

e-ISSN: 2980-1397

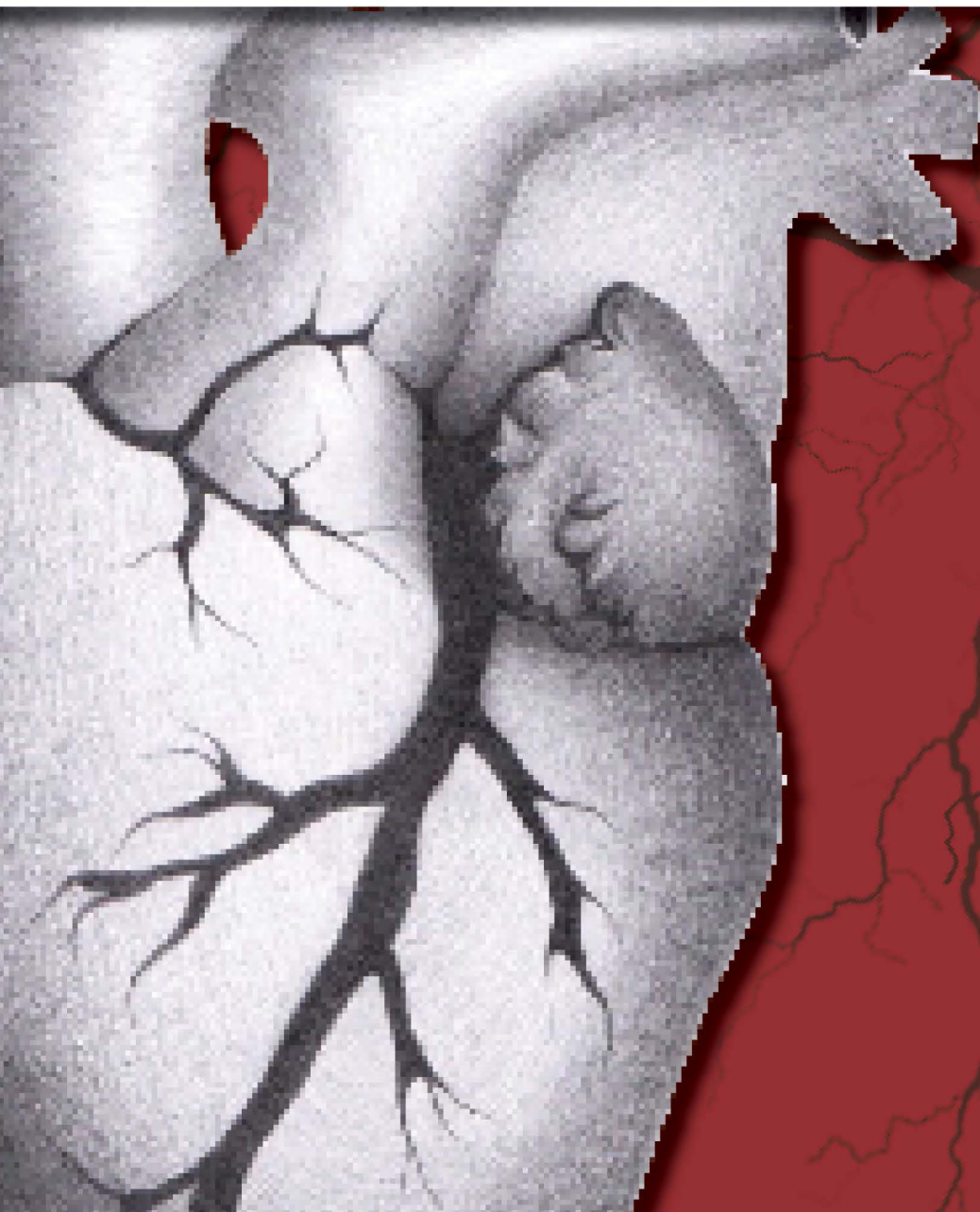
Journal of
**CARDIOLOGY & CARDIOVASCULAR
SURGERY**

Volume: 1

Issue: 4

Year: 2023

JCCVS



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Dear Colleagues,

I feel excited to welcome you in the the last issue of the year of Cardiology & Cardiovascular Surgery.

This issue included 7 original research articles and 1 interesting case.

In the first original article, Koç et al. investigated the hemodynamic effects of etomidate anesthesia induction in diabetic and non-diabetic patients.

In the second original article, Ozdemir et al. investigated the impacts of YouTube videos on the patients diagnosed with hypertension in Turkish population.

The third original article entitled "*Evaluation of atrial conduction properties and atrial arrhythmia propensity in vitiligo patients*" presented interatrial and intraatrial electromechanical delay findings in vitiligo patients.

The fourth original article entitled "*Determination of cardiovascular risks in adult individuals and assessment of the level of knowledge of cardiovascular risk factors*" emphasized the importance of cardiovascular risk assessment in family medicine outpatient clinics.

In the fifth original article, Yılmaz et al. presented the results of evaluation of right ventricle functions in acute pulmonary thromboembolism using tissue doppler imaging.

The sixth article entitled "*Evaluation of the risk of sudden cardiac death in obstructive sleep apnea syndrome patients with Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio*" presented the results of ECG findings and its impact on early risk stratification in patents with obstructive sleep apnea syndrome.

In the seventh original article, Keleşoğlu et al. investigated the role new electrocardiographic parameters to determine the risk of atrial fibrillation in patients with ischemia with no obstructive arteries.

Lastly, the interesting case with J-point elevation and AV complete block presenting with recurrent syncope attacks was reported by Sakallı et al.

I would like to thank the authors, reviewers, editorial team and publisher for their hard work and dedication throughout the year. We look forward to bringing you the latest developments in cardiology and cardiovascular surgery, which will increase even more in the coming year, and we will strive to mediate all your contributions to science in the highest quality way.

Sincerely,

İbrahim Halil İNANÇ, MD
Editor-in-Chief

Volume: 1 Issue: 4 Year: 2023

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How much are videos on YouTube sufficient for Turkish hypertension patients?

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Cite this article: Özdemir S, Gültekin N, Göl M, Altınsoy KM, Türkbeyler İH. How much are videos on YouTube sufficient for Turkish hypertension patients? *J Cardiol Cardiovasc Surg.* 2023;1(4):56-60.

