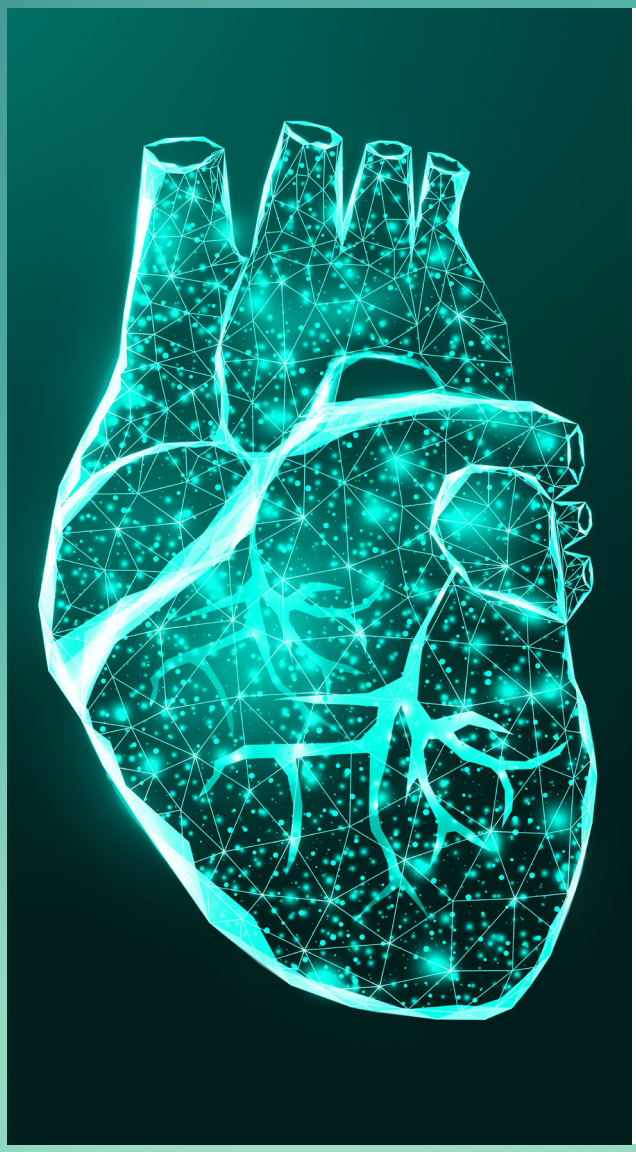
E-ISSN: 2405-819X

CARDIOVASCULAR ACADEMY SOCIETY

INTERNATIONAL JOURNAL OF THE CARDIOVASCULAR ACADEMY

OFFICIAL PUBLICATION OF THE CARDIOVASCULAR ACADEMY SOCIETY

VOLUME: 11 ISSUE: 1 MARCH 2025



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Web: www.galenos.com.tr
Publisher Certificate Number: 14521
Publication Date: March 2025
ISSN: 2405-8181 **E-ISSN:** 2405-819X
International scientific journal published quarterly.

INTERNATIONAL JOURNAL OF THE CARDIOVASCULAR ACADEMY

OFFICIAL PUBLICATION OF THE CARDIOVASCULAR ACADEMY SOCIETY

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Owner: Ömer Kozan on behalf of the Cardiovascular Academy Society

Responsible Manager: Mehdi Zoghi

VOLUME: **11**
ISSUE: **1**
MARCH **2025**

INTERNATIONAL JOURNAL OF THE CARDIOVASCULAR ACADEMY

OFFICIAL PUBLICATION OF THE CARDIOVASCULAR ACADEMY SOCIETY

CONTENTS

REVIEW

DOI: 10.4274/ijca.2024.70288
Int J Cardiovasc Acad 2025;11(1):1-5

Assessment Tools and Performance Development in Sports Cardiology

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Abstract

Sports cardiology is a multidisciplinary field that has evolved to evaluate and optimize the cardiovascular health of athletes. The field focuses on improving exercise-related physical performance, reducing cardiovascular risks, and detecting potential diseases early. Sports cardiology monitors the heart health of athletes while also evaluating their cardiovascular responses during exercise. This process plays a critical role in increasing training intensity, managing fatigue, and preventing heart disease. In addition, one of the areas of interest of sports cardiology is performance medicine. A sports cardiologist and sports physician is a part of the athletic process from the athlete's first examination to the final step of athletic success. Sports cardiology and performance medicine provide athletic and economic value to the sports industry by preventing injuries, objectively assessing performance, rapidly and effectively improving performance, and enhancing athletic success. In this review, we aim to present the assessment tools, and study areas of sports cardiology.

Keywords: Sports cardiology, performance medicine, cardiorespiratory fitness

INTRODUCTION

Sports cardiology has emerged as a significant area of academic research in recent years. The vast majority of sports cardiology literature so far has focused on sudden cardiac death (SCD) and the relationship between sports and disease.[1] However, there are few cardiology articles related to performance medicine, an area of interest in sports cardiology. Athletic features related to muscles and joints have reached the upper limits of human performance in today's elite athletes. Along with external development, internal development is essential for elite athletes in order to remain competitive. Consequently, sports cardiology and performance medicine arise as a scientific discipline that has the potential to positively impact elite athletes. Evaluating performance medicine with a cardiologist's perspective may provide novel and beneficial support for sports and athletes. Moreover, sports cardiology and performance medicine present injury prevention, objective performance monitoring, accelerated and efficient performance enhancement, and economic savings and profitability for the sports industry in many situations. This review provides an overview of sports cardiology and performance.

Athlete in Sports Cardiology

The definition of an athlete can vary depending on the purpose and duration of training. In a proposed classification of athletes according to the minimum volume of exercise, "elite" athletes (i.e., national team members, olympians, and professional athletes) typically engage in over 10 hours per week, "competitive" athletes (i.e., high school, college, and older master club level athletes) participate in over 6 hours

To cite this article: Torun A, Kılıç Ş, Işık Ö. Assessment tools and performance development in sports cardiology. Int J Cardiovasc Acad. 2025;11(1):1-5

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Received: 17.10.2024
Accepted: 17.12.2024
Publication Date: 18.03.2025

per week, and "recreational" athletes exercise for more than 4 hours per week.[2] The term "athlete's heart" refers to many alterations and adaptations, including structural, functional, physiological, and electro-physiological changes resulting from sport-specific cardiac remodeling.[3] Not only the duration of training but also the content of training in elite athletes reveals different variations of the athlete's heart.[4] In sports cardiology and performance medicine, the nature of the sport, age, and position of the athlete, and, if it is a team sport, the task expectations from the athlete on the field are elements that should be taken into consideration.

Athlete Examination and Sudden Cardiac Death

Despite ongoing debate on the funding and economic resources for systematic screening programs, there is a consensus that a cardiological examination should at least be performed. In the United States, only a medical history and directed physical examination are recommended; however, in Europe, a 12-lead electrocardiogram (ECG) is also included in the examination.[5]

Sports-related SCD is a phenomenon previously linked to both competitive and recreational sports activity. Screening strategies must be tailored to the target group and the specific diseases with the highest risks. The incidence of SCD in college-aged males is 1 in 35,000 person-years and 1 in 18,000 person-years for black males, with elevated risks associated with men's basketball, men's soccer, and American football. Inherited cardiomyopathies and electrical disorders comprise approximately two-thirds of sudden cardiac arrest/death cases and can be identified by an ECG.[6] SCD in young athletes results from many structural and electrical heart problems, such as cardiomyopathies, ion channel abnormalities, coronary anomalies, and acquired cardiac illnesses.[7,8] Atherosclerotic coronary artery disease is the predominant condition resulting in significant adverse cardiovascular events in adult and senior athletes.[9] Sports-related SCD has been observed to occur 5-33 times less frequently in women than in men, with this sex disparity being evident despite a swift rise in female engagement in sports.[10] ECG, echocardiography options, exercise test protocols, cardiopulmonary exercise tests (CPETs), tomography, and magnetic resonance imaging provide effective approaches in the examination of professional athletes. The presence of symptoms and family history should be taken into consideration prior to considering these options. In the examination of a team or the evaluation of an individual athlete, the presence of any cardiac symptoms or family history should be questioned first. Further examination can be planned according to these answers.

Athletic Performance Assessment and Development Tools in Sports Cardiology

Echocardiography

Echocardiography is a cost-effective method that facilitates the detection of the main causes of preventable sudden death, including cardiomyopathies, anomalies in coronary artery origin, and aortic disorders. In numerous competitive athletes, the left ventricular end-diastolic volume and diameter may above the established "normal" ranges for chamber quantification.[11] The left ventricular wall thickens symmetrically due to conditioning and can occur in isolation (concentric hypertrophy), in strength-focused activities or alongside an increase in chamber dilation (eccentric hypertrophy) in athletes engaged in sports necessitating both strength and endurance stimuli, such as swimming and rowing. Asymmetric hypertrophy and left ventricular wall thickness above 15 mm, should prompt concerns for pathological cardiomyopathy, especially in athletes participating in isometric exercises. Conditioned persons generally exhibit a normal left ventricular ejection fraction (LVEF) at rest; nevertheless, the regulation of stroke volume in a bigger ventricle occurs via the ejection of a diminished fraction of the end-diastolic volume. This may present as a low-normal or somewhat abnormal LVEF.[12] Despite the misleading decrease in LVEF, the systolic function remains intact or exceeds normal levels, as demonstrated by standard LV strain measurements.[13]

Another important aspect of echocardiography in performance medicine is analyzing the conditioned heart and elucidating the exercise methods that best form the athlete's heart. Our observation is that the rate of athletes' hearts is higher in endurance sports that require water mechanics, such as rowing, swimming, and canoeing. Fast and effective methods can be developed with the future specific training methodology studies.

Heart Rate Recovery Time and Vagal Tone

The heart exhibits physiological adaptations in response to prolonged and intense exercises, leading to distinct changes.[4] Vagal activity contributes to the differences observed in the athlete's heart.[14] While various cardiac arrhythmias and conduction abnormalities can be considered as pathology in untrained individuals, they are considered normal in athletes due to increased vagal tone.[15] Intensive level sports cause an increase in vagal tone in the heart. Vagal tone and heart rate recovery (HRR) are directly related to athletic success.[16] During postexercise recovery, heart rate initially falls

rapidly, followed by a period of slower decrease, until resting values are reached.[17] HRR is an important parameter for the monitoring and evaluation of attack potential, the ability to maintain race pace, and the endurance.

For sports performance doctors, HRR and vagal tone should target the development of athletic success. The cranial electrical stimulator is a device that can enhance sports performance via vagal stimulation.[18] The parasympathetic system plays a crucial role in restructuring and recovery during rest periods, significantly alleviating athlete fatigue and enabling early recovery. Vagus nerve stimulation, the principal component of the parasympathetic system, can influence several cardiovascular, pulmonary, and metabolic parameters during both rest and exercise.[19] In addition, various breathing exercises are used to develop vagal tone and shorten the HRR time.[20] More scientific studies are needed to investigate vagal tone in the preservation and development of athletic capacity in performance medicine.

Cardiopulmonary Exercise Testing

CPET is a form of stress test that is primarily carried out on a treadmill or cycle ergometer. During this test, the O_2 (VO_2) in the air the patient breathes, CO_2 levels in the air given off, minute ventilation, minute respiratory rate, anaerobic threshold, heart rate, tidal volume, inspiratory capacity, oxygen saturation, 12-lead ECG rhythm, work done, exercise duration, and blood pressure are monitored. Sometimes more invasive measurements, such as blood lactate levels or arterial blood gases, are also taken.[21] CPET is the gold standard in determining the metabolic status of the organism and evaluating the functional capacities of the cardiac, pulmonary, and neuromuscular systems.[22] The purpose of CPET is to implement a certain amount of stress on the organs involved in the exercise. Therefore, during the test, large muscle exercises that use lower extremity muscles are preferred.[21,22] CPET can be used to optimize athletes' training programs or evaluate their cardiovascular health status. VO_2 max measured in this test indicates the individual's maximum oxygen consumption capacity and is an important parameter reflecting aerobic capacity. Resting VO_2 is 3.5 mL/kg/min. The highest values for women are 35 mL/kg/min and for men, 45 mL/kg/min. The average athlete can consume up to 60 mL/kg/min.[23] For this reason, athletes, runners, and individuals involved in other endurance sports often implement training programs aimed at increasing VO_2 max.[24,25] Many fitness watches offer VO_2 max measurement functionality, but this functionality needs improvement. Nowadays, it is possible to make measurements in the field and during exercise with portable CPETs. CPET provides information about the athlete's exercise capacity, peak performance indicators, and physiological responses to exercise through the professional team evaluation and analysis of special software.

Heart Rate Variability

Heart rate variability (HRV) reveals variations in the intervals between consecutive heartbeats, offering insights into cardiac autonomic function and overall physiological condition. High HRV indices typically reflect the presence of efficient autonomous systems, which are characteristic of an individual in a healthy state.[26] Endurance athletes generally exhibit better cardiac autonomic function than non-athletes, characterized by reduced resting heart rates and increased variability. The accessibility and use of HRV measures have expanded among the general population and may be especially beneficial for endurance athletes.[27] HRV monitoring enables the understanding of an athlete's internal dynamics. Daily measurement of autonomic nervous system activity by spectral analysis of HRV during training load appears to be a promising tool for improving performance.[28] In addition, HRV is a preferred parameter in the analysis of athletes' injury risk (Figure 1). HRV can provide a new approach to overuse injuries both in terms of athlete health and financial value in the sports industry. However, studies examining the use of HRV using consistent methodologies are limited, and more comprehensive studies are needed on this subject.

Performance Improvement

The limits of athletic performance have been a subject of speculation and discussion for a long time. Nonetheless, a noticeable plateau in sports performance has emerged in recent years, suggesting that the potential for further development of people's physical ability may be limited.[29] Consequently, doping substances have become increasingly seen as a controversial issue among professional athletes. Due to the wide variety of chemicals and the frequent introduction of new designer medications, the World Anti-Doping Agency (WADA) annually updates its list of prohibited substances and methods. Cardiac function is likely one of the most fundamental factors of athletic performance. This casts significant questions on the utilization of certain cardiac medications as performance-

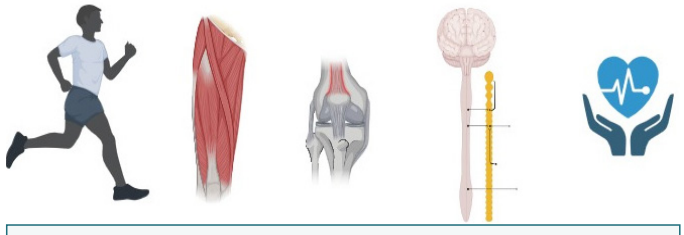

Figure 1: As a result of strain and inadequate recovery, overuse injuries begin to occur in athletes. The low-grade inflammatory process that occurs before the pain symptom causes changes in the autonomic nervous system. The effect on the autonomic nervous system can be detected by heart rate variability analysis and may be useful as a predictive tool for overuse injuries

enhancing substances. The inclusion of trimetazidine in WADA's prohibited list as a doping agent in 2014 marks the commencement of this period. Other currently suspected drugs are ranolazine, sacubitril/valsartan and dapagliflozin. Therefore, a performance doctor should primarily be an ethical consultant to the athlete.[30,31]

In both aerobic and resistance exercise consultancy, the performance doctor should aim to increase training efficiency. Resistance exercise is rapidly gaining popularity in both cardiology patient groups and healthy individuals, and is one of the most important elements of athletic performance.[32] The exercise dose-response relationship differs among various populations. The optimal strength gains for untrained persons are achieved at an average training intensity of 60% of their one-repetition maximum (1RM), performed three times weekly, with an average training volume of four sets per muscle group. Recreationally trained non-athletes get optimal strength increases with an average training intensity of 80% of 1RM training twice weekly and performing an average of 4 sets. In athletic populations, optimal strength increases are achieved with training twice weekly at an average intensity of 85% 1RM and a volume of 8 sets per muscle group.

Heart rate-focused training approaches should be implemented for objectives such as injury rehabilitation, aerobic capacity enhancement, and anaerobic threshold improvement. Exercise intensity can be quantified as a percentage of an individual's heart rate reserve, calculated by taking a percentage of the difference between maximum heart rate max and resting heart rate, then adding this value to the resting heart rate, as per the Karvonen formula.[33] When calculating the athlete's target heart rate with the Karvonen formula, the type of sport and the player's task expectations should be taken into consideration. For example, if acceleration and sprint frequency are targeted for a football winger, it is necessary to work in zone 5. However, if the aim is simply to maintain performance, a training model in zone 3 is sufficient for the endurance athlete. In addition, the interval method will increase efficiency in aerobic training and make it easier to obtain long-term exercise responses.[34] Methods such as ischemic heart rate training, water mechanics training, and blood flow restriction will contribute to performance medicine in the future.

Additionally, artificial intelligence-based injury analysis methods and wearable technologies used in performance monitoring, are becoming widespread in both predicting training loads and providing objective performance data for athletes. Artificial intelligence applications that are integrated with tracking parameters such as HRV and catapult are the first examples of these technologies.

CONCLUSION

Sports cardiology and performance medicine focus on performance development in addition to athlete health. It can be beneficial in preventing injury, analyzing performance, and enhancing it to an optimal level, especially in industrial sports branches. More studies are needed in performance medicine, both in the prevention of performance issues and in the development of performance.

Footnotes

Authorship Contributions

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

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

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

REFERENCES

1. Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, *et al*. 2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease. Eur Heart J. 2021;42:17-96.
2. McKinney J, Velghe J, Fee J, Isserow S, Drezner JA. Defining Athletes and Exercisers. Am J Cardiol. 2019;123:532-5.
3. Liu PY, Tsai KZ, Lima JAC, Lavie CJ, Lin GM. Athlete's heart in Asian military males: the CHIEF heart study. Front Cardiovasc Med. 2021;8:725852.
4. Torun A, Erdem A, Doğan S, Orhan AL, Acar B, Simsek U, *et al*. Comparison of the effects of resistance, aerobic and mixed exercise on athlete's heart. J Sports Med Phys Fitness. 2024;64:88-93
5. Boraita A. Muerte súbita y deporte. 'Hay alguna manera de prevenirla en los deportistas? [Sudden death and sport. Is there a feasible way to prevent it in athletes?]. Rev Esp Cardiol. 2002;55:333-6.
6. Harmon KG. Incidence and Causes of Sudden Cardiac Death in Athletes. Clin Sports Med. 2022;41:369-88.
7. Harmon KG, Asif IM, Maleszewski JJ, Owens DS, Prutkin JM, Salerno JC, *et al*. Incidence, cause, and comparative frequency of sudden cardiac death in national collegiate athletic association athletes: a decade in review. Circulation. 2015;132:10-9.
8. Peterson DF, Siebert DM, Kucera KL, Thomas LC, Maleszewski JJ, Lopez-Anderson M, *et al*. Etiology of sudden cardiac srrest and death in US Competitive athletes: a 2-year prospective surveillance study. Clin J Sport Med. 2020;30:305-14.
9. Finocchiaro G, Papadakis M, Robertus JL, Dhutia H, Steriotis AK, Tome M, et al. Etiology of sudden death in sports: insights from a United Kingdom regional registry. J Am Coll Cardiol. 2016;67:2108-15.
10. Rajan D, Garcia R, Svane J, Tfelt-Hansen J. Risk of sports-related sudden cardiac death in women. Eur Heart J. 2022;43:1198-206.
11. Parry-Williams G, Sharma S. The effects of endurance exercise on the heart: panacea or poison? Nature reviews. Cardiology. 2020;17:402-12.

12. Baggish AL, Battle RW, Beaver TA, Border WL, Douglas PS, Kramer CM, *et al*. Recommendations on the use of multimodality cardiovascular imaging in young adult competitive athletes: a report from the American society of echocardiography in collaboration with the society of cardiovascular computed tomography and the society for cardiovascular magnetic resonance. J Am Soc Echocardiogr. 2020;33:523-49.

13. Addis DR, Townsley MM. Imaging Considerations for the athletically conditioned heart: an echocardiography-focused overview of the 2020 American society of echocardiography recommendations on the use of multimodality cardiovascular imaging in young adult competitive athletes. J Cardiothorac Vasc Anesth. 2020;34:2867-70.

14. Coote JH, White MJ. CrossTalk proposal: bradycardia in the trained athlete is attributable to high vagal tone. J Physiol. 2015;593:1745-7.

15. Zorzi A, Vio R, Bettella N, Corrado D. Criteria for interpretation of the athlete's ECG: A critical appraisal. Pacing Clin Electrophysiol. 2020;43:882-90.

16. Peinado AB, Benito PJ, Barriopedro M, Lorenzo I, Maffulli N, Calderón FJ. Heart rate recovery in elite Spanish male athletes. J Sports Med Phys Fitness. 2014;54:264-70.

17. Torun A, Kilic S, Uzun M, Simsek U, Aslan GY, Kahraman G. Evaluation of high altitude training camps with heart rate recovery and heart rate variability analysis: beneficial effect in elite swimmers. J Sports Med Phys Fitness. 2024;64:1026-30.

18. Güçlüer EÖ, Ural İH, Özden AV, Alptekin HK, Hatık SH. Effects of auricular vagus nerve stimulation on cardio-respiratory functions after aerobic exercise. International Journal of Disabilities Sports &Health Sciences. 2024;7:494-501.

19. Hatik SH, Asrlan M, Demirbilek Ö, Özden AV. The effect of transcutaneous auricular vagus nerve stimulation on cycling ergometry and recovery in healthy young individuals. Brain Behav. 2023;13:e3332.

20. Balban MY, Neri E, Kogon MM, Weed L, Nouriani B, Jo B, et al. Brief structured respiration practices enhance mood and reduce physiological arousal. Cell Rep Med. 2023;4:100895.

21. Albouaini K, Egred M, Alahmar A, Wright DJ. Cardiopulmonary exercise testing and its application. Postgrad Med J. 2007;83:675-82.

22. Ceylan E. Kardiyopulmoner egzersiz testleri. Journal of Clinical and Experimental Investigations. 2014;5:504-9.

23. Shin K, Minamitani H, Onishi S, Yamazaki H, Lee M. Assessment of training-induced autonomic adaptations in athletes with spectral analysis of cardiovascular variability signals. Jpn J Physiol. 1995;45:1053-69.

24. Štursová P, Budinská X, Nováková Z, Dobšák P, Babula P. Sports activities and cardiovascular system change. Physiol Res. 2023;72:S429-44.

25. Chtara M, Chamari K, Chaouachi M, Chaouachi A, Koubaa D, Feki Y, *et al.* Effects of intra-session concurrent endurance and strength training sequence on aerobic performance and capacity. Br J Sports Med. 2005;39:555-60.

26. Mendes RG, Simões RP, De Souza Melo Costa F, Pantoni CB, Di Thommazo L, *et al*. Short-term supervised inpatient physiotherapy exercise protocol improves cardiac autonomic function after coronary artery bypass graft surgery--a randomised controlled trial. Disabil Rehabil. 2010;32:1320-7.

27. Lundstrom CJ, Foreman NA, Biltz G. Practices and applications of heart rate variability monitoring in endurance athletes. Int J Sports Med. 2023;44:9-19.

28. Botek M, McKune AJ, Krejci J, Stejskal P, Gaba A. Change in performance in response to training load adjustment based on autonomic activity. Int J Sports Med. 2014;35:482-8.

29. Berthelot G, Sedeaud A, Marck A, Antero-Jacquemin J, Schipman J, Saulière G, *et al*. Has Athletic Performance Reached its Peak? Sports Med. 2015;45:1263-71.

30. Jarek A, Wójtowicz M, Kwiatkowska D, Kita M, Turek-Lepa E, Chajewska K, *et al*. The prevalence of trimetazidine use in athletes in Poland: excretion study after oral drug administration. Drug Test Anal. 2014;6:1191-6.

31. Li YJ, Wang PH, Chen C, Zou MH, Wang DW. Improvement of mechanical heart function by trimetazidine in db/db mice. Acta Pharmacol Sin. 2010;31:560-9.

32. Torun A. Role of Resistance exercise in cardiology. Anatol J Cardiol. 2024;28:217–21.

33. Myers J, Hadley D, Oswald U, Bruner K, Kottman W, Hsu L, *et al*. Effects of exercise training on heart rate recovery in patients with chronic heart failure. Am Heart J. 2007;153:1056-63.

34. Mueller S, Winzer EB, Duvinage A, Gevaert AB, Edelmann F, Haller B, *et al*. Effect of high-intensity interval training, moderate continuous training, or guideline-based physical activity advice on peak oxygen consumption in patients with heart failure with preserved ejection fraction: a randomized clinical trial. JAMA. 2021;325:542-51.

RESEARCH ARTICLE

DOI: 10.4274/ijca.2025.70298
Int J Cardiovasc Acad 2025;11(1):6-14

The Impact of Patient Education on Rehospitalization Rate and Quality of Life in Heart Failure Patients

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Abstract

Background and Aim: Heart failure (HF) with reduced ejection fraction (HFrEF) significantly impairs quality of life (QoL), leading to frequent hospitalizations, high mortality and high healthcare costs. This study sought to investigate whether education of patients could enhance QoL and reduce rehospitalization rates in patients with HFrEF.

Materials and Methods: A randomized, follow-up trial was conducted in our center including 64 patients diagnosed with HFrEF, all of whom were receiving guideline-directed medical therapy. Participants were randomly assigned to two groups: the nurse-led education group (n=32), which received structured education on HF management from trained nurses, and the routine care group (n=32), who received standard medical care without additional educational support. QoL was assessed using a validated questionnaire and clinical evaluations after 3 months, focusing on the performance of everyday activities (various aspects of daily life and depression), as well as the rehospitalization rate.

Results: Educated group demonstrated significantly improved QoL. Additionally, none of the educated patients had rehospitalizations, while 34% of the non-educated group did.

Conclusion: Education of patients has a positive impact on both the physical and psychological well-being of patients with HFrEF, thereby improving their QoL, reducing rehospitalizations and lowering healthcare costs.

Keywords: Heart failure, education, quality of life, rehospitalizations

INTRODUCTION

Heart failure (HF) is a major global public health problem. The mortality rate is still high, as well as the rate of rehospitalizations despite current therapeutic options.

Advanced HF is a condition with a poor prognosis, with a prognosis worse than many metastatic cancers. We have novel, potent medications helping us in managing patients with HF, especially in HF with reduced ejection fraction (HFrEF). But there are unmet needs. Obstacles and challenges lurk around the corner. Could we do better?

Are we able to help our patients (and their caregivers) not just to survive but to have better quality of life (QoL)? HF can significantly affect the patient's physical, emotional, and social well-being. The limitations due to fatigue, shortness of breath, and frequent hospitalizations can lead to feelings of frustration, helplessness, and isolation having strong impact on QoL.

To cite this article: Dizdarevic-Hudic L, Halilovic E, Brkic S, Loncar D, Jahic NA, Hudic I, *et al.* The impact of patient education on rehospitalization rate and quality of life in heart failure patients. Int J Cardiovasc Acad. 2025;11(1):6-14

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Received: 26.01.2025
Accepted: 03.03.2025
Publication Date: 18.03.2025

HF guidelines stressed the importance of patient education regarding treatment adherence, lifestyle changes, symptom monitoring, and response to possible deterioration.[1]

Are our patients well educated? Are we listening to them, their needs, their complaints, their QoL wishes? Are we explaining to them simple but potentially life-changing hacks, such as regarding water and salt intake or nutrition tips?

Could better education of patients make a significant change for HF patients? Utopia or reality?

We hypothesized that **patient education** plays a crucial role in managing HF, as it empowers individuals to understand their condition, make informed decisions, and take active steps in their care and impact on QoL.

HF can significantly affect the patient's physical, emotional, and social well-being. The limitations due to fatigue, shortness of breath, and frequent hospitalizations can lead to feelings of frustration, helplessness, and isolation. Education that supports self-management, promotes adherence to treatment, and encourages a healthy lifestyle can improve both physical and psychological outcomes, ultimately enhancing QoL. For patients with HF, the level of knowledge about the disease process is positively correlated with recognizing and managing symptoms and improving QoL.[1,2] Nurse-led HF inpatient hospital education (covering disease management, medication adherence, lifestyle changes, symptom monitoring and when to seek medical help) has been demonstrated to improve knowledge, self-care behaviours and readmissions.[3,4]

METHODS

This study involved two groups of patients with chronic HFrEF receiving optimized guideline-directed therapy. Group 1 (32 patients) received structured education from a trained nurse, covering disease management, medication adherence, lifestyle changes, symptom monitoring, and when to seek medical help. Group 2 (32 patients) received standard routine care without additional detailed education.

Key aspects of nurse-led patient education in HF:

1. Understanding HF

- What is HF? HF means that the heart does not pump effectively and is unable to meet the body's needs.

- Causes: Discuss the underlying causes like coronary artery disease, hypertension, diabetes, and valve disorders.

- Symptoms: Help patients recognize symptoms of worsening HF, such as shortness of breath, fatigue, weight gain, and swelling.

2. Medication adherence

- Importance of medications: Emphasize the need to take prescribed medications regularly to manage symptoms, improve survival and prevent hospitalizations.

- Side effects: Teach patients to recognize common side effects and know how to handle them.

3. Lifestyle modifications

- Dietary changes: Advise limiting sodium and fluid intake, and following a heart-healthy diet rich in fruits, vegetables, and whole grains.

- Exercise: Encourage regular physical activity based on individual tolerance to prevent deconditioning.

- Smoking and alcohol cessation and advices

4. Self-monitoring

- Daily weight monitoring: Teach patients to weigh themselves daily, as sudden weight gain can indicate fluid retention or worsening HF.

- Symptom tracking: Encourage tracking symptoms like shortness of breath or swelling, and reporting changes to healthcare providers.

5. When to seek medical help

- Provide clear guidance on when to contact healthcare providers (via phone or email), such as: rapid weight gain (2-3 pounds in one day), increased swelling or shortness of breath, chest pain or signs of a heart attack, new or worsening fatigue

6. Psychosocial support

- Discuss the emotional challenges of living with HF, including anxiety or depression.

- Encourage participation in support groups or counseling to enhance mental well-being.

7. End-of-life planning (when appropriate)

For advanced HF patients, discuss goals of care and end-of-life wishes, ensuring the patient's preferences are respected

Patients were recruited at our institution, either during hospitalization or in outpatient clinics. Hospitalized patients received education from a nurse, which began during their inpatient treatment (group 1). Patients who came for a check-up in the outpatient clinic and had optimized therapy were evaluated and continue to be monitored through follow-up appointments in the outpatient setting (group 2).

Key inclusion criteria included participants being aged 18-85 and diagnosed with HFrEF (ejection fraction ≤40%). Exclusion criteria included cognitive impairments and patients' refusal to participate.

Both groups were on optimized, guideline-directed medical therapy (GDMT) for HFrEF according to the current European Society of Cardiology (ESC) guidelines for HFrEF,[5] which included the maximum tolerable dose of angiotensin receptor-neprilysin inhibitor (sacubitril valsartan), a diuretic, a beta-blocker, magnetic resonance angiography (eplerenone or spironolactone, 25 or 50 mg), and sodium-glucose cotransporter 2 (empagliflozin or dapagliflozin, 10 mg).

Outcome Measures:

- Primary outcomes:

- QoL assessed via a customized questionnaire at baseline and after 3 months, focusing on effort tolerance, daily activities, and mood (anxiety/depression).

- Hospitalizations for HF within the 3-month follow-up.

- Secondary outcomes:

- Medication adherence.

- Patient-reported symptoms and functional status (New York Heart Association class).

- Death.

All patients were followed for 3 months. Data were collected at baseline and at follow-up. The study was approved by the Ethics Committee of University Clinical Center Tuzla Institution before starting the research (approval number: 02-09/2-53/21, date: 08.06.2022)., and informed consent was obtained from all participants, ensuring their full adherence to appropriate privacy and confidentiality standards.

After 3 months, QoL was assessed in both groups at follow-up examinations. QoL was assessed with a set of questions, via an interview or survey, modeled on the ESC questionnaire (the questions were adapted to the demographic characteristics of our population, and the questionnaire is provided as a Supplement 1). We compiled a set of questions concerning the patients responded to which QoL in HF and took into account the degree of tolerance to effort, the ability to perform usual daily and life activities, and the mood of the patients, such as the assessment of possible anxiety or depression. The survey questionnaire is attached as a the Supplement 1.

Statistical Analysis

Comparative analysis used t-tests for continuous variables and chi-square for categorical variables ($P < 0.05$ considered significant). ANOVA was used for data analysis. The visual analogue scale assessed symptom intensity and QoL, with patients marking their subjective experiences, as detailed in the Supplement 1.

RESULTS

The study involved 64 patients with HFrEF (85% male, 15% female), with most participants aged 56-65 years. The t-test showed no significant difference in age ($P < 0.05$) between groups. There was no significant difference among groups regarding the etiology of HFrEF, as shown in Table 1. As aforementioned in the methodology section both groups were on GDMT and there were no differences in medications. There were 4 patients with implantable cardioverter-defibrillator/cardiac resynchronization therapy in the first group versus 5 patients in the second group (no statistically significant difference).

Significant differences were found between educated and uneducated patients in various aspects of daily life (Figure 1). Educated patients reported fewer problems with usual activities, including walking. About 38% of educated patients had no issues walking, compared to 68% of uneducated patients. Furthermore, 19% of uneducated patients were unable to walk at all (Figure 2), while no educated patient reported this ($P = 0.038$). There was also a significant difference in responses regarding chest pain (Figure 3), with educated patients reporting less pain ($P = 0.0011$).

Table 1: Etiology of heart failure in groups

Diagnosis (etiology of HFrEF)	Group 1 (n=32)	Group 2 (n=32)	*P*-value
Ischemic post infarction heart disease	17 (53.13%)	15 (46.88%)	0.80
Valvular heart disease	7 (21.88%)	9 (28.13%)	0.77
Dilated CMP	5 (15.63%)	6 (18.75%)	1.00
Other CMP/etiology	3 (9.38%)	2 (6.25%)	1.00
Overall difference between groups			0.86

HFrEF: Heart failure with reduced ejection fraction, CMP: Cardiomiopathy

Regarding anxiety and depression, educated patients showed significantly lower levels, with 54% reporting no anxiety compared to 28% in uneducated patients (Figure 4). Conversely, 72% of uneducated patients experienced moderate or severe anxiety/depression ($P = 0.034$; $P = 0.042$).

Additionally, none of the educated patients had rehospitalizations, while 34% of uneducated patients did, highlighting the positive impact of education in reducing hospitalizations, improving QoL, and lowering healthcare costs.

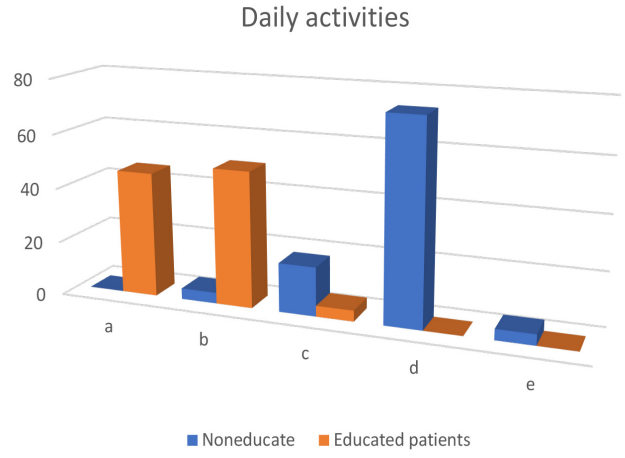


Figure 1: Comparison of results between educated and non-educated group regarding daily activities (a, b, c, d and e on X axis are answers on questions given in Supplement 1, Y axis shows proportions of patients)

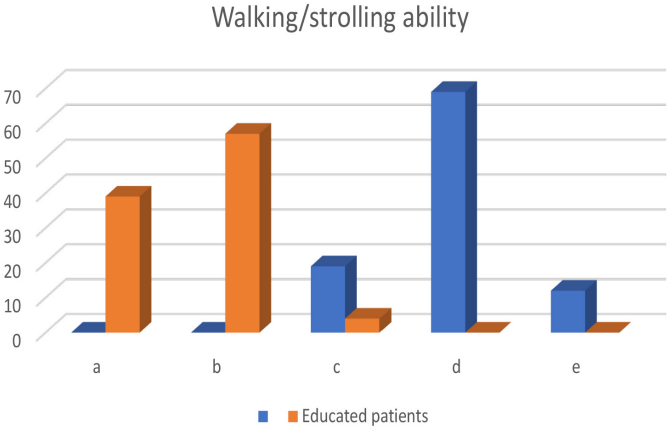


Figure 2: Comparison of results between educated and non-educated group regarding walking disability (a, b, c, d and e on X axis are answers on questions given in Supplement 1, Y axis shows proportions of patients)

DISCUSSION

This study highlights several key findings regarding the impact of education on HF patients' QoL, symptom management, and overall well-being. The sample of 64 subjects, predominantly male (85%) and aged 56-65 years, reflects the typical demographic profile for HFrEF. No statistically significant difference in age was found between the educated and uneducated groups ($P > 0.05$), suggesting age did not confound the study results.

A major finding was the significant improvement in the ability to perform daily activities among educated patients. For instance, while 68% of uneducated patients reported walking as a problem, only 19% of educated patients did, with none reporting an inability to walk. Statistically significant differences in walking difficulties were observed ($P = 0.038$ for

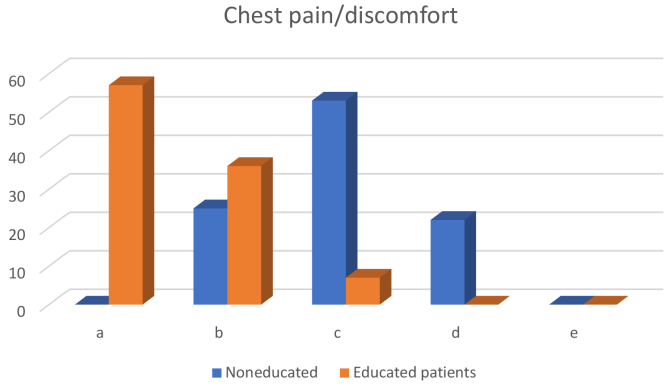


Figure 3: Comparison of results between educated and non-educated group regarding chest pain/discomfort (a, b, c, d and e on X axis are answers on questions given in Supplement 1, Y axis shows proportions of patients)

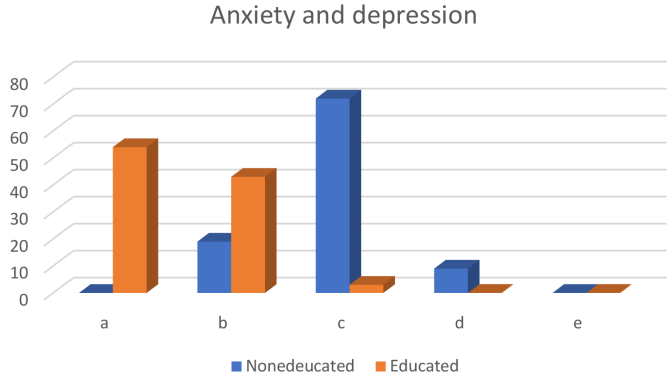


Figure 4: Comparison of results between educated and non-educated group regarding anxiety and depression (a, b, c, d and e on X axis are answers on questions given in Supplement 1, Y axis shows proportions of patients)

"big problem", $P = 0.044$ for "small problem"), indicating that education positively influences mobility and physical activity.

Regarding chest pain, educated patients reported fewer instances of pain or discomfort. A significant difference was found in the "no chest pain or discomfort" response ($P = 0.0011$) between the groups, though no significant differences were noted for mild, severe, or extreme pain. This suggests education may help alleviate mild to moderate discomfort but might not have a significant impact on more severe pain.

The study also found that educated patients had significantly lower levels of anxiety and depression. Specifically, 54% of educated patients reported no anxiety, compared to 28% in the uneducated group, while 72% of uneducated patients experienced moderate to severe symptoms of anxiety or depression. The statistical significance of these findings ($P = 0.034$ for "not anxious", $P = 0.042$ for "moderately anxious") underscores the mental health benefits of patient education.

Finally, a key outcome was the absence of rehospitalizations among educated patients, while 34% of uneducated patients experienced rehospitalizations. This suggests that education is crucial in reducing hospital readmissions, as educated patients are likely more adept at managing symptoms, adhering to treatment, and seeking timely medical care.

Overall, the results suggest that patient education can significantly improve both physical and psychological outcomes for HF patients, while also reducing the need for rehospitalizations.

This not only improves the patients' QoL but also has important implications for reducing healthcare costs, as rehospitalizations are a significant financial burden.[4] For instance, Saito et al.[6] conducted a meta-analysis and concluded that patients with HF, particularly those with comorbidities, poor physical condition, a history of readmissions, or inconsistent medication adherence, are at a higher risk of readmission. These patients could benefit significantly from the additional support provided by nurse-led interventions, which often include home visits and personalized education. Feltner et al.[7] and Takeda et al.[8], further corroborated the positive impact of home visits on both readmissions and mortality rates. In contrast, other studies comparing the effectiveness of home visits with telephone calls or telemonitoring found that remote interventions were less effective than face-to-face consultations.[9-11] These findings underscore the value of in-person interactions in improving patient outcomes, particularly for high-risk populations like those with HF.

The impact of education programs on patients with HF has been a topic of ongoing investigation, and recent meta-analytic findings continue to confirm its importance in reducing HF-related readmissions, as well as all-cause readmissions and mortality. A pooled analysis confirmed that interventions, such as nurse-led education programs, had a meaningful effect on reducing HF-related readmission rates and improving survival outcomes. Notably, interventions that included home visits appeared more effective than those without this component. These findings align with previous research suggesting that home visits can be an essential factor in improving patient outcomes post-discharge.[4]

However, some studies have questioned the broader efficacy of nurse-led HF self-care education. Son et al.[3] found that nurse-led education, specifically on self-care, did not lead to significant improvements in QoL or HF knowledge, raising concerns about the generalizability of nurse-led education programs. They argued that while many studies highlight the positive outcomes of such interventions, the evidence supporting the effectiveness of the nurse-led approach remains limited. This point raises an important consideration regarding the methodology used in many trials, which often focuses only on positive health outcomes without addressing potential methodological flaws.

In contrast, the present meta-analysis addressed this gap by including a comprehensive set of interventions. All randomized controlled trials (RCT) included in the meta-analysis incorporated education on managing comorbidities and medications, such as diabetes, hypertension, and obesity-factors that can significantly affect cardiac outcomes. Additionally, three of the studies included mandatory exercise as part of the intervention. These findings suggest that education programs, when tailored to a patient's broader health management needs, may be more effective in improving HF outcomes.

Despite the overall positive findings regarding nurse-led interventions, it is essential to consider the methodological issues identified in previous studies. Ditewig et al.[11] highlighted that self-management interventions often suffered from various methodological shortcomings, such as non-RCT designs, which could explain why some studies failed to show any significant impact on readmission rates or mortality. In contrast, the current meta-analysis demonstrated a positive effect on HF-related readmission and the composite outcome of all-cause readmission/death, though no significant effect was observed for all-cause readmissions or all-cause death, alone. These nuanced results are consistent with the broader literature, which suggests that improving patients' knowledge about HF could help reduce exacerbations and prevent readmissions.[12-14]

Moreover, Van Spall et al.[15] examined post-discharge programs for HF patients and found that nurse-led home visits were the most effective in reducing all-cause mortality, followed by

disease management clinics. When it comes to readmissions, home visits proved once again to be the most effective. However, the data did not support a reduction in all-cause readmissions. These discrepancies could stem from differences in the study designs, patient populations, or outcome measures.

In conclusion, while nurse-led education programs-particularly those including home visits-show promise in improving HF-related readmissions and patient survival, there are still questions about the broader impact on all-cause readmissions and mortality. The evidence suggests that tailored, comprehensive interventions that address both disease management and comorbidities, alongside active patient engagement through home visits, are likely to be the most effective strategies for reducing readmission rates and improving outcomes in HF patients.

It is well known that patient education plays an important role in patients with HF, especially when it comes to improving the QoL of educated patients. However, there is not enough research that discusses to what extent education affects patients who are on modern, and optimized therapy according to the latest ESC guidelines for the treatment of HF. Additionally, insufficient implementation of patient and family education in everyday clinical practice is one of the main reasons for the unsatisfactory statistics regarding HF (in terms of mortality, morbidity, and QoL). Due to the insufficient number of healthcare workers (doctors and nurses) per capita in our country, as well as in many other countries, there is often not enough time dedicated to patient education. However, we believe that this research, even though it has a small sample size, emphasizes the importance of education and not just therapy optimization. In the long run, this ultimately saves time and resources by reducing the number of emergency doctor visits, hospitalizations, and improved QoL.

Study Limitations

While the study provides valuable insights into the effects of education on HF patients, there are some limitations. The sample size of 64 patients is relatively small, and the study was cross-sectional in nature, limiting the ability to draw precise conclusions about causality. Furthermore, the study did not assess the specific content or format of the educational interventions, which could vary in effectiveness depending on delivery methods. Future studies with larger, more diverse populations and longitudinal designs are needed to confirm these findings and explore the long-term effects of education on HF patients. Additionally, investigating the specific components of educational programs that contribute to improvements in physical activity, mental health, and hospitalization rates could further enhance the understanding of effective interventions for HF management. QoL was assessed with a set of questions, via an interview or survey, modeled on the questionnaire of the ESC. We adapted the questions to the demographic characteristics of our population; hence, we did not obtain accreditation.

CONCLUSION

In conclusion, the findings from this study underscore the significant benefits of education for patients with HF. Educated patients reported fewer problems with daily activities, less chest pain and discomfort, lower levels of anxiety and depression, and a reduction in rehospitalizations. These results suggest that incorporating educational interventions into the management of HF could lead to improved patient outcomes, enhanced QoL, and reduced healthcare costs. A comprehensive educational program for HF patients, which emphasizes self-care, symptom monitoring, and lifestyle changes, can significantly improve outcomes. By helping patients understand their condition and actively participate in their treatment plan, we can enhance their overall QoL and reduce hospital admissions and complications.

Future research should further investigate the impact of different educational approaches and explore their long-term benefits for HF patients.

Ethics

Ethics Committee Approval: Approval was obtained from the Ethics Committee of University Clinical Center Tuzla Institution before starting the research (approval number: 02-09/2-53/21, date: 08.06.2022).

Informed Consent: Informed consent was obtained from all participants, ensuring their full adherence to appropriate privacy and confidentiality standards.

Footnotes

Authorship Contributions

Surgical and Medical Practices: L.D.H., E.H., S.B., I.H., Z.S., Concept: L.D.H., S.B., D.L., N.A.J., I.H., Z.S., Design: L.D.H., E.H., S.B., D.L., N.A.J., I.H., Z.S., Data Collection or Processing: L.D.H., E.H., D.L., N.A.J., Analysis or Interpretation: L.D.H., E.H., N.A.J., A.M.I., Literature Search: L.D.H., E.H., N.A.J., A.M.I., Writing: L.D.H., A.M.I., Z.S.

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

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

REFERENCES

1. Jaarsma T, Hill L, Bayes-Genis A, La Rocca HB, Castiello T, Čelutkienė J, *et al.* Self-care of heart failure patients: practical management recommendations from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2021;23:157-74.
2. Ferreira JP, Kraus S, Mitchell S, Perel P, Piñeiro D, Chioncel O, *et al.* World Heart Federation roadmap for heart failure. Global Heart. 2019;14:197-214.
3. Son YJ, Choi J, Lee HJ. Effectiveness of nurse-led heart failure self-care education on health outcomes of heart failure patients: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17:6559.
4. Tian C, Zhang J, Rong J, Ma W, Yang H. Impact of nurse-led education on the prognosis of heart failure patients: a systematic review and meta-analysis. Int Nurs Rev. 2024; 71:180-8.
5. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2023;44:3627-39. Erratum in: Eur Heart J. 2024;45:53.
6. Saito M, Negishi K, Marwick TH. Meta-analysis of risks for short-term readmission in patients with heart failure. Am J Cardiol. 2016;117;626-32.
7. Feltner C, Jones CD, Cené CW, Zheng ZJ, Sueta CA, Coker-Schwimmer EJ, *et al.* Transitional care interventions to prevent readmissions for persons with heart failure: a systematic review and meta-analysis. Ann Intern Med. 2014;160:774-84.
8. Takeda A, Martin N, Taylor RS, Taylor SJ. Disease management interventions for heart failure. Cochrane Database Syst Rev. 2019;1:2752.
9. McCall N, Cromwell J. Results of the Medicare Health Support disease-management pilot program. N Engl J Med. 2011;365:1704-12.
10. O'Connor CM, Miller AB, Blair JE, Konstam MA, Wedge P, Bahit MC, *et al.* Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduced left ventricular ejection fraction: results from efficacy of vasopressin antagonism in heart failure outcome study with tolvaptan (EVEREST) program. Am Heart J. 2010;159:841-9
11. Ditewig JB, Blok H, Havers J, van Veenendaal H. Effectiveness of self-management interventions on mortality, hospital readmissions, chronic heart failure hospitalization rate and quality of life in patients with chronic heart failure: a systematic review. Patient Educ Couns. 2010;78:297-315.
12. Abshire M, Xu J, Baptiste D, Almansa JR, Xu J, Cummings A, *et al.* Nutritional interventions in heart failure: a systematic review of the literature. J Card Fail. 2015;21:989-99.
13. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, *et al.* 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. J Am Coll Cardiol. 2022;79:263-421.
14. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al.* 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42:3599-726.
15. Van Spall HGC, Rahman T, Mytton O, Ramasundarahettige C, Ibrahim Q, Kabali C, *et al.* Comparative effectiveness of transitional care services in patients discharged from the hospital with heart failure: a systematic review and network meta-analysis. Eur J Heart Fail. 2017;19:1427-43.

Supplement 1-Addendum: Appendix (Questionnaire)

General section

1. Gender

a) Male

b) Female

2. Age

a) 18-25 years

b) 26-35 years

c) 36-45 years

d) 46-55 years

e) 56-65 years

f) 66-75 years

g) 76 years and older

Part I - Usual activities

3. a) I have no problems performing everyday activities.

b) I have minor problems performing everyday activities.

c) Performing everyday activities is a moderate problem for me.

d) Performing everyday activities is a major problem for me.

e) I am unable to perform everyday activities.

4. a) I have no problems walking or strolling.

b) Walking or strolling is a minor problem for me.

c) Walking or strolling is a moderate problem for me.

d) Walking or strolling is a major problem for me.

e) I am unable to walk.

Part II - Pain/discomfort

5. a) I have no pain or discomfort in my chest.

   b) I have mild chest pain or discomfort.

   c) I have moderate pain or discomfort in the chest.

   d) I have severe pain or discomfort in the chest.

   e) I have very severe pain in my chest.

Part III - Anxiety and Depression

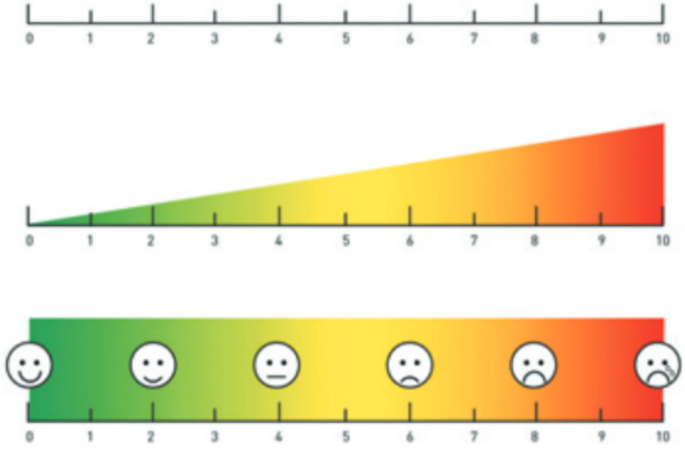
6. a) I am not anxious or depressed.

   b) I am mildly anxious or depressed.

   c) I am moderately anxious or depressed.

   d) I am severly anxious or depressed

   e) I am very severely anxious or depressed



VAS scale The VAS scale is used to assess the intensity of symptoms and the QoL of patients. Patients mark their subjective experience on a 10 cm long line, where the endpoints represent the extreme values of the symptoms.

RESEARCH ARTICLE

DOI: 10.4274/ijca.2025.43433
Int J Cardiovasc Acad 2025;11(1):15-22

Electrocardiogram Changes in Patients with Hyponatremia: A Retrospective Study

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Abstract

Background and Aim: Hyponatremia is defined as a serum sodium level lower than 135 mEq/L. It is the most common clinical electrolyte disorder. Electrolyte disorders are known to affect electrical conduction in the human heart. As the severity of sodium deficiency increases, the clinical picture becomes more severe, but this may not always be directly reflected in the electrocardiogram (ECG). In our study, we aimed to detect common ECG findings seen in patients with hyponatremia.

Materials and Methods: The study was designed retrospectively. Patients who applied to the cardiology and/or nephrology outpatient clinic between January 2020 and 2023, were detected to have hyponatremia in laboratory tests, and had an ECG taken on the same day were included in the study. Changes in the ECG were recorded.

Results: Thirty-four patients were included in the study. When the ECG examinations of the patients were evaluated, P mitrale was detected in 8 patients and bundle branch block (left bundle branch block, right bundle branch block and incomplete bundle branch block), was detected in 7 patients. T-wave changes were frequently observed in hyponatremic patients. The most common cause of hyponatremia in patients was determined to be hypovolemic hyponatremia.

Conclusion: In conclusion, the investigation into ECG changes associated with hyponatremia reveals critical insights into the complex interplay between electrolyte disturbances and cardiac function. While the study identified specific ECG abnormalities like P mitrale and various bundle branch blocks, these findings underscore the necessity for careful interpretation, as they may not be solely attributable to hyponatremia. The lack of distinctive ECG patterns correlating exclusively with sodium deficiency suggests that clinicians should employ a holistic approach when evaluating patients with hyponatremia, considering accompanying medical conditions and pharmacological influences. Ultimately, further research is imperative to explore the underlying mechanisms and enhance the diagnostic utility of ECG in managing electrolyte imbalances effectively.

Keywords: P mitrale, hyponatremia, electrocardiogram, bundle branch blocks

INTRODUCTION

The complexity of electrolyte imbalances in clinical medicine requires comprehensive examination, particularly regarding their impact on cardiovascular health. Hyponatremia, characterized by abnormally low serum sodium levels, is a common and potentially dangerous condition that can lead to various health complications.[1] It is frequently encountered in patients with heart failure (HF), where the interplay between neurohormonal activation and fluid retention further exacerbates sodium deficiency. Alterations in serum sodium levels can induce significant changes in cardiac electrical activity, as can be detected by observable electrocardiogram (ECG) abnormalities.

To cite this article: İyigün U, Hüzmeli C. Electrocardiogram changes in patients with hyponatremia: a retrospective study. Int J Cardiovasc Acad. 2025;11(1):15-22

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Received: 19.01.2025
Accepted: 07.03.2025
Publication Date: 18.03.2025

Symptoms of patients with hyponatremia range from being asymptomatic to coma. Patients with acute (<48 h) or severe (sodium levels less than 120 mmol/L) hyponatremia may present with serious complications such as dizziness, coma, seizures, respiratory depression, and death. Others may present with only non-specific symptoms such as nausea, vomiting, and headache. Chronic moderate (sodium levels 120-129 mmol/L) and mild (sodium levels 130-134 mmol/L) hyponatremia can cause fatigue, cognitive impairment, gait deficits, falls, impaired bone metabolism, and fractures.[2]

Electrolyte imbalances, particularly those affecting sodium levels, have significant implications for health, especially in patients with chronic conditions. Hyponatremia can arise from a myriad of factors, including excessive fluid intake, renal impairment, or the side effects of medications, particularly in the context of cancer treatment.[3]

Identification of changes in the ECG, such as T-wave changes and conduction defects, in cases of hyponatremia may provide early prediction of clinical deterioration.[4]

There is a complex relationship between hyponatremia and ECG changes, and in some cases it can cause arrhythmias with serious cardiac consequences. ECG changes such as P mitrale, bundle branch blocks and T-wave changes have been described in some studies, and it has been noted that more pronounced ECG changes can be seen at lower sodium levels. These changes may occur due to electrolyte imbalances affecting myocardial repolarization and conduction and may lead to increased susceptibility to fatal arrhythmias.[5]

The evaluation of cardiac complications associated with electrolyte imbalances is crucial to understanding their implications in clinical practice. In the context of hyponatremia, the aim of this retrospective study was to identify ECG changes occurring in affected patients. Hyponatremia is often associated with poor health outcomes and, in some cases, affects populations with pre-existing cardiac conditions. Therefore, it is important to detect these changes early. The aim of the study is not only to enable early recognition of ECG changes in hyponatremia, but also to increase awareness and improve patient management and prevent further complications.

METHODS

This retrospective study included patients who presented to the cardiology and/or nephrology outpatient clinic between January 2020 and January 2023, were diagnosed with hyponatremia, and had their ECG taken on the same day. Data were collected from patient records, specifically targeting those diagnosed with hyponatremia, defined as serum sodium levels less than 135 mEq/L. The study included 34 patients, mostly older adults, with a significant prevalence of chronic health conditions such as HF, which is known to complicate the clinical picture of hyponatremia. It was planned to evaluate the possible effects of hyponatremia by detecting all abnormal changes in the ECG.

The selection of participants for the study on ECG changes in patients with hyponatremia involved stringent inclusion and exclusion criteria to ensure valid and reliable results. Individuals aged 18 and older, with confirmed hyponatremia defined as serum sodium levels less than 135 mEq/L, were included to create a focused cohort that accurately reflects the population affected by this electrolyte imbalance. Furthermore, patients exhibiting significant comorbid conditions, such as chronic kidney disease (CKD) or cardiac disorders, were scrutinized to assess their impact on ECG results, which aligns with findings suggesting that underlying health issues complicate hyponatremia and its cardiac implications. Exclusion criteria eliminated those with psychiatric illnesses or previous electrolyte disorders to avoid confounding variables, thereby enhancing the study's power and ensuring that the captured ECG changes were indeed reflective of hyponatremia itself. The study protocol was reviewed and approved by the Ethics Committee of Hatay Mustafa Kemal University (decision number:19, date:12.10.2023).

Statistical Analysis

The SPSS 20 package program was used to analyze statistical data for evaluation. Descriptive analytic methods were used in this study. Data statistics, number, and percentage distributions were analyzed using the chi-square and Mann-Whitney U tests. A P of <0.05 was considered significant.

RESULTS

This study included 34 patients, of whom 20 (58.5%) were women and 14 (41.5%) were men. The average age of the patients was 67.5±13.0 (34-94) years. Hypertension was present in 18 (52.9%) of the patients; CKD in 13 (38.2%) of the patients, with four undergoing hemodialysis; coronary artery disease in 7 (20.5%) of the patients. HF was diagnosed in 5 (14.7%) patients. Twenty-one of the 34 patients included in the study were aged 65 years and older. When the etiologies of hyponatremia were investigated, hypervolemic hyponatremia was found in 10 patients, hypovolemic hyponatremia was found in 19 patients (2 of whom had malnutrition), and euvolemic hyponatremia was found in five patients.

One patient had hypokalemia. However, the ECG was found to be normal in this patient. Potassium levels were increased in two patients (5.5 mmol/L). These patients did not exhibit any signs of hyperkalemia, such as T peaking and QRS widening. Furthermore, twelve (35%) patients were using diuretics (6 of them were using loop diuretics, while the others were using thiazides). Notably, patients with hypervolemic hyponatremia

are generally associated with HF and/or CKD. Eight of the hypervolemic hyponatremia patients (ten overall) had accompanying CKD, with five of these patients having HF and three having HF and CKD. Four of the patients had inappropriate antidiuretic hormone (ADH) syndrome (12.5%). Twelve patients were taking diuretics (35.2%). The demographic, laboratory, and ECG results of the patients are shown in Table 1.

When the ECGs of the patients were evaluated, P mitrale was found in ten patients, and bundle branch block was detected in eight patients (left bundle branch block in four patients, right bundle branch block in three patients, and incomplete bundle branch block in one patient). Two patients experienced atrial fibrillation (AF) (this finding was confirmed by information in the patients' files). One patient had supraventricular tachycardia at the time of admission. Other patients were in the sinus rhythm. T flattening was found in five patients. T negativity was found in thirteen patients. However, the regions of these changes varied from patient to patient (in some patients, they were seen in D1-aVL, whereas in others, they were in the chest leads). ECG changes according to hyponatremia levels are shown in Table 2.

None of the patients had serious complications such as neurological deterioration or death. Twenty of the thirty-four patients had general weakness and headache-like complaints, while six patients had nausea. These symptoms were seen in all hyponatremia patients, regardless of sodium levels.

DISCUSSION

Hyponatremia has been associated with poor outcomes in a variety of clinical settings. This situation can have negative consequences on patients with HF, coronary artery disease, heart valve disease, elderly patients, patients who have undergone cardiac surgery, and patients with renal dysfunction. The pathogenesis of sinus arrest or cardiac conduction defects caused by hyponatremia has yet to be elucidated, and there is insufficient information in the literature regarding this condition. Clinical observations have shown that a low extracellular sodium concentration can decrease the depolarization of the cardiac action potential and reduce its amplitude in the atrioventricular (AV) node. Furthermore, low sodium levels in the fluid perfusing isolated cardiac muscle can reduce contraction frequency, reduce excitability, and reduce conduction velocity.[6]

Hyponatremia caused by fluid retention increases atrial wall tension, which can lead to atrial arrhythmias.[7] In our study, supraventricular tachycardia was found in one patient. However, the patient had previously experienced palpitations similar to those described. There was insufficient evidence to directly link this condition with hyponatremia.

Severe symptomatic hyponatremia (serum sodium of ≤120 mEq/L) can lead to life-threatening or fatal complications, such as cerebral edema and permanent neurological disability, due to osmotic demyelination.[8] In our study, 20 patients (58.8%) had severe hyponatremia (serum sodium of ≤120 mEq/L). There were no neurological events reported in any patient.

In patients with congestive HF, the number of ventricular premature beats was found to be equally related to the severity of hyponatremia and hypokalemia. Mouallem et al.[9] described three patients who developed reversible cardiac conduction defects associated with transient hyponatremia. During hyponatremia, two of these patients had complete or second-degree AV block (both patients had preexisting heart disease and were taking antiarrhythmic drugs). The other patient developed first-degree AV block during hyponatremia. Second-degree AV block improved with treatment, while first-degree AV block persisted after treatment of hyponatremia. Kottwitz et al.[10] reported a first-degree AV block due to hyponatremia in a 76-year-old male patient, who complained of malnutrition, dysarthria, disorientation, weakness, and fatigue, and had a history of alcohol use and dementia. It was shown that a patient who developed first-degree AV block, followed by second and third-degree AV block, during an attack of severe hyponatremia (serum sodium 98 mmol/L), experienced AV block conditions that were completely reversed once the serum sodium level was corrected.

Previous studies have shown that changes similar to the Brugada pattern can occur in patients with hyponatremia. Brugada syndrome is a genetic condition that increases the risk of ventricular fibrillation and sudden cardiac death in a structurally normal heart. The Brugada type 1 ECG pattern can occur independently of the actual syndrome, and this clinical phenomenon is commonly known as the Brugada phenocopy. A 49-year-old male patient admitted to the emergency department with delirium (due to his use of thiazide diuretics and angiotensin-converting enzyme inhibitors for hypertension) was diagnosed with antihypertensive drug-induced hypovolemic hyponatremia (serum sodium 108 mmol/L, low serum osmolality, high urine osmolality, and urine sodium <20 mmol/L). On admission, the patient's ECG revealed a sloping ST-segment elevation in leads V1 and V2, with high J-dots indicating a Brugada type 1 pattern. The patient improved after treatment. It was believed that his findings were the result of antihypertensive medication. He was discharged after his antihypertensive medications were changed, and the incident did not occur again.[11] In our study, no changes in this pattern were observed in any patient.

The most common causes of hyponatremia in patients with HF are autonomic imbalance caused by diuretic use, sympathetic nervous system response, and renin-angiotensin

Table 1: Demographic, laboratory, and ECG findings of the patients

Case	Gender/age	Serum/urine Na	Serum K	Thyroid hormone/ cortisol	Additional diagnosis	Hyponatremia etiology	ECG finding
1	M/64	102/171	4.5	N/N	COPD	Inappropriate ADH	NSR, 75/min
2	M/69	124	5.1	N/N	HT	Diuretic use (Thiazide)	NSR, 1mm ST in d2-d3-avf
3	M/68	121	5.5	N/N	DM, CKD	Hypervolemic hyponatremia	NSR, p mitrale, 50/min
4	F/70	108/22	3.8	N/N	DM, HT	Diuretic use (Loop), dehydration	NSR, left bundle branch block, frequent VES (Quadrigemine)
5	F/84	124/34	5.1	N/N	Heart failure, HT, AF	Hypervolemic hyponatremia	AF, d1-avl T (-), 72/min
6	M/64	124/12	3.8	N/N	DM, HT, CKD	Hypervolemic hyponatremia	NSR, 90/min, P mitrale
7	F/58	104/10	3.6	N/N	No features	Dehydration	NSR, 106/min
8	M/48	124	4.2		CKD	Hypervolemic hyponatremia	NSR, 71/min, right bundle branch block, d1-d2 T (-), p mitrale
9	F/63	122/31	4.3	N/N	HT, kidney transplant	Diuretic use (thiazide)	NSR, 86/min
10	M/63	113	4.5		AKI	Dehydration	NSR, 100/min, d3-avf T (-)
11	M/61	119	4.8	N/N	Heart failure, CKD	Hypervolemic hyponatremia	NSR, Left bundle branch block, p mitrale, d1-avl T (-)
12	F/80	128/27	4.9	N/N	HT	Diuretic use (thiazide)	NSR, T (-) in V1, 1 mm ST depression in V6
13	F/72	111/23	5.2	N/N	DM, HT	Dehydration	NSR, 75/min, T (-) at V6
14	F/80	116/54	3.8	N/N	DM	Inappropriate ADH	NSR, 62/min, T (-) in V4-V6
15	F/94	111	2.8	N/N	DM, HT	Diuretic use (loop)	NSR, 85/min
16	M/67	127	4.3	N/N	DM, HT, CKD, AF	Hypervolemic hyponatremia	AF, ıncomplete left bundle branch block, VES
17	F/53	116/87	4.7	N/N	HT	Diuretic use (thiazide)	NSR, 71/min
18	F/52	105/38	4.2	N/N	Bronchiectasis, CKD	Diuretic use (loop)	NSR, 70/min
19	F/52	119/18	4.3	N/N	Anorexia nervosa	Dehydration	NSR, T (-) in V1
20	F/71	123/50	4.2	N/-	HT	Diuretic use (thiazide)	NSR, p mitrale
21	M/84	123/38	3.6	N/N	HT, gallbladder cancer	Inappropriate ADH	NSR, right bundle branch block, p mitrale
22	F/32	125	4.2	N/N	ABH	Dehydration	NSR, diffuse T flattening
23	M/79	119/12	5.0	N/N	HT, CKD	Diuretic use (loop), gastroenteritis	NSR, 52/min
24	F/60	119/41	4.0		HT, CKD	Diuretic use (loop)	NSR, 72/min, d1-avL T flattening
25	M/72	114/13	5.5	N/-	CKD, colon cancer	Malnutrition	NSR, 75/min, p mitrale, aVL'de T (-)
26	F/75	123/33	4.0	N/N	HT, CKD	Diuretic use (loop)	NSR, 75/min, p mitrale, T (-) in aVL
27	F/73	105/29	2.7	N/N	HT, COPD	Malnutrition	NSR, 80/min, p mitrale, T (-) in d1-aVL

Table 1: Continued

Case	Gender/age	Serum/urine Na	Serum K	Thyroid hormone/ cortisol	Additional diagnosis	Hyponatremia etiology	ECG finding
28	F/50	118	4.7	N/-	CKD	Hypervolemic hyponatremia	NSR, 90/min, p mitrale, T (-) in d1-aVL
29	F/65	113	4.7	N/-	Heart failure, HT, CKD	Hypervolemic hyponatremia	SVT, 114/min, right bundle branch block, 1 mm ST depression in v4-v6, T(-) in v1-v3 and aVL
30	F/65	124/65	4.8	N/-	DM, HT, CKD, hypothyroidism	Diuretic use (thiazide)	NSR, SVES, 65/min
31	M/84	119	4.2	N/-	Heart failure, CKD	Hypervolemic hyponatremia	NSR, left bundle branch block, T (-) in D1-aVL, q(+) in the inferior
32	F/82	118	4.7	N/-	Heart failure	Hypervolemic hyponatremia	NSR, Diffuse ST depression, ST elevation in V1
33	M/68	128/32	4	N/-	No features	Inappropriate ADH	NSR, 98/min, T flattening in aVL
34	M/82	111/90	4.0	N/N	Lung cancer	Inappropriate ADH	NSR, 82/min, T flattening in aVL

F: Female, M: Male, ECG: Electrocardiogram, COPD: Chronic obstructive pulmonary disease, ADH: Antidiuretic hormone, NSR: Normal sinus rhythm, HT: Hypertension, DM: Diabetes mellitus, CKD: Chronic kidney disease, AF: Atrial fibrillation, AKI: Acute kidney injury, ABH: Acute bronchitis

Table 2: The table shows the accompanying ECG changes according to the levels of hyponatremia. The numbers in the columns indicate the number of patients

Serum Na (mEq/L)	T-wave alternans	Atrial fibrillation	LBBB	RBBB	P mitrale
120 and higher	7	2	1	2	6
110-119	13	None	2	1	3
100-109	1	None	1	None	1

ECG: Electrocardiogram, LBBB: Left bundle branch block, RBBB: Right bundle branch block

system activation, as well as the subsequent neurohormonal response. The primary cause of hyponatremia associated with HF is increased non-osmotic release of ADH as a result of the reduced circulating effective volume.[12]

Although the rate of AF was found to be higher in patients with hyponatremia than in patients with normonatremia, logistic regression analysis did not reveal a direct relationship between hyponatremia and AF.[13] However, for the first time in the literature, hyponatremia has been shown to be independently associated with an increased risk of AF.[14] Another study found a higher incidence of AF and diabetes mellitus in patients with hyponatremia. Fasting glucose, mineralocorticoid receptor antagonists, and digoxin use were found to be higher in the hyponatremia group than in the normonatremia group. However, no correlation was found between sodium levels and AF in patients with HF with preserved ejection fraction. The slowing of the sinoatrial nodal rate caused by low sodium and potassium levels may contribute to an increased risk of AF during hyponatremia or hypokalemia.[15] In our study, AF was found in two patients; however, these patients had pre-existing AF (as confirmed by reviewing their previous records), which was not associated with hyponatremia. In our study, five patients had hyponatremia associated with HF. Hypervolemic hyponatremia was found in each of them.

Hyponatremia may be associated with cardiac conduction abnormalities and some ECG changes. However, with current knowledge, direct ECG assessment cannot be used to determine whether a patient has hyponatremia. Recognizing diseases associated with hyponatremia and identifying conditions that may cause it, such as medication use, can provide early warning signs for the prevention and diagnosis of this electrolyte disorder.

Hyponatremia may prolong the hospital stay and increase mortality. Hyponatremia is especially common in patients with HF who are using diuretics and in the elderly, and therefore, more care should be taken in these patients. Although our study findings do not identify specifics to hyponatremia, they may be useful in taking precautions, especially in patients in the risk group. The heterogeneity of the findings

detected in ECGs supports the possibility that this condition may also occur due to other concomitant heart diseases. However, the retrospective nature of our study and the lack of echocardiographic evaluations of the patients make it difficult to evaluate this relationship. Therefore, it should be evaluated in larger patient groups to clarify its direct relationship with hyponatremia.

Early diagnosis with ECG can contribute to disease management when the possible risks associated with hyponatremia are evaluated. Therefore, methods other than laboratory measurements can be used to detect ECG changes that may occur due to hyponatremia. Similar to previous studies, the current study shows that physician evaluation with ECG alone is not sufficient to diagnose hyponatremia. In addition, the inadequacy of ECG in the diagnosis of hyponatremia emphasizes the need for the development of new methods. Machine learning-based approaches may increase the success of early diagnosis in patient groups where sufficient information about hyponatremia cannot be obtained through ECG evaluation. However, further studies are needed before they can be used in clinical settings.

Future research is needed to understand the complexities that constitute ECG changes in patients with hyponatremia. It is necessary to investigate how low sodium levels affect cardiac electrophysiology, particularly given the high prevalence of ECG abnormalities in these patients. The retrospective nature of the current study highlights the necessity of prospective, longitudinal studies that capture a broader demographic, allowing for more generalized conclusions about cardiac implications in different health conditions. Future studies with larger sample sizes may deepen the understanding of how hyponatremia affects cardiac health and guide clinical practice for monitoring high-risk populations.

Identification and management of ECG changes in patients with hyponatremia is important, especially given their potential to affect cardiac function. In this retrospective study, a number of ECG abnormalities were noted in patients with serum sodium levels less than 135 mEq/L, highlighting their risk for future arrhythmias and poor clinical outcomes. Clinicians should be vigilant in monitoring sodium levels, especially in high-risk populations such as those with preexisting heart conditions or CKD. Furthermore, the association of severe hyponatremia with cardiac conduction defects highlights the need to include comprehensive electrolyte assessments in routine cardiovascular assessments. By recognizing the interaction between hypoosmolality and cardiac health, healthcare providers can implement early interventions that can significantly improve patient prognosis and prevent adverse events related to arrhythmias.

The findings of this retrospective study underscore the critical interplay between electrolyte balance and cardiac function, specifically focusing on instances of hyponatremia. A notable percentage of the 34 patients observed displayed ECG abnormalities, with conditions such as P mitrale and T-wave changes being present in those with serum sodium levels less than 135 mEq/L. While no severe neurological events were directly linked to these changes, the connection between electrolyte imbalances and arrhythmias remains a compelling area for further exploration, particularly given that hyponatremia is prevalent in individuals with other cardiac conditions, as highlighted in the study. It is crucial to consider that, despite the documented impacts of hyponatremia on cardiac action potentials, the study's data suggest, a lack of definitive correlation with arrhythmogenic events, which should be further examined in larger cohorts. The necessity for ongoing monitoring and evaluation of ECG changes in patients at risk of hyponatremia cannot be overstated, as it could significantly affect clinical outcomes and management strategies.

The investigation into ECG changes in patients suffering from hyponatremia yielded several significant findings that underscore the condition's impact on cardiac function. In a sample population averaging 67.5 years old, a notable prevalence of comorbidities, such as CKD and HF, was observed. Key ECG abnormalities included P mitrale, bundle branch blocks, and various T-wave changes, indicating that hyponatremia can interfere with cardiac action potentials and provoke arrhythmias. Despite earlier studies suggesting a link between severe hyponatremia and cardiac conduction disturbances, this study found no direct association between severe hyponatremia and neurological events in patients with significant electrolyte imbalances. Moreover, among 20 patients with serum sodium levels at or below 120 mEq/L, ECG results did not reflect expected conduction defects, which resonates with findings that the ECG alone may not suffice in diagnosing hyponatremia-associated changes. Overall, these results highlight the complexity of hyponatremia's arrhythmogenic potential and call for increased awareness in clinical practice.

The relationship between electrolyte imbalances and cardiac function is critical for understanding the ECG changes observed in patients with hyponatremia. In this context, hyponatremia, defined as a serum sodium level below 135 mEq/L, can produce significant alterations in the cardiac electrical conduction system, which are reflected in the ECG patterns. Notably, key abnormalities such as P mitrale, bundle branch blocks, and T-wave changes were prevalent among patients studied, corroborating findings from (Table 2). Moreover, while severe hyponatremia has been implicated in leading to various arrhythmias, the study emphasizes the absence of direct links between these instances and AF in

affected patients. Such findings align with previous research suggesting that ECG may not consistently reflect electrolyte levels, heightening the importance of vigilant monitoring and diagnostic clarity. Thus, the comprehensive interpretation of ECG changes emerges as essential for the management of hyponatremia and its potential cardiac consequences.

Study Limitations

The findings of the current study on ECG changes in patients with hyponatremia highlight significant limitations that must be considered when interpreting the data. First, the retrospective design inherently limits the ability to establish causative relationships between observed ECG changes and hyponatremia levels. Furthermore, the study's small sample size, comprising only 34 participants, restricts the generalizability of its conclusions, particularly when considering the diverse clinical backgrounds of the patients, as described in. Additionally, the lack of follow-up ECG data post-treatment diminishes the understanding of potential reversibility, of the observed changes. Lastly, while the analysis does contribute valuable insights, it must be contextualized within a broader scope of research, which includes studies on cardiac conduction abnormalities. A more comprehensive approach involving larger, prospective studies is necessary to validate the findings.

CONCLUSION

In reviewing the implications of the findings from this study, it becomes evident that abnormal sodium levels can have significant cardiac effects, warranting further clinical attention. The correlations highlight the need for thorough monitoring of ECGs in patients exhibiting signs of hyponatremia, particularly those with underlying cardiovascular conditions. While our study did not identify direct links between severe hyponatremia and significant arrhythmias, existing literature suggests that electrolyte imbalances may contribute to conduction abnormalities, underscoring the importance of proactive management. Clinicians must remain vigilant in recognizing the potential for long-term consequences associated with these cardiac changes, as even mild hyponatremia can precipitate serious health issues. This research reinforces the necessity for larger, prospective studies to enhance our understanding and improve patient outcomes effectively.

Future research should focus on elucidating the precise mechanisms by which hyponatremia affects ECG changes, as current studies have emphasized correlations rather than causal relationships. In particular, examining the interaction between varying degrees of hyponatremia and specific ECG findings may provide valuable information regarding patient prognosis and management strategies. Furthermore, longitudinal studies evaluating the effects of treatment interventions on both sodium levels and ECG findings may increase our understanding of potential synergies in therapeutic approaches. Consequently, comprehensive multicenter studies are necessary to validate these emerging hypotheses and guide clinical practice.

Ethics

Ethics Committee Approval: The study protocol was reviewed and approved by the Ethics Committee of Hatay Mustafa Kemal University (decision number:19, date:12.10.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: U.I., C.H., Design: U.I., C.H., Data Collection or Processing: U.I., C.H., Analysis or Interpretation: U.I., C.H., Literature Search: U.I., C.H., Writing: U.I., C.H.

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

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

REFERENCES

1. Rondon H, Badireddy M: Hyponatremia. In. StatPearls. StatPearls Publishing, Treasure Island; 2023.
2. Christopoulou E, Liamis G, Naka K, Touloupis P, Gkartzonikas I, Florentin M. Hyponatremia in patients with heart failure beyond the neurohormonal activation associated with reduced cardiac output: a holistic approach. Cardiology. 2022;147:507-20.
3. De las Peñas R, Escobar Y, Henao F, Blasco A, Rodríguez CA; Spanish Society for Medical Oncology. SEOM guidelines on hydroelectrolytic disorders. Clin Transl Oncol. 2014;16:1051-9.
4. Nakazone MA, Otaviano AP, Machado MN, Bestetti RB. Does left ventricular reverse remodeling influence long-term outcomes in patients with Chagas cardiomyopathy? Cardiol J. 2022;29:44-52.
5. Kapłon-Cieślicka A, Balsam P, Ozierański K, Tymińska A, Peller M, Galas M, *et al.* Resting heart rate at hospital admission and its relation to hospital outcome in patients with heart failure. Cardiol J. 2014;21:425-33.
6. Rosner MH. Hyponatremia in heart failure: the role of arginine vasopressin and diuretics. Cardiovasc Drugs Ther. 2009;23:307-15.
7. Zou S, Zhang Q, Gao S, Luo M, Gan X, Liang K. Electrocardiogram manifestations of hyponatraemia. Cardiovasc J Afr. 2022;33:98-100.
8. Sterns RH. Treatment of severe hyponatremia . Clin J Am Soc Nephrol. 2018;13:641-9.
9. Mouallem M, Friedman E, Shemesh Y, Mayan H, Pauzner R, Farfel Z. Cardiac conduction defects associated with hyponatremia. Clin Cardiol. 1991;14:165-8.
10. Kottwitz J, Akdis D, Duru F, Heidecker B. Severe hyponatremia leading to complete atrioventricular block. Am J Med. 2016;129:243-4.
11. Ramsaroop K, Seecheran R, Seecheran V, Persad S, Giddings S, Mohammed B, *et al.* Suspected hyponatremia-induced Brugada phenocopy. Int Med Case Rep J. 2019;12:61-5.

12. Rodriguez M, Hernandez M, Cheungpasitporn W, Kashani KB, Riaz I, Rangaswami J, *et al*. Hyponatremia in heart failure: pathogenesis and management. Curr Cardiol Rev. 2019;15:252-61.

13. Akyüz A, Baykız D, Gür DÖ, Gökçek S, Efe MM, Alpsoy Ş. Role of sodium levels on atrial fibrillation in heart failure: active player or a bystander? Arq Bras Cardiol. 2022;118:712-8.

14. Cavusoglu Y, Kaya H, Eraslan S, Yilmaz MB. Hyponatremia is associated with occurrence of atrial fibrillation in outpatients with heart failure and reduced ejection fraction. Hellenic J Cardiol. 2019;60:117-21.

15. Rafaqat S, Rafaqat S, Khurshid H, Rafaqat S. Electrolyte's imbalance role in atrial fibrillation: pharmacological management. Int J Arrhythm. 2022;23:1-10.

RESEARCH ARTICLE

DOI: 10.4274/ijca.2024.96268
Int J Cardiovasc Acad 2025;11(1):23-28

A Study of Serum Magnesium Levels in Patients with Acute Myocardial Infarction in the Rural Population of Vijayapura District

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Abstract

Background and Aim: Magnesium is an essential element for the proper functioning and regulation of cardiovascular physiology. It acts as a vital helper molecule in various enzyme systems and is involved in multiple cardiovascular processes. These processes include intracardiac conduction, myocardial contraction, atherogenesis, thrombosis, regulation of vascular tone, and the proliferation and migration of endothelial cells and vascular smooth muscle. The aim of this study was to evaluate the relationship between serum magnesium concentration and their correlation with complications and in-hospital outcomes in acute myocardial infarction (AMI) patients.

Materials and Methods: This observational study included patients who were admitted to a tertiary care centre in India from December 2019 to September 2021. A total of 100 patients with AMI were enrolled in the study. Serum magnesium concentration was assessed using the calmagite method. The patients were followed up for 7 days during their hospitalization to monitor complications and in-hospital outcomes.

Results: The serum magnesium concentration was between 1.1 mg/dL and 4.0 mg/dL. There were 28 patients with hypomagnesemia and 11 patients with hypermagnesemia. The study population consisted of 57% male, and the majority of patients were in the age group of 60-80 years (38%). A typical clinical presentation was observed in 61% of the patients, while 39% of patients displayed an atypical clinical presentation. Higher proportions of patients with typical clinical presentation were significantly observed to have hypomagnesemia ($P = 0.037$). Among the total patient population, 20% experienced QT-prolongation in our study. Patients with hypomagnesemia experienced more complications, but patients with hypermagnesemia were associated with an increased rate of mortality.

Conclusion: In patients with AMI, hypomagnesemia was associated with an increased incidence of complications. Conversely, hypermagnesemia was linked to increased mortality among patients.

Keywords: Hypermagnesemia, hypomagnesemia, mortality, myocardial infarction, outcomes

To cite this article: Bangi SMH, Hidayethulla M, Golla A, Kausar ST, Kadloor P. A study of serum magnesium levels in patients with acute myocardial infarction in rural population of Vijayapura district. Int J Cardiovasc Acad. 2025;11(1):23-28

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Received: 25.10.2024
Accepted: 26.12.2024
Publication Date: 18.03.2025

INTRODUCTION

Ischemic heart disease (IHD) is one of the prominent causes of morbidity and mortality globally. Myocardial ischemia due to atherosclerotic coronary artery disease (CAD) can result in acute myocardial infarction (AMI), unstable angina, or effort angina.[1] Out of all, AMI is the most common and serious event leading to emergency hospital admissions.[1] In the human body, magnesium is an important element following calcium, potassium, and sodium, also it plays a crucial role of being co-factor in numerous enzyme systems holding noteworthy role in production of DNA, RNA, adenosine triphosphate, and in the proper regulation of cardiovascular physiology; such as maintenance of ion channels, energy production, intracardiac conduction, contraction. Additionally, it also helps in atherogenesis, thrombosis, vascular tone regulation, endothelial cell and vascular smooth muscle proliferation, and migration.[2] Hence, the constant supply of magnesium to our body is essential.[3] A normal healthy range of serum magnesium concentration in our body is 0.72-1.15 mmol/L.[4] Persistent deficiency of magnesium leads to various clinical and subclinical conditions, like neuropsychiatric disorders, depression, hypertension, atherosclerosis, cardiac arrhythmias, stroke, type 2 diabetes mellitus, metabolic syndrome, changes in lipid metabolism, osteoporosis.[5] Thus, it is very important to identify how magnesium levels can be correlated with the diagnosis and treatment of cardiovascular disease.[6] Magnesium deficiency is observed in approximately 8% to 30% of in-hospital patients.[7] Patients with AMI often show hypomagnesemia.[1] In AMI, magnesium moves inside the cell compartments from the extracellular compartments because of lipolysis induced by adipocytes, following catecholamine activity, and then magnesium combines with the by-products of lipolysis. The total magnesium levels may not change during AMI, but there is a decline in extracellular magnesium concentration specifically during the first 24 to 48 hours after the onset of MI. This can cause post AMI complications such as ventricular tachycardia, sudden cardiac death (SCD), or even another heart attack.[1] Accordingly, our aim was to study the effect of serum magnesium concentration in patients with AMI and to investigate the associated complications and in-hospital outcomes.

METHODS

Study Design and Population

This is an observational, cross-sectional single-centred study conducted at a tertiary care centre in India from December 2019 to September 2021. A total of 100 patients diagnosed with AMI were included in the study. Eligibility criteria for the study were determined by the inclusion and exclusion criteria. Patients older than 18 years diagnosed with AMI based on their history, clinical examination, electrocardiogram (ECG) changes, and biochemical markers for MI were included in the study. Based on the type of clinical presentation, the patients were divided into typical and atypical types of symptoms. Atypical symptoms usually include epigastric pain, back pain and are characterized by indigestion, burning or stabbing. Typical symptoms are those that include chest pain, arm pain, or pain in the jaws.[8] Patients with history and any cause of hepatitis, history of MI or diagnosed with Crohn's disease, cirrhosis of liver and patients with chronic malnutrition were excluded from the study. Patients on drugs such as thiazide diuretics, and loop diuretics, and antibiotics including aminoglycosides, amphotericin, pentamidine, gentamycin, tobramycin, and other drugs such as digitalis and adrenergics were also excluded from the study. After detailed counseling, all the patients in the study provided written consent in their own language before being included. The study was conducted in accordance with the Declaration of Helsinki, and after receiving approval from the Al-Ameen Medical College Ethical Committee of the institution with (approval number: IEC/AAMC/2019/0098, date: 20.10.2019).

Data Collection

Patients were observed for complications, including conduction abnormalities like sinus bradycardia, bradyarrhythmia (conduction blocks), tachyarrhythmia (ventricular tachycardia, supraventricular tachycardia, atrial fibrillation), ventricular ectopies, and heart failure in the emergency and intensive coronary care unit departments of our institution. A detailed history of patients along with general examination, systemic examination and investigations was performed. The estimated serum magnesium concentration ranged from 1.1 mg/dL to 4.0 mg/dL in the study. The mean serum magnesium level in the present study was 2.1 mg/dL.

Laboratory Investigation

The serum magnesium concentration of patients was collected on the day of admission. Other investigations, including random blood sugar, ECG, cardiac biomarkers, trop-T/CPK-MB, 2D-ECHO/DOPPLER, were also done. The Calmagite method was used to determine the serum magnesium concentration. In this method, the magnesium combines with calmagite in an alkaline medium to form a red complex. By using selected binding agents and detergents, the test eliminates calcium and protein interference. Colour intensity increases in direct proportion to the sample's magnesium concentration.

Follow-up Schedule

The patients were followed up for 7 days during their hospitalization and observed for development of complications before discharge.

Definition

Concentrations of serum magnesium between 1.7 and 2.55 mg/dL are considered normal for all individuals, regardless of age or gender. When a patient's serum magnesium falls below 1.7 mg/dL, it's classified as hypomagnesemia. Conversely, if serum magnesium exceeds 3.0 mg/dL, the condition is termed hypermagnesemia.

Statistical Analysis

SPSS Software v.23 (IBM Statistics, Chicago, USA) was used to analyze the collected data. Mean and standard deviation were used for continuous variables and number and percentage were used for categorical data. For association between two categorical variables, the chi-square (χ^2) test was used. The Fisher-Freeman-Halton exact test was employed in cases of more than 30% cell frequency <5 to determine the significance of the differences among the groups of categorical data. The results were statistically significant if the p-value was <0.05.

RESULTS

A total of 100 patients were included in the study. The gender composition showed a slight male predominance, with 57 male patients and 43 female patients. Age distribution revealed a predominant representation of older patients, with the largest group aged 60-80 years (n=38). There were 3 patients who were less than 20 years old, 14 patients were between the age group of 20-40 years old, 26 patients 40-60 years old, and 19 patients belonged to the age group greater than 80 years old. Serum magnesium level analysis showed that 28 patients had hypomagnesemia (<1.8 mg/dL), 61 patients had normal levels of magnesium (1.8-2.5 mg/dL) and 11 patients had hypermagnesemia (>2.5 mg/dL). Enrolled patients were grouped based on their addictive habits. Thirty patients were observed to have addictive habits. Smoking was found to be the most common of all examined risk factors. Fourteen were smokers, hypomagnesemia was present in 2 (7.1%) patients, 11 (18%) had normal levels of serum magnesium and only 1 (9.1%) had hypermagnesemia. Tobacco chewing was done by 12 patients, of whom 2 (16.7%) patients had hypomagnesemia, 7 (58.3%) (11.5%) patients had normal serum magnesium concentration, and 3 (25%) (27.3%) had hypermagnesemia. Alcohol consumption was seen in 2 patients, of whom 1 (1.6%) had normal serum magnesium concentration and 1 (9.1%) had hypermagnesemia.

Figure 1 illustrates the association between serum magnesium concentration and age.

Based on the clinical presentation, patients were classified into groups exhibiting typical and atypical symptoms. Around 61% of patients showed typical presentation, and 39% atypical presentation. The correlation of clinical presentation and ECG changes with serum magnesium concentration is shown in Table 1. Patients were classified into ST elevation MI (STEMI) and non-STEMI (NSTEMI) based on their ECG changes. The STEMI was found in 67% of the patients and NSTEMI in 33%. Bedside echocardiography was performed to identify which region of the heart was involved. The echocardiographic findings are shown in Figure 2. In our study, echocardiography for three patients was not performed because they died before the procedure could be conducted. Complications were seen in 22 patients over a period of 5 days during their hospital stay. During the course of hospitalization, a total of 9 patients did not survive. Table 2 shows the data of correlation between complications and cause of death in association with serum magnesium concentration in patients. The rate of complications was high in patients with hypomagnesemia, and patients who did not survive had hypermagnesemia.

Among the total patient population, 20% demonstrated QT-interval prolongation on their ECG, with a significant

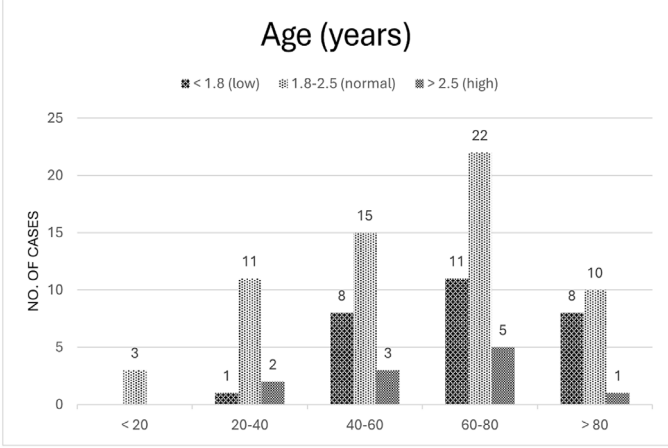

Figure 1: Association among serum magnesium concentration and age

Table 1: Correlation of serum magnesium with clinical presentation and ECG changes

Variables	<1.8 (low) (n=28 patients)	1.8-2.5 (normal) (n=61 patients)	>2.5 (high) (n=11 patients)	*P*-value
Clinical presentation				
Typical	20 (71.4)	38 (62.3)	3 (27.3)	0.037
Atypical	8 (28.6)	23 (37.7)	8 (72.7)	
ECG changes				
STEMI	21 (75)	41 (67.2)	5 (45.5)	0.210
NSTEMI	7 (25)	20 (32.6)	6 (54.5)	

Data are expressed as n (%). *P*-value <0.05 was considered statistically significant.

ECG: Electrocardiogram, NSTEMI: Non-ST segment elevation myocardial infarction, STEMI-ST: Segment elevation myocardial infarction

prevalence observed in patients with STEMI. QT-prolongation was notably associated with several cardiac complications, including sinus bradycardia and ventricular ectopy. Of particular clinical significance, patients experiencing SCD and ventricular tachycardia also exhibited QT-prolongation, which was identified as a potentially contributing factor to patient mortality.

DISCUSSION

This study investigated the relationship between the levels of serum magnesium and its effects on complications and cause of death in patients diagnosed with AMI. Over the past decades, studies have been carried out regarding the role of serum magnesium in the etiology,[9] and the pathophysiology of AMI. It was found that patients with AMI had hypomagnesemia during the first 24 hours of admission to hospital.[10] Even though serum magnesium measurements may not precisely indicate intracellular magnesium content, disturbances in its levels can cause cardiovascular disease.[11] Rahman et al.[12] in their study observed 76% of the patients were male and 70% of patients were smokers in the study group with AMI. In the present study, 57% of patients were male and 14% were smokers. In our study, most of the patient population with AMI belonged to the age group of 60-80 years (38%). In concordance with our study, another study also showed that a majority of the patient population between the ages of 61-70 years (32.5%).[13]

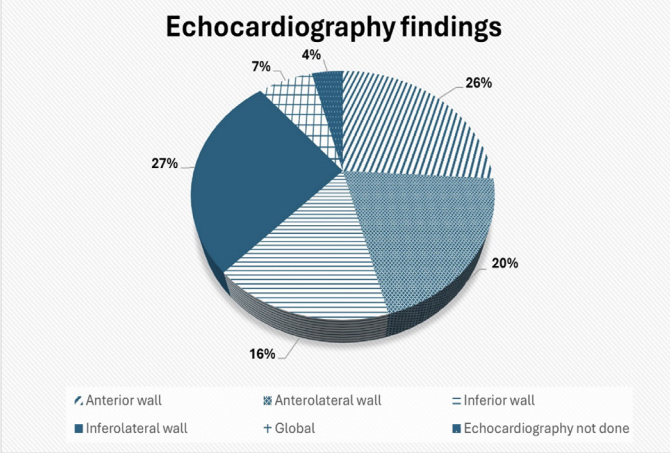

Figure 2: Echocardiographic findings

Table 2: Complications and causes of death in association with serum magnesium concentration

Variables	<1.8 (low) (n=28 patients)	1.8-2.5 (normal) (n=61 patients)	>2.5 (high) (n=11 patients)	*P*-value
Complications				
Bradyarrhythmia	6 (21.42)	2 (3.2)	0 (0.0)	0.802
Tachyarrhythmia	3 (10.7)	3 (4.9)	1 (9.09)	
Sinus bradycardia	0 (0.0)	3 (4.9)	1 (9.09)	
CCF	1 (3.5)	1 (1.6)	0 (0.0)	
Ventricular ectopy	1 (3.5)	0 (0.0)	0 (0.0)	
Cause of death				
Cardiac failure	1 (3.5)	0 (0.0)	0 (0.0)	0.161
VT	0 (0.0)	1 (1.6)	0 (0.0)	
CHB	0 (0.0)	0 (0.0)	2 (18.1)	
Sudden cardiac death	0 (0.0)	2 (3.2)	3 (27.2)	

Data are expressed as n (%). *P*-value <0.05 was considered statistically significant.

CCF: Congestive cardiac failure, CHB: Complete heart block, VT: Ventricular tachycardia

Based on the presenting complaints, patients were classified as having either typical or atypical clinical presentations in our study. Among these, chest pain emerged as the predominant clinical presentation, affecting 61% of the patients. Taha et al.[14] in their study conducted on the prevalence of hypomagnesemia in patients with AMI and its correlation to intra-hospital complications noted that 92% of patients presented with chest pain. In another study, 94% of patients complained about chest pain, which was highest among other presenting complaints.[15] Breining et al.[16] found that 66% of the patients showed a typical presentation. STEMI was diagnosed in 67% of patients while NSTEMI in 33% of patients. A study reported that out of 100 cases, 82% had STEMI and 18% had NSTEMI.[15] In contrast to our study, Singh et al.[13] found that 45% of patients had STEMI and 55% of patients had NSTEMI.

The majority of the patients were affected by inferolateral MI (27%), anterior wall MI (26%), followed by anterolateral MI (20%) which was revealed through echocardiography. While Sharma et al.[15] in their study found that patients were majorly affected by anterior wall MI (34%) followed by (21%) inferior wall MI.

The estimated serum magnesium concentration in the present study ranged from 1.1 mg/dL to 4.0 mg/dL. Among all patients, 28 had hypomagnesemia, 61 had normal levels of serum magnesium, and 11 showed hypermagnesemia. Akila et al.[9] in their study found that 16% of patients with AMI experienced hypomagnesemia with levels less than 1.6 mg/dL during admission and between 1.6-2.4 mg/dL in 34% of patients. Zia Sabah et al.[17] found that out of 160 patients in their study, 52.5% of patients with AMI on admission showed hypomagnesemia.

Out of the total patient groups, 22 experienced complications related to AMI. Half of these patients presented with reduced serum magnesium concentration. The most frequently observed complications in this subgroup were bradyarrhythmia and tachyarrhythmia. A study done by Wahid et al.[18] found that 39% of patients with hypomagnesemia were more prone to develop complications.

The rate of mortality was 9% in our study. Of, 4% of total patients had hypermagnesemia. The cause of death for 2 patients was complete heart block, while 3 patients died of SCD. In contrast to our study, Kieboom et al.[19] reported that there was an association between patients with hypomagnesemia and increased risk of coronary heart disease mortality [heart rate (HR): 1.36, 95% cardiac index (CI): 1.09-1.69] and high risk of SCD (HR: 1.54, 95% CI: 1.12-2.11). In our study, one patient with hypomagnesemia died due to heart failure. Another study found that 2.5% of patients with hypomagnesemia in their study had cardiac failure, which was similar to our findings.[18] Various observational studies have been found to be linked to hypomagnesemia causing adverse form of cardiovascular disease risk factors and events, also it was found that patients were at 2.5 times greater risk of developing heart failure who had hypomagnesemia.[20] Hypomagnesemia is also found to be linked with mortality in elderly people with chronic kidney disease and the overall cause of death in patients admitted to the intensive care unit in the hospital.[21] Additionally, the literature shows that it is linked with increased incidence of hip fracture and progression of Alzheimer's.[22,23]

It has been found in a study that hypermagnesemia can cause cardiovascular symptoms like dysrhythmia suggestive of electrocardiographic imbalances causing bradycardia and malignant ventricular tachycardia.[21] In concordance with that, in our study, the cause of death for 2 patients was complete heart block, whereas 3 patients died of SCD.

Study Limitation

This single-center study has several notable limitations. The relatively small sample size may limit the generalizability of our findings. We did not correlate serum magnesium levels with other biochemical markers, particularly renal function values, nor did we conduct risk factor identification for CAD and IHD. The absence of follow-up data and lack of multivariate analysis for mortality restricted our understanding of patient prognosis. Additionally, the study did not account for patient comorbidities, which could have provided valuable insights into the relationship between serum magnesium concentration and the clinical presentation and course of AMI. To address these limitations, larger multi-center studies with extended follow-up periods and comprehensive patient assessments are needed.

CONCLUSION

The present study examined magnesium levels in patients with AMI and found that increasing age predicted low levels of serum magnesium. Patients with hypomagnesemia had higher complication rates; the majority of them had bradyarrhythmia or tachyarrhythmia. In those with hypermagnesemia, the rate of mortality was high, caused by complete heart block or SCD.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki, and after receiving approval from the Al-Ameen Medical College Ethical Committee of the institution with (approval number: IEC/AAMC/2019/0098, date: 20.10.2019).

Informed Consent: Written consent in their own language before being included.

Footnotes

Authorship Contributions

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

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

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

REFERENCES

1. Jaffery MH, Shaikh K, Baloch GH, Shah SZA. Acute myocardial infarction; hypomagnesemia in patients. Professional Med J. 2014;21:258-63.
2. Tangvoraphonkchai K, Davenport A. Magnesium and cardiovascular disease. Adv Chronic Kidney Dis. 2018;25:251-60.
3. Chrysant SG, Chrysant GS. Association of hypomagnesemia with cardiovascular diseases and hypertension. Int J Cardiol Hypertens. 2019;1:100005.
4. Gröber U, Schmidt J, Kisters K. Magnesium in prevention and therapy. Nutrients. 2015;7:8199-226.
5. Kostov K, Halacheva L. Role of magnesium deficiency in promoting atherosclerosis, endothelial dysfunction, and arterial stiffening as risk factors for hypertension. Int J Mol Sci. 2018;19:1724.
6. Kolte D, Vijayaraghavan K, Khera S, Sica DA, Frishman WH. Role of magnesium in cardiovascular diseases. Cardiol Rev. 2014;22:182-92.
7. Ismail A, Ismail NA. Magnesium: A mineral essential for health yet generally underestimated or even ignored. J Nutr Food Sci. 2016;6:1-8.
8. DeVon HA, Mirzaei S, Zègre-Hemsey J. Typical and atypical symptoms of acute coronary syndrome: time to retire the terms? J Am Heart Assoc. 2020;9:e015539.
9. Akila A, Anandraj J, Karthikayan S. Serum magnesium levels in acute myocardial infarction. IOSR J Dent Med Sci. 2017;16:35-40.
10. Subramanyam NT, Vakrani GP. Serum magnesium in acute myocardial infarction. JEMDS. 2015;4:10460-8.
11. de Baaij JH, Hoenderop JG, Bindels RJ. Magnesium in man: implications for health and disease. Physiol Rev. 2015;95:1-46.
12. Rahman MA, Parvez MS, Lita AI. Serum magnesium level in patients with acute myocardial infarction and its relation with arrhythmia. Medico Research Chronicles. 2021;8:179-89.

13. Singh H, Khosla P, Kaur J. A study of serum magnesium levels in acute myocardial infarction and its association with clinical outcome. Natl J Physiol Pharm Pharmacol. 2023;13:286-91.

14. Taha MM, Azhary A, Alkhatim WAS, Daoud MH, Mohmed MHA, Idris MYM, et al. Prevalence of hypomagnesaemia among patients with acute myocardial infarction and its correlation to intra-hospital complications. 2024.

15. Sharma R, Chowdhary I, Sharma A. Arrhythmia and its risk factors post myocardial infarction: a prospective study. JAD. 2022;11:26-31.

16. Breining A, Negers A, Mora L, Moïsi L, Golmard JL, Cohen A, et al. Determinants of clinical presentation on outcomes in older patients with myocardial infarction. Geriatr Gerontol Int. 2018;18:1591-6.

17. Sabah Z, Wani J, Deajim M, Al Zomia AS, Asiri A, Alqahtani AA, et al. Serum magnesium in patients with acute myocardial infarction and its effect on cardiac complications and mortality in myocardial infarction patients. Cureus. 2023;15:e38147.

18. Wahid SB, Ara S, Ali A, Payel FS, Rahaman MA, Yasmin F. Evaluation of prognostic significance of serum magnesium level in patients with acute myocardial infarction. Mediscope. 2024;11:27-33.

19. Kieboom BC, Niemeijer MN, Leening MJ, van den Berg ME, Franco OH, Deckers JW, et al. Serum magnesium and the risk of death from coronary heart disease and sudden cardiac death. 2016;5:e002707.

20. Lutsey PL, Alonso A, Michos ED, Loehr LR, Astor BC, Coresh J, et al. Serum magnesium, phosphorus, and calcium are associated with risk of incident heart failure: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Clin Nutr. 2014;100:756-64.

21. Van Laecke S. Hypomagnesemia and hypermagnesemia. Acta Clin Belg. 2019;74:41-7.

22. Sakaguchi Y, Hamano T, Wada A, Hoshino J, Masakane I. Magnesium and risk of hip fracture among patients undergoing hemodialysis. J Am Soc Nephrol. 2018;29:991-9.

23. Kieboom BCT, Licher S, Wolters FJ, Ikram MK, Hoorn EJ, Zietse R, et al. Serum magnesium is associated with the risk of dementia. Neurology. 2017;89:1716-22.

CASE REPORT

DOI: 10.4274/ijca.2025.85866

Int J Cardiovasc Acad 2025;11(1):29-33

Starr-Edwards Mechanical Prosthesis for More Than 53 Years in the Mitral Position: A Case Report

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Abstract

Valvular heart disease affects approximately 2.5% of the global population. Starr-Edwards (SE) prosthetic valves are commonly used in the aortic and mitral positions, with reported durability extending up to 40 years. We report the case of a 77-year-old woman with a SE mechanical prosthesis in the mitral position, which was implanted 53 years ago. Imaging studies revealed the prosthesis to be intact, with no signs of degeneration. This case underscores the remarkable longevity of the SE valve and provides valuable insights into the long-term durability and performance of these valves, suggesting that valvular dysfunction may occur less frequently than previously estimated.

Keywords: Case report, mechanical prosthesis, valve, Starr-Edwards, mitral stenosis, durability

INTRODUCTION

Heart valve disease represents a significant clinical challenge, affecting approximately 2.5% of the global population. For decades, Starr-Edwards (SE) prosthetic valves were widely used in the aortic and mitral positions.[1] Studies have shown that these valves can last up to 40 years, with a notable reduction in hemolysis and valve thrombosis rates in contemporary series, reaching values as low as 0.10% and 0.06% per patient per year, respectively. However, there remains an increased risk of thromboembolic events and valve dysfunction, with a freedom from thromboembolic events ranging from 74% to 87% at 10 years.[2]

More than half a million SE valves were implanted globally between 1960 and 2007, with around 300,000 of them placed in the last 7 years of their production. These valves have proven to be reliable in the long term, offering considerable durability and have reoperation rates comparable to other recent mechanical valves in terms of complications.[3]

In this context, it is being discussed whether valve dysfunction associated with these prostheses is less prevalent than suggested by some experts. There are case reports of patients with SE valves with survival of 48 years, 40 years, and 51 years.[4,5] The case presented involves a patient with an SE valve that has lasted 53 years.

This case is unique due to the extraordinary longevity of the SE valve prosthesis, which has functioned for 53 years without showing expected signs of degeneration. This challenges common conceptions about the lifespan of these valves and suggests that valve dysfunction associated with these prostheses

To cite this article: Macías Cervantes RC, Fernandez Gutierrez LMA, Martínez EA. Starr-Edwards mechanical prosthesis for more than 53 years in mitral position: Case report. Int J Cardiovasc Acad. 2025;11(1):29-33

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Received: 24.10.2024
Accepted: 18.02.2025
Publication Date: 18.03.2025

may be less prevalent than previously estimated. This report adds significant evidence regarding the durability and long-term performance of SE valves, thereby contributing to a better understanding of patients with these prostheses.

CASE REPORT

A 77-year-old female patient with a history of mitral stenosis was treated in 1971 with the implantation of a SE 6120 2M (silastic) mechanical prosthesis. In 2016, she received a permanent ventricular impulse rate medtronic® pacemaker due to blocked atrial fibrillation. The patient was being managed with warfarin, telmisartan, atorvastatin, levothyroxine, and clonazepam.

Currently, the patient presented with mixed-origin dyspnea and was classified as functional class IV according to the New York Heart Association, with symptoms and signs of global heart failure even at rest. Six months ago, she had community-acquired pneumonia, requiring hospitalization and treatment with a dual antibiotic regimen. Since her discharge, she needed supplemental oxygen at 5-7 L/min to maintain an oxygen saturation above 80%.

Additionally, she experienced episodes of depression and low food intake, leading to malnutrition. On inspection, she appeared cachectic, with signs of dehydration, including dry mucous membranes and positive skin turgor.

Laboratory tests revealed macrocytic anemia, moderate thrombocytopenia, an estimated glomerular filtration rate of 52 mL/min/1.73 m^2, abnormal pancreatic and liver function tests, and prolonged coagulation times [partial thromboplastin time of 62.4 s, prothrombin time of 39.1 s, and international normalized ratio (INR) of 3.55].

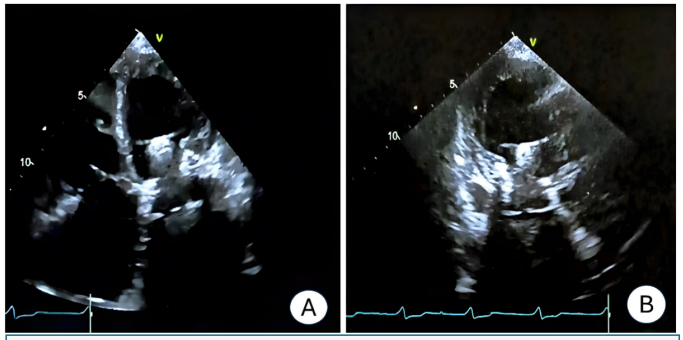

Figure 1: The echocardiogram shows the Starr-Edwards type mechanical mitral prosthesis, which is functioning normally with no pathological leaks. Proper movement of the ball within the cage is observed, as well as the absence of significant gradients or paravalvular regurgitation

To assess her cardiac and pulmonary status, she underwent an echocardiogram (Figures 1-4), an electrocardiogram (Figure 5), and a chest X-ray (Figure 6).

The echocardiogram revealed a mixed cardiopathy of degenerative atherosclerotic and hypertensive origin. The SE mechanical prosthesis in the mitral position demonstrated proper ball movement in the closure position with a maximum diastolic gradient of 25 mmHg and an average of 5.7 mmHg, without pathological leaks. The tricuspid valve exhibited slight thickening of the leaflets, moderate annular dilation (38 mm), leaflet tethering (11.5 mm), and a tenting area of 1.4 cm^2.

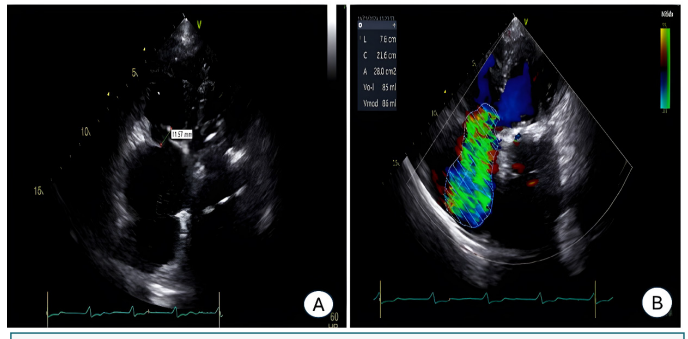

Figure 2: (**A**) Transthoracic echocardiogram in 2D mode, apical four-chamber view, showing the apical systolic displacement of the tricuspid valve (tethering) with a maximum distance from the valvular plane of 11.5 mm. (**B**) In the same apical four-chamber view, in color Doppler mode, the severe secondary (functional) tricuspid regurgitation is visible, extending up to the atrial roof, with a regurgitant volume of 86 mL and a regurgitant area of 28 cm^2

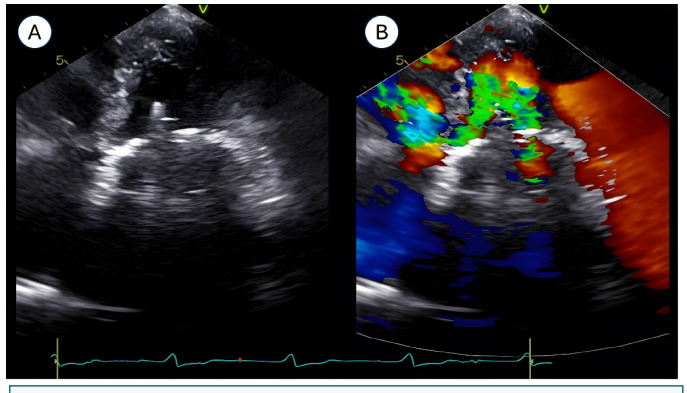

Figure 3: (**A**) Hows an echocardiogram in the apical four-chamber view where the Starr-Edwards mechanical prosthesis is observed, with the ball moving towards the cage during diastole. (**B**) In the same view, a comparative image in color Doppler mode shows the high profile of the prosthesis, allowing diastolic flow to pass along the sides of the ball

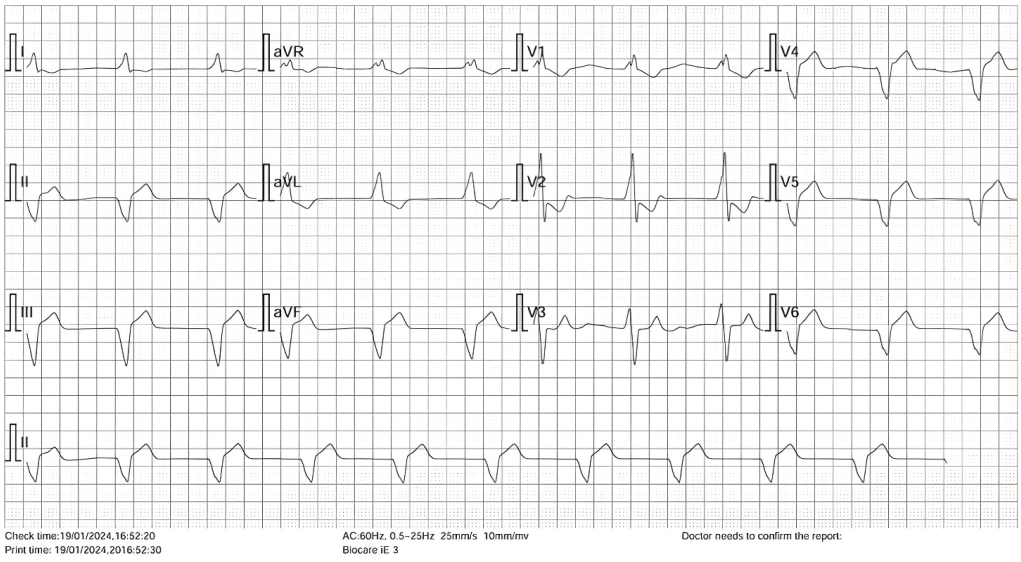

Figure 4: **(A)** Displays the transvalvular gradient across the Starr-Edwards mechanical prosthesis, with a maximum diastolic gradient of 25 mmHg, a mean of 5.7 mmHg, and a valve area of 2.8 cm^2. **(B)** Shows the retrograde gradient of the tricuspid regurgitation assessed using continuous Doppler, revealing a maximum systolic regurgitant velocity of 4.0 m/s and a maximum systolic regurgitant gradient of 64 mmHg. These findings estimate a pulmonary artery systolic pressure of 79 mmHg

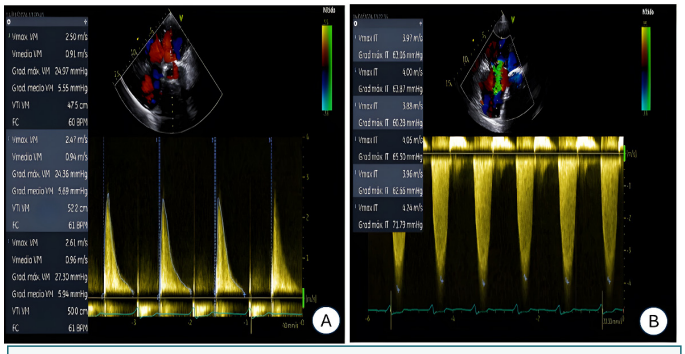

Figure 5: The electrocardiogram shows atrial fibrillation, with a permanent pacemaker capture and 100% ventricular pacing at a heart rate of 60 bpm. It also shows a left bundle branch block and right ventricular hypertrophy. In the right precordial leads, there are increased voltage R waves (R/S index in V2: 1.62) and asymmetrical inverted T waves with negative ST-segment depression, secondary to systolic overload caused by pulmonary arterial hypertension

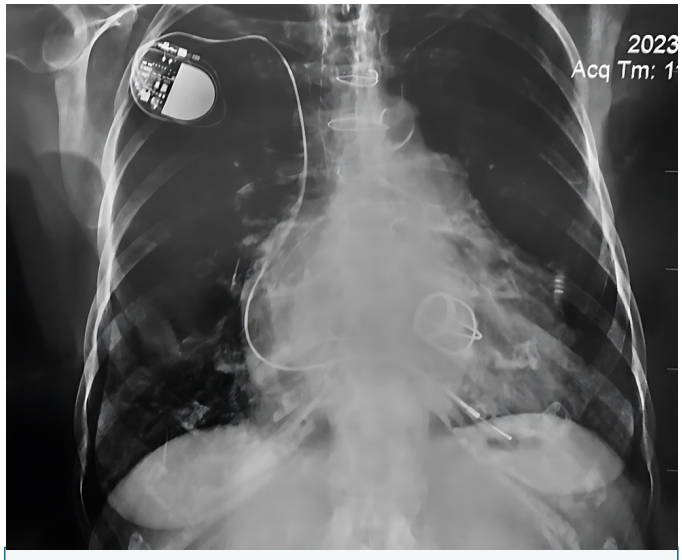

Figure 6: The posteroanterior chest X-ray shows the pacemaker electrode in the right ventricle, directed towards the apex, and connected to the right subclavian generator. The Starr-Edwards mechanical prosthesis is also visible in the mitral position, showing the Teflon ring and polypropylene fabric, continuing with the cobalt-chromium cage; the ball is not visible due to its silicone (silastic) composition. The image highlights moderate to severe cardiomegaly with a cardiothoracic index of 0.6, significant enlargement of both atria, and a prominent pulmonary arch due to pulmonary arterial hypertension

There was severe regurgitation extending to the atrial roof, with a vena contracta of 7.8 mm, regurgitant volume of 85 mL, regurgitant area of 28 cm^2, and maximum systolic regurgitant velocity of 4.0 m/s. Mild functional pulmonary insufficiency was also noted.

Biventricular systolic function was normal, with a left ventricular ejection fraction of 59% as per the automated biplane method, a shortening fraction of 43%, a Tei index of 0.36, and global longitudinal strain of -20%. Severe, irreversible restrictive biventricular diastolic dysfunction was present, with a left atrial volume index (LAVi) of 160 mL/m^2, isovolumetric relaxation time of 69 ms, deceleration time of 147 ms, e' wave velocity of 3 cm/s, flow propagation velocity of pulse

(Vp) of 37 cm/s, and VPd greater than VPs. Segmental wall motion abnormalities were observed in the left ventricle, with dyskinesia and reduced systolic thickening in the basal third of the posterior septum, while the distal two-thirds showed mild hypokinesia. Moderate to severe hypokinesia was also seen in the lateral wall and inferolateral region (both in basal thirds), without areas of fibrosis.

The right ventricle showed an increased end-diastolic diameter (47 mm x 31 mm x 65 mm), hypertrophy of the free wall (9 mm), and normal wall motion. A pacemaker lead was observed to be directed toward the apex. Right ventricular systolic function was borderline, with a TAPSE of 19 mm, a dP/dt of 315 mmHg/sec, and a lateral tricuspid S' wave velocity of 11 cm/s.

The left atrium was severely dilated, with a LAVi of 160 mL/m^2. It measured 67 mm in M-mode in the parasternal long-axis view, and 82x62 mm in longitudinal and horizontal diameters. No thrombi were observed inside. The right atrium showed moderate dilation (65x50 mm in longitudinal and horizontal diameters in the 2D4C view). The inferior vena cava was dilated, exhibiting an expiratory diameter of 34 mm and an inspiratory diameter of 30 mm, with 12% inspiratory collapse.

There was a high likelihood of pulmonary arterial hypertension (PAH), with positive criteria for severe group 2 PAH. Right atrial pressure was 15 mmHg, mean pulmonary artery pressure was 43 mmHg, pulmonary artery diastolic pressure was 18 mmHg, and pulmonary artery systolic pressure was 79 mmHg.

Treatment

The established treatment included warfarin 2.5 mg tablets every 24 hours; maintaining an INR of 3.5, telmisartan 20 mg daily, spironolactone 25 mg orally, furosemide 20 mg orally, and levothyroxine 50 mg, all administered every 24 hours.

Prognosis

The prognosis is poor for both function and life expectancy due to multiple comorbidities, including depression, severe malnutrition (cachexia), congestive hepatopathy secondary to cardiac cirrhosis, and community-acquired pneumonia. Close and multidisciplinary follow-up was initiated to improve the patient's quality of life.

Written informed consent was obtained from the patient for the publication of this case and the associated images.

DISCUSSION

Albert Starr documented his longest-living patient with a SE valve in the aortic position in 2015, with a survival of 51.7 years and a functioning mitral valve for 44.4 years. Durability was a priority in the prosthesis design, aiming for an indefinite lifespan. The cage-ball valve, with no hinges, distributed stress evenly. Additionally, the biocompatibility of the materials and manufacturing techniques were optimized. After eight modifications between 1960 and 1965, the SEV 6120 model remained unchanged until 2004.[3]

Cases of patients with SE valves lasting 48, 40, and 51 years have been documented.[1,4,5] However, this case stands out due to the 53-year duration of a SE valve in the mitral position, which represents one of the longest reported durations and surpasses the expectations of many experts. This is a key point in discussing the durability and long-term performance of these prostheses in clinical practice.

Over time, the patient maintained good clinical and functional stability. This is despite the unfavorable long-term prognosis of this type of prosthesis, due to thromboembolic complications and resistance to flow, which make these prostheses less physiological. This case illustrates the effective function of the SE prosthesis, which was revolutionary in cardiac surgery at the time, significantly improving the quality of life and life expectancy of many patients with valvular disease.

However, the case limitations included the difficulty in correlating the clinical condition with the prosthesis' functionality and hemodynamics, mainly due to the patient's severe general deterioration from chronic malnutrition, community-acquired pneumonia in the last 6 months, and abnormal liver function tests associated with cardiac cirrhosis secondary to right heart failure.

Although SE mechanical prostheses are no longer implanted, we will continue to encounter patients with them due to their proven durability in case reports. However, there is no evidence from larger case series, associating survival with prosthesis durability. Patients with SE mechanical prostheses require close follow-up. Maintaining optimal coagulation profiles is necessary to reduce thromboembolic and hemorrhagic risks. Additionally, hemodynamic profiles, cardiac function, and pulmonary pressures should be evaluated through serial echocardiography. It is crucial to detect and treat comorbidities that deteriorate patients' clinical conditions and increase mortality.

Ethics

Informed Consent: Written informed consent was obtained from the patient for the publication of this case and the associated images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: R.C.M.C., L.M.A.F.G., E.A.M., Concept: R.C.M.C., Design: L.M.A.F.G., Data Collection or

Processing: L.M.A.F.G., E.A.M., Analysis or Interpretation: R.C.M.C., Literature Search: L.M.A.F.G., E.A.M., Writing: R.C.M.C., L.M.A.F.G., E.A.M.

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

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

REFERENCES

1. Raymundo-Martínez GIM, Gopar-Nieto R, Araiza-Garaygordobil D, Cabello-López A, Martínez-Amezcua P, Farjat-Ruiz JI, et al. A 51-year-old Starr-Edwards caged-ball valve. Arch Cardiol Mex. 2020;90:361-2.
2. Amrane M, Soulat G, Carpentier A, Jouan J. Starr-Edwards aortic valve: 50+ years and still going strong: a case report. Eur Heart J Case Rep. 2017;1:ytx014.
3. Dimitrakakis G, Wheeler R, von Oppell U. Starr-Edwards mitral valve-48 years till redo surgery, with over 54 years of patient survival after primary mitral valve replacement. Interact Cardiovasc Thorac Surg. 2021;33:640-2.
4. Powell S, Choxi R, Gunda S, Jovin IS. A 43-year-old functional Starr-Edwards ball and cage mechanical aortic valve. Gen Thorac Cardiovasc Surg. 2021;69:97-9.
5. Jadán Luzuriaga G del C, Paladines Jimenez RF, Viera ML, Fernandes F. Starr-Edwards prosthesis current and functional for more than 40 years. 2022;21:e861.

CASE REPORT

DOI: 10.4274/ijca.2024.96168
Int J Cardiovasc Acad 2025;11(1):34-37

Persistent False-Positive Troponin I Elevation Due to Heterophile Antibody Interference: A Case Report

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Abstract

Troponins are important biomarkers in the diagnosis of acute coronary syndrome (ACS). In this case report, we present the clinical course of an 80-year-old female patient who presented with complaints of fever, sore throat, and fatigue. Although the patient was initially diagnosed with non-ST elevation myocardial infarction and coronavirus disease-2019 infection, detailed examinations revealed that elevated troponin I levels were due to heterophile antibodies and that the diagnosis of ACS was excluded. It was understood that the consistently elevated troponin I levels in the patient, who had previously undergone coronary angiography and long-term dual antiplatelet therapy with a diagnosis of ACS, were due to the presence of these antibodies. This case report demonstrates that clinicians should be aware of potential false-positive troponin results due to heterophile antibodies, particularly in patients with persistently elevated troponin levels without typical clinical and diagnostic findings.

Keywords: Acute coronary syndrome, troponins, heterophile antibodies

INTRODUCTION

Troponins are essential biomarkers for diagnosing acute coronary syndromes (ACS) and assessing myocardial injury.[1] The interpretation of troponin levels can be complicated by various factors, including heterophile antibodies.[2] These antibodies can cross-react with assay components, potentially leading to false-positive results that may misguide clinical decisions.[3] We present a case of a patient suspected of having ACS, whose elevated troponin I levels were erroneously attributed to heterophile antibody interference. This case emphasizes the importance of considering alternative explanations for elevated troponin levels and highlights the need for clinicians to recognize potential assay interferences. Our report aims to raise awareness about heterophile antibody interference in troponin testing and promote careful interpretation of results.

CASE REPORT

An 80-year-old woman came to the emergency department with complaints of fever, sore throat, and fatigue lasting two days. She did not report chest pain or difficulty in breathing. She had a history of hypertension and coronary artery disease. She underwent coronary angiography for ACS 6 years, and 1 year ago, both of which revealed no significant stenosis, aside from the presence of coronary plaques. Her daily medications included acetylsalicylic acid (100 mg), clopidogrel (75 mg), metoprolol (50 mg), atorvastatin (20 mg), and amlodipine/valsartan (5/160 mg).

On admission, her blood pressure was 130/80 mmHg, heart rate was 86 bpm, body temperature was 38.1 °C, and oxygen saturation was 92% on room air. Physical examination showed

To cite this article: Akıncı S, Arıkan S, Akbay E, Adar A. Persistent false-positive troponin I elevation due to heterophile antibody interference: a case report. Int J Cardiovasc Acad. 2025;11(1):34-37

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Received: 05.11.2024
Accepted: 24.12.2024
Epub: 11.03.2025
Publication Date: 18.03.2025

oropharyngeal hyperemia, but cardiac and pulmonary examinations were normal. Laboratory tests revealed an elevated C-reactive protein level of 38.3 mg/dL and a slightly elevated D-dimer level of 604.5 mg/L, while other biochemical parameters were within normal limits. The complete blood count revealed neutrophil predominance (Table 1). The patient tested positive for coronavirus disease-2019 (COVID-19) antigen, and troponin I levels [ARCHITECT STAT assay, abbot laboratories, Illinois, United States of America (USA)] were markedly elevated at 37,430 ng/L (reference range: 0-16 ng/L). Based on these findings, we initially diagnosed non-ST elevation myocardial infarction (NSTEMI) and COVID-19 infection and admitted the patient to the intensive care unit.

Despite the marked troponin I elevation, the electrocardiogram (ECG) remained normal (Figure 1), and transthoracic echocardiography revealed only mild left ventricular hypertrophy with preserved systolic function. In the absence of ischemic symptoms, we did not proceed with early invasive intervention. Treatment consisted of enoxaparin (60 mg subcutaneously, twice daily) and molnupiravir (800 mg, twice daily), in addition to her regular medications. Throughout hospitalization, there was no progression of COVID-19 symptoms or cardiac findings.

Serial troponin I measurements remained consistently elevated (37,430 ng/L, 33,052 ng/L, 31,876 ng/L, and 33,183 ng/L), similar to levels documented during her previous ACS admission one year earlier (Figure 2). The absence of dynamic troponin changes, typical ischemic findings on ECG, and echocardiography, or other clinical evidence of ACS, prompted us to suspect a false-positive result. A subsequent troponin T assay yielded <10 ng/L (reference range: 0-14 ng/L). Testing troponin I in a heterophile antibody-blocking tube (Scantibodies Laboratory, CA, USA) produced a significantly

Table 1: Patient laboratory results at admission

Hematology	Result	Reference range
Hemoglobin (g/dL)	15.4	12-16.5
WBC (×10³/mL)	9.66	4.5-11
Platelets (×10³/mL)	207	140-440
Neutrophils (%)	74	40-72
Lymphocytes (%)	13	20-47
Chemistry		
Glucose (mg/dL)	82	80-110
Creatinine (mg/dL)	0.86	0.5-1.2
Sodium (mmol/L)	141	132-145
Potassium (mmol/L)	3.89	3.5-5.5
AST (U/L)	20	5-35
HDL cholesterol (mg/dL)	57	40-80
LDL cholesterol (mg/dL	120	60-130
Triglycerides (mg/dL)	96	55-150
CRP (mg/L)	38.8	0-5
Creatine kinase (U/L)	40	<168
D-dimer (mg/L)	604.5	<500
Troponin I (ng/L)	37430.5	0-16

WBC: White blood cells, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, CRP: C-reactive protein, AST: Aspartate aminotransferase

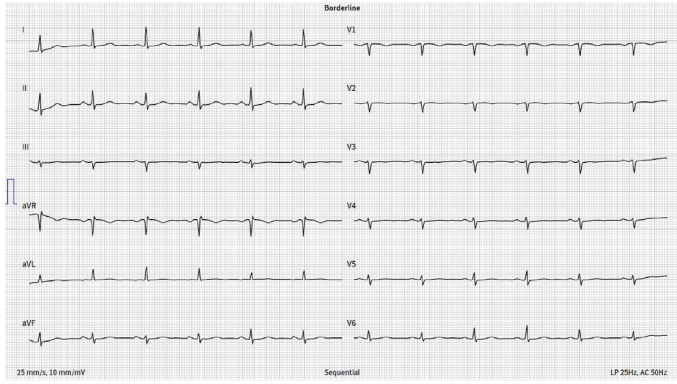

Figure 1: Patient's baseline electrocardiogram

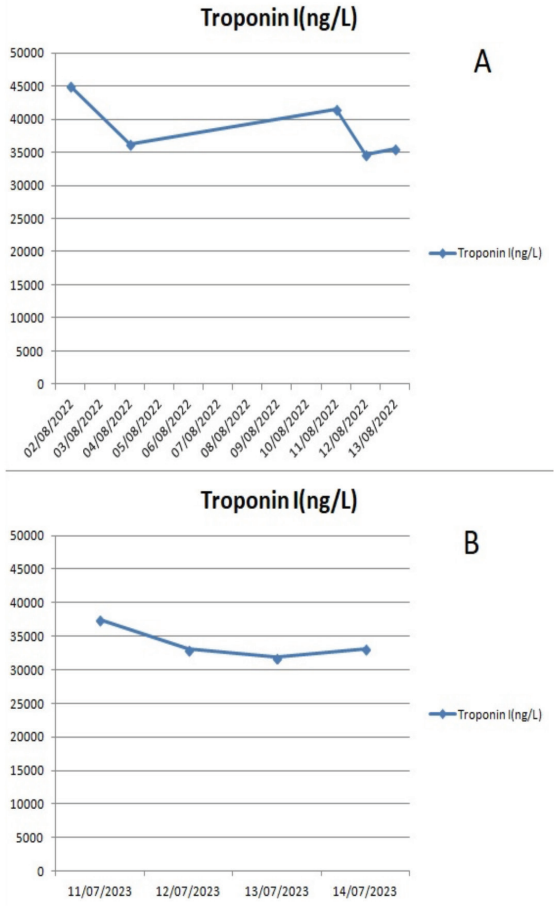

Figure 2: Graph of the patients troponin levels. **(A)** Hospitalization one year ago; **(B)** Current hospitalization

lower value of 62 ng/L, confirming heterophile antibody interference. This finding led us to exclude ACS. We discharged the patient with stable COVID-19 status, discontinued clopidogrel, and maintained her other medications. One-year follow-up demonstrated continued stability. Informed consent was obtained.

DISCUSSION

Cardiac troponins have become the preferred biomarkers for diagnosing acute myocardial infarction and levels above the 99th percentile of a healthy reference population are considered diagnostic for myocardial infarction.[4] Even small elevations in troponins correlate with higher risk of death and recurrent ischemic events in ACS patients. Patients with elevated troponins benefit most from more intensive medical therapy and early invasive management. On the other hand, troponins do not discriminate between ischemic and non-ischemic causes of myocardial injury and the clinical presentation is crucial.[4]

Although troponins are highly specific for myocardial necrosis, false positive elevations can occur in various clinical conditions other than ACS. Renal failure, myocarditis, cardiomyopathy, pulmonary embolism, sepsis, stroke, and other critical illnesses can cause troponin elevation.[5,6] In one study, 41% of patients with elevated troponin T did not have ACS, and the positive predictive value was only 56%.[7]

Elevated troponin levels are commonly observed in patients with COVID-19 infection, with studies reporting that up 10-45% of hospitalized patients have elevated troponin levels.[8] This elevation may be due to several factors, including myocardial injury, myocarditis, stress cardiomyopathy, or supply-demand mismatch. In this case, the patient's troponin levels were initially thought to be indicative of NSTEMI, leading to her admission to the intensive care unit and initiation of appropriate treatment. In the follow-up, it was determined that the elevated troponin levels were not genuine but were caused by test interference due to heterophile antibodies. Consequently, troponin elevation related to COVID-19 infection was ruled out. Although there are reports in the literature of falsely elevated test results for substances such as D-dimer in COVID-19 patients due to heterophile antibodies, no such data exist regarding troponin.[9] Furthermore, it remains unclear whether the heterophile antibodies observed in these cases are associated with COVID-19 infection. In our case, we observed similarly elevated troponin levels a year prior, leading us to conclude that the heterophile antibodies were not related to COVID-19 infection.

Heterophile antibodies are an under-recognized cause of false-positive troponin results. These antibodies can interfere with immunoassays like troponin tests, and cause false positive results. The prevalence of false-positive troponin elevations due to heterophile antibodies is estimated to be around 0.17-3.1%. In one study, 15% of troponin elevations in rheumatoid factor-positive subjects were found to be false positives.[10] The antibodies can bind to the assay reagents and lead to a potentially high troponin result not reflective of actual myocardial injury.

False-positive troponin results caused by heterophile antibodies can lead to unnecessary diagnostic procedures and treatments, as seen in this patient, who underwent coronary angiography twice and received dual antiplatelet therapy for an extended period. When interference is suspected, the laboratory can use blocking reagents, test with a different assay, or look for characteristic dynamics of troponin rise and fall to address the issue.[11] In this case, the patient's initial troponin I values were found to be consistently elevated, even when she was admitted with ACS a year ago. The absence of typical ECG and echocardiographic findings, as well as the lack of progression in COVID-19 symptoms, raised suspicion of a false-positive troponin result. Further testing with a troponin T assay and a heterophilic antibody blocking tube confirmed the presence of heterophilic antibodies, leading to the exclusion of ACS as the primary diagnosis.

In this case, although we demonstrated that there was no actual myocardial injury using troponin T levels, cardiac magnetic resonance imaging (MRI), could have provided additional insights by assessing myocardial damage and COVID-19 involvement. In similar cases, cardiac MRI may offer additional information about the condition. Furthermore, the presence of heterophile antibodies was identified using heterophile blocking tubes and alternative tests. Methods such as serial dilution could also have been employed as alternative approaches.

This case emphasizes the importance of correlating laboratory findings with the clinical presentation and other diagnostic tests. While elevated troponin levels are commonly associated with myocardial injury, it is essential to consider other potential causes, such as heterophilic antibodies, which can lead to false-positive results.

Ethics

Informed Consent: Informed consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.A., S.Ar., E.A., A.A., Data Collection or Processing: S.A., S.Ar., Analysis or Interpretation: S.A., S.Ar., E.A., A.A., Literature Search: S.A., E.A., A.A., Writing: S.A., E.A., A.A.

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

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

REFERENCES

1. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al*. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2021;42:1289-367.
2. Chaulin AM. False-Positive Causes in Serum Cardiac Troponin Levels. J Clin Med Res. 2022;14:80-7.
3. Lakusic N, Sopek Merkas I, Lucinger D, Mahovic D. Heterophile antibodies, false-positive troponin, and acute coronary syndrome: a case report indicating a pitfall in clinical practice. Eur Heart J Case Rep. 2021;5:ytab018.
4. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, *et al*. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol. 2018;72:2231-64.
5. Giannitsis E, Katus HA. Cardiac troponin level elevations not related to acute coronary syndromes. Nat Rev Cardiol. 2013;10:623-34.
6. Zaki HA, Shaban AE, Shaban AE, Shaban EE. Interpretation of cardiac and non-cardiac causes of elevated troponin T levels in non-acute coronary syndrome patients in the emergency department. Cureus. 2022;14:e22703.
7. Alcalai R, Planer D, Culhaoglu A, Osman A, Pollak A, Lotan C. Acute coronary syndrome vs nonspecific troponin elevation: clinical predictors and survival analysis. Arch Intern Med. 2007;167:276-81.
8. De Michieli L, Jaffe AS, Sandoval Y. Use and prognostic implications of cardiac troponin in COVID-19. Heart Fail Clin. 2023;19:163-76.
9. Ozbalci D, Doguc DK, Yilmaz G, Ozturk O, Sirin FB, Akcam FZ. Interference of D-dimer levels from heterophilic antibody in COVID-19: a serious concern in treatment and follow-up of patients. Int J Lab Hematol. 2022;44:e13-6.
10. Krahn J, Parry DM, Leroux M, Dalton J. High percentage of false positive cardiac troponin I results in patients with rheumatoid factor. Clin Biochem. 1999;32:477-80.
11. Lippi G, Aloe R, Meschi T, Borghi L, Cervellin G. Interference from heterophilic antibodies in troponin testing. Case report and systematic review of the literature. Clin Chim Acta. 2013;426:79-84.