ability to regenerate inner ear structures pre-metamorphosis provides a unique opportunity to explore the molecular and cellular processes underlying hair cell regeneration, which could inform future strategies for hearing restoration in humans. In mammals, the loss of regenerative capacity in hair cells leads to irreversible hearing loss. Understanding the factors that enable axolotls to regenerate these cells and identifying what changes occur during metamorphosis that halt this process could yield critical knowledge applicable to therapeutic interventions. Furthermore, the use of a bone vibrator for ABR testing establishes a non-invasive method that could be applied to other regenerative models or even species that undergo auditory changes as part of their development.

In addition to the findings from axolotls, the auditory tests conducted on rats yielded consistent ABR waveforms across the tested frequencies (8, 12, 16, and 20 kHz). The determined thresholds reflect stable auditory processing in rats, offering a useful point of comparison with the auditory responses of axolotls. While axolotls exhibited alterations in auditory function subsequent to metamorphosis, the rats exhibited consistent auditory thresholds across frequencies, thereby establishing them as a reliable model for baseline auditory function. This contrast serves to underscore the potential for comparative studies to elucidate species-specific auditory mechanisms.

Future studies could investigate how regenerative capacity varies across different developmental stages and how auditory function is restored post-injury, potentially leading to breakthroughs in treating auditory damage caused by trauma or age-related degeneration.

Study Limitations

This study has several limitations. First, the small sample size of three axolotls may restrict the generalizability of the findings. Additionally, the absence of molecular or histological analyses limits the understanding of the cellular mechanisms underlying the changes in auditory function observed pre- and post-metamorphosis. Lastly, variability in bone vibrator pressure could have influenced the amplitude of ABR measurements, suggesting a need for further investigation to ensure consistent pressure application across developmental stages and different specimens.

CONCLUSION

This study is the first to apply ABR testing with a bone vibrator in axolotls, evaluating auditory function before and after metamorphosis. Although different frequencies and conduction methods were used for axolotls and rats due to species-specific differences, a comparison was necessary to interpret and set a base point for the axolotl data. Aware of this limitation, we selected rats and air-conduction ABR-one of the most widely accepted methods in hearing research-as a scientific reference point. This approach enabled a meaningful comparison and revealed significant changes in axolotl auditory thresholds and latencies following metamorphosis. These findings support the feasibility of objective auditory testing in axolotls and highlight their potential as a model in auditory and regenerative research.

Ethics

Ethics Committee Approval: This study was approved by the Istanbul Medipol University Animal Experiments Local Ethics Committee (decision no: 17, date: 10.02.2025).

Informed Consent: This study did not involve human participants; therefore, informed consent was not required.

Footnotes

Author Contributions: Surgical and Medical Practices - F.B.; Concept - F.B.; Design - F.B., M.B.Ş; Data Collection and/or Processing – F.B.; Analysis and/or Interpretation- F.B., Ş.T.Ö., M.B.Ş; Literature Search - F.B., Ş.T.Ö; Writing - F.B., Ş.T.Ö.

Conflict of Interest: The authors have no conflict of interest to declare.

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Comparison of Outcomes of Total Extraperitoneal Repair and Transabdominal Preperitoneal Approach in Inguinal Hernia Surgery

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ABSTRACT

Objective: This study compares the outcomes of transabdominal preperitoneal (TAPP) and totally extraperitoneal (TEP) techniques in inguinal hernia repair, focusing on the relationship between the number of tacks used for mesh fixation and the incidence of chronic postoperative pain. Despite advancements in minimally invasive surgery, chronic pain remains a significant complication.

Methods: This retrospective study analyzes retrospectively collected data from patients who underwent elective laparoscopic inguinal hernia repair (TEP or TAPP) between 2019 and 2023. It compares early and late postoperative complications, examining the relationship between the number of tacks used for mesh fixation and chronic pain or recurrence.

Results: This study includes 164 patients who underwent TEP (n=117) or TAPP (n=47) for inguinal hernia repair. No significant differencec in chronic pain and recurrence rates between the groups were detected. TAPP patients had larger hernias (p=0.024), had more frequent recurrent operations (p=0.042), and higher seroma rates (p=0.003). Operative times and tack numbers were greater in TAPP (p=0.086, p<0.001). American Society of Anesthesiologists class 3, presence of recurrence, and early hematoma were associated with recurrence. Chronic pain correlated with the number of tacks used for mesh fixation (p=0.001) but not with seroma or hematoma (p=0.313, p=0.578). Recurrence rates were similar between groups (p=0.228). The number of tacks used was identified as an independent risk factor for chronic pain in the multivariate analysis (p=0.001, odds ratio: 5,103, %95 confidence intervals: 2,093-12,446).

Conclusion: Comparisons between TEP and TAPP techniques have shown similar outcomes in terms of intraoperative and postoperative complications. Reducing the number of mechanical fixations may help decrease the incidence of chronic pain.

Keywords: Minimal invasive surgery, inguinal hernia, totally extraperitoneal, transabdominal preperitoneal

INTRODUCTION

In recent years, the role of minimally invasive surgery (MIS) in the treatment of inguinal hernia has significantly expanded. Among these, transabdominal preperitoneal (TAPP) and totally extraperitoneal (TEP) techniques are the most employed minimally invasive approaches in inguinal hernia repair. In high-resource countries, the rates of TAPP and TEP procedures have significantly increased. According to the German Herniamed registry, TAPP and TEP account for 64% of inguinal hernia surgeries (1). In the TAPP technique, hernia repair is performed with a wider field of view by accessing the preperitoneal space through entry into the abdominal cavity; however, this approach carries a higher risk of intra-abdominal organ injury. In contrast, the TEP technique reaches the preperitoneal space without entering the abdominal cavity, though with a more restricted field of view (2). The TEP technique requires a longer learning curve compared to TAPP; however, both methods are complex procedures that demand an extended learning curve (3). Advances in surgical techniques, a more comprehensive understanding of the myopectineal orifice anatomy, and the development of superior prosthetic materials have collectively enhanced the success of minimally invasive inguinal hernia surgery (4). It offers advantages such as reduced postoperative pain, earlier return to work, fewer wound site complications, and prevention of new hernia formation by covering the entire myopectineal orifice with mesh (5). With increased surgical experience and a more detailed understanding of the myopectineal orifice anatomy, recurrence rates in MIS for inguinal hernia have shown comparable outcomes to open surgery in recent studies (6). Despite these improvements, chronic postoperative pain remains the primary limitation of minimally invasive inguinal hernia surgery (7). Various studies have been conducted to mitigate this drawback associated with MIS (8,9).

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Postoperative chronic pain remains the most significant complication associated with MIS in hernia repair. While the incidence of chronic postoperative pain ranges from 0.75% to 75%, the incidence of chronic pain that impacts daily life is between 2% and 12%. This wide range is thought to be due to variations in the definition of chronic pain (9). Although its pathophysiology is not yet fully understood, various studies have investigated its risk factors. The aim of this study is to compare the outcomes of patients who underwent TEP or TAPP procedures, and to explore the relationship between the number of tacks used for mesh fixation and the incidence of chronic pain.

METHODS

This research was conducted in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to their inclusion in the study. Ethical approval was granted by the University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital Non-Interventional Ethics Committee (approval no: 67, date: 20.11.2024).

Data from patients who underwent laparoscopic inguinal hernia repair between 2019 and 2023 were retrospectively analyzed. The study included patients aged 18 to 80 years who underwent elective TEP or TAPP procedures for primary or recurrent groin hernias. Exclusion criteria included patients with incomplete preoperative data (e.g., missing demographic information, comorbid conditions, or hernia characteristics), those without at least one year of postoperative follow-up data, and those who underwent emergency surgery due to strangulation or bowel obstruction. Additionally, patients with previous pelvic surgery or pelvic radiation therapy that would affect the feasibility of laparoscopic repair were excluded. Furthermore, cases for which the surgical report did not specify the number and type of tacks used during the procedure were excluded from the analysis (Figure 1).

Patient characteristics, including hernia size, hernia side, history of recurrence, body mass index (BMI), and history of heavy sports or labor, were documented. Preoperative clinical and demographic characteristics, intraoperative complications, characteristics of the mesh and tacks used, and early (within the first 90 days) and late (after 90 days) postoperative complications were recorded through a review of hospital records. The HerniaSurge group defines postoperative chronic pain as moderate pain lasting longer than 3 months and impacting daily life. In our study, we also set 90 days as the threshold period to identify chronic complications and diagnosed chronic pain according to this definition (10). The patients were categorized into two groups according to the surgical technique performed: TEP and TAPP. Postoperative complications, both early and late, were evaluated and compared between these groups. For subgroup analysis, patients were categorized based on the development of chronic pain and recurrence to identify risk factors associated with these outcomes. Variables with a p-value <0.1 in univariate analysis were further assessed separately through multivariate analysis, for chronic pain and recurrence. The diagnosis of inguinal hernia was established through ultrasound and physical examination. The diagnoses of hematoma, seroma, recurrent, and ischemic orchitis were confirmed using ultrasound and Doppler imaging. All TAPP and TEP procedures were performed by surgeons experienced in MIS. General anesthesia was administered for all patients. A minimum 10 cm x 15 cm polypropylene mesh was used in each case. In cases where mesh fixation was performed, a variable number of absorbable tacks were used, ensuring that tacks were anchored at least 2 cm superior to the iliopubic tract. For TAPP procedures, the peritoneum was closed with absorbable barbed sutures. All patients underwent surgery using one 10 mm trocar and two 5 mm trocars, without routine use of a bladder catheter.

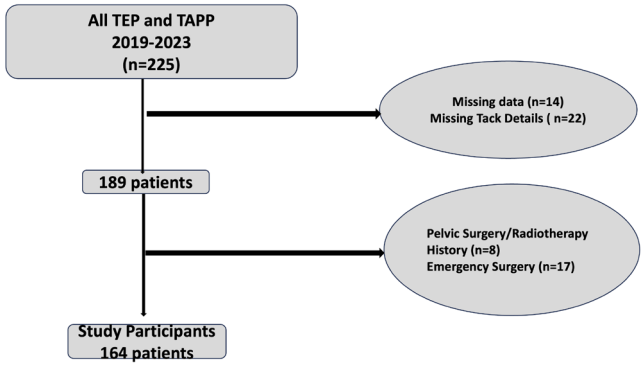

Figure 1. Flowchart for patient selection
TEP: Total extraperitoneal, TAPP: Transabdominal preperitonea

Statistical Analysis

Statistical analyses were performed using SPSS version 27.0. The assessment of data distribution normality was conducted via the Kolmogorov-Smirnov test. For normally distributed data, results were expressed as mean±standard deviation, while non-normally distributed data were reported as median and interquartile range. Independent group comparisons were carried out using the Student's t-test for normal distributions and the Mann-Whitney U test for non-normal distributions. Categorical variables were analyzed using the chi-square test or Fisher's exact test. Variables with a p-value <0.1 in univariate analysis were pre-selected for inclusion in the multivariate logistic regression model. Logistic regression was utilized to determine independent risk factors, and the odds ratio (OR) and 95% confidence intervals (CI) were calculated. Statistical significance was defined as a p-value <0.05. The goodness-of-fit of both logistic regression models was assessed using the Hosmer-Lemeshow test, which evaluates whether the observed event rates match expected event rates.

RESULTS

In this study, 164 consecutive patients who underwent TEP (n=117) and TAPP (n=47) for inguinal hernia were included. Of these, 18 (10.98%) were female, and 146 (89.02%) were male. A statistically significant higher number of patients in the TAPP group had hernias larger than 3 cm (p=0.024). Additionally, the TAPP group

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Table 1. Demographic and preoperative characteristics of patients

Variables		Group 1: TEP (n=117)	Group 2: TAPP (n=47)	p-value
Age (mean±SD)		49.91±13.10	49.34±13.11	0.803
BMI (median-IQR)		26.30-2.99	25.95-3.38	0.481
Height in cm (median-IQR)		78.00-11.00	77.00-7.00	0.861
Weight in kg (median-IQR)		170,00-6.00	170-8.00	0.282
Type of hernia	Indirect n,%	89 (76.10%)	33 (70.20%)	0.142
	Direct n,%	24 (20.50%)	11 (23.40%)	
	Femoral n,%	0 (0.00%)	2 (4.30%)	
	Combined n,%	4 (3.40%)	1 (2.10%)	
Hernia side	Right n,%	39 (33.30%)	23 (48.90%)	0.842
	Left n,%	29 (24.80%)	9 (19.10%)	
	Bilateral n,%	49 (41.90%)	15 (31.90%)	
Hernia size	<1.5 cm n,%	56 (47.90%)	17 (36.20%)	0.024
	1.5-3 cm n,%	53 (45.30%)	20 (42.60%)	
	>3 cm n,%	8 (6.80%)	10 (21.30%)	
Follow-up duration (in months) (median-IQR)		17.00-22.00	16.00-17.00	0.504
History of heavy labor or sports, yes n,%		66 (56.40%)	25 (53.20%)	0.708
Presence of recurrence, yes n,%		16 (13.70%)	13 (27.70%)	0.042
Smoking	Yes (n,%)	52 (44.40%)	24 (51.10%)	0.491
	No (n,%)	23 (48.90%)		
Sex	Female n, %	9 (7.70%)	9 (19.10%)	0.051
	Male n, %	38 (80.90%)		
ASA class	1,2 (n, %)	114 (97.40%)	46 (97.90%)	1.000
	3, (n, %)	1 (2.10%)		

IQR: Interquartile range, BMI: Body mass index, ASA: American Society of Anesthesiologists, TAPP: Transabdominal pre-peritoneal, TEP: Totally extraperitoneal repair, SD: Standard deviation

Table 2. Comparison of intraoperative characteristics and early and late postoperative complications

Variables		Group 1: TEP (n=117)	Group 2: TAPP (n=47)	p-value
90-day complications	None n, %	77 (65.8%)	21 (44.7%)	
	Hematoma n, %	8 (6.8%)	3 (6.4%)	1.000
	Seroma n, %	22 (18.8%)	20 (42.6%)	0.003
	Pain n, %	2 (1.7%)	1 (2.1%)	0.198
	Ischemic orchitis n, %	4 (%3.4)	0 (0.0%)	0.579
	Recurrence n, %	4 (3.4%)	2 (4.3%)	1.000
Intraoperative complications	None n, %	103 (88.0%)	43 (91.5%)	
	Hemorrhage n, %	5 (4.3%)	2 (4.3%)	1.000
	Conversion to open surgery n, %	4 (3.4%)	1 (2.1%)	1.000
	Anesthesia complication n,%	0 (0.0%)	1 (2.1%)	0.287
Late-term complications	None n, %	105 (89.7%)	39 (83.0%)	
	Chronic pain n, %	8 (6.8%)	4 (8.5%)	0.744
	Recurrence n, %	4 (3.4%)	4 (8.5%)	0.228
Operation time (in min) (median-IQR)		60.00-25.00	70.00-15.00	0.086
Number of tacks used for mesh fixation (median-IQR)		4.00-2.00	4.00-1.00	**<0.001**

IQR: Interquartile range, TAPP: Transabdominal pre-peritoneal, TEP: Totally extraperitoneal repair

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had a higher proportion of patients who underwent surgery due to recurrent inguinal hernia (27.70% vs. 13.70%, p=0.042) (Table 1). Among early complications, only seroma occurred at a significantly higher rate statistically in the TAPP group (p=0.003). While early recurrence rates were similar, ischemic orchitis was observed in 4 (3.4%) patients in the TEP group. No significant difference was observed between the groups concerning chronic pain and recurrence rates (p=0.744, p=0.228). Although not statistically significant, the median operative times were longer in the TAPP group (70.00-1.00 minutes vs. 60.00-25.00 minutes, p=0.086). Patients in the TAPP group underwent mesh fixation with a higher number of tacks (p<0.001) (Table 2). Conversion to TAPP was required in 5 (4.3%) patients initially planned for TEP, and their data were analyzed in the TAPP group. The presence of ASA class 3 comorbidities, recurrence, and the development of early postoperative hematoma was found to be associated with recurrence (Table 3). In multivariate analysis, the ASA classification was not found to be significant for recurrence. However, recurrence and early postoperative hematoma were identified as independent risk factors for recurrence (OR: 6,537, p=0.029, 95% CI: 1,210-35,330; OR: 8,109, p=0,039, 95% CI: 1,111-59,185, respectively) Table 4. The occurrence of early hematoma and seroma was not found to be associated with chronic pain, with p=0.578 for hematoma and p=0.313 for seroma, respectively (Table 3). The number of tacks used for mesh fixation was an independent risk factor for chronic pain (p=0.001, OR: 5,103, 95% CI: 2,093-12,446) but was not associated with recurrence (p=0.557) (Table 4). The Hosmer-Lemeshow test results demonstrated a good fit for the models, with p=0.741 for the chronic pain model and p=0.719 for the recurrence model, indicating no significant difference between observed and predicted outcomes.

Table 3. Subgroup analysis based on chronic pain and recurrence status

Variables		Chronic pain group (n=12)	Non-chronic pain group (n=152)	p-value	Recurrent group (n=8)	Non-recurrent group (n=156)	p-value
Number of tacks used for mesh fixation median (IQR)		5.00 (1.00)	4.00 (1.00)	**<0.001**	4.00 (0.00)	4.00 (1.00)	0.557
BMI median (IQR)		25.73 (3.23)	26.28 (3.16)	0.716	27.68 (2.09)	26.15 (3.19)	0.158
Height median (IQR)		170.00 (9.00)	170.00 (6.00)	0.995	170.00 (6.00)	170.00 (6.00)	0.265
Weight median (IQR)		77.50 (6.00)	78.00 (9.00)	0.929	80.00 (12.00)	78.00 (8.00)	0.693
Age median (IQR)		54.50 (20.00)	51.00 (16.00)	0.394	51.00 (18.00)	51.00 (18.00)	0.593
Sex, male n, %		11 (91.7%)	135 (89.4%)	1.000	6 (75.0%)	140 (89.7%)	0.214
Operation duration median (IQR)		72.50 (18.00)	64.50 (20.00)	0.103	70.00 (4.00)	64.50 (20.00)	0.385
ASA classification, ASA 3/4 n, %		0 (0.00%)	4 (2.6%)	1.000	2 (25.0%)	2 (1.3%)	**0.012**
Hernia size	<1.5 cm n, %	6 (50.0%)	67 (44.4%)	0.659	1 (12.5%)	72 (46.2%)	0.600
	1.5-3 cm n, %	4 (33.3%)	69 (45.4%)		7 (87.5%9	66 (42.3%)	
	>3 cm n, %	2 (16.7%)	16 (10.5%)		0 (0.0%)	18 (11.5%)	
Smoking, yes n, %		7 (58.3%)	69 (45.4%)	0.387	4 (50.0%)	72 (46.2%)	1.000
History of heavy labor or sports, yes n, %		9 (75.0%)	82 (53.9%)	0.158	5 (62.5%)	86 (55.1%)	0.733
Presence of recurrence		4 (33.3%)	25 (16.4%)	0.228	4 (50.0%)	25 (16.0%)	**0.034**
Early hematoma		1 (8.3%)	10 (6.6%)	0.578	3 (37.5%)	8 (5.1%)	**0.011**
Seroma		5 (41.7%)	40 (26.3%)	0.313	3 (37.5%)	42 (26.9%)	0.685

IQR: Interquartile range, BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 4. Logistic Regression Analysis of Variables Associated with chronic pain and recurrence

Logistic regression models		Odds ratio	%95 CI	p-value
Variables associated with chronic pain	Number of tacks used for mesh fixation	5.103	2.093-12.446	**<0.001**
Variables associated with recurrent	ASA classification, ASA 3	15.311	0.971-241.363	0.052
	Presence of recurrence	6.537	1.210-35.330	**0.029**
	Early hematoma	8.109	1.111-59.185	**0.039**

CI: Confidence interval, ASA: American Society of Anesthesiologists

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DISCUSSION

Minimally invasive techniques, particularly laparoscopic approaches, have revolutionized inguinal hernia repair, offering advantages such as reduced postoperative pain and faster recovery. While open repair remains a commonly performed technique, laparoscopic methods, including TAPP and TEP approaches, have gained widespread acceptance due to their potential benefits. A comprehensive meta-analysis comparing open and laparoscopic inguinal hernia repairs demonstrated that laparoscopic techniques are associated with reduced postoperative pain and a shorter recovery period, while recurrence rates remain comparable between the two approaches (11). Furthermore, among laparoscopic techniques, it is still unclear whether TEP or TAPP provides better outcomes, as both methods have shown similar efficacy in previous studies (12). Given this ongoing uncertainty, our study aimed to directly compare TEP and TAPP to further clarify their respective advantages and potential drawbacks. Consistent with prior research, our findings revealed no statistically significant differences between the two techniques in terms of recurrence or chronic pain. However, we observed that the number of tacks used during the procedure was associated with an increased incidence of chronic pain, suggesting that fixation strategies may play a critical role in postoperative outcomes.

A population-based study conducted between 1995 and 2006, comparing the short-term outcomes of over 4,500 patients who underwent either TEP or TAPP, reported a significantly higher rate of intraoperative and postoperative complications with the TEP technique. The same study also found a longer operative time for TEP (66.6 minutes vs. 59.0 minutes, p<0.001). Conversely, the length of hospital stay was significantly longer in patients who underwent TAPP (2.9 vs. 2.3 days, p=0.002) (2). Two recent meta-analyses of randomized controlled trials have shown no significant difference between TEP and TAPP regarding postoperative pain, hematoma, seroma, and recurrence rates (5,13). Although earlier studies with large cohorts conducted during the initial years of laparoscopic hernia surgery, suggested that TEP might be at a disadvantage, recent research indicates no significant differences in postoperative complications between TAPP and TEP. This shift may be attributed to a better understanding of the procedure, improved knowledge of myopectineal orifice anatomy, and advances in laparoscopic equipment with enhanced image quality. Krishna et al. (14) reported no significant difference in operative time between TEP and TAPP in a cohort of 100 MIS patients (p=0.343); and, unlike our study, they observed a higher incidence of seroma in TEP cases (37.8% vs. 17.0%, p=0.021). In the same study, a cost comparison between TEP and TAPP showed no statistically significant difference (14). Although we did not conduct a formal cost analysis for each case, the relatively higher cost of TAPP at our center may be attributed to the greater number of tacks used and the application of absorbable barbed sutures for peritoneal closure. In our study, seroma was found to be significantly more prevalent in the TAPP group (18.8% vs. 42.6%, p=0.003), while hematoma, postoperative pain, and early recurrence rates were comparable. The higher seroma rate observed in the TAPP group could be related to the larger proportion of patients with hernias exceeding 3 cm and/or recurrent hernias in this group (15).

In a study on bilateral inguinal hernias, Hidalgo et al. (16) reported a significant increase in laparoscopic surgery, rising from 22% in 2016 to 94% in 2020. At our center, as the rates of laparoscopic hernia surgery have increased over the years, approximately 30% of all inguinal hernias in 2023 were treated laparoscopically. In the same study, 46% of cases utilized the TEP approach, while 54% employed TAPP. Although TAPP had a significantly longer operation time (107.2±31.29 vs. 82.99±30.84 minutes, p<0.001), there were no statistically significant differences in postoperative complications (any complication, p=0.672) (16). Some studies have also documented longer operative times for TEP compared to TAPP. In our cohort, there were 65 patients with bilateral inguinal hernia, with 49 (75%) undergoing TEP and 15 (25%) undergoing TAPP. All TAPP cases demonstrated a trend toward longer operation times (25.00-60.00 vs. 15.00-70.00 minutes, p=0.086). Despite reports in the literature indicating longer times for TEP, we find the longer operative times required for TAPP to be reasonable, given the additional peritoneal suturing required and the tendency to prefer TAPP for larger hernias.

Recent randomized controlled trials have demonstrated that laparoscopic hernia surgery reduces the incidence of chronic pain compared to open surgery (5,6,17,18). In a meta-analysis by Scheuermann et al. (19), comparing Lichtenstein repair with TAPP, patients who underwent TAPP experienced significantly lower rates of chronic pain than those in the open surgery group (OR: 0.42, 95% CI: 0.23-0.78, p=0.006). Additionally, studies comparing laparoscopic and open surgery, particularly those conducted in the early years of laparoscopic inguinal hernia repair, have reported mixed results regarding chronic pain, with some indicating no significant difference and others suggesting a higher incidence of chronic pain associated with laparoscopic surgery (20,21).

In a meta-analysis comparing the outcomes of TEP and TAPP, Aiolfi et al. (5) found no significant difference in terms of chronic pain. In a prospective randomized controlled study, pain scores at 1 month and 3 months were significantly higher in the TAPP group compared to the TEP group, but by 6 months, no significant difference was observed between the groups, (respectively, p=0.001, p=0.002, p=0.231) (14). An international study analyzing 782 TEP and 1464 TAPP cases also showed no difference between the techniques in terms of chronic pain. Chronic pain requiring treatment was observed in 4.48% of the TEP patients and 3.41% of the TAPP patients (p=0.206) (22). Similarly, in our study, no significant difference was found between TEP and TAPP in terms of chronic pain (p=0.744).

Female sex, younger age, high preoperative pain sensitivity, surgery for recurrent hernia, open surgery, inadequate mesh fixation, low-weight mesh, early severe pain, postoperative hematoma, and wound infection have been identified as

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independent risk factors for chronic pain following inguinal hernia surgery (23-26). In this study, only the number of tacks used in mesh fixation was found to be a significant risk factor for chronic pain. Kim et al. (26) reported that benign prostatic hyperplasia (BPH) and low BMI were statistically significant risk factors for chronic pain following TEP and TAPP (p=0.035 and p=0.043, respectively). In the multivariate analysis of the same study, BPH was found to be the only significant independent risk factor (OR: 5,363; CI: 1,028-27,962, p=0.046) (26). In this study, no notable correlation was identified between BMI and the development of chronic pain (p=0.716). In their meta-analysis, Shi et al. (24) reported no significant difference in recurrence rates or chronic pain between mesh fixation using fibrin glue and tack fixation methods. Another study found a higher incidence of pain among patients who underwent mesh fixation with non-absorbable staples or self-adhesive mesh. Conversely, in the group where no fixation was applied, a lower incidence of chronic pain was reported (25). Buyukasik et al. (27) conducted a study comparing the outcomes of patients who underwent TEP repair with and without fixation and reported that fixation did not reduce the recurrence rate but increased the risk of complications. A recent randomized controlled trial compared permanent tacks and absorbable tacks in 333 patients who underwent laparoscopic inguinal hernia repair, focusing on their association with chronic pain. The number of tacks used was also identified as a risk factor for chronic pain development. However, in multivariate analysis, neither the type of tack (permanent vs. absorbable) nor the number of tacks was found to be statistically significant in predicting chronic pain outcomes (23). Another randomized controlled trial reported that using more than six tacks significantly increased pain incidence (p=0.008) (28). In the present study, an increase in the number of attacks was also identified as an independent risk factor for chronic pain.

Study Limitations

The primary limitation of the study is its retrospective design. The small number of patients, particulary the limited number of cases undergoing TAPP, represents another important limitation.

CONCLUSION

In conclusion, recent studies have demonstrated that minimally invasive inguinal hernia surgery offers comparable recurrence rates to open surgery, with the added benefit of reduced postoperative pain. Comparisons between TEP and TAPP techniques have shown similar outcomes in terms of intraoperative and postoperative complications. Reducing the number of mechanical fixations may help decrease the incidence of chronic pain.

Ethics

Ethics Committee Approval: Ethical approval was granted by the University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital Non-Interventional Ethics Committee (approval no: 67, date: 20.11.2024).

Informed Consent: Written informed consent was obtained from all participants prior to their inclusion in the study.

Footnotes

Author Contributions:

Surgical and Medical Practices - M.G., D.G.; Concept - M.G., D.G.; Design - M.G., D.G.; Data Collection and/or Processing - M.G., D.G.; Analysis and/or Interpretation - M.G., D.G.; Literature Search - M.G., D.G.; Writing – M.G., D.G.

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Evaluation of the Pediatric Clinical Test of Sensory Interaction for Balance in Children Aged 6-9 Years

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ABSTRACT

Objective: The Pediatric Clinical Test of Sensory Interaction for Balance (P-CTSIB) provides information on the utilization and integration of sensory inputs as well as postural sway during postural control tasks under various static conditions in children. The evaluation of the P-CTSIB performance in healthy children aged 6-9 years aims to obtain normative data.

Methods: A total of 81 children aged 6-9 years were included in the study. The participants were asked to maintain an upright posture in two different stance positions (feet together and heel-toe position) under six test conditions: eyes open or closed on a firm surface with a dome, and eyes open or closed on a foam pad with a dome. The amount of postural sway (anterior-posterior/medial-lateral), test duration, and test scores for each condition were recorded, and the data were compared across groups.

Results: In the study, descriptive statistics for the sway, test duration, and test scores obtained under all conditions in the feet together and heel-toe positions were determined. No significant difference was found between genders in terms of sway, duration, and scores under all test conditions. In the feet together position, a significant difference was found between groups in terms of sway in three test conditions and test scores in four test conditions. In the heel-toe position, a significant difference was found between groups in terms of sway measured in 4 test conditions and test scores in 2 test conditions ($p<0.05$).

Conclusion: The P-CTSIB is a cost-free test that can assess postural sway under different static test conditions without the need for any equipment. Measuring postural sway provides valuable information in the assessment of balance. It is expected that our findings will serve as a foundation for ensuring the availability of the test in our country. Age-specific normative data obtained from Turkish children will provide reference data for future studies involving children with balance-affecting pathologies.

Keywords: Child, postural control, balance, sway, normative

INTRODUCTION

Balance: it is a complex motor control task that requires the integration of sensory information, neural processing, and biomechanical factors (1). Effective balance control requires the combination of vestibular, proprioceptive, and visual system performance. Neurological factors responsible for balance provide sensory processing and motor output mechanisms, which form the neurophysiological basis, while musculoskeletal factors provide the mechanical structure for the response (2). Sensory inputs from the vestibular, visual, and somatosensory/proprioceptive systems are directed to the vestibular nuclei and cerebellum for processing and regulation. In response to these inputs, the vestibular nuclear complex forms connections with the muscles that control the eyes, neck, and spinal cord (3). These motor outputs result in three vestibular reflexes that maintain balance: the vestibulo-ocular (4), vestibulospinal (5), and vestibulocollic reflexes (citation needed). The examination of these reflexes is important in detecting vestibular dysfunction (6). The vestibular system provides postural control and visual stabilization through the vestibulo-ocular reflex and vestibulo-spinal reflex (7). The maintenance of postural control requires an active sensorimotor control system. Postural control involves sensory feedback, and the integration of visual and proprioceptive inputs is required for the center of pressure to move in phase with the center of mass. Postural control is a key component of physical movement, particularly in standing and walking (8,9).

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The development of vestibular function in children is associated with two important factors: postural control related to motor skills and the ability to stabilize vision during head movements (10). These aspects of vestibular function facilitate children's ability to adapt to environmental stimuli and movements. This highlights the importance of motor and sensorimotor control in the developmental process. It is known that between the ages of 6 and 10, children's ability to integrate visual and vestibular stimuli becomes more pronounced (11). The proprioceptive, visual, and vestibular systems develop more slowly than the automated motor processes that mature during early childhood (12). Balance assessment in children is considered an important component of their developmental evaluation (13). In adults, sensory systems involved in postural control are mature. Although these systems are anatomically developed, they are not functionally mature in children. The functional development of the afferent sensory pathways, which include the vestibular, proprioceptive, and visual systems, occurs gradually and hierarchically, beginning after the early maturation of low-level automatic motor processes (14).

It is recommended that a comprehensive clinical, otological, neurological, and vestibular examination be performed on children with complaints of dizziness and imbalance before resorting to expensive and unnecessary complementary test methods (15). In this context, there is a need for inexpensive, effective, and reliable methods for assessing balance in children.

Considering these challenges, the more accessible Clinical Test of Sensory Interaction for Balance (CTSIB) was developed (16). The CTSIB is a method suitable for static balance assessment that does not require a computerized force platform and is easy to use in clinical settings. The pediatric version of this test is called the Pediatric-CTSIB (P-CTSIB) (17). The P-CTSIB reflects the child's ability to integrate and use different sensory information to respond in various positions during static balance.

In this study, the evaluation of P-CTSIB performance in healthy children aged 6-9 years is planned, thus providing normative data for an inexpensive, easy-to-apply, and reliable test method for this population. The aim is for these data to be used as a reference for children at risk of balance disorders.

METHODS

Participants

A total of 81 healthy children were included in the study. The children included in the study were divided into four age groups. The first group included 19 children (9 female, 10 male) aged 6 years to 6 years 11 months. The second group included 18 children (11 female, 7 male) aged 7 years to 7 years 11 months. The third group included 23 children aged 8 years to 8 years 11 months. The fourth group included 21 children (14 female, 9 male) aged 9 years to 9 years 11 months.

Children were included in the study based on the following criteria:

- No reported neurological disorders (according to parental information),
- No uncorrected visual impairments,
- No history of developmental motor disorders or musculoskeletal system conditions,
- No engagement in regular physical exercise programs,
- No use of sedative or performance-enhancing medications that could affect the nervous or balance systems.

Children who did not meet one or more of the above criteria were excluded from the study.

Ethics Committee Information

This study was approved by the Ethics Committee of the Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (decision no: 835, date: 06.01.2022). The children included in the study were those attending primary school. With permission obtained from the Ministry of National Education, children from primary schools were included in the study. The purpose and procedure of the study were explained to the parents, and they were asked to sign a written informed consent form.

Pediatric Clinical Test of Sensory Interaction for Balance

The P-CTSIB evaluates the child's ability to use visual, somatosensory, and vestibular inputs to maintain standing balance (17). All children included in the study were asked to maintain an upright standing position in six test conditions, including positions where one or more of the visual or proprioceptive inputs were impaired. At the beginning, the children were informed about the test and the importance of cooperation. The test procedure was reviewed before each stage. The duration of static balance, the amount of anterior-posterior body sway, and the medio-lateral body sway were evaluated under six different sensory conditions and two different standing positions (6 evaluations in the feet together position and 6 in the heel-to position, totaling 12 evaluations). The combination of three conditions for the visual variable (eyes open, eyes closed, and with dome) and two conditions for the support surface variable (on a firm surface and on a foam pad) formed the six sensory condition levels of the test. These six conditions were as follows:

1. Eyes open, on a firm surface;
2. Eyes closed, on a firm surface;
3. Eyes open with dome, on a firm surface;
4. Eyes open, on a foam pad;
5. Eyes closed, on a foam pad;
6. Eyes open with dome, on a foam pad (Table 1).

The relationship between the P-CTSIB conditions and sensory systems is shown in Table 2.

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Table 1. Images of the example participant in different postural positions

Conditions	Feet together position	Heel toe position
Condition 1 Firm surface Eyes open		
Condition 2 Firm surface Eyes closed		
Condition 3 Firm surface Visual conflict dome		
Condition 4 Foam pad Eyes open		
Condition 5 Foam pad Eyes closed		

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Table 1. continued

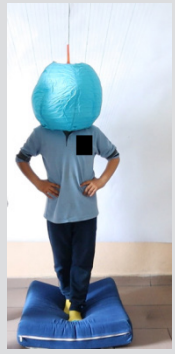
Conditions	Feet together position	Heel toe position
Condition 6 Foam pad Visual conflict dome		

Table 2. Conditions of the Pediatric Clinical Test of Sensory Interaction for Balance (P-CTSIB) and the relationship between sensory systems

Conditions	Available sensory input	Absent/inaccurate sensory input
Condition 1 **Firm surface** **Eyes open**	Vestibular Proprioceptive Vision	-
Condition 2 **Firm surface** **Eyes closed**	Vestibular Proprioceptive	Absent vision input
Condition 3 **Firm surface** **Visual conflict dome**	Vestibular Proprioceptive	Inaccurate vison input
Condition 4 **Foam pad** **Eyes open**	Vestibular Vision	Inaccurate proprioceptive input
Condition 5 **Foam pad** **Eyes closed**	Vestibular	Absent vision input inaccurate proprioceptive input
Condition 6 **Foam pad** **Visual conflict dome**	Vestibular	Inaccurate proprioceptive input inaccurate vison input

Sway Analysis

The participants were asked to maintain an upright standing position in each of the 6 test conditions: (eyes open/closed on a firm surface with a dome, eyes open/closed on a foam pad with a dome, for two different standing positions (feet together and heel-to-toe). The best trial score for each condition was recorded (either the trial with the longest duration or the trial with the least sway). The children were asked to maintain balance for 30 seconds or until a new postural adjustment occurred in all test positions. If the child made a postural adjustment (by moving their hands, feet, or eyes), the timing was stopped.

The child's performance in all test conditions was recorded with a camera. The children were placed in front of a floor marked with 2-degree increments to measure the amount of sway. A background with millimeter markings was placed behind the children in a 1x1 meter area, to assess the degree of sway. A paper screen with lines spread across a total of 32 degrees in 2-degree increments was used to measure the degree of sway. After the tests were completed, the camera recordings were reviewed by two audiologists, and the amount of postural sway and test duration were recorded for each condition. The materials used in the sway analyses are shown in Figure 1.

Test Duration

Before each task, the participants were shown the postures, and measurements began after they assumed the correct posture. The standing duration (static balance) and the degrees of medial-lateral and anterior-posterior sway were recorded. The standing duration was defined as the time from the start of the test until a new postural adjustment occurred, and this time was measured in seconds using a stopwatch. To prevent fatigue in children, the maximum standing duration was set to 30 seconds. Movement of one or both feet from the starting position, opening of the eyes in the closed-eye condition, or the need for assistance from the researcher to prevent a fall were defined as "postural adjustment", and participants were recorded as having "fallen" (18). The test scores of the participants were determined based on the duration of the posture in the given conditions. The scores were determined as follows.

Scoring points:

0. The child cannot assume any position,

I. Test duration less than 3 seconds,

II. Test duration between 4-10 seconds,

III. Test duration between 11-29 seconds or sway greater than 15 degrees for 30 seconds,

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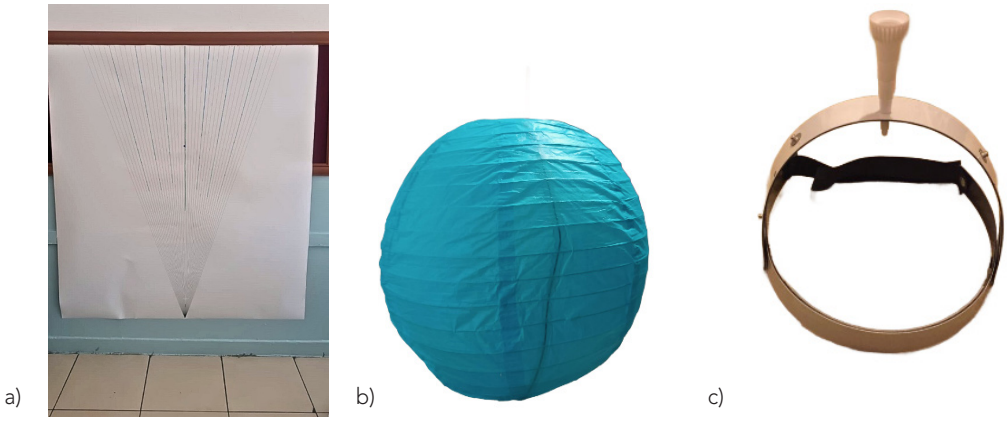

Figure 1. Experimental materials.
a) A paper screen with 1x1 m dimensions, containing lines spread over 32 degrees with 2-degree increments, b) visual conflict dome, c) a cap for measuring the degree of sway

IV. Test duration of 30 seconds, with sway between 6-15 degrees,

V. Test duration of 30 seconds, with sway less than 5 degrees.

In our study, evaluating the P-CTSIB test performance, recording, and reviewing for each child took approximately 60 minutes in total.

Statistical Analysis

The IBM SPSS Statistics Version 23 software program was used to analyze the data. The normality of the data distribution was evaluated using histograms, probability plots, and the Kolmogorov-Smirnov/Shapiro-Wilk tests. Because the data did not show a normal distribution, the Kruskal-Wallis test was used to compare the data among the four groups. The chi-square test was used to compare gender between groups. The statistical significance level was set at $p<0.05$. In case of a significant difference between groups, the Dunn-Bonferroni post-hoc test was applied. Descriptive statistics included the use of mean, median, minimum, maximum, 25th and 75th percentile.

RESULTS

Table 3 shows the distribution of gender across the groups. There was no significant difference between the groups in terms of gender.

Sway Percentage Normative Data

Table 4 presents the normative data for anterior-posterior sway obtained in the feet-together position and medial-lateral sway obtained in the heel-toe position for all groups. The corresponding column graphs are presented in Figure 2 for the feet together position and in Figure 3 for the heel-toe position.

Normative Data for Test Durations

Table 5 presents the normative data for test durations obtained in the heel-toe position across all groups. Since all individuals were able to maintain a standing feet-together position for 30 seconds in each test phase , the data obtained from this test position are not presented. The corresponding column graphs are presented in Figure 4.

Table 3. Distribution of gender by groups

Grup	Female (n)	(%)	Male (n)	(%)	p-value
Group 1	9	47	10	53	
Group 2	11	61	7	39	
Group 3	14	61	9	39	0.686
Group 4	10	48	11	52	
Total	44	54	37	46	

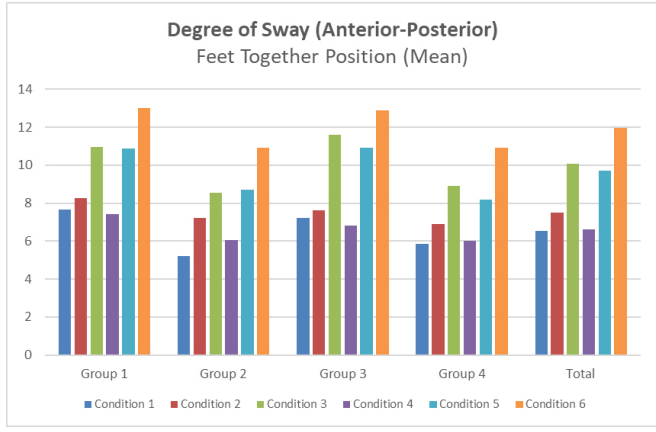

Figure 2. Normative anterior-posterior sway values (mean) in the feet together position (column graph)

Test Scores Normative Data

Table 6 presents the normative data for the test scores obtained in the feet together and heel toe positions across all groups. The corresponding column graphs are presented in Figure 5 for the feet together position and in Figure 6 for the heel-toe position.

Table 4. Normative values of sway (anterior-posterior and medial-lateral)

Degree of sway (anterior-posterior)				
Feet together position				
Variables	**Mean**	**Median**	**SD**	**Min./25%/75% percentile/max.**
Group 1 (n=19)				
Condition 1	7.68	7	2.60	4/6/10/13
Condition 2	8.26	8	2.55	4/6/10/13
Condition 3	10.94	11.5	2.72	5.5/10/12.5/17
Condition 4	7.4	7	1.77	5/6/8/11
Condition 5	10.89	10.5	2.30	8/9/12.5/16.5
Condition 6	13	12	3.70	7.5/11/15/21.5
Group 2 (n=18)				
Condition 1	5.2	4.5	1.60	3/4/7/8
Condition 2	7.2	7.5	1.93	4/5.7/9/11
Condition 3	8.55	8	3.42	0/7/9.62/17
Condition 4	6.05	6	2.13	2/4.5/8/10
Condition 5	8.69	9	3.02	0/6.8/10.37/12.5
Condition 6	10.9	12	3.7	0/16.5/13.12/8.7
Group 3 (n=23)				
Condition 1	7.2	7	2.39	3/6/10/11
Condition 2	7.6	7	2.14	4/6/9/12
Condition 3	11.6	10	4.65	7/8.5/14/28
Condition 4	6.8	6	1.86	5/12/8/5
Condition 5	10.91	10.5	2.74	7/9/12.5/19.5
Condition 6	12.87	11.5	4.5	7.5/10/17.5/24
Group 4 (n=21)				
Condition 1	5.85	6	2.85	3/4/6.5/16
Condition 2	6.9	6	2.71	4/5/9/14
Condition 3	8.9	9	2.37	5.5/7/10.75/13.5
Condition 4	6	6	1.80	3/4.5/8/9
Condition 5	8.2	8.5	1.99	4.5/7.5/9/14.5
Condition 6	10.9	10	3.03	6.5/19.5/12.5/8.7
Total (n=81)				
Condition 1	6.55	6	2.57	3/4/8/16
Condition 2	7.51	7	2.36	4/6/9/14
Condition 3	10.08	9.5	3.64	0/7.5/12/28
Condition 4	6.61	6	1.93	2/5/8/12
Condition 5	9.72	9.5	2.78	0/8/11.25/19.5
Condition 6	11.96	11.50	3.85	0/9.5/14/24
Heel toe position (medial-lateral)				
Group 1 (n=19)				
Condition 1	13.42	11	6.7	5/8.5/17/29
Condition 2	16	15	5.3	6.5/13/21/25
Condition 3	17.5	17	7.36	6/12/21/35
Condition 4	11.68	11	4.18	6/8/14/21.5
Condition 5	22.18	23	6.61	13/16.5/28/32
Condition 6	24.69	25	7.12	12/17.7/28.75/39

Table 4. continued

Degree of sway (anterior-posterior)				
Feet together position				
Variables	**Mean**	**Median**	**SD**	**Min./25%/75% percentile/max.**
Group 2 (n=18)				
Condition 1	8.13	8	2.31	4/6/9.75/13.5
Condition 2	14.55	14.25	7.25	0/9.8/19.25/30
Condition 3	15.44	15.25	8.75	0/8.3/19.37/36
Condition 4	8.5	7.5	3.47	5.5/18/10/6
Condition 5	13.94	15	8.38	0/9/21.25/27
Condition 6	16.59	15	6.85	6/12.5/20/34
Group 3 (n=23)				
Condition 1	12.21	10.9	6.92	5.5/7.5/12.5/34.5
Condition 2	15.53	14	7.38	0/11/19.5/30
Condition 3	16.65	14	8.48	6/10.5/20/39.5
Condition 4	12.13	9	7	5/7.5/17/29.5
Condition 5	20.71	20	9.93	8/12/28/45
Condition 6	18.13	17	7.20	6/12.5/18/38
Group 4 (n=21)				
Condition 1	8.09	7	4.67	3/5/9.75/24
Condition 2	14.88	13	6.72	7/10.5/17.75/34
Condition 3	12.11	13	4.02	6/8.5/15/19.5
Condition 4	8.78	7	4.27	5/5.74/11.25/24
Condition 5	15.90	15	8.36	0/9.5/23.50/32.5
Condition 6	18	16.50	5.92	10/34/20/14
Total (n=81)				
Condition 1	10.52	8.5	5.97	3/7/12/34.5
Condition 2	15.25	14	6.65	0/10.75/19/34
Condition 3	15.42	14	7.53	0/9.5/18.25/39.5
Condition 4	10.37	8.5	5.23	5/7/11.87/29.5
Condition 5	18.36	18	8.96	0/11.5/24/45
Condition 6	19.29	17.25	7.31	6/14/24.5/39

SD: Standard deviation, Min.: Minimum, Max.: Maximum

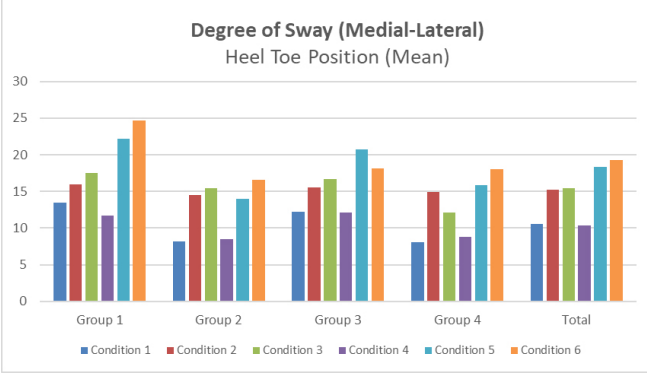

Figure 3. Normative medial-lateral sway values (mean) in the heel toe position (column graph)

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Intergroup Comparison

In the feet together position, significant differences were found in the anterior-posterior sway scores between four groups in Condition 1, 3, and 5 ($p<0.05$). In the Dunn-Bonferroni post hoc analysis, pairwise comparisons showed a significant difference only in Condition 1 between Group 4 and Group 1 ($p=0.001$) and between Group 4 and Group 3 ($p<0.001$).

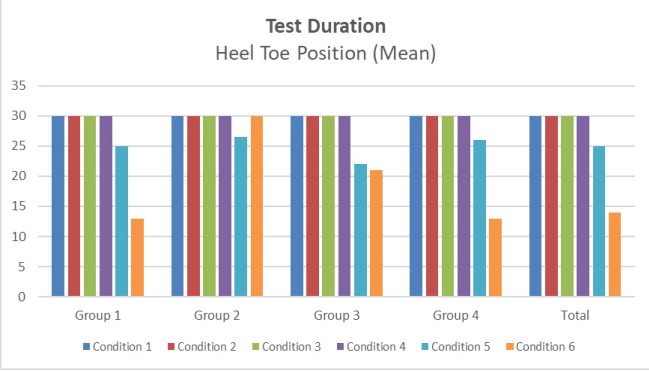

Figure 4. Normative values (mean) of test duration in heel toe position (column graph)

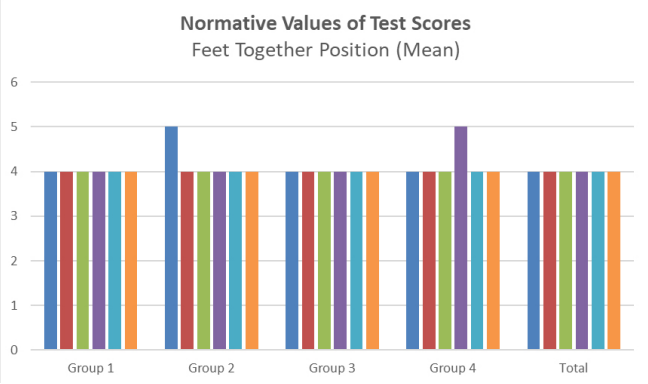

Figure 5. Normative values (mean) of test scores in the Feet Together position (column graph)

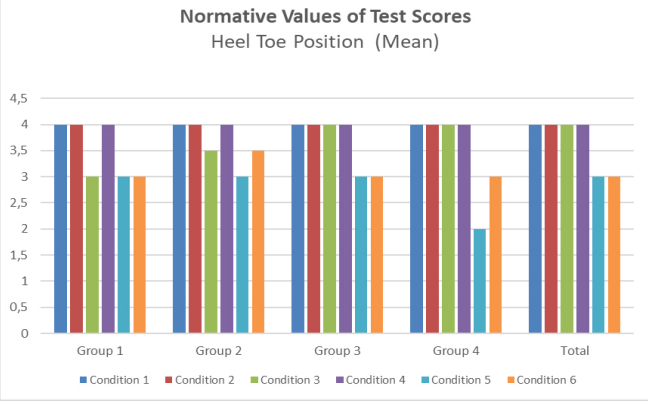

Figure 6. Normative values (mean) of test scores in heel toe position) (column graph)

In the heel-toe position, significant differences were found in the medial-lateral sway scores among four groups across Conditions 1, 4, 5, and 6 ($p<0.05$). In the Dunn-Bonferroni post-hoc analysis pairwise comparisons showed significant differences between Group 4 and Group 1 in Condition 1 ($p=0.002$), and between Group 1 and Group 2 in Condition 6 ($p=0.004$) (Table 5).

Table 5. Normative values of test duration (heel toe position)

Test duration				
Heel toe position				
Variables	**Median**	**Mean**	**SD**	**Min./25%/75% percentile/max.**
Group 1 (n=19)				
Condition 1	30	30	30	30/30/30/30
Condition 2	29	30	4.35	11/30/30/30
Condition 3	28	30	4.3	17/30/30/30
Condition 4	27	30	7.06	4/30/30/30
Condition 5	22.47	25	7.82	10/14/30/30
Condition 6	15	13	9.39	3/7/23/30
Group 2 (n=18)				
Condition 1	30	30	30	30/30/30/30
Condition 2	23.75	30	10.17	2/14.1/30/30
Condition 3	25	30	8.24	6/24.7/30/30
Condition 4	29.6	30	1.64	23/30/30/30
Condition 5	20.27	26.5	10.99	3/8/30/30
Condition 6	20.41	30	11.7	3/7/30/30
Group 3 (n=23)				
Condition 1	28.21	30	4.57	11/30/30/30
Condition 2	24.78	30	8.76	5/20/30/30
Condition 3	27.5	30	5.41	12/30/30/30
Condition 4	26	30	8.44	6/28/30/30
Condition 5	19.71	22	10.60	3/9/30/30
Condition 6	19.30	21	10.56	4/8.5/30/30
Group 4 (n=21)				
Condition 1	28.26	30	5.76	5/30/30/30
Condition 2	27.85	30	6.1	5/30/30/30
Condition 3	28.76	30	3.30	18/30/30/30
Condition 4	29.04	30	4.36	10/30/30/30
Condition 5	20.69	26	10.69	3.5/10.2/30/30
Condition 6	15.97	13	9.92	3/7.7/30/30
Total (n=81)				
Condition 1	29.04	30	3.85	5/30/30/30
Condition 2	26.34	30	7.82	2/30/30/30
Condition 3	27.53	30	5.56	6/30/30/30
Condition 4	27.99	30	6.17	4/30/30/30
Condition 5	20.7	25	10	3/11/30/30
Condition 6	17.67	14	10.46	3/8.2/30/14

SD: Standard deviation, Min.: Minimum, Max.: Maximum

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Table 6. Normative values of test scores (heel toe position)

Test scores				
Feet together position				
Variables	**Median**	**Mean**	**SD**	**Min/25%/75% percentile/max**
Group 1 (n=19)				
Condition 1	4.11	4	0.31	4/4/4/5
Condition 2	4.11	4	0.31	4/4/4/5
Condition 3	4.05	4	0.22	4/4/4/5
Condition 4	4.11	4	0.31	4/4/4/5
Condition 5	4	4	0	4/4/4/4
Condition 6	3.79	4	0.4	3/4/4/4
Group 2 (n=18)				
Condition 1	4.5	5	0.51	4/4/5/5
Condition 2	4.2	4	0.42	4/4/4.25/5
Condition 3	3.67	4	1	0/4/4/4
Condition 4	4.11	4	1.13	0/4/5/5
Condition 5	3.7	4	0.94	0/4/4/4
Condition 6	3.7	4	0.95	0/4/4/4
Group 3 (n=23)				
Condition 1	4.2	4	0.42	4/4/4/5
Condition 2	4.13	4	0.34	4/4/4/5
Condition 3	3.74	4	0.68	2/4/4/4
Condition 4	4.26	4	0.44	4/4/5/5
Condition 5	3.83	4	0.57	2/4/4/4
Condition 6	3.70	4	0.47	3/3/4/4
Group 4 (n=21)				
Condition 1	4.33	4	0.73	2/4/5/5
Condition 2	4.36	4	0.49	4/4/5/5
Condition 3	4.10	4	0.30	4/4/4/5
Condition 4	4.52	5	0.51	4/4/5/5
Condition 5	4.14	4	0.05	4/4/4/5
Condition 6	3.95	4	0.21	3/4/4/4
Total (n=81)				
Condition 1	4.3	4	0.52	2/4/5/5
Condition 2	4.21	4	0.41	4/4/4/5
Condition 3	3.89	4	0.65	0/4/4/5
Condition 4	4.26	4	0.66	0/4/5/5
Condition 5	3.94	4	0.57	0/4/4/5
Condition 6	3.79	4	0.56	0/4/4/4
Heel toe position				
Group 1 (n=19)				
Condition 1	3.79	4	0.53	3/3/4/5
Condition 2	3.53	4	0.51	3/3/4/4
Condition 3	3.26	3	0.45	3/3/4/4
Condition 4	3.74	4	0.56	4/4/4/4
Condition 5	3.21	3	0.53	2/3/4/4
Condition 6	2.68	3	0.47	2/2/3/3

Table 6. continued

Test scores				
Feet together position				
Variables	**Median**	**Mean**	**SD**	**Min/25%/75% percentile/max**
Group 2 (n=18)				
Condition 1	4.06	4	0.23	4/4/4/5
Condition 2	3.22	4	1.1	0/2.7/4/4
Condition 3	3.22	3.50	1.06	0/3/4/4
Condition 4	3.83	4	1.04	0/4/4/5
Condition 5	2.78	3	1.06	0/2/4/4
Condition 6	3.11	3.50	0.96	2/2/4/4
Group 3 (n=23)				
Condition 1	3.83	4	0.49	3/4/4/5
Condition 2	3.48	4	0.66	2/3/4/4
Condition 3	3.61	4	0.49	3/3/4/4
Condition 4	3.65	4	071	2/3/4/5
Condition 5	3.09	3	0.84	2/2/4/4
Condition 6	3.04	3	0.82	2/2/4/4
Group 4 (n=21)				
Condition 1	4.10	4	0.76	2/4/5/5
Condition 2	3.62	4	0.59	2/3/4/4
Condition 3	3.76	4	4.36	3/3.5/4/4
Condition 4	4.14	4	0.65	2/4/4.4/5
Condition 5	3.19	2	0.81	2/2.5/4/4
Condition 6	2.90	3	0.76	2/2/3.5/4
Total (n=81)				
Condition 1	3.94	4	0.55	2/4/4/5
Condition 2	3.47	4	0.74	0/3/4/4
Condition 3	3.48	4	0.67	0/3/4/4
Condition 4	3.84	4	0.76	0/4/4/5
Condition 5	3.07	3	0.83	0/2.5/4/4
Condition 6	2.94	3	0.78	2/2/4/4

SD: Standard deviation, Min.: Minimum, Max.: Maximum

In terms of the test score, significant differences were found among 4 Groups: in Condition 1, 3, 4, and 5, in the feet together position; and in Condition 3 and 4, in the heel toe position ($p<0.05$). In the Dunn-Bonferroni post hoc analysis, no significant differences were found in pairwise comparisons (Table 7).

No significant differences were found between females and males in terms of anterior-posterior sway, medial-lateral sway, test duration, and test scores ($p>0.05$) (Table 8).

DISCUSSION

It has been shown that the vestibular system is anatomically developed from birth and can respond functionally (19). The vestibular system continues to develop postnatally in terms of both morphology and function (20). Knowing and understanding

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Table 7. Comparison of sway, test duration and test scores between groups

Condition	p-value of sway (feet together)	p-value of test scores (feet together)	p-value of test duration (feet together)
Condition 1	**0.003**	**0.022**	-
Condition 2	0.309	0.123	-
Condition 3	**0.007**	**0.044**	-
Condition 4	0.113	**0.047**	-
Condition 5	**<0.001**	**0.033**	-
Condition 6	0.251	0.145	-
Condition	**p-value of sway (heel toe)**	**p-value of test scores (heel toe)**	**p-value of test duration (heel toe)**
Condition 1	**<0.001**	0.099	0.091
Condition 2	0.706	0.745	0.041
Condition 3	0.080	**0.017**	0.436
Condition 4	**0.011**	**0.025**	0.118
Condition 5	**0.023**	0.561	0.898
Condition 6	**0.004**	0.391	0.400

Table 8. Comparison of sway, test duration and test scores between genders

Condition	p-value of sway (feet together)	p-value of test scores (feet together)	p-value of test duration (feet together)
Condition 1	0.836	0.794	-
Condition 2	0.160	0.337	-
Condition 3	0.812	0.172	-
Condition 4	0.791	0.374	-
Condition 5	0.875	0.992	-
Condition 6	0.374	0.064	-
Condition	**p-value of sway (heel toe)**	**p-value of test scores (heel toe)**	**p-value of test duration (heel toe)**
Condition 1	0.500	0.189	0.537
Condition 2	0.140	0.230	0.180
Condition 3	0.390	0.219	0.857
Condition 4	0.062	0.225	0.868
Condition 5	0.225	0.577	0.089
Condition 6	0.436	0.062	0.410

the status of vestibular responses in infants, children, adolescents, and adults is of great importance in the assessment and diagnosis of vestibular pathology (21-25). Vestibular disorders occur in children with a frequency of 7% to 15%, and this condition can have negative effects on a child's academic performance and quality of life (26).

During vestibular assessment, children can be tested using any of the techniques employed for adults (27). Most assessment methods can be adapted for children to provide reliable results. Videonystagmography and caloric tests, which are frequently used in assessments, are generally challenging for children (28). The rotational chair test, however, is disadvantageous due to its high cost and unavailability in all clinics. Similarly, the sensory organization test (SOT) in computerized dynamic posturography, used to assess balance performance, provides a more comprehensive balance evaluation (18), however, its clinical use is limited due to high costs and the need for expensive equipment. However, these assessments are not specific to poor postural control and vestibular dysfunction in the pediatric group. Although the P-CTSIB does not provide detailed sway parameters or measures of vestibular function, studies have shown moderate correlations between P-CTSIB performance and posturography findings (29). Gagnon et al. (30) investigated the comparability of the SOT and P-CTSIB in children. They found that although both tests are related to age, they do not measure sensory organisation skills in the same way, suggesting that each provides different and complementary information about children's balance skills. Therefore, the P-CTSIB serves as a useful screening tool to complement more instrumented methods, particularly in large or resource-limited paediatric evaluations.

In our study, we used the P-CTSIB test, assesses postural control. The obtained data provided insights into balance performance in different standing positions, the ability of children to process inputs from visual, somatosensory, and vestibular systems, and

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the integration skills of sensory systems. This study provided normative data for a more practical, and easily applicable method of clinically adapted sensory interaction in the pediatric population. No other study has been found in our country that obtained normative data for Turkish children using P-CTSIB.

In our study, normative data for anterior-posterior sway, test duration, and test scores in six different test positions were obtained for Turkish children. These normative data are intended to serve as baseline data in studies where postural control will be evaluated in children with balance disorders. In our study, significant differences were found between age groups in terms of anterior-posterior sway, medial-lateral sway , and P-CTSIB test scores. In pairwise comparisons, significant differences were found in anterior-posterior sway in Condition 1 between Group 4 and Groups 1 and 3 in the feet-together position, while in medial-lateral sway in Condition 6, significant differences were found between Group 1 and Group 2 in the heel-to position. These differences were attributed to less sway in the older age groups. The sensory organization system in younger children is less efficient than older children (31). This result is consistent with previous reports that found significant differences in balance performance between age groups (32,33). This finding is consistent with the view that the development of postural control ability results from the development of the proprioceptive, visual, and vestibular systems, and that observable improvements in balance tests occur with age throughout childhood (34). Similar to our study findings, Riach and Hayes (32) found significant differences in postural sway between age groups: older children were more stable compared to younger children. Similar to our study, Deitz et al. (33), in their study examining balance performance with P-CTSIB in children aged 6-9, showed that older age groups were able to maintain their balance better under challenging sensory conditions. The study by Pandian et al. (35) on healthy children aged 7-12, found that the P-CTSIB test scores increased with age, indicating an improvement in balance control skills, which is consistent with the findings of our study.

Sayadi et al. (36) stated that the P-CTSIB is an effective test method for identifying sensory integration difficulties in assessing postural control in children aged 4-6. Improvements in balance have been observed with increasing age, including longer static stance duration and less sway.

Similarly, other studies (37,38) have validated the reliability of P-CTSIB in measuring anterior-posterior sway, test duration, and other balance variables, highlighting its usefulness as a clinically applicable alternative. The heel-toe position reflects the degree of postural stability in the medial/lateral direction, and has been used as an indicator of proprioceptive system abnormalities (39).

Our study focused solely on children with typical development. Future research is recommended to include studies involving larger populations, and children with sensory-motor issues. Additionally, the normative data obtained can serve as a foundation for more effective applications in both clinical and educational settings. In future studies with children who have balance problems, individual differences (such as physical activity level or motivation) and factors that may affect performance can also be examined.

Study Limitations

While these findings contribute significantly to the understanding of postural stability and balance, this study has several limitations, including the prolonged testing duration, which may have caused fatigue in children, potentially affecting their performance. In our study, no additional tests were applied to compare the measured postural sway. Including such tests could have provided a more comprehensive evaluation and strengthened the study's findings.

Conclusion

P-CTSIB is a cost-free test that can measure postural sway under different static test conditions without the need for any equipment. Measuring postural sway provides valuable information in the assessment of balance. It is expected that our findings will serve as a basis for ensuring the usability of P-CTSIB in children with balance disorders in our country. Age-specific normative data obtained from Turkish children using the P-CTSIB test will provide reference data for future studies involving children with balance-affecting pathologies.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of the Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (decision no: 835, date: 06.01.2022).

Informed Consent: Patient consent was obtained for this study.

Footnotes

Author Contributions: Concept - B.M., Ş.Ç., H.M.K., S.Ö., F.D.Ş.; Design - B.M., Ş.Ç., H.M.K., S.Ö., F.D.Ş.; Data Collection and/or Processing - B.M., Ş.Ç., H.M.K., S.Ö., F.D.Ş.; Analysis and/or Interpretation - B.M., Ş.Ç., H.M.K., S.Ö., F.D.Ş.; Literature Search - B.M., Ş.Ç., H.M.K., S.Ö., F.D.Ş.; Writing - B.M., Ş.Ç., H.M.K., S.Ö., F.D.Ş.

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The Effectiveness of Structured Vestibular Assessment Form in the Diagnosis Process

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ABSTRACT

Objective: This study investigated the role of vestibular assessment form in the differential diagnosis of peripheral vestibular disorders, and disorders originating from central or other non-vestibular causes.

Methods: Data from individuals aged 18 and older who visited the audiology unit with complaints of dizziness and/or balance disorders and underwent vestibular/balance evaluation were analyzed. The vestibular disease diagnoses of the individuals and their responses to the vestibular assessment form were evaluated. The vestibular assessment form included questions about the episodes, associated symptoms, auditory symptoms, exacerbating factors, comorbidities, and relieving factors.

Results: The study included 56 individuals with peripheral vestibular pathology (mean age: 48.41±18.15 years, range: 18-77 years) and 29 individuals with non-peripheral vestibular pathology (mean age: 54.55±16.99 years, range: 21-80 years). Vertigo and vestibulo-visual symptoms were more common in individuals with peripheral vestibular pathology, whereas dizziness and postural symptoms were more frequent in individuals with non-peripheral vestibular pathology ($p<0.01$). Auditory symptoms and relieving factors were more common in individuals with peripheral vestibular pathologies ($p<0.05$). In contrast, symptoms such as headache, photophobia, and phonophobia were more frequent in those with non-peripheral vestibular pathologies ($p<0.01$).

Conclusion: The presence of auditory symptoms, vertigo, vestibulo-visual symptoms, neurovegetative symptoms (such as nausea and vomiting), the relieving effect of standing still or resting, and the response to medical treatment in the patient's history, suggest peripheral vestibular pathology. A detailed history is crucial for selecting the appropriate clinical examination, determining the need for additional tests, and ensuring a time- and cost-effective evaluation of patients with vestibular symptoms.

Keywords: Vertigo, dizziness, vestibular symptoms, vestibular disorders, positional vertigo, medical history

INTRODUCTION

Vertigo and dizziness are common reasons for medical consultation, accounting for 2.6% of primary care visits and 3.3-4.4% of emergency department visits (1). Vertigo and dizziness may stem from various sources, including central or peripheral neurological disorders, peripheral organ pathology, and systemic conditions such as hyperlipidemia, diabetes, hypertension, coronary artery disease, and asthma. Therefore, experiencing vertigo and dizziness alone is not enough to make a diagnosis. Associated symptoms, episode details, exacerbating and relieving factors, and comorbidities are crucial for an accurate diagnosis. A detailed medical history is essential to obtain this information. The medical history is a crucial part of the evaluation, where the patient and clinician collaborate to communicate the patient's symptoms (2). Van de Berg and Kingma (3) suggest four key steps in history-taking: i) identifying episodes of dizziness and/or vertigo, ii) identifying chronic vestibular symptoms, iii) screening for psychological and psychiatric comorbidities, and iv) providing a comprehensive diagnosis that considers all possible co-occurring vestibular symptoms.

Many diseases and/or disorders, primarily otological, neurological, and systemic, may play a role in causing symptoms of vertigo and dizziness. The characteristics, presentation, and accompanying symptoms of vertigo and dizziness vary depending on the affected centers and systems (2). In vestibular diseases, many typical features such as exacerbating factors, episode duration, and accompanying symptoms are key to the differential diagnosis (4). For example, neurological symptoms are diagnostic signs

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of vestibular migraine, while auditory symptoms are key for diagnosing Meniere's disease (5,6). However, excluding specific diseases, the differential criteria in the vestibular assessment form for distinguishing between peripheral and non-peripheral vestibular pathologies in clinical patients remain unclear. Therefore, it is important to narrow the range of differential criteria for vestibular pathologies and classify diseases to improve understanding and diagnosis (7).

Based on this information, the study aimed to investigate the role of the vestibular assessment form in the differential diagnosis of vestibular pathologies. The study focused on differentiating between peripheral vestibular pathologies and non-peripheral vestibular disorders, with the latter referring to central vestibular conditions and other diseases related to vertigo. It was anticipated that an effective, well-planned patient assessment process where the clinician addresses all relevant questions about symptoms would save both time and money in reaching a diagnosis.

METHODS

This retrospective study was conducted between January 1, 2022, and April 30, 2022, and included data from individuals aged 18 years and older who presented to Hacettepe University Adult Hospital with complaints of dizziness and/or balance disorders. All participants were referred to the Audiology Unit for vestibular and/or balance evaluation following an examination by an otorhinolaryngologist.

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki, and ethical approval was obtained from the Hacettepe University Non-Interventional Clinical Research Ethics Committee (decision no: 2022/10-7, date: 07.06.2022).

The inclusion criteria for the study were as follows: participants had to be 18 years of age or older, have completed the vestibular assessment form (updated on January 1, 2022), and have both hearing and vestibular evaluation results available. Participants were excluded from the study if they failed to complete the vestibular assessment form thereby limiting the assessment of subjective vestibular symptoms or if there was no confirmed or documented final diagnosis, which would have prevented proper interpretation of clinical findings within a diagnostic framework.

Vestibular Evaluation Procedure

A detailed medical history (anamnesis) was obtained from all patients as part of the vestibular evaluation procedure. Following bedside physical examination, all patients underwent a videonystagmography test battery. This battery included spontaneous nystagmus assessment, oculomotor tests, and positional tests, all of which were administered to every participant.

Additional tests, including the caloric test, cervical and ocular vestibular evoked myogenic potentials, video head impulse test, and computerized dynamic posturography, were administered selectively based on clinical judgment regarding the appropriateness and necessity for each patient.

The results of all tests performed were documented in the vestibular assessment form (Appendix 1).

The vestibular assessment form consisted of seven main sections, in addition to demographic information. These sections included: (i) Episodes (onset and duration, recovery between episodes, imbalance between episodes, viral infection, fullness, and tinnitus before the episode); (ii) Symptoms (dizziness, lightheadedness, vestibulo-visual symptoms, postural symptoms); (iii) Exacerbating factors (spontaneous, active body movement, active head movement, cervical rotation, sound, physical stress, mental stress); (iiii) Auditory symptoms (hearing loss, tinnitus, earache, fluctuations in hearing, fullness); (vi) Associated symptoms (nausea, vomiting, pallor, motion sickness, childhood motion sickness, headache, neck pain, visual impairment, photophobia, osmophobia); (vi) Comorbidities (metabolic diseases, cardiovascular diseases, eye diseases, neurological diseases); and (vii) Relieving factors (spontaneous, standing still, resting, cervical rotation, medication use). The relationship between participants' responses on the vestibular assessment form and the diagnosis of vestibular disease, as determined by clinical examination, was analyzed.

Statistical Analysis

The research data were analyzed using the SPSS v28 program. Since the data collected consisted of categorical variables, descriptive statistics such as percentages and frequencies were used. The comparison of groups (peripheral and non-peripheral) was carried out using the chi-square test, with a statistical significance value of 5%.

RESULTS

The study analyzed data from 85 individuals who were divided into two groups based on their diagnoses: group 1 for those with peripheral vestibular pathology and group 2 for those with non-peripheral vestibular pathology. Group 1 consisted of 56 individuals (mean age: 48.41±18.15 years; 33 females, 23 males), while group 2 included 29 individuals (mean age: 54.55±16.99 years; 22 females, 7 males). No statistical significance was observed in the gender distribution comparison between group 1 and group 2 (p=0.197). No significant difference in age was observed between the groups (p=0.792). This indicates that both groups were comparable regarding gender and age.

Diagnoses of peripheral vestibular pathology in the study (65.8%, n=56) were as follows: benign paroxysmal positional vertigo (BPPV): 25.8% (n=22); idiopathic dizziness: 15.3% (n=13); unilateral vestibulopathy: 11.8% (n=10); presbyopia/presbyvestibulopathy: 7.1% (n=6); and bilateral vestibulopathy: 5.8% (n=5). Non-peripheral vestibular pathologies (34.2%, n=29) included dizziness/drowsiness of cardiological origin, 9.45% (n=8), vestibular migraine, 9.45% (n=8), psychogenic dizziness/drowsiness, 8.2% (n=7), and dizziness/drowsiness of neurological origin, 7.1% (n=6). When comparing the groups with peripheral and non-peripheral vestibular pathologies, a statistically significant difference was found in Figure 1 in terms of vertigo (p=0.005), dizziness (p=0.010),

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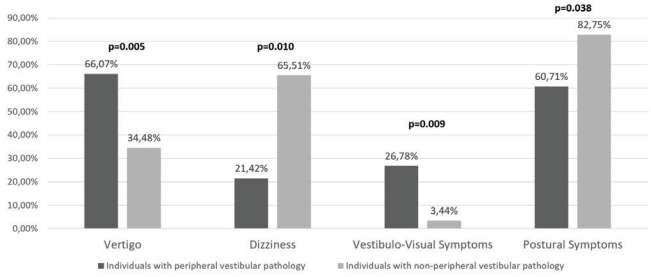

Figure 1. Comparison of the presence of vestibular symptoms in individuals with peripheral and non-peripheral vestibular pathology

vestibulo-visual symptoms (p=0.009), and postural symptoms (p=0.038). Vertigo and vestibulo-visual symptoms were more commonly observed in peripheral vestibular pathologies, while dizziness and postural symptoms were more frequent in non-peripheral vestibular pathologies.

A comparison of the information regarding episodes, associated symptoms, and auditory symptoms from the vestibular assessment form is presented in Table 1. A statistically significant difference was observed between the groups regarding episode duration and onset (p<0.01). Complaints of hearing loss, hearing fluctuations, and fullness were more prevalent in individuals with peripheral vestibular pathology (p<0.05).

When the co-occurrence of auditory symptoms among individuals with peripheral vestibular pathology was compared, the simultaneous occurrence of hearing loss and tinnitus was found to be statistically significant (p<0.001). However, no significant relationship was found between hearing loss and symptoms of fluctuation in hearing (p=0.937), earache (p=0.466), and ear fullness (p=0.596). Similarly, no statistically significant difference was observed between symptoms of tinnitus and hearing fluctuation (p=0.253), earache (p=0.891) and fullness (p=0.149). On the other hand, it was determined that participants with complaints of fluctuation in hearing were also significantly more likely to have the symptom of ear fullness (p<0.001).

Additionally, the distribution of comorbidities, exacerbating and relieving factors, in those with peripheral vestibular pathology and non-peripheral vestibular pathology is shown in Table 2. Cenation (food and beverage) and sound were more commonly identified as exacerbating factors in individuals with peripheral vestibular pathology compared to those with non-peripheral vestibular pathology (p<0.05). Additionally, standing still and consuming medication were reported more frequently as relieving factors in individuals with peripheral vestibular pathology (p<0.05). The spontaneous occurrence of symptoms without a triggering factor was absent in individuals with peripheral pathology; however, it was significantly more prevalent in those with non-peripheral pathology (p=0.001). Analysis of comorbidities revealed higher rates of neurological diseases, photophobia, and phonophobia to among individuals with non-peripheral vestibular pathology (p=0.004).

DISCUSSION

The patient's complaint is the first point of contact between the patient and the clinician, providing valuable insight into the nature and scope of the symptoms. The first step of the vestibular assessment, history-taking, should allow time for careful listening, enabling the patient to discuss not only their symptoms but also how the disease has impacted their daily life (8,9). Treatment and rehabilitation are determined by the diagnosis, physical findings, and the impact of the disease on daily activities. The severity of conditions underlying vestibular symptoms spans a wide clinical spectrum, ranging from benign to life-threatening (9). This study was conducted to investigate the diagnostic value of the responses to the questions in the vestibular assessment form, with the aim of making the history-taking process more effective and structured. As a result of this study, a correlation was observed between the clinical diagnoses of the patients and their responses in the vestibular assessment form.

Peripheral vestibular pathology was diagnosed in 65.8% (56 patients) and non-peripheral vestibular pathology in 34.2% (29 patients) of the individuals who presented to the audiology unit during the specified period for this retrospective study. The study findings are consistent with the literature, indicating a higher prevalence of peripheral vestibular pathologies (10-12). In the group with peripheral vestibular pathology, the most common diagnosis was BPPV (39.3%), followed by unilateral vestibulopathy, presbyvestibulopathy, and bilateral vestibulopathy. In the group with non-peripheral vestibular pathology, the most common diagnosis was vertigo or dizziness of cardiological origin (9.5%), followed by vestibular migraine, psychogenic or neurologically-originated vertigo. Numerous studies have identified BPPV as the most prevalent cause of dizziness of peripheral origin (11,13,14).

The Barany Society classifies vestibular symptoms into four categories: vertigo, dizziness, vestibulo-visual symptoms, and postural symptoms (15). In our study, these categories were used to classify vestibular symptoms. A statistically significant difference was found between patients with peripheral and non-peripheral vestibular pathology, in each of these categories (p<0.05). In our study, vertigo and vestibulo-visual symptoms were more common in patients with peripheral vestibular pathology, while dizziness and postural symptoms were more prevalent in patients with non-peripheral vestibular pathology. These findings are consistent with those described in the literature (16,17).

Since vertigo and dizziness are to often triggered symptoms and many vestibular disorders are characterized by the presence or absence of specific exacerbating factors, it is important to provide detailed definitions of these symptoms when exacerbated (15). When analyzing symptom exacerbating factors, it was observed that episodes were triggered in all individuals with peripheral vestibular pathology (e.g., head-body movement, sound, etc.), whereas, 27.5% of individuals with non-peripheral vestibular pathology experienced episodes that started spontaneously without any identifiable trigger. Similar findings have been

Table 1. Comparative analysis of vertigo episode informations and associated symptoms for peripheral and non-peripheral vestibular disorders

	Peripheral vestibular pathologies (n=56%) n (%)	Non-peripheral vestibular pathologies (n=29%) n (%)	p-value*
Vertigo episode	Suddenly: 40 (71.4%)	Suddenly: 25 (86.2%)	0.120
	Gradually: 16 (28.6%)	Gradually: 4 (13.8%)	
Onset of episode	In a week: 4 (7.1%)	In a week: 0 (0%)	**0.007**
	In a month: 11 (19.7%)	In a month: 0 (0%)	
	3 months ago: 4 (7.1%)	3 months ago: 8 (27.6%)	
	6 months ago: 5 (8.9%)	6 months ago: 2 (6.9%)	
	1 year ago: 11 (19.7%)	1 year ago: 3 (10.4%)	
	Over 1 year: 21 (37.5%)	Over 1 year: 16 (55.1%)	
Duration of episode	Sec/min: 29 (51.8%)	Sec/min: 20 (69%)	**0.001**
	Hours: 18 (32.1%)	Hours: 0 (0%)	
	Days: 8 (14.3%)	Days: 3 (10.3%)	
	Months: 1 (1.8%)	Months: 6 (20.7%)	
Recovery between episodes	39 (69.6%)	18 (62.1%)	0.480
Imbalance between episodes	33 (58.9%)	10 (34.5%)	**0.030**
Viral infection before the episode	5 (9%)	4 (34.5%)	0.490
Tinnitus before the episode	16 (28.6%)	6 (20.7%)	0.430
Fullness before the episode	12 (21.5%)	4 (13.8%)	0.390
Associated symptoms			
Nausea	39 (69.6%)	6 (20.7%)	**0.010**
Vomiting	28 (50%)	2 (6.9%)	0.090
Paleness	13 (23.2%)	4 (13.8%)	0.670
Motion sickness	5 (9%)	2 (6.9%)	0.740
Childhood motion sickness	6 (10.7%)	7 (24.1%)	0.100
Headache	9 (16%)	14 (48.3%)	**0.002**
Neck pain	4 (7.1%)	2 (6.9%)	0.140
Visual impairment	23 (41.1%)	8 (27.5%)	0.220
Light sensitivity	4 (7.1%)	8 (27.5%)	**0.010**
Hyperosmia	13 (23.2%)	4 (13.8%)	0.300
Auditory symptoms			
Hearing loss	31 (55.4%)	8 (27.5%)	**0.010**
Tinnitus	35 (62.5%)	18 (62.1%)	0.960
Earache	6 (10.7%)	4 (13.8%)	0.670
Fluctuation in hearing	7 (12.5%)	0 (0%)	0.040
Fullness	9 (16%)	0 (0%)	**0.020**

Statistically significant values are shown in bold
Chi-square test

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Table 2. Comparison of comorbidities and exacerbating and relieving factors during the vertigo episode in participants with peripheral and non-peripheral vestibular disorders

	Peripheral vestibular pathologies (n=56%) n (%)	Non-peripheral vestibular pathologies (n=29%) n (%)	p-value
Comorbidities			
Metabolic disease	24 (42.9%)	12 (41.4%)	0.890
Cardiovascular disease	24 (42.9%)	14 (48.3%)	0.630
Eye diseases	2 (3.5%)	4 (13.8%)	0.080
Neurological diseases	0 (0%)	4 (13.8%)	**0.004**
Head and neck trauma	8 (14.3%)	2 (6.9%)	0.310
Mental disorders (anxiety, depression etc.%)	9 (16%)	3 (10.4%)	0.470
Photophobia	0 (0%)	4 (13.8%)	**0.004**
Phonophobia	0 (0%)	4 (13.8%)	**0.004**
Exacerbating factors			
Spontaneous	0 (0%)	8 (27.5%)	**0.001**
Active body movement	17 (30.4%)	8 (27.5%)	0.790
Active head movement	34 (60.7%)	12 (41.4%)	0.090
Cenation	8 (14.3%)	0 (0%)	**0.032**
Sound	8 (14.3%)	0 (0%)	**0.032**
Physical stress	24 (42.9%)	12 (41.4%)	0.890
Mental stress	32 (57.1%)	17 (58.6%)	0.890
Relieving factors			
Spontaneous	31 (55.4%)	10 (34.5%)	0.060
Stand still	34 (60.7%)	6 (20.7%)	**0.001**
Take a rest	26 (46.5%)	20 (69%)	0.050
Cenation	0 (0%)	2 (6.9%)	0.050
Consuming medication	18 (32.2%)	3 (10.4%)	**0.020**

Statistically significant values are shown in bold

reported in the literature, suggesting that symptoms associated with peripheral pathology are more specific and closely linked to external factors (18-20). In contrast, symptoms in individuals with non-peripheral pathology may be exacerbated by internal mechanisms that are more specific. The types of exacerbating factors also highlight an important distinction. The majority of individuals with peripheral vestibular pathology (60.7%) reported that active head movements triggered their symptoms, whereas most individuals with non-peripheral vestibular pathology (58.6%) experienced symptom exacerbation due to mental stress. This underscores the differences in the causes and manifestations of peripheral and non-peripheral vestibular disorders.

An analysis of symptom-relieving strategies revealed notable differences between individuals with peripheral and non-peripheral vestibular pathologies. Spontaneous relief was more frequently reported by individuals with peripheral vestibular disorders, potentially reflecting the episodic and self-limiting nature of conditions such as BPPV and vestibular neuritis. In addition, remaining still was identified as a more effective strategy for symptom alleviation in this group, which may be attributed to the movement-provoked nature of peripheral symptoms a hallmark of peripheral vestibular involvement. Furthermore, individuals with peripheral vestibular pathology demonstrated a higher rate of symptom improvement following medical treatment, aligning with prior findings that pharmacological interventions are often more beneficial in cases involving localized and well-defined lesions.

In the present study, auditory symptoms were more frequently observed in individuals with peripheral vestibular pathology. This finding aligns with previous research highlighting the concurrent involvement of the peripheral auditory and vestibular systems, largely attributed to their close anatomical proximity within the inner ear (21-24). Specifically, 55.4% of individuals with peripheral involvement reported hearing loss, 62.5% experienced tinnitus, 12.5% noted hearing fluctuations, and 16% reported aural fullness. In contrast, these symptoms were less frequently observed among those with non-peripheral vestibular pathology, suggesting that peripheral damage may more directly impact auditory structures.

Peripheral vestibular disorders, such as Meniere's disease and labyrinthitis, frequently involve both cochlear and vestibular

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structures, leading to a range of auditory symptoms including hearing loss, tinnitus, aural fullness, and hearing fluctuation (5). In the current study, a statistically significant association was identified between hearing loss and tinnitus in individuals diagnosed with peripheral vestibular pathology. In contrast, no significant correlations were observed between hearing loss and other auditory symptoms such as hearing fluctuation, otalgia, or aural fullness. Similarly, tinnitus was not significantly associated with these accompanying symptoms. These findings suggest that while hearing loss and tinnitus often co-occur, other auditory complaints may manifest more inconsistently and could reflect different underlying mechanisms or stages of disease progression. Taken together, these findings underscore the clinical importance of evaluating auditory symptoms in the differential diagnosis of vestibular disorders. The presence, combination, and severity of these symptoms can provide valuable clues for distinguishing peripheral from non-peripheral vestibular conditions and for guiding diagnostic and therapeutic decision-making.

Analysis of symptom profiles in individuals with peripheral vestibular pathologies demonstrated a predominance of autonomic and emetic manifestations. Nausea (69.6%), vomiting (50%), and paleness (23.2%) were frequently reported, aligning with the established role of vestibulo-autonomic pathways in mediating motion-induced autonomic responses. The symptom profile of individuals with non-peripheral vestibular pathology follows a different pattern. In this group, symptoms such as nausea (20.7%), vomiting (6.9%), and paleness (13.8%) are less common, while headache (48.3%) and light sensitivity (27.5%) are more prevalent. The findings suggest that the peripheral vestibular system is more closely linked to emetic and autonomic reactions. Nausea and vomiting are more commonly associated with peripheral vestibular pathologies, while non-peripheral vestibular pathologies are more closely related to neurological symptoms such as headache and photophobia.

The findings regarding the episodes align with those reported in the literature (16,24). In our study, episodes in individuals with peripheral vestibular pathology typically lasted seconds to minutes or seconds to hours (83.9%). In contrast, episodes in individuals with non-peripheral vestibular pathology were mostly brief (seconds to minutes), with 20.7% of cases experiencing episodes lasting for months. These data reveal significant differences in episode duration between individuals with peripheral and non-peripheral vestibular pathology, which may aid in the differential diagnosis.

Additionally, when the onset of episodes was examined, it was found that individuals with non-peripheral vestibular pathology seek care at otolaryngology and audiology clinics later than those with peripheral vestibular pathology. This delay may be attributed to the shorter diagnostic period for individuals with peripheral vestibular pathology compared to those with non-peripheral vestibular pathology, who often consult multiple departments, thus prolonging the diagnostic process. Another important finding of this study is that 38.8% of individuals with peripheral vestibular pathology experience imbalance between episodes, compared to 11.8% of individuals with non-peripheral vestibular pathology. These results indicate that imbalance is more commonly reported between episodes in individuals with peripheral vestibular pathology. This finding could be valuable for guiding the rehabilitation processes of patients. When comorbidities were assessed, our study found no significant difference in the prevalence of metabolic, cardiovascular, and psychiatric diseases between individuals with peripheral and non-peripheral vestibular pathologies. Neurological diseases, photophobia, and phonophobia were not observed in any of the individuals with peripheral vestibular pathology, but were present in 13.8% of those with non-peripheral vestibular pathology. In addition, migrainous headaches, visual aura, and moderate to severe vestibular symptoms serve as important indicators for the diagnosis of vestibular migraine (25).

Study Limitations

The limited number of individuals with non-peripheral vestibular pathologies was insufficient to identify generalizable symptoms for these conditions. Moreover, the broad spectrum of diseases within this group further complicates the identification of common symptoms. A larger sample size may enable the determination of pathology-specific symptom rates.

Although summary reports of patients' hearing and vestibular evaluations were available in the form of clinician-generated conclusions, detailed findings were not accessible to a degree that would allow for parameter-based analysis. As a result, it was not possible to assess correlations between patients' subjective symptoms and objective test parameters. In future studies, we recommend including objective audiovestibular test results to enable such analyses. While vestibular history forms cannot replace objective assessments in audiovestibular evaluations, they can serve as a strong foundation for guiding the selection of appropriate diagnostic tests and for supporting potential diagnoses.

CONCLUSION

The most important step in the diagnostic process of patients with vertigo or dizziness, particularly for otolaryngologists and audiologists, is distinguishing between peripheral and non-peripheral vestibular pathologies. In some non-peripheral vestibular pathologies, the information obtained from the patient is crucial for differential diagnosis, particularly when objective tests may yield normal results. For this reason, asking the right questions on the vestibular assessment form is crucial. In our study, individuals with peripheral vestibular pathology commonly experienced vertigo and vestibulo-visual symptoms, while those with non-peripheral vestibular pathologies more frequently reported dizziness and postural symptoms. Additionally, individuals with peripheral vestibular pathology experienced higher rates of auditory symptoms, while relieving factors such as standing still/resting and medical support were more commonly observed. These findings are expected to aid clinicians and

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researchers by enhancing the history forms they use, serving as both a supplement to and a precursor for objective tests.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the principles outlined in the Declaration of Helsinki, and ethical approval was obtained from the Hacettepe University Non-Interventional Clinical Research Ethics Committee (decision no: 2022/10-7, date: 07.06.2022).

Informed Consent: Retrospective study.

Footnotes

Author Contributions: Concept - S.Ö., N.B.A.; Design - S.Ö., N.B.A., Ö.Y.; Data Collection and/or Processing - S.Ö., N.B.A., Ö.Y.; Analysis and/or Interpretation- S.Ö., N.B.A., Ö.Y.; Literature Search - S.Ö., N.B.A., Ö.Y.; Writing - S.Ö., N.B.A., Ö.Y.

Conflict of Interest: There is no potential conflict of interest between the authors and/or their family members and scientific and medical committee membership or relationships with committee members. Additionally, there is no conflict due to consultancy, expert witness status, employment status in any company, shareholding status, or similar status regarding this study.

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Appendix Link: https://l24.im/HdQ

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Evaluation of Changes in Ventricular Repolarization Parameters After Surgical Mitral Valve Repair in Patients with Mitral Valve Prolapse

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ABSTRACT

Objective: To evaluate the changes in ventricular repolarization parameters in preoperative and postoperative electrocardiograms (ECGs) of patients who underwent mitral valve repair (MVR) for mitral valve prolapse (MVP).

Methods: Patients who underwent MVR due to MPV with severe mitral regurgitation were included in the study. A resting 12-lead ECG was recorded both preoperatively and 6 months postoperatively. QT, QTc, cQTd, JT, JTc, and Tp-e were measured; Tp-e/QT and Tp-e/QTc ratios were calculated.

Results: The study included 53 patients (58.5% male), with a mean age of 52.7±13 years. The durations of PR, QRS, QT, cQT, cQTd, JT, cJT, and Tp-e were reduced significantly ($p<0.001$) six months after repair.

Conclusions: The repolarization parameters changed after MVR surgery. Shortening of the QT, cQT, cQTd, JT, cJT, and Tp-e durations after the repair procedure may reduce the risk of sudden cardiac death, and arrhythmias in MVP.

Keywords: Mitral valve prolapse, mitral valve regurgitation, mitral valve repair, sudden cardiac death, ventricular arrhythmia, ventricular repolarization

INTRODUCTION

In developed countries, mitral valve prolapse (MVP) is the leading cause of primary mitral regurgitation (MR) (1). However, rheumatic mitral valve disease continues to be more common in developing countries (2). MVP is associated with several significant complications, including severe MR, heart failure, transient ischemic attacks, cerebrovascular events, ventricular arrhythmias (VAs), infective endocarditis, and sudden cardiac death (SCD) (3). While several studies have indicated that MVP may increase the risk of SCD, the exact incidence remains undefined. Research has shown a reduction in VAs following mitral valve surgery (4,5). VAs are a leading cause of SCD in MVP (6). Furthermore, alterations in the electrocardiogram (ECG) repolarization phase have been associated with VAs and SCD (7). Parameters such as JT, QT, and Tp-e intervals, when measured and compared on an ECG, are valuable indicators for assessing the risk of VAs and SCD. While the QT interval reflects overall repolarization, the JT interval is more specific to repolarization, and the Tp-e interval reflects the dispersion of ventricular repolarization. This study aimed to assess preoperative and postoperative differences in the JT, QT, and Tp-e intervals on 12-lead ECGs of patients with MVP undergoing mitral valve repair (MVR).

METHODS

In accordance with the Declaration of Helsinki, the study was conducted after obtaining approval İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (decision no: 954, date: 10.11.2022), and written informed consent was secured from all participants. The 53 patients who underwent MVR for MVP with severe MR between January 2019 and December 2022 were included in the study. Baseline characteristics were recorded for all patients. Patients with persistent atrial fibrillation before or after surgery, chronic ischemic heart disease, decreased left ventricular ejection fraction (LVEF), right or left bundle block or atrioventricular blocks, structural heart disease, valve pathology other than MVP, and decreased LVEF function after surgery were excluded. A 12-lead ECG was recorded at rest before surgery and 6 months after surgery.

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ECG recordings of all patients were obtained with a standard machine (Nihon Kohden Cardiofax ECG-1950 VET) with an amplitude of 10 mm/mV and using all 12 leads: I–III, aVR, aVF, V1-V6, at a speed of 25 mm/s in the supine position. ECG samples were evaluated by two different cardiologists. QT, QTc, cQTd, JT, JTc, and Tp-e were measured. Corrected QT dispersion was calculated by subtracting the minimum corrected QT interval (QTc) from the maximum QTc interval. The PR interval was calculated from the beginning of the P wave to the commencement of the QRS complex. The QRS duration was determined from the onset of the Q wave to the end of the S wave. The Tp-e interval was manually measured from the peak of the T wave to the lowest point of the wave in the precordial leads (V4, V5, and V6). The QT interval was measured from the onset of the QRS complex to the end of the T wave, or from the onset of the QRS complex to the point where the T wave returned to baseline in cases where a U wave was present. The QTc interval was calculated using the Bazett formula.

Normal QTc values range from 360 to 460 ms in women and from 350 to 450 ms in men (8). The JT interval was measured from the J point to the end of the T wave in the precordial leads. Measurements were taken until the nadir of the Tp-e, and the QTc ratios were subsequently calculated.

MR severity, anatomy of the mitral leaflets, left ventricular function, left ventricular diameters, and left atrial diameter were evaluated with GE Philips Health Care Vivid T8 cardiovascular ultrasound machines, with transthoracic transducers.

Statistical Analysis

The normality of continuous variables was assessed using the Kolmogorov-Smirnov test and analyzing histogram plots. Normally distributed variables were given as the mean and standard deviation. The other categorical variables were shown as absolute numbers and percentages. The paired-sample t-test was used to investigate whether there was a statistically significant difference in the preoperative and postoperative values of the electrocardiographic and echocardiographic parameters for the normally distributed variables. The threshold of statistical significance in the study results was established as a p-value <0.05. The IBM Statistics, version 26, program was used for all statistical analyses (IBM Corporation, NY, USA).

RESULTS

The mean age of the patients included in the study was 52.7±13 years. Table 1 summarizes the clinical, echocardiographic, and procedural features of the patients. There were 31 (58.5%) male and 22 (41.5%) female patients. Anterior prolapse was observed in 7 (13.2%), posterior prolapse in 27 (50.9%), and bileaflet prolapse in 19 (35.8%) patients. Tricuspid valve prolapse was observed in 29 patients (54.7%), and tricuspid annuloplasty was performed in addition to MVR in 18 of these patients (34%). Mitral chordal and leaflet augmentation was performed in 47 (88.7%) patients, and mitral ring annuloplasty was performed in 34 (64.2%) patients.

There were significant improvements in the left ventricular end-systolic, end-diastolic diameters, left atrial diameter, and pulmonary artery systolic pressure 6 months after the operation. Pre-operative and postoperative electrocardiographic findings of patients are shown in Table 2. The mean heart rate of patients was 82.2±15.8 beats per minute (bpm) before the operation and was reduced to 70.2±10.5 bpm after six months of MVR. The mean PR duration was 162.1±30.9 ms before, 142.6±28.8 in 6 months after the operation (p<0.001). Similar to the shortening of the PR interval, the duration of the QRS (from 91.1±11.2 to 86.9±9.3), the QT (from 424.8±40.1 to 394.4±34.3 ms), the constant Q transform

Table 1. Clinical, echocardiographic and procedural features of the study population (n=53)

	Mean±SD / n (%)		
Age, years	52.7±13.1		
Gender (male)	31 (58.5%)		
Hypertension	22 (41.5%)		
Diyabetes mellitus	5 (9.4%)		
Dyslipidemia	8 (15.1%)		
Coronary artery disease	10 (18.9%)		
Anterior/posterior/bi-leaflet prolapse	7 (13.2%)/27 (50.9%)/19 (35.8%)		
Tricuspid valve prolapse	29 (54.7%)		
Tricuspid ring annuloplasty	18 (34%)		
Mitral cordal augmentation	47 (88.7%)		
Mitral ring annuloplasty	34 (64.2%)		
	Pre-op	**Post-op**	**p-value**
LVEF (%)	61.1±5.7	57.4±7.7	<0.001*
LVESD (mm)	40.1±4.9	36.1±3.1	<0.001*
LVEDD (mm)	58.3±4.8	45.7±7.5	<0.001*
LAD (mm)	47.1±5.2	42.8±5.7	<0.001*
sPAP (mmHg)	40.2±13.9	27.3±7.6	<0.001*

*Paired-sample t-test was used
LVEF: Left ventricle ejection fraction, LVESD: Left ventricle end-systolic diameter, LVEDD: Left ventricle end-diastolic diameter, LAD: Left atrial diameter, sPAP: Systolic pulmonary artery pressure

Table 2. Pre-operative and postoperative comparison of the electrocardiographic findings

	Pre-op	Post-op	p-value
Heart rate, bpm	82.2±15.8	70.2±10.5	<0.001*
PR, ms	162.1±30.9	142.6v28.8	<0.001*
QRS, ms	91.1±11.2	86.9±9.3	0.001*
QT, ms	424.8±40.1	394.4±34.3	<0.001*
cQT, ms	439.6±39.6	419.2±22.9	0.002*
cQTd, ms	42.9±7.9	36.7±7.9	<0.001*
JT, ms	331.1±46.1	311.7±29.4	0.01*
cJT, ms	351.2±35.9	336.1±18.1	<0.001*
Tp-e, ms	87.9±13.1	81.2±9.2	<0.001*

*Paired-sample t-test was used

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(cQT) (from 439.6±39.6 to 419.2±22.9 ms), the cQTd (from 42.9±7.9 to 36.7±7.9 ms), the JT (from 331.1±46.1 to 311.7±29.4 ms), the cJT (from 351.2±35.9 to 336.1±18.1 ms), and the Tp-e (from 87.9±13.1 to 81.2±9.2 ms) were reduced significantly after MVR ($p<0.001$).

DISCUSSION

In this article, we analyzed QT, cQT, cQTd, JT, cJT, and Tp-e interval durations of MVP patients before and at six months after MVR surgery. A significant reduction in these parameters was observed following successful MVR.

According to our study, MVR appears to exert a beneficial effect on the regression of ventricular repolarization parameters, potentially lowering the incidence of VAs. However, data regarding repolarization changes following cardiac surgery remain limited. A short-term prolongation of the QT interval is observed postoperatively. General anesthetic agents, antibiotic agents, cardioactive drugs, antiarrhythmic drugs, or increased inflammatory activation after surgery are among the causes. The ventricular repolarization parameters reach normal values, 3-6 months after surgery (9).

The prevalence of MVP is 2-3% (10). Although MVP is usually described as a benign disease, it is associated with SCD. Humphries and McKusick (11) first described inferior T wave inversions (TWI) in patients with mitral valve disease, which was later defined as MVP. The SCD was higher in patients with inferior TWI (12). In case reports, the VAs were suppressed, and inferior (TWI) improved after MVR, due to MVP (13). The study aimed to evaluate changes in ventricular repolarization parameters following surgical MVR for MVP, which have not been previously assessed in the literature. Unfortunately, there is no definitive treatment option to prevent SCD in MVP patients. Despite their widespread use in managing VAs associated with MVP, the evidence supporting the efficacy of beta-blockers remains insufficient. A recent study demonstrated that ventricular ectopic impulses of fascicular and papillary muscle can trigger ventricular fibrillation (VF). This study indicates that catheter ablation may play a role in mitigating the complications associated with symptomatic arrhythmias and reducing the necessity for implantable cardioverter defibrillators (14).

Arrhythmogenesis in MVP is significantly influenced by the Purkinje system. Suppression of VA after MVR has been shown in limited case reports (15,16). Vaidya et al. (17) revealed that after surgical correction of bileaflet MVP, the surgical correction reduced the malignant arrhythmia and appropriate shocks.

The exact mechanism of VAs in patients with MVP and their relationship with mechanical, electrical, or hemodynamic factors is yet to be clearly established. It is believed that arrhythmias in MVP may arise from myocardial stretching or endocardial friction lesions due to the retraction of the valve leaflet over the papillary muscle (18). The presence of late gadolinium enhancement at the papillary muscle level or adjacent free wall has been associated with the origin of VAs. In MVP, SCD is generally attributed to VF, with some studies suggesting that VF may be caused by excessive leaflet motility, which leads to mechanical stretching of the valve apparatus, followed by stretch-induced fibrosis and ectopic foci.

Variations in the QT interval, QT dispersion, and J-point elevation may be implicated in the pathogenesis of VAs in MVP patients. By demonstrating improvements in ventricular repolarization parameters post-surgery, this study provides valuable insights to the existing literature on MVP. It has been shown in previous studies that the QT interval, JT interval, and Tp-e measurements are important predictors of Vas (19-21). In our findings, repolarization abnormalities reverted to normal after MVP surgery. In a published case, TWIs, one of the key ventricular repolarization parameters, were observed to return to normal on the first day after surgery, a change attributed to hemodynamic factors rather than structural modifications.

The prolapse of the mitral valve induces mechanical stress on the left atrium. Theoretically, timely MVR prevents the development of scar tissue and may reduce the risk of VAs. Following MVR, left ventricular volume decreases due to hemodynamic effects. Because QRS duration correlates with left ventricle end-diastolic volume, prolonged QRS duration has been associated with elevated cardiovascular mortality (22). Consequently, MVR may improve ventricular repolarization parameters by reducing mechanical stretch, decreasing left ventricular volume, and potentially preventing the development of VAs.

Study Limitations

The retrospective design of our study and the limited number of cases included are notable limitations. One of the key factors contributing to this is the small number of centers in our country where MVP repair can be performed. ECG changes were compared before the operation and 6 months after the operation; and follow-ups of ECGs were not performed during this period. however

CONCLUSION

Ventricular repolarization parameters were altered following MVR surgery. Shortening of QT, cQT, cQTd, JT, cJT and Tp-e intervals after repair of MVP may reduce the risk of SCD and arrhythmia in these patients. Surgical repair of MVP plays a crucial role in normalizing ventricular repolarization parameters and preventing SCD.

Ethics

Ethics Committee Approval: Approval was obtained for this study from the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (decision no: 954, date: 10.11.2022).

Informed Consent: Written informed consent was secured from all participants.

Footnotes

Author Contributions: Surgical and Medical Practices - Ü.S, A.A., A.H.; Concept - Ü.S.; Design - Ü.S. A.H.; Data Collection and/or Processing - Ü.S.; Analysis and/or Interpretation - A.A.; Literature Search - Ü.S.; Writing - Ü.S.

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Evaluation of the Impact of Epileptic Seizures on Cardiac Electrical Activity Through Postictal Electrocardiography (ECG): an Observational Prospective Study

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ABSTRACT

Objective: Epileptic seizures affecting higher autonomic control centers may disrupt parasympathetic-sympathetic balance, contributing to cardiovascular dysfunction and increased morbidity and mortality. This study aimed to evaluate the impact of epileptic seizures on cardiac electrical activity using post-ictal electrocardiography (ECG).

Methods: This prospective cohort study evaluated patients presenting to the emergency department with epileptic seizures. Demographic data, laboratory results, and ECG parameters (heart rate, rhythm, wave durations, and morphologies) were recorded. Patients were categorized as newly diagnosed or known epilepsy cases, with further classification based on antiepileptic drug use. The frequency of ECG abnormalities was analyzed, comparing conduction disturbances between groups.

Results: This study included 205 cases of epileptic seizures. Among the patients, 35 (17.1%) were newly diagnosed. Sinus tachycardia was observed in 24.4%, T wave inversion in 30.2%, and first-degree atrioventricular block in 4.9%. PR interval abnormalities were detected in 7.8% and corrected QT interval (QTc) abnormalities in 10.7%. Prolonged PR interval was more common in newly diagnosed patients (14.3% vs. 2.9%, p=0.036), while the mean QTc interval was shorter in these patients compared to controls (p=0.040). No significant differences were found in tachycardia/bradycardia (p=0.403), ST segment changes (p=0.680), QRS duration (p=0.204), or ECG parameters based on antiepileptic drug use. Intensive care unit (ICU) patients had higher leukocyte (p=0.036) and neutrophil counts (p=0.009), with lower pH (p=0.004) and bicarbonate levels (p=0.009).

Conclusion: Sinus tachycardia is the most prevalent ECG abnormality in epileptic seizures. Elevated lactate and decreased bicarbonate levels may predict seizure duration and ICU admission. No significant association was found among epilepsy, anti-epileptic drugs, and severe arrhythmias.

Keywords: Electrocardiography, anti-epileptics, epileptic seizure, autonomic dysfunction, cardiac conduction abnormalities

INTRODUCTION

Epilepsy is a complex neurological condition involving abnormal, hypersynchronous neuronal activity. It manifests with a wide range of symptoms, including involuntary motor movements such as muscle contractions, automatisms like chewing and swallowing, autonomic disturbances, and varying degrees of altered consciousness (1). Although different theories have been proposed, it is thought to occur due to an imbalance in the excitation-inhibition dynamics of neurons (2). Epileptic seizures cause transient disruption of brain functions and can lead to severe complications by impacting multiple physiological systems simultaneously. In this regard, epileptic seizures represent a potentially life-threatening and prevalent public health concern.

Various mechanisms have been proposed for the pathophysiology of epileptic seizures. However, the cellular mechanisms are not fully understood. Among the most widely accepted mechanisms are the inhibition of Gamma-aminobutyric acid (GABA) ergic interneurons and ion channel mutations (3). Ion channel mutations disrupt excitatory-inhibitory balance, leading to increased neuronal excitability. One of the systems most directly associated with ion channels is the cardiac conduction system. This relationship is a key point that suggests a potential link between epilepsy, epileptic seizures, and cardiac arrhythmias.

Epileptic discharges involving higher autonomic control centers may disrupt the balance between parasympathetic and sympathetic activity. This can lead to autonomic dysfunction and

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result in various cardiovascular abnormalities during seizures (4). Cardiovascular abnormalities are often characterized by alterations in heart rate and rhythm. These effects are linked to an increased risk of early mortality and morbidity, primarily due to their association with cardiovascular disease (4).

The primary aim of this study is to evaluate the effect of epileptic seizures on the electrical activity of the heart through electrocardiography (ECG) obtained during the post-ictal period. Additionally, it aims to investigate the association between anti-epileptic drugs and ECG abnormalities in patients with known epilepsy. The secondary aim of our study is to identify key parameters, such as vital signs, ECG findings, and laboratory results, that can help determine the need for admission and assess the requirement for intensive care unit admission in patients with epileptic seizures.

METHODS

Ethical committee approval for the study was obtained from Haydarpaşa Numune Training and Research Hospital, Clinical Research Ethics Committee, University of Health Sciences (approval no: HNEAH-KAEK 2022/KK/117, date:13.06.2022). This study was conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from all subjects or their relatives.

Case Selection

This study was conducted on patients admitted to the Emergency Medicine Clinic of Haydarpaşa Numune Training and Research Hospital, University of Health Sciences Türkiye, between July 13, 2022, and January 13, 2023, with active epileptic seizures or in the postictal period. Inclusion criteria were age over 18 years, a known or newly diagnosed epilepsy, and presentation either with an active seizure or during the postictal period. Exclusion criteria included pregnancy, seizures secondary to increased intracranial pressure (e.g., hemorrhagic or ischemic stroke, mass lesions, or traumatic hemorrhage), unconfirmed epileptic seizure diagnosis during follow-up, and a history of cardiac arrhythmia or coronary artery disease.

Case Classification

Patients diagnosed with epilepsy for the first time in the emergency department were categorized as "newly diagnosed"; while those with a known history of epilepsy were categorized as "known epilepsy". Patients receiving a single anti-epileptic drug were classified under monotherapy, while those receiving more than one anti-epileptic drug were classified under polytherapy. The cases were further categorized based on the type of epileptic seizure as partial (focal) or generalized.

Electrocardiogram Recording

Electrocardiogram (ECG) was performed in the post-ictal period to assess the effects of epileptic seizures on cardiac electrophysiology. The heart rate, rhythm, wave durations, and wave morphologies were individually recorded for each patient. Thus, the frequency of ECG abnormalities and the relationship between epilepsy and cardiac conduction disturbances were examined. ECG parameters were compared between the "newly diagnosed" and "known epilepsy" groups, as well as among "known epilepsy" patients based on the type and number of anti-epileptic drugs used. Thus, ECG findings potentially associated with anti-epileptic drug use and those that could help distinguish known epilepsy cases from newly diagnosed ones were investigated. Additionally, ECG findings related to discharge-admission decisions were identified and analyzed.

Diagnostic Tests

The patients' characteristics, including age, gender, history of known epilepsy or newly diagnosed, and medications, were recorded. Age, gender, comorbidities, hemogram, blood urea nitrogen, creatinine, sodium, potassium, calcium, magnesium, phosphorus, chloride, creatine kinase, albumin, high-sensitive troponin tests, and venous blood gas (lactate, bicarbonate level, pH) were compared between the newly diagnosed and known epilepsy patient groups. Additionally, cerebral imaging tests (computed tomography, magnetic resonance imaging) were used for etiology and differential diagnosis.

Statistical Analysis

Descriptive statistics were expressed as frequency (n), percentage (%), mean, standard deviation, median, and interquartile range [interquartile range (IQR) 25-75 percentiles]. The relationship between categorical variables was examined using Pearson's chi-square and Fisher Exact tests. The normality of the data was tested using the Shapiro-Wilk test. Differences in continuous variables between independent groups were assessed using the Mann-Whitney U test and Kruskal-Wallis test, when the data did not follow a normal distribution, and the independent t-test and one-way analysis of variance when the data followed a normal distribution. In non-parametric comparisons of three or more groups, the Bonferroni correction was applied for post hoc tests, while the Türkiye hypermobility spectrum disorder test was used for parametric comparisons. The data analysis was performed using IBM Statistical Package for the Social Sciences 23.0 software (IBM Corp., Armonk, NY), and p-values less than 0.05 were considered statistically significant.

RESULTS

Our study included 205 patients. The mean age was 33 years (IQR: 24-41). Among the patients, 117 (57.1%) were male and 88 (42.9%) were female. The majority of the patients had a known diagnosis of epilepsy, while 35 patients (17.1%) were newly diagnosed. A significant proportion of the patients (90.7%) were discharged following treatment and follow-up in the emergency department, while 7 patients (3.4%) were admitted to the neurology ward, and 12 patients (5.9%) were transferred to the intensive care unit for further management. The age (p=0.081) and gender (p=0.993) distributions between patients with newly diagnosed and known epilepsy were similar. The demographic characteristics, vital

parameters, laboratory findings, and admission-discharge status of patients with known epilepsy and newly diagnosed epilepsy are shown in Table 1.

ECG analysis revealed that 88.3% of the patients had normal sinus rhythm, 24.4% had sinus tachycardia, 30.2% exhibited T wave inversion, and 4.9% had first-degree atrioventricular (AV) block. ST segment changes were absent in 199 patients (97.1%). PR interval abnormalities were observed in 16 patients (7.8%), while corrected QT (QTc) interval abnormalities were detected in 22 patients (10.7%). The overall mean PR interval duration was 154.29±23.58 ms, the mean QTc interval duration was 417.61±27.68 ms, and the mean QRS complex duration was 90.83±11.09 ms.

The baseline rhythm characteristic, (p=0.269), the presence of tachycardia or bradycardia, (p=0.403), ST segment changes, (p=0.680), PR interval abnormalities, (p=0.255), QTc interval abnormalities, (p=0.619), and QRS complex duration (p=0.204) were comparable between the newly diagnosed and known epilepsy groups. Although the rate of T wave negativity was higher in patients with known epilepsy, this difference was not statistically significant (p=0.064). The rate of first-degree AV block was significantly higher in the newly diagnosed group compared to, the known epilepsy group (14.3% vs. 2.9%, p=0.015). The proportion of prolonged PR interval was significantly higher in the newly diagnosed group compared to the known epilepsy group (14.3% vs. 2.9%, p=0.036). Additionally, the mean QTc interval duration was observed to be shorter in the newly diagnosed group (p=0.040). The ECG findings of patients in the newly diagnosed and known epilepsy groups are shown in Table 2.

Table 1. Comparison of demographics, laboratory parameters, and admission status

Parameters	All patients	Newly diagnosed	Known epilepsy	p-value
Number of patients, (%)	205	35 (17.1)	170 (82.9)	-
Age (year)	33 (24-41)	39 (26-51)	32 (24-41)	0.081
Gender				
Male	117 (57.1)	20 (57.1)	97 (57.1)	0.993
Female	88 (42.9)	15 (42.9)	73 (42.9)	
Blood sugar (mg/dL)	113 (97-130)	121 (108-140)	110 (96-127)	**0.014**
Body temperature (°C)	36.6 (36.4-36.8)	36.6 (36.5-36.8)	36.5 (36.4-36.8)	0.254
Heart rate (atım/dk)	86 (73-98)	83 (69-94)	86 (74-99)	0.185
SBP (mmHg)	123 (110-134)	123 (111-142)	122 (110-132)	0.216
Leukocyte (/uL)	8270 (6760-10860)	8300 (7040-12480)	8100 (6720-10840)	0.253
Neutrophil (/uL)	5290 (3690-7090)	5400 (4030-7020)	5285 (3660-7110)	0.416
Lymphocyte (/uL)	2220 (1600-3210)	2500 (1590-3740)	2165 (1600-3050)	0.260
Hemoglobin (g/dL)	13.52±1.88	13.5±1.85	13.53±1.89	0.942
Hct (%)	40.82±5.26	40.79±5.44	40.82±5.24	0.973
Platelets (103/uL)	256 (209-297)	285000 (208-323)	252 (209-291)	0.254
CRP (mg/dL)	1.63 (0.63-4.75)	3.17 (0.7-7.56)	1.51 (0.59-4.09)	0.189
Urea (mg/dL)	24.4 (19.3-30.2)	27 (18.8-33)	24.05 (19.3-29.3)	0.126
BUN (mg/dL)	11.4 (9.01-14.11)	12.62 (8.79-15.42)	11.24 (9.01-13.69)	0.123
Creatinine (mg/dL)	0.76 (0.65-0.93)	0.75 (0.65-0.98)	0.76 (0.65-0.93)	0.518
Sodium (mEq/L)	138 (136-140)	138 (135.1-140.4)	138 (136.2-139.9)	0.872
Chloride (mEq/L)	102.2 (99.9-103.9)	101.3 (99.1-103.5)	102.25 (99.9-104)	0.280
Na-Cl	35.88±3.05	36.06±3.32	35.84±3	0.704
HS-troponin (ng/L)	3.46 (3-5.89)	4 (3-5.51)	3.44 (3-6)	0.605
pH	7.35 (7.31-7.38)	7.35 (7.3-7.37)	7.35 (7.31-7.38)	0.716
Bicarbonate (mEq/L)	22.4 (20-24)	21.6 (17.8-23)	22.6 (20.2-24.2)	**0.013**
Lactate (mmol/L)	2.4 (1.51-5.12)	4.41 (2.3-8.16)	2.25 (1.46-4.85)	**0.001**
Admission status				
Discharged	186 (90.7)	30 (85.7)	156 (91.8)	0.265
Ward	7 (3.4)	1 (2.9)	6 (3.5)	
ICU	12 (5.9)	4 (11.4)	8 (4.7)	

The results are presented as mean±SD, median (IQR), or n (%). Independent t-test, Mann-Whitney U test, Pearson Chi-square test, Fisher's Exact test
BUN: Blood urea nitrogen, Na-Cl: Sodium chloride, CRP: C-reactive protein, Hct: Hematocrit, HS: High sensitive, ICU: Intensive care unit, SBP: Systolic blood pressure, IQR: Inpatient quality reporting, SD: Standard deviation

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In our study, we determined that 186 patients were discharged after emergency department follow-up, 7 patients were admitted to the neurology ward for further observation, and 12 patients were transferred to the ICU. No statistically significant relationship was found between patients' baseline rhythm characteristics (p=0.217), ST segment abnormalities (p=0.156), PR interval duration (p=0.225), QTc interval abnormalities (p=0.707), QTc interval duration (p=0.337), and their admission status. The rates of tachycardia and T wave negativity (p=0.108 and p=0.355), as well as the average QRS complex duration (p=0.090), were higher in patients with status epilepticus admitted to the ICU, although the differences were not statistically significant. The frequency of P-wave absent rhythm (8.3%) was significantly higher in patients followed in the ICU compared to those admitted to the ward (0%) (p=0.027). The ECG findings based on the patients' admission status are presented in Table 3.

In terms of vital parameters, the heart rate was higher in the ICU group compared than the other groups; however, this difference was not statistically significant. Among patients followed in the ICU, leukocyte (p=0.036) and neutrophil (p=0.009) counts were significantly higher, while pH (p=0.004) and bicarbonate (p=0.009) levels were notably lower compared to the other groups. There were no significant differences in other laboratory findings based on admission status (p>0.05). Vital parameters and laboratory

Table 2. Comparison of ECG parameters based on new diagnosis vs. known epilepsy

ECG parameters	All patients (n=205)	Newly diagnosed (n=35)	Known epilepsy (n=170)	p-value
Basic rhythm				
Sinus rhythm	181 (88.3)	29 (82.9)	152 (89.4)	0.269
RBBB	4 (2)	2 (5.7)	2 (1.2)	
AF	1 (0.5)	0 (0)	1 (0.6)	
Sinus arrhythmia	19 (9.3)	4 (11.4)	15 (8.8)	
Heart rate				
Tachycardia	50 (24.4)	6 (17.1)	44 (25.9)	0.403
Bradycardia	11 (5.4)	3 (8.6)	8 (4.7)	
Normal	144 (70.2)	26 (74.3)	118 (69.4)	
T wave abnormality				
Absent	143 (69.8)	29 (82.9)	114 (67.1)	0.064
T wave negativity	62 (30.2)	6 (17.1)	56 (32.9)	
ST segment abnormality				
Absent	199 (97.1)	34 (97.1)	165 (97.1)	0.680
ST elevation	3 (1.5)	1 (2.9)	2 (1.2)	
ST depression	3 (1.5)	0 (0)	3 (1.8)	
AV block				
Absent	195 (95.1)	30 (85.7)	165 (97.1)	**0.015**
First-degree	10 (4.9)	5 (14.3)	5 (2.9)	
PR interval				
Normal duration	189 (92.2)	29 (82.9)[a]	160 (94.1)[b]	**0.036**
Short PR	5 (2.4)	1 (2.9)[a]	4 (2.4)[a]	
Long PR	10 (4.9)	5 (14.3)[a]	5 (2.9)[b]	
P wave absent rhythm	1 (0.5)	0 (0)[a]	1 (0.6)[a]	
PR interval (msn)	154.29±23.58	158.43±30.46	153.43±21.9	0.255
QTc interval				
Normal duration	183 (89.3)	33 (94.3)	150 (88.2)	0.619
Short QT	1 (0.5)	0 (0)	1 (0.6)	
Long QT	21 (10.2)	2 (5.7)	19 (11.2)	
QTc interval (msn)	417.61±27.68	408.86±28.33	419.42±27.28	**0.040**
QRS complex (msn)	90.83±11.09	93±11.52	90.38±10.99	0.204

The results are presented as mean±SD or n (%). Independent t-test, Pearson Chi-square test, Fisher's Exact test. The same lowercase letters in a row indicate no significant difference between the groups
AF: Atrial fibrillation, RBBB: Right bundle branch block, AV: Atrioventricular, SD: Standard deviation, ECG: Electrocardiography

findings according to patients' discharge and admission status between admission and discharge are shown in Table 4.

In our study, patients were divided into two groups based on the number of seizures before admission: single-seizure and multiple seizure patients. No statistically significant differences were found between single seizure and multiple-seizure patients regarding ECG rhythm characteristics.

Patients with multiple seizures before admission, had significantly higher systolic blood pressure (p=0.042), neutrophil count (p=0.028), bicarbonate (p=0.043), and neutrophil-to-lymphocyte ratio (p=0.002); while lymphocyte count (p=0.023) was significantly lower. Although high-sensitivity troponin and platelet-lymphocyte ratio were higher in the multiple seizure group, the differences were not statistically significant (p=0.063 and p=0.080). Lactate levels were lower in the multiple seizure group, but the difference was not significant (p=0.053). The other laboratory findings were similar between the two groups (p>0.05). The comparison of vital signs and laboratory findings based on the number of epileptic seizures is presented in Table 5.

In our study, it was found that 114 out of 170 patients with known epilepsy received monotherapy, while 56 received polytherapy. There were no statistically significant differences between the monotherapy and polytherapy groups in terms of baseline rhythm (p=0.189), presence of tachycardia/bradycardia (p=0.426),

Table 3. Comparison of ECG parameters based on hospitalization status

ECG parameters	Discharged (n=186)	Ward (n=7)	Intensive care unit (n=12)	p-value
Basic rhythm				
Sinus rhythm	164 (88.2)	7 (100)	10 (83.3)	0.217
RBBB	4 (2.2)	0 (0)	0 (0)	
AF	0 (0)	0 (0)	1 (8.3)	
Sinus arrhythmia	18 (9.7)	0 (0)	1 (8.3)	
Heart rate				
Tachycardia	41 (22)	2 (28.6)	7 (58.3)	0.108
Bradycardia	11 (5.9)	0 (0)	0 (0)	
Normal	134 (72)	5 (71.4)	5 (41.7)	
T wave abnormality				
Absent	132 (71)	5 (71.4)	6 (50)	0.355
T wave negativity	54 (29)	2 (28.6)	6 (50)	
ST segment abnormality				
Absent	181 (97.3)	7 (100)	11 (91.7)	0.156
ST elevation	3 (1.6)	0 (0)	0 (0)	
ST depression	2 (1.1)	0 (0)	1 (8.3)	
AV block				
Absent	176 (94.6)	7 (100)	12 (100)	0.999
First-degree	10 (5.4)	0 (0)	0 (0)	
PR interval				
Normal duration	173 (93)[a]	6 (85.7)[a]	10 (83.3)[a]	**0.027**
Short PR	3 (1.6)[a]	1 (14.3)[a]	1 (8.3)[a]	
Long PR	10 (5.4)[a]	0 (0)[a]	0 (0)[a]	
P wave absent rhythm	0 (0)[a]	0 (0)[a]	1 (8.3)[b]	
PR interval (msn)	150 (140-170)	140 (140-160)	140 (130-160)	0.225
QTc interval				
Normal duration	166 (89.2)	7 (100)	10 (83.3)	0.707
Short QT	1 (0.5)	0 (0)	0 (0)	
Long QT	19 (10.2)	0 (0)	2 (16.7)	
QTc interval (msn)	420 (400-435)	412 (399-428)	432 (399.5-447.5)	0.337
QRS complex (msn)	90 (80-100)	80 (80-90)	95 (90-102.5)	0.090

Findings are presented as median (IQR) or n (%), Kruskal-Wallis test, Fisher's Exact test, The same lowercase letters in a row indicate no significant difference between groups.
AF: Atrial fibrillation, ICU: Intensive care unit, RBBB: Rright bundle branch block, AV: Atrioventricular

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T wave abnormalities (p=0.231), ST segment abnormalities (p=0.999), AV block (p=0.333), PR interval pathology (p=0.599), PR interval (p=0.381), QTc interval (p=0.173), and QRS complex duration (p=0.346). In our study, 95 patients used levetiracetam, 52 carbamazepine, 51 valproate, and 25 lamotrigine. There was no statistically significant relationship between the use of anti-epileptic agents and heart rate, rhythm, wave durations, wave morphologies, segments, or intervals.

DISCUSSION

In our study, sinus tachycardia was the most common ECG abnormality in patients with epileptic seizures. Additionally, we observed a higher frequency of prolonged QT intervals. In patients admitted to the ICU with status epilepticus, serum lactate levels were elevated, while bicarbonate levels were significantly lower compared to other patients. However, no significant relationship was found between the type or number of anti-epileptic drugs (monotherapy vs. polytherapy) and ECG parameters. In our study, sinus arrhythmia was detected in 9% of the cases, and tachycardia was detected in 24%. Additionally, in patients with epileptic seizures, abnormalities were observed in all ECG waveforms, segments, and intervals. Specifically, T wave inversion was present in 30% of the cases, QT interval abnormalities (both shortened and prolonged) in 11%, PR interval abnormalities (both shortened and prolonged) in 7%, and ST segment abnormalities (depression and elevation) in 3%. Furthermore, first-degree AV block was identified in 5% of the cases.

One of the mechanisms implicated in the development of epileptic seizures is an ion channel mutation. This association is a potential cause for the severe cardiac conduction system abnormalities observed during seizures. In patients with epileptic seizures, the hyperadrenergic state induced by the release of epinephrine and norepinephrine into systemic circulation within the first 30 minutes leads to an increase in heart rate and cardiac output. This response also enhances the utilization of glucose and oxygen throughout the body (5). These mechanisms can result in tachycardia in some patients. Zijlmans et al. (6) reported that 59.6% of patients with epileptic seizures developed tachycardia,

Table 4. Comparison of vitals and laboratory findings based on hospitalization status

Parameters	Discharged (n=186)	Ward (n=7)	Intensive care unit (n=12)	p-value
Blood sugar (mg/dL)	112.5 (98-130)[a]	94 (78-99)[b]	123 (105-151.5)[a]	**0.009**
Body temperature (°C)	36.5 (36.4-36.8)	36.5 (36.5-36.7)	36.7 (36.6-37.05)	0.159
Heart rate (heartbeat/dk)	85 (72-96)	85 (78-101)	105.5 (79.5-134.5)	0.095
SBP (mmHg)	123 (111-133)	126 (115-142)	120.5 (94.5-144)	0.786
Leukocyte (/uL)	8185 (6720-10780)[a]	7250 (5900-10380)[a]	11590 (7905-15360)[b]	**0.036**
Neutrophil (/uL)	5155 (3680-7020)[a]	4480 (3550-6770)[a]	7275 (5655-9230)[b]	**0.009**
Lymphocyte (/uL)	2225 (1590-3070)	2280 (1230-3420)	2105 (1645-5030)	0.792
Hemoglobin (g/dL)	13.4 (12.3-14.8)	13.7 (11.8-15.2)	13.9 (11.7-14.75)	0.943
Hct (%)	40.55 (37.4-44.3)	42.1 (35.4-44.2)	42.45 (36.6-45.6)	0.912
Platelets (10^3/uL)	255.5 (209-295)	372 (193-386)	233 (199-340)	0.180
CRP (mg/dL)	1.67 (0.65-4.77)[a]	0.4 (0.34-1.31)[b]	3.66 (0.96-7.32)[a]	**0.037**
Urea (mg/dL)	24.25 (19.3-29.3)	32.2 (23.7-44.8)	22.05 (16.2-34.05)	0.135
BUN (mg/dL)	11.33 (9.02-13.69)	15.04 (11.07-20.93)	10.3 (7.57-15.91)	0.135
Creatinine (mg/dL)	0.76 (0.65-0.93)	1 (0.6-1.07)	0.75 (0.54-1.02)	0.596
Sodium (mEq/L)	138 (136-139.9)	137.3 (136-141.7)	138.95 (137.55-141.5)	0.440
Chloride (mEq/L)	102.15 (99.9-103.9)	101.3 (99.4-103.9)	102.25 (96.05-105.05)	0.844
Albumin (gr/L)	44.68 (42.56-47.07)	44.14 (40.73-46.49)	42.85 (41.05-46.01)	0.333
Na-Cl	35.6 (34.1-37.3)	37.8 (33.7-43.3)	35.8 (34.05-40.85)	0.295
HS-troponin (ng/L)	3.46 (3-5.89)	3.88 (3-5)	4.07 (3-47.69)	0.678
pH	7.35 (7.32-7.38)[a]	7.34 (7.23-7.36)[a,b]	7.27 (7.07-7.34)[b]	**0.004**
Bicarbonate (mEq/L)	22.4 (20.2-24.1)[a]	22.8 (15.4-24.6)[a]	18.25 (14.3-20.85)[b]	**0.009**
Lactate (mmol/L)	2.35 (1.5-4.9)	2.2 (1.2-14.2)	5.56 (3.21-12.67)	0.062
NLR	2.01 (1.4-3.33)	1.96 (1.63-2.61)	3.53 (2.55-4.72)	0.181
PLR	108.15 (76.08-155.71)	160.34 (95.32-203.33)	95.35 (60.31-141.9)	0.185
CRP/albumin	35.98 (14.62-102.69)[a]	8.8 (6.88-29.68)[b]	86.82 (21.36-166.1)[a]	**0.037**

The results are presented as median IQR: Kruskal-Wallis test, The same lowercase letters in a row indicate no significant difference between groups
BUN: Blood urea nitrogen, Na-Cl: Sodium chloride, CRP: C-reactive protein, Hct: Hematocrit, HS: High sensitive, ICU: Intensive care unit, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SBP: Systolic blood pressure

with 93% of these patients showing a heart rate increase of 10 beats, 80% a 20-beat increase, and 15% a decrease of 10 beats. In the same study, sinus arrhythmia was observed in 18.3% of the patients, atrial extrasystole in 11.5%, ventricular extrasystole in 7%, and sinus arrest in 6%. In our study, tachycardia was observed in a quarter of the patients, while the majority (70%) had a normal heart rate, and only 5% exhibited bradycardia. In our study, the majority of cases (88%) had sinus rhythm, 9% had sinus arrhythmia, and 2% had right bundle branch block. Only one case exhibited atrial fibrillation as the baseline rhythm. The main reason for the difference in tachycardia frequency compared to the literature is that in our study, the heart rhythm was assessed using an ECG obtained during the postictal period, rather than during the epileptic seizure itself.

In cases of prolonged seizure duration, cerebral autoregulation is impaired due to decompensation, leading to a decrease in cardiac output, the development of hypotension, and widespread hypoperfusion. This cascade of events results in diminished cellular energy metabolism, mitochondrial dysfunction, and an increased reliance on anaerobic metabolism. A study by Wijdicks and Hubmayr (7) demonstrated that metabolic and lactic acidosis developed in cases with status epilepticus. In a study conducted by Kılıc et al. (8) in the emergency department, it was found that a pH below 7.24, a bicarbonate level below 17 mmol/L, and a lactate level above 7.65 mmol/L increased the risk of recurrent seizures. In our study, in cases admitted to the ICU with status epilepticus, the average pH value was 7.27 (p=0.004) and the average bicarbonate level was 18.25 mmol/L (p=0.009). This suggests that metabolic acidosis is an important finding that can be used to predict prolonged seizure activity and the need for ICU in patients presenting with epileptic seizures. Similar to prolonged seizure activity, metabolic acidosis may be observed in cases with multiple seizures. However, in our study, no significant differences were observed in pH, bicarbonate, and lactate levels between the groups with multiple seizures and a single seizure. One of the main reasons for the lack of similar statistical results may be the variability in seizure duration and factors such as the

Table 5. Comparison of vitals and laboratory findings based on number of epileptic seizures

Parameters	Single seizure (n=159)	Multiple seizures (n=46)	p-value
Blood sugar (mg/dL)	112 (96-127)	117 (101-138)	0.203
Body temperature (°C)	36.5 (36.4-36.8)	36.6 (36.4-36.8)	0.422
Heart rate (heartbeat/dk)	86 (74-98)	84.5 (71-105)	0.896
SBP (mmHg)	121 (110-131)	131 (109-142)	**0.042**
Leukocyte (/uL)	8080 (6720-10780)	8535 (7200-11960)	0.191
Neutrophil (/uL)	5060 (3660-6880)	6110 (3880-8210)	**0.028**
Lymphocyte (/uL)	2290 (1680-3240)	1865 (1290-2720)	**0.023**
Hemoglobin (g/dL)	13.52±1.86	13.53±1.97	0.976
Hct (%)	40.75±5.09	41.06±5.87	0.726
Platelets (10^3/uL)	259 (208-302)	242.5 (213-297)	0.572
CRP (mg/dL)	1.63 (0.63-4.2)	1.72 (0.59-6.43)	0.436
Urea (mg/dL)	24.9 (20-30.2)	22.75 (17.4-30.3)	0.206
BUN (mg/dL)	11.63 (9.34-14.11)	10.63 (8.13-14.15)	0.204
Creatinine (mg/dL)	0.77 (0.65-0.94)	0.71 (0.62-0.93)	0.232
Sodium (mEq/L)	138 (136.5-139.8)	137.65 (136-140)	0.681
Chloride (mEq/L)	102.2 (99.7-103.9)	102.15 (100-104.6)	0.624
Albumin (gr/L)	44.73±3.58	43.93±4.64	0.214
Na-Cl	35.96±2.91	35.58±3.51	0.450
HS-troponin (ng/L)	3.42 (3-5.08)	4.93 (3-8.36)	0.063
pH	7.35 (7.31-7.37)	7.36 (7.33-7.39)	0.159
Bicarbonate (mEq/L)	22.1 (19.8-23.7)	22.75 (21-25)	**0.043**
Lactate (mmol/L)	2.5 (1.53-6.1)	1.84 (1.43-3.6)	0.053
NLR	1.96 (1.33-3.31)	2.85 (1.94-5.01)	**0.002**
PLR	104.33 (75.67-144.89)	139.05 (78.55-205.45)	0.080
CRP/albumin	35.65 (14.15-91.23)	38.43 (14.16-136.49)	0.489

The results are presented as median (IQR), independent t-test, Mann-Whitney U test, The same lowercase letters in a row indicate no significant difference between groups
BUN: Blood urea nitrogen, Na-Cl: Sodium chloride, CRP: C-reactive protein, Hct: Hematocrit; HS: High sensitive, ICU: Intensive care unit, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SBP: Systolic blood pressure

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time to hospital arrival in cases with multiple seizures. In addition, there were no significant differences in ECG parameters between the two groups.

Anti-epileptic drugs exert their effects by enhancing GABA receptor activation, blocking N-methyl-D-aspartate receptors, and altering the permeability of ion channels such as sodium, potassium, and calcium, which are crucial for neuronal transmission. This condition causes antiepileptic drugs to affect not only the neuronal transmission system but the entire body as well, leading to abnormalities in laboratory parameters. Numerous antiepileptic drugs have been reported to be associated with hematological disorders, ranging from mild thrombocytopenia and neutropenia to anemia, aplastic anemia, and bone marrow failure (9). Beyond the use of antiepileptic drugs, it is suggested that drug interactions in patients undergoing polytherapy may result in hematological and biochemical abnormalities, osteomalacia, and liver failure (10). In our study, the lymphocyte count, hemoglobin level, hematocrit percentage, and lactate level were found to be lower in the polytherapy group compared to the monotherapy group.

The interactions of antiepileptic drugs can induce abnormalities in the cardiac conduction system, leading to abnormal ECG findings. It has been shown that frequent generalized seizures can trigger cardiac pathologies, and that polytherapy with anti-epileptic drugs can lead to cardiac involvement in patients (11). Krishnan and Krishnamurthy (12) reported that the average QT interval duration was shorter in patients with polytherapy for epilepsy compared to those on monotherapy. The same study reported no significant difference in PR interval duration between the two groups. We found that 19 patients (11.2%) using anti-epileptic drugs had QT interval pathology (either prolonged or shortened). Only one of these patients was receiving polytherapy, while the others were receiving monotherapy. Our findings indicate that QT interval prolongation was observed in the monotherapy group. However, neither the type nor the number of anti-epileptic drugs appeared to have an impact on QT interval duration.

Various anti-epileptic drugs and pharmacological agents, with off-label use, are often preferred in the treatment of epilepsy. We found that the most commonly used agents in patients with epilepsy were levetiracetam (55.9%), carbamazepine (30.6%), valproate (29.4%), and lamotrigine (14.7%).

There are numerous studies in the literature that have found a relationship between antiepileptic drugs and cardiac conduction abnormalities (13-15). Aydin and Korkut (13) reported no significant changes in any ECG parameters before and after levetiracetam therapy. Siniscalchi et al. (14) reported an approximately 25 ms increase in QTc in patients treated with levetiracetam. Levetiracetam is a widely preferred anti-epileptic drug that exerts its effects primarily through calcium channel inhibition. In the literature, there are case-based reports suggesting an association between levetiracetam and long QT syndrome, as well as torsades de pointes (15). However, Hulhoven et al. (16) reported no statistical relationship between the increase in levetiracetam dosage and QTc prolongation. In our study, we did not observe significant pathological changes related to levetiracetam in the ECG.

The majority of studies investigating antiepileptic–cardiovascular interactions have concentrated on carbamazepine. In our study, carbamazepine was the second most commonly used drug after levetiracetam, with a frequency of 30.6%. Apfelbaum et al. (17) reported that carbamazepine overdose did not lead to a statistically significant change in heart rate in their case series of carbamazepine intoxication. It has been reported that carbamazepine can cause negative chronotropy (18). Hojer et al. (19) reported that sinus tachycardia is the most common side effect of carbamazepine; additionally, at toxic doses, sinus bradycardia, AV blocks, and junctional escape rhythms may be observed. The effect of carbamazepine on heart rate remains unclear in the literature. Nonetheless, it is widely accepted that its cardiovascular impact differs between therapeutic and toxic concentrations. Surges et al. (20) have reported an association between carbamazepine and a short QTc interval. In our study, the mean QTc interval was significantly shorter in patients receiving carbamazepine. However, the observed values did not fall within the pathological range defined as "short QT".

Study Limitations

The limitations of this study include its single-center design, which may limit the generalizability of the findings to other populations. Additionally, the relatively small sample size may have reduced the statistical power to detect subtle differences between groups. The study only included patients presenting to the emergency department with active seizures or in the post-ictal period, potentially leading to selection bias by excluding individuals with well-controlled epilepsy or those who did not seek emergency care. Another limitation is the reliance on post-ictal ECG recordings rather than continuous ECG monitoring, which may have missed transient arrhythmias occurring during the ictal phase. Lastly, the study did not account for potential confounding factors such as medication adherence and seizure triggers, that might have influenced ECG findings. Future research involving larger, multi-center cohorts and continuous ECG monitoring during seizures would offer more comprehensive insights.

CONCLUSION

Our study indicates that sinus tachycardia is the most common ECG abnormality in patients with epileptic seizure. The frequency of a prolonged QT interval increases in patients with epileptic seizures. Furthermore, our study suggests that elevated serum lactate and decreased bicarbonate levels may serve as predictors of seizure duration and the need for ICU admission. We did not find a significant relationship among epileptic seizures, status epilepticus, the use and number of antiepileptic drugs, and serious cardiac arrhythmias. Large-scale prospective studies are required to investigate the relationship between the types of antiepileptic drugs, the number of drugs (monotherapy/polytherapy), and ECG abnormalities in patients with epileptic seizures.

Ethics

Ethics Committee Approval: Ethical committee approval for the study was obtained from Haydarpaşa Numune Training and Research Hospital, Clinical Research Ethics Committee, University of Health Sciences Türkiye, (approval no: HNEAH-KAEK 2022/KK/117, date:13.06.2022).

Informed Consent: Informed written consent was obtained from all subjects or their relatives.

Footnotes

Author Contributions: Concept – A.Ş., K.Y.; Design – A.Ş., İ.A., K.Y., S.D., B.G.Y.; Data Collection and/or Processing -A.Ş., S.D., B.G.Y.; Analysis and/or Interpretation - İ.A., K.Y., S.D.; Literature Search -B.G.Y.; Writing - A.Ş., İ.A.

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