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Received: 18/09/2023

Accepted: 23/10/2023

Published: 29/12/2023

ABSTRACT

Aims: The quality of YouTube videos has been studied across various medical specialties and for numerous diseases. The aim of this study is to assess the quality, adequacy, and reliability of video content related to hypertension (HT) created on the YouTube platform.

Methods: Considering that the native language of most patients and physicians is Turkish in our country, the term 'Hipertansiyon' was searched in the YouTube search section on September 1, 2023. Only videos from the last ten years were included. Video quality and reliability, included in the study data, were defined using the 'Global Quality Score' (GQS) and 'Modified DISCERN Scores' (MDS), which have been previously used in many internet-based studies.

Results: A total of 99 videos were included. The mean number of subscribers was $107,997.77 \pm 25,850.54$, and the most frequently encountered content in the videos was hypertension and its treatment. The mean MDS scores were 4.61 and 4.44, while the mean GQS scores were 3.94 and 3.91. Considering that the majority of the videos were created by expert academic medical doctors or specialists, the content was found to be satisfactory. Academicians hold academic titles and conduct educational and research activities at universities, whereas non-academic individuals are typically specialist medical doctors.

Conclusion: Videos created by expert academic medical doctors should be preferred.

Keywords: Hypertension, general information, global quality score, modified DISCERN score, treatment, video content

INTRODUCTION

Systolic blood pressure represents the pressure exerted on the vessel walls by the blood ejected by the contraction of the left ventricle, while diastolic blood pressure is the pressure applied when the left ventricle is at rest. Despite the existence of specific graded levels and definitions, hypertension (HT) is simply defined as SBP above 140 mmHg or DBP above 90 mmHg. The diagnosis of HT increases the risk of morbidity and mortality due to cardiovascular, cerebrovascular, or renal diseases.¹

According to data published by the Turkish Hypertension and Kidney Diseases Association in 2012, the prevalence of hypertension in the adult population was found to be 32.3% in women, 28.4% in men, and 30.3% in the entire adult population. By age groups, hypertension is most common among the 60-69 age group and can reach as high as 85.2% in this group. Additionally, as an individual's body mass index increases, blood pressure also increases.² High blood pressure, which is one of the most important causes of cardiovascular mortality, causes 7.5 million deaths worldwide every year, accounting for 12.8% of all deaths.³ Hypertension is the leading risk factor among preventable deaths.^{4,5}

Hypertension has become an important public health problem in developing countries, especially in the last 30 years, due to the epidemiological transience in these countries. In a recent study, data from 136 countries is used and the number of individuals with uncontrolled hypertension is found to have been reached three billion in the last 30 years.⁶ After all, the economic burden caused by this disease is approximately 370 billion dollars, which corresponds to 10% of all healthcare costs.⁷ Masked HT and subtle organ dysfunction/failure are among the most feared phenomena regarding HT.^{8,9} However, associated cardiovascular complications such as heart failure, coronary heart diseases, ischemic and hemorrhagic stroke, peripheral vascular diseases, renal failure and visual disturbances can be easily prevented with early diagnosis, lifestyle changes and appropriate treatment.¹⁰ Studies have shown that although there are recently drastic improvements in diagnosis and treatment proficiencies in developed countries, awareness about the HT and ratio of controlled cases are maintaining to remain lower in developing countries.¹¹ Nevertheless, studies in our country indicate that the frequency of HT varied between 25% and 32%, and ratio of controlled cases is varying between 16.4% and 28.7%.¹²⁻¹⁴

Individuals often use the internet to find answers to questions they have about their own health problems. Although health professionals provide patients with reliable and regular information about diseases, surgical procedures or various complications, individuals often prefer to access information via the internet and social media. According to the 2021 Household Information Technologies Utilization Survey of the Turkish Statistical Institute (TSI), internet utilization rate in our country was found to be 82.6% among individuals in the 16-74 age group, and the rate of internet access among households was 92.0%.¹⁵ The internet and social media are important parts of our daily lives and provide people with a lot of information with the help of a handheld device. YouTube was launched on 15th of February, 2005, provides services in many areas and is one of the most frequently used social media sites. It provides approximately one billion users with the opportunity to watch millions of video content per day.¹⁶ Although the increase in the use and popularity of YouTube in society is in many different areas, its use in the field of health is increasing day by day. It is claimed to be an effective and powerful means for health education.¹⁷ It has been stated that internet usage and following health-related news on the internet are highly widespread in Turkey. 69.6% of our society research health-related information such as diseases, injuries, nutrition, and health improvement on the internet (15). Health literacy in monitoring chronic diseases offers benefits such as screening and understanding general information, benefiting from early diagnosis programs, and provides increased quality of self-care.^{18,19} It is declared that effective treatment of chronic diseases and prevention of complications are directly associated with health literacy, which is qualified by the ability to access and use information.^{19,20} Individuals, along with healthcare providers, should be actively involved in the management of patients with chronic diseases. In order to increase the health literacy of patients, it is recommended that healthcare professionals make educational plans and benefit from resources such as written and visual materials. Undoubtedly, one of these resources is the social media environment furnished by the World Health Organization.

Content on YouTube and other social media platforms can be created by many people and sources; however, information can be uploaded to the relevant platforms without any control or audit. Patients' expectations from the healthcare system are affected at different levels due to the information they access from those sources. Today, the amount of medical data accessible via the internet has been constantly increasing, and the reliability and adequacy of these contents are not clearly known.^{21,22} The quality, accuracy, adequacy, and reliability of YouTube videos have been studied by many medical specialties and for many diseases. Our aim in conducting this study is to evaluate the quality, adequacy and reliability of video content created on the YouTube platform regarding HT.

METHODS

Our study did not require ethical committee approval since access to YouTube videos is legally open to the public. All procedures were carried out in accordance with the ethical rules and the principles. To find videos related to hypertension (HT), the term 'Hipertansiyon' was entered into the YouTube search section in Turkish on September 1, 2023.

In order to access the most up-to-date videos, those from the last ten years were included in the study. The search history on the computer was cleared before browsing, and documented lists that did not involve cookies were recorded. Videos were filtered by relevance in the YouTube filters section.

Videos that were not in Turkish, not related to hypertension, or did not contain audio were excluded from the study. Additionally, videos that were required to be shorter than one minute and thus had a time constraint, known as 'shorts' videos, were excluded from the study. Video content that was not 'shorts' but less than one minute in duration was included in the study as there was no time limit. There were no upper- or lower-time limits for the videos included. Copied video contents were evaluated as a single video that started with the first encountered video. Due to the increase in the number of videos that met the exclusion criteria, especially after the first 99 videos, and the fact that patients generally do not watch videos beyond the 250th video, our study data was generated with 99 video contents.

The videos included in our study were evaluated by independent researchers who were competent experts in hypertension (HT), its diagnosis, treatment, and follow-up. In this evaluation, video durations, view counts, likes, and comment counts were recorded. Additionally, the presence of information about the disease, diagnosis, epidemiology, treatment, diet, complications, etc., was checked in the video content. The individuals providing information in the video content were categorized as either academicians or non-academicians. "Academicians hold academic titles and conduct educational and research activities at universities, whereas non-academic individuals are typically specialist medical doctors."

Statistical Analysis

The quality and reliability of the videos included in the study were assessed using the 'Global Quality Score' (GQS) and the Modified 'DISCERN' Score (MDS), which have been used in many internet-based studies. GQS is a scoring system created by Bernard et al. This scoring system measures the quality of information obtained from the internet. The highest score of five indicates that the video is of high quality and contains clear information, while the lowest score of one indicates that the video quality is very poor and most information is missing. The MDS includes five questions with yes/no answers. It is a scale where yes answers receive one point, and no answers receive zero points, so the highest score is five, and the lowest score is zero. With this scoring system, the objectivity, reliability, and understandability of the video are evaluated in terms of sources. The Cronbach alpha was 0.72 for reliability of MDS and 0.70 for GQS.

RESULTS

Out of the 99 YouTube video contents, 93 were created by healthcare professionals, while the remaining portion was created by non-healthcare professionals. The video contents were classified based on their publication date into two categories;

1. The last five years (2019-2023)
2. The five years before that (2014-2018)

The majority of the videos (n:67, 67.7%) were from the last five years. When we analyzed the contents of the YouTube videos, we found that among them, 92 were including the information about HT definition, 89 about diagnosis, 85 about epidemiology, 92 about treatment, 91 about dietary recommendations, and 89 about complications in **Table 1**.

	Available	Not available
Definition	92 (92.9%)	7 (7.1%)
Diagnosis	89 (89.9%)	10 (10.1%)
Epidemiology	85 (85.9%)	14 (14.1%)
Treatment	92 (92.9%)	7 (7.1%)
Recommendations about diet	91 (91.9%)	8 (8.1%)
Complications	89 (89.9%)	10 (10.1%)

In terms of the mean values of the screened and watched videos in our study, the average number of subscribers was 107,997.77 ± 25,850.54, the average number of views was 23,574.08, the average number of likes was 378.43, and the average number of comments was 73.30 in **Table 2**.

	Mean	Minimum	Maximum
Number of subscribers	107997.77	39	1450000
Number of views	23574.08	34	457000
Number of likes	378.43	0	9100
Number of comments	73.30	0	5000

The videos were evaluated by each researcher with both GQS and MDS. The proportion of videos gaining 5 points in MDS from both experts were 72.7% and 62.6%, respectively. First expert gave 0 point with MDS to none of the videos, and second expert gave 0 to only video. With GQS, first expert gave 1 point to 3 videos and second expert to 4 videos. The proportion of videos obtaining 5 points in GQS from both experts were 40.4% and 33.3%, respectively in **Table 3**.

Modifiye 'DISCERN' score (MDS)	First expert	Second expert
0 points	0	1 (1.0%)
1 points	1 (1.0%)	0
2 points	3(3.0%)	5 (5.1%)
3 points	3 (3.0%)	4 (4.0%)
4 points	20 (20.2%)	27 (27.3%)
5 points	72 (72.7%)	62 (62.6%)
Gobal quality score (GQS)	First expert	Second expert
1 puan	3 (3.0%)	4 (4.0%)
2 puan	6 (6.1%)	6 (6.1%)
3 puan	25 (25.3%)	18 (18.2%)
4 puan	25 (25.3%)	38 (38.4%)
5 puan	40 (40.4%)	33 (33.3%)

The comparison of two evaluations is depicted in **Table 4**. Since the distribution was not a normal distribution, the Spearman correlation test was used. There is a highly positive and significant relationship between the two experts' ratings.

	First expert M±SD	Second expert M±SD	r	p
Modified 'DISCERN' score	4.61 ± 0.78	4.44 ± 0.92	0.71	0.000*
Global quality score	3.94 ± 1.09	3.91 ± 1.06	0.83	0.000*

*p<0.01, r: Spearman's correlation test

The relationship between the average of the scores in each of MDS and GQS and the number of views, number of likes and number of comments was examined. Since the distribution was not normal, Spearman correlation test analysis was used. No significant relationship was detected between neither MDS nor GQS and the number of views, likes, comments and subscribers in **Table 5 and 6**.

Countable features of the videos	Count	r	p
Number of views	99	-0.12	0.052
Number of likes	99	-0.07	0.47
Number of comments	99	-0.11	0.26
Number of subscribers	99	-0.07	0.51

Countable features of the videos	Count	r	p
Number of views	99	-0.20	0.2
Number of likes	99	-0.05	0.62
Number of comments	99	-0.17	0.08
Number of subscribers	99	-0.18	0.08

Video content	Groups	Count	Mean MDS	p
Occupation	Medical doctor	93	4.61	.47
	Other than medical doctor	6	3.16	
Definition	Available	92	4.56	.16
	Not available	7	4.00	
Diagnosis	Available	89	4.62	.02
	Not available	10	3.70	
Epidemiology	Available	85	4.71	.000
	Not available	14	3.39	
Treatment	Available	92	4.62	.001
	Not available	7	3.29	
Diet	Available	91	4.63	.000
	Not available	8	3.38	
Complication	Available	89	4.68	.000
	Not available	10	3.15	

Video content	Groups	Count	Mean GQS	p
Occupation	Medical doctor	93	4.61	.47
	Other than medical doctor	6	3.16	
Definition	Available	92	4.56	.16
	Not available	7	4.00	
Diagnosis	Available	89	4.62	.02
	Not available	10	3.70	
Epidemiology	Available	85	4.71	.000
	Not available	14	3.39	
Treatment	Available	92	4.62	.001
	Not available	7	3.29	
Diet	Available	91	4.63	.000
	Not available	8	3.38	
Complication	Available	89	4.68	.000
	Not available	10	3.15	

It was examined whether there was a significant difference between the MDS and GKS average scores of the videos according to the profession of the content producer. The occupational group was divided into two categories:

1) Doctors, and 2) Professions other than doctors. Content created by doctors was found to be significantly higher than content producers other than doctors in terms of MDS score. On the other hand, there is no significant difference between the groups in terms of GQS. Both the average scores of MDS and GQS of videos containing diagnostic, epidemiological, treatment, dieting, and complication information are higher than the averages of videos that do not contain these parameters.

At the same time, when look over at the relationship between these parameters and the average scores of each of MDS and GQS, there is statistical significance ($p < 0.05$) in **Table 7 and 8**.

DISCUSSION

It is thought that 85-90% of CHD cases are multifactorial (There have been many video analysis studies regarding the YouTube and other social media platforms since recent years. However, studies examining videos about HT on YouTube are almost absent in Turkey. For this reason, in our study, we looked over at HT videos on YouTube and the profession of the video producer and their content by using GQS and MDS scales.

As seen in previous studies, the owners of health-related video contents are from various professional groups, but a significant portion of them are physicians. For example, in a study where fibromyalgia videos are evaluated, it is reported that the 28% of the videos are uploaded by doctors²³, in another study where 200 videos about spondylarthrititis are evaluated, it is found that 62% those are uploaded by healthcare professionals²⁴, and 39.2% of videos about exercises applied to ankylosing spondylitis patients are uploaded by universities/professional organizations/associations.²⁵

In our study, 93 of the content owners of the 99 videos examined were medical doctors, and most of them were uploaded to the YouTube platform in the last 5 years. As it is known, hypertension is one of the most common chronic diseases in the world and correct treatment, follow-up and current and accurate information are of great importance. In this regard, YouTube provides ease of access to information since it is a public and easily accessible platform. At the same time, YouTube ranks second among the most frequently used internet platforms in the world.²⁶ However, this convenience can sometimes be beneficial and sometimes harmful. This has a great impact on the correct guidance of patients. The lack of references in YouTube videos has been criticized in some studies, as it may mislead viewers.^{27,28} In that study which is on fibromyalgia videos, more than 50% were grouped as “very weak” and “underweight” according to the MDS scale.²³ In another study conducted by Lee and colleagues on YouTube videos about gallstones, more than half of the videos were found to be misleading.²⁹ In their study where Gonzalez-Estrada et al.³⁰ examine 200 asthma-related videos, and show that the content of the videos was most often related to alternative medicine and the MDS scores of videos of health professionals are higher than those of other producers.

Although a significant part of the studies in the literature are found to be weak in terms of content, in our study, the video contents were found to be rich in the analysis of both experts. We think that the reason for this is that the majority of the video content in our study was created by physicians or academicians. At the same time, we found statistical

significance in comparing the evaluations of two experts with each other.

When the video contents are examined, it can be seen that in one of the studies evaluating disc herniation videos, non-surgical approaches (40%) were mentioned most frequently, followed by general information (30%).³¹ Özsoy et al.²³ report that video contents involve general information about fibromyalgia with 55% and treatment approaches with 23%. In our study the mostly encountered video content was definition and treatment of HT, with 92.9%.

Unlike in our study, in studies examine the videos on social platforms, scales such as DISCERN and JAMA, which are actually used to evaluate written scientific materials, are usually applied, however, it is recommended to create distinct appropriate scales and methodologies for the evaluation of the quality visual publications.³²

Study Limitations

Our study is focused on videos in the Turkish language. This does not provide an opinion on the quality and content of videos in other languages. Therefore it does not provide insights into what kind of information videos in different languages offer regarding hypertension.

CONCLUSION

Our results also indicate that video content related to hypertension generally covers important topics such as diagnosis, treatment, epidemiology, dietary recommendations, and complications. This suggests that videos related to hypertension are generally informative and educational.

Among the limitations of our study, it is important to remember that YouTube videos are constantly updated, and new content continues to be added. Therefore, the videos we examined reflect a snapshot in time. Additionally, it should be understood that the scoring systems used to assess the quality and reliability of videos may be subjective and may not always be comprehensive for all viewers.

In conclusion, we demonstrate that YouTube videos related to hypertension are generally created by reliable sources, and we believe that patients can use these videos for informational purposes. However, caution should always be exercised, and consultation with healthcare professionals is advisable. These videos can assist in understanding and managing hypertension but should not replace official medical advice.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study did not require ethical committee approval since access to YouTube videos is legally open to the public. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: This study did not require informed consent since access to YouTube videos is legally open to the public.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Hemodynamic effects of etomidate anesthesia induction in diabetic and non-diabetic patients: Importance of heart rate variability in early detection of cardiac autonomic dysfunction

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Cite this article: Koç A, Uzman S. Hemodynamic effects of etomidate anesthesia induction in diabetic and non-diabetic patients: Importance of heart rate variability in early detection of cardiac autonomic dysfunction. *J Cardiol Cardiovasc Surg.* 2023;1(4):61-65.

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Received: 07/03/2023

Accepted: 25/10/2023

Published: 29/12/2023

ABSTRACT

Aims: Cardiovascular diseases represent the primary cause of perioperative morbidity among diabetic patients. Etomidate, an anesthetic agent with minimal cardiovascular effects, is commonly used in these patients. Diabetic patients often experience cardiovascular autonomic neuropathy, a severe complication of diabetes. In recent years, measuring heart rate variability has become increasingly important for early detection of cardiac autonomic dysfunction. The aim of this study was to compare the hemodynamic effects of etomidate anesthesia induction between diabetic and non-diabetic patients.

Methods: This was a prospective randomized study that enrolled consecutive ASA I-III patients scheduled for various elective surgeries under general anesthesia. The patients were divided into two groups: Group D (diabetic, n=21) and Group ND (non-diabetic, n=21). Heart rate variability analyses were performed using a Norav-800 Holter on the day before surgery. On the day of the operation, after premedication and monitoring, general anesthesia was induced with etomidate. Hemodynamic parameters were measured before induction (T1), after induction (T2), and 2 min (T3), 5 min (T4), and 10 min (T5) after endotracheal intubation. Hemodynamic changes and heart rate variability were compared between the two groups.

Results: Group D showed a statistically significant decrease in systolic arterial pressure values at T2, T4, and T5 compared to baseline values ($p < 0.001$), while Group ND showed no significant differences in any period. Diastolic blood pressure decreased significantly in Group D compared to baseline values in the preintubation period ($p < 0.001$), but there was no significant change in Group ND. Heart rate did not significantly differ between the two groups during any measurement period, and there was no correlation between heart rate variability and hemodynamic changes.

Conclusion: The results suggest that etomidate anesthesia induction provides hemodynamic stability in patients with type 2 diabetes mellitus. Despite its potential utility, heart rate variability measured during resting conditions may not provide sufficient diagnostic accuracy for predicting the presence of autonomic neuropathy, particularly in individuals with diabetes mellitus. Therefore, additional measures may be needed for early detection of cardiac autonomic dysfunction in these patients.

Keywords: Autonomic dysfunction, etomidate, diabetes mellitus, heart rate variability

INTRODUCTION

Diabetes mellitus (DM) is presently recognized as the foremost endocrine ailment worldwide, with a heightened demand for surgical interventions and ICU admissions when compared to the nondiabetic population. This clinical observation highlights the pressing need for continued research and development of improved management strategies for patients with DM.¹ Cardiovascular autonomic neuropathy (CAN) is a common and severe complication of diabetes. It has been reported that CAN is present in 22.1% of type 2 diabetics and 16.8% of type 1 diabetics.² CAN is caused by damage to the autonomic nerve fibers that supply the heart and blood vessels. This damage to nerve fibers leads

to disturbances in heart rate control and hemodynamics. Clinically, it manifests itself as postural hypotension, exercise intolerance, intraoperative cardiovascular lability, and silent myocardial ischemia/infarction in diabetic patients.³ Cardiovascular reflex tests are sensitive, reproducible, simple, and noninvasive tests that provide a comprehensive diabetic cardiovascular autonomic neuropathy assessment. These include heart rate at rest, beat-to-beat heart rate variability, blood pressure response to the Valsalva maneuver, heart rate and systolic blood pressure during standing and diastolic blood pressure during prolonged exercise. Reduced 24-hour heart rate variability is a new test that is more sensitive than the standard reflex test and detects cardiac autonomic dysfunction earlier. The recording of 24-hour heart rate

variability can reveal abnormal circadian rhythms regulated by sympathovagal activity. The high-frequency component of heart rate variability is decreased in vagal dysfunction. On the other hand, the low-frequency and very low-frequency components decrease sympathetic dysfunction. In advanced cardiac autonomic neuropathy, all three components are decreased, as is the ratio between low and high frequencies, which indicates sympathovagal balance.⁴

Cardiovascular instability has been shown to increase during anesthesia, and abnormal cardiovascular responses can occur during anesthetic induction and intubation in patients with CAN.³ These patients have been shown to have a greater need for surgical intervention and intensive care hospitalization than nondiabetic patients and to have higher perioperative mortality and morbidity.¹ Etomidate is a fast-acting hypnotic used for the induction of anesthesia. Etomidate administration results in minimal hemodynamic changes while maintaining hemodynamic stability by preserving sympathetic outflow and autonomic reflexes.⁵

Hemodynamic instability that may occur during the induction of anesthesia in diabetic patients may make etomidate a suitable option for these patients. We aimed to compare the hemodynamic effects during anesthesia induction and intubation in type 2 diabetic and nondiabetic patients.

METHODS

After patient consent was obtained, elective surgery requiring endotracheal intubation was performed in 42 patients enrolled in the ASA I - III score group. The study was planned as a prospective, randomized, single-blind trial. Patients with uncontrolled hypertension, type 1 diabetes and another condition causing hyperglycemia, hepatic or renal insufficiency, an endocrine or metabolic disorder other than diabetes mellitus, a known allergy to the drugs to be used, and patients in whom difficult intubation was contemplated were excluded from the study. According to their hospitalization date, the patients were divided into two groups of 21 each. Those with type 2 diabetes whose blood glucose was controlled by oral antidiabetics were classified as Group D, whereas those without DM were classified as Group ND. HbA1c was measured in diabetic patients. Heart rate variability analysis was performed the day before surgery, according to the recommendations of the HRV Task Force.⁶ The 5-minute ECG recording with the Norav-800 Holter was recorded on the SD memory card and transferred to the computer environment. Heart rate variability was determined by analyzing data on the NH-300 operating system based on time and rate.

The patient, who received 1 mg of midazolam in the preoperative room, was brought to the operating table and monitored with electrocardiography, noninvasive blood pressure, and peripheral oxygen saturation. For premedication, 1 mg of midazolam was administered. In induction, 1 mcg/kg fentanyl, 0.3 mg/kg etomidate and 0.6 mg/kg rocuronium were administered. After muscle relaxation, endotracheal intubation was performed. After endotracheal intubation, sevoflurane was administered at a concentration of 2% and 4 l/min at a rate of 50-50% in a flow rate O₂-air mixture to maintain anesthesia. Hemodynamic parameters such as systolic arterial pressure (SAP), diastolic

arterial pressure (DAP), mean arterial pressure (MAP), and heart rate (HR) were measured and recorded.

Hemodynamic parameters were measured after monitoring (T1), before induction (T2), and 2 minutes (T3), 5 minutes (T4), and 10 minutes (T5) after endotracheal intubation. Hemodynamic alterations and heart rate variability were evaluated and compared between both groups.

Statistical Analysis

The data obtained were analyzed using the prepackaged statistical program SPSS 16.0. The chi-square test was used to compare the quantitative data between groups, and Student's t test was used to compare the qualitative data. Two-way analysis of variance was performed for a within-group comparison of hemodynamic data. The variance distribution was evaluated with the Kolmogorov-Smirnov test. Data are expressed as the mean \pm standard deviation or median (interquartile range). The accepted level of significance in this study was $p < 0.05$.

RESULTS

There was no difference between the weight, height, sex, and ASA group distribution groups. The age of the patients in group D was significantly higher than that in group ND ($p < 0.05$). Fasting blood glucose levels and percent HbA1c were significantly higher in diabetic patients than in nondiabetic patients ($p < 0.05$) (Table 1).

Table 1. Demographic characteristics of the groups

	Group D (n=21)	Group ND (n=21)
Age (year)	53.3 \pm 11.7	44.7 \pm 13.9
Weight (kg)	81.6 \pm 10.6	73.9 \pm 14.9
Gender (F/M)	16/5	16/5
Fasting blood glucose	115 \pm 22	89 \pm 17
HbA1c (%)	6.94 \pm 0.9	5.17 \pm 0.81
ASA II/III	18/3	14/7

While the SAP values measured in the T2, T4, and T5 periods were statistically significantly lower in Group D than in the baseline values ($p < 0.001$), no significant difference from the baseline values was observed in Group ND in any period (Figure 1).

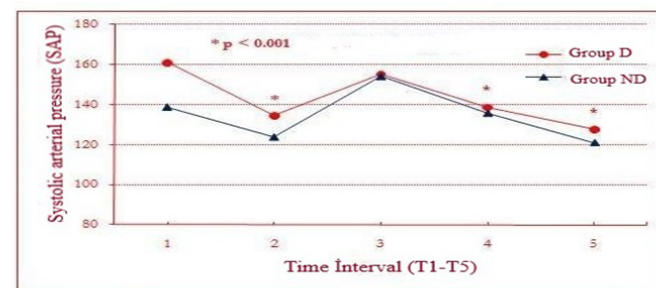


Figure 1. SAP values according to measurement periods, after monitoring (T1), before induction (T2), 2th minute (T3), 5th minute (T4), 10 minutes (T5) after endotracheal intubation.

There was no significant difference in DAP values at each measurement period between the two groups. In Group D, there was a significant decrease in DAP compared with

baseline values in the period before intubation ($p < 0.001$). There was no significant change in the other measurement periods and Group ND (Figure 2).

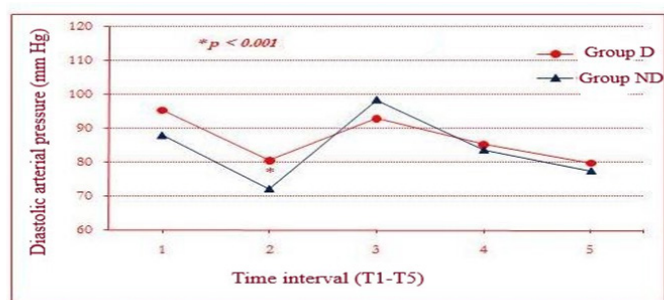


Figure 2. Diastolic arterial pressure values for measurement periods after monitoring (T1), before induction (T2), 2th minute (T3), 5th minute (T4), 10 minutes (T5) after endotracheal intubation.

Group D had a considerably higher baseline MAP than Group ND ($p < 0.001$). Other periods showed no notable differences. It was found that the MAP values in Group D significantly decreased in the T2, T4, and T5 intervals compared to baseline values ($p < 0.001$). In Group ND, there was a significant decrease in MAP in the T2 interval compared to baseline values, while a significant increase was observed in the postintubation period ($p < 0.01$) (Figure 3).

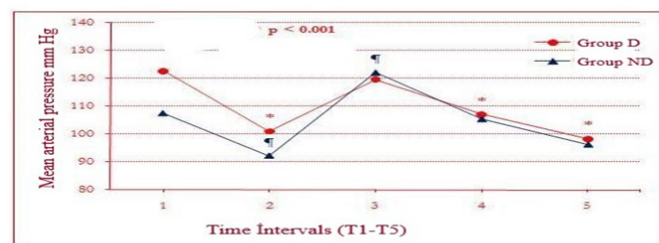


Figure 3. MAP values according to measurement periods. 1. Baseline 2. Before intubation 3. 2 minutes after intubation 4. 5 minutes after intubation 5. 10 minutes after intubation.

There were no significant differences observed in heart rate between the two study groups throughout the measurement periods, and no relationship was identified between heart rate variability and hemodynamic changes (Table 2, 3).

	Group D (n=21)		Group ND (n=21)	
	Mean	Median	Mean	Median
SDNN	137.73	123.7	134.79	128.2
RMSSD	34.83	20.73	32.56	22.1
Triangular index	4.26	3.75	4.75	4.45
VLF.nu	269.72	253.26	277.13	259.55
LF.nu	178.59	164.25	175.14	158.18
HF.nu	127.65	122.49	127.42	126.57
LF/HF	1.57	1.57	1.6	1.59

	Group H (n=11)		Group NH (n=31)	
	Mean	Median	Mean	Median
SDNN	137.1	123.6	136	130.9
RMSSD	40.6	18.1	37.9	20.1
Triangular index	3.92	3.74	4.71	4.14
VLF.nu	283.3	284.6	287.13	260.4
LF.nu	205.8	205.2	195.14	187.13
HF.nu	130.5	122.5	128.16	126.61
LF/HF	1.81	1.78	1.6	1.57

DISCUSSION

Cardiovascular autonomic neuropathy is a significant long-term complication of diabetes mellitus. This can lead to hemodynamic instability during the induction and maintenance of anesthesia. Etomidate preserves sympathetic outflow and autonomic reflexes in induction. Keyl et al.⁷, in their study using etomidate together with HRV analysis in 60 patients, 30 of whom had diabetes and who underwent coronary artery bypass grafting, concluded that autonomic dysfunction during anesthetic induction does not require hemodynamic instability. We reached a similar conclusion. The most important finding of our study was that both diabetic and nondiabetic patients had significant decreases in MAP compared to baseline values after anesthetic induction with etomidate. These decreases were less pronounced than in the Keyl study and, although statistically significant, were not clinically significant. The most significant MAP decreases after etomidate anesthetic induction identified in the study by Keyl et al.⁸ may be because of the more pronounced autonomic dysfunction in patients with myocardial perfusion defects.

Induction of anesthesia in people with diabetes should always be considered an aberrant cardiovascular response. According to Linstedt et al.⁹, the findings of their study compared circulatory changes in diabetic and nondiabetic patients undergoing eye surgery. They contend that the Valsalva technique, deep breathing, and monitoring heart rate fluctuations while seated can help identify these individuals. Latson et al.¹⁰ reported that the incidence of hypotension increased during the induction of anesthesia in patients with autonomic reflex dysfunction. The study conducted by Burgos et al.¹¹ aimed to evaluate the incidence of intraoperative cardiac morbidity among diabetic patients undergoing elective ophthalmic surgery. In their investigation, 38 patients were included, of whom 17 were diagnosed with diabetes mellitus. The authors reported significantly elevated reductions in blood pressure and heart rate during anesthesia induction among the diabetic population. Moreover, diabetic patients necessitated a higher dose of intraoperative vasopressors. The results suggest that preoperative assessment of autonomic functions using conventional methods may aid in identifying patients at risk of cardiac morbidity. Thiopental was used for anesthesia induction and was administered at a dose of 3-5 mg/kg in the study. Vohra et al.¹² conducted a study to investigate the impact of diabetes mellitus on cardiovascular responses to anesthesia induction and tracheal intubation. All diabetic patients showed abnormal results in standard cardiovascular autonomic function tests. There was no significant difference in preoperative cardiovascular status between the two groups. After induction of anesthesia, both groups showed a decrease in mean arterial pressure and vascular resistance, but the

diabetic group's heart rate did not change, and the cardiac index decreased. After tracheal intubation, the diabetic group exhibited a more significant increase in mean arterial pressure, vascular resistance, and heart rate than the control group. This suggests that an increased pressure response to tracheal intubation in diabetic patients may be indicative of autonomic dysfunction.

We used HRV analysis instead of traditional autonomic neuropathy testing because it takes less time. Diabetic and nondiabetic subjects had the same time and frequency-based characteristics. Again, there was no difference in HRV between subjects with a mean blood pressure drop-off over 30% (Group H) and those without (Group NH) (Table 3). HRV analysis is an indicator used in recent years in patients undergoing spinal anesthesia to determine the risk of hypotension. It has been reported that the risk of hypotension is higher in cases with an LF/HF ratio of 2.5 or more. Although such a precise value has not been reported to determine the risk of hypotension after intravenous induction, the existence of an association between HRV analysis and hypotension after induction of anesthesia has been reported.^{13,14} In contrast, we did not find any association between hypotension and the results of HRV analysis. In the study by Knuettgen et al.¹³, the difference between HRV results in diabetic patients who developed hypotension and those who did not may be because thiopental was used as an induction agent. Sympathetic outflow and autonomic reflexes are preserved because of the induction of anesthesia with etomidate. Schwarzkopf et al.¹⁵ conducted a study to compare the efficacy of preanesthesia administration of etomidate or midazolam in preventing etomidate-induced myoclonus. The study included 60 premedicated patients who were divided into three groups of 20 each. The first group received 0.05 mg/kg IV etomidate 90 seconds before induction, the second group received 0.015 mg/kg IV midazolam, and the third group received IV normal saline as a placebo. Anesthesia was induced with sufentanil and rocuronium one minute after the onset of hypnosis. Myoclonic movements were observed from the preinduction period of midazolam or etomidate administration to the end of anesthesia and were recorded on a scale of 0 to 3. The results showed that myoclonus was significantly lower (4 out of 20 patients) in those who received 0.015 mg/kg midazolam before induction with etomidate. The current study involved the administration of 1-1.5 mg midazolam and 1 mg/kg fentanyl IV to all patients 3-5 minutes before anesthesia induction. Slow induction of etomidate within 20 seconds did not result in myoclonus in any of the 20 patients. The results indicate that premedication with fentanyl and midazolam, along with a slow injection of etomidate, may prevent myoclonus.

CONCLUSION

As a result, cardiovascular autonomic neuropathy (CAN) is a common and severe complication of diabetes that can lead to hemodynamic instability during anesthesia. HRV is a new test that is more sensitive than the standard reflex test and detects cardiac autonomic dysfunction earlier. In this study, the hemodynamic effects during anesthesia induction and intubation were compared between type 2 diabetic and nondiabetic patients. Etomidate administration resulted in minimal hemodynamic changes while maintaining hemodynamic stability by preserving sympathetic outflow

and autonomic reflexes in diabetic patients. The study concluded that etomidate may be a suitable option for anesthesia induction in diabetic patients with CAN. Furthermore, we feel that HRV evaluated at rest may not be adequate for detecting autonomic neuropathy in some instances.

Acknowledgments

This article is a publication of the anesthesiology and reanimation specialty thesis of Alparslan Koç, which was completed in 2010.

This article was presented orally at the 7th Balkan States Anesthesia Days (ARUD 2021) as summary text, and at the 5th International Health Science and Life Congress (IHSLC 2022) as full text.

ETHICAL DECLARATIONS

Ethics Committee Approval: This article is a publication of the anesthesiology and reanimation specialty thesis of Alparslan Koç, which was completed in 2010. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Evaluation of atrial conduction properties and atrial arrhythmia propensity in vitiligo patients

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Cite this article: Çetinkaya Z, Keleşoğlu Ş, Ergün G et al. Evaluation of atrial conduction properties and atrial arrhythmia propensity in vitiligo patients. *J Cardiol Cardiovasc Surg.* 2023;1(4):66-70.

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Received: 03/11/2023

Accepted: 06/12/2023

Published: 29/12/2023

ABSTRACT

Aims: Vitiligo is a skin condition characterized by melanocyte loss. It is thought to have a robust association with various systemic and metabolic disorders, such as insulin resistance, atherosclerotic cardiovascular disease, and metabolic syndrome. Atrial fibrillation (AF) is a prevalent disorder in clinical practice and appears to be predictable by atrial electromechanical delay (EMD). This study aimed to detect atrial conduction time through tissue Doppler echocardiography, a non-invasive method used for patients with vitiligo.

Methods: We conducted this study with 32 patients diagnosed with generalized vitiligo and 38 age and sex-matched controls. This study was designed as a prospective, single-center, and cross-sectional study. We evaluated all participants' blood samples, including neutrophil/lymphocyte ratio (NLR), high-sensitivity C-reactive protein (hs-CRP), and other laboratory parameters. Then, we calculated atrial EMD, intra-atrial EMD, and left atrial EMD.

Results: We found neutrophil count, NLR levels, and hs-CRP levels to be significantly higher in the vitiligo group (6 ± 1.4 vs. 4.5 ± 2.3 , $p=0.001$; 3.5 ± 1.4 vs. 2.5 ± 1.9 , $p=0.024$; 6.2 ± 1.9 mg/dl vs. 4.1 ± 1.3 mg/dl, $p<0.001$, respectively). In addition, inter-atrial and intra-atrial EMD were significantly higher in the vitiligo group compared to the control group (36.3 ± 8.5 vs. 24.2 ± 10.8 , $p<0.001$; 18.1 ± 8.3 vs. 10.9 ± 5.8 , $p<0.001$, respectively). Finally, left atrial EMD was higher in the vitiligo group, but we could not reach statistical significance (15.3 ± 6.9 vs. 13.2 ± 7.2 , $p=0.33$).

Conclusion: We concluded that intra-atrial EMD and inter-atrial EMD were significantly prolonged in the vitiligo patients. Our results suggest that vitiligo patients are at risk for atrial fibrillation.

Keywords: Atrial conduction time, atrial fibrillation

INTRODUCTION

Vitiligo, a skin condition characterized by selective loss of melanocytes, affects an estimated 0.5-2% of the population worldwide.¹ It is a chronic depigmentation disorder of the skin characterized by white patches. Skin lesions seen in this disorder initially start as hypopigmented lesions and later appear as depigmented macules or patches. Vitiligo is classified as an autoimmune condition and is associated with other autoimmune skin disorders. It also acts as a systemic disease rather than a condition that only affects the skin. It is thought to have a robust relationship with various systemic and metabolic disorders, such as insulin resistance, lipid abnormalities, atherosclerotic cardiovascular disease, and metabolic syndrome.^{2,3} Although the etiopathogenesis of vitiligo is not clear, activation of the proinflammatory system involved in the pathogenesis of atherosclerosis and atrial arrhythmias, expression of cytokines/chemokines, increase in oxidative stress, and an elevation in catecholamine discharge play a role in its etiopathogenesis.^{4,5}

Atrial fibrillation (AF) is a vital heart rhythm disorder. It is common in clinical practice, causes hemodynamic disorders, frequent hospitalizations, and thromboembolic events, and affects 1-2% of the general population.⁶ Although the exact mechanisms that cause AF are not fully understood, diastolic dysfunction, inflammation, endothelial dysfunction, and catecholamine discharge have a place in its pathogenesis.⁶

Atrial conduction time (ACT) refers to the interval between sinus impulses and atrial mechanical contraction. A non-invasive technique called tissue Doppler imaging (TDI) is good at finding heart rhythm problems like atrial fibrillation (AF). It measures atrial electromechanical delay (EMD), which is the lengthening of the conduction time within and between atrial cells.^{7,8} Previously, TDI measurement of atrial EMD has been shown to correlate well with invasive measurements.¹⁴ Also, atrial EMD was once found to be prolonged in chronic skin disorders such as psoriasis and lichen planus.^{9,10}

To the best of our knowledge, cardiac evaluation has not been performed on patients with vitiligo before. Therefore, we aimed to evaluate the atrial conduction time in vitiligo patients with TDI. We also explored a relationship between atrial conduction time, disease severity, and inflammation marker levels.

METHODS

We conducted the study in dermatology and cardiology clinics at Kayseri City Training and Research Hospital between March and May 2021. Thirty-two (22 females, 10 males) patients diagnosed with generalized vitiligo and age- and sex-matched 38 (24 females, 14 males) controls participated in the study. The approval of the ethics committee, Kayseri City Training and Research Hospital, dated 07.01.2021 and numbered 2021/253 was obtained before the study. All procedures were carried out in accordance with the ethical rules and the principles, and it was conducted in accordance with the Declaration of Helsinki.

This study was designed as a prospective, single-center, and cross-sectional study. From all patients, we obtained a detailed medical history, physical examination, 12-channel electrocardiography (ECG), complete blood count, and serum biochemistry tests. We performed a thorough transthoracic echocardiographic examination on all patients. There was no atrial or ventricular conduction anomaly in the ECG of both the patient and the control groups. In addition, none of the patients included in the study or their families had a history of paroxysmal AF.

Vitiligo is divided into three types: localized, generalized, and universal. We selected our patient group among generalized vitiligo patients since it, the most common form of the disorder, is assumed to be systemic rather than just a depigmenting skin disorder.^{2,3}

People who had ischemic heart disease, diabetes mellitus (DM), no sinus rhythm, a pacemaker, severe valvular heart disease, structural heart disease, renal failure, severe comorbidities, use of any cardiovascular medications, obesity [body mass index (BMI) 30 kg/m²], or abnormal thyroid function or serum electrolyte levels were not allowed to participate.

Echocardiography

We performed 2-dimensional, M-mode, pulse wave, continuous wave, color Doppler, and TDI, as well as conventional echocardiography, using the Philips EPIQ 7 ultrasound system (Andover, Massachusetts, USA). We also recorded ECG simultaneously during all measurements. Conventional echocardiographic images were obtained from parasternal and apical images, according to the guidelines of the American Echocardiography Association. We measured left ventricular (LV) diameter and wall thickness from a parasternal image using the M-mode echocardiography method. Simpson's method was used to calculate the LV ejection fraction. We utilized the parasternal long-axis view in measuring LA diameter, while the left atrial area and mitral inflow rate were measured through the apical window.

Atrial Electromechanical Time

We performed TDI using converter frequencies of 3.5-4.0 MHz. We adjusted spectral-pulsed Doppler signal filters until achieving a Nyquist limit of 15-20 cm/sec and used the minimum optimal gain. Myocardial TDI velocities [peak systolic (S'), early diastolic (E'), and late diastolic velocities (A')] were measured by spectral-pulsed Doppler from the apical 4-chamber view. The ultrasound beam tilt did not exceed 15% to achieve the optimal viewing angle. We set the monitor scan rate to 50-100 mm/sec to optimize the spectral display of myocardial velocities. Then, we defined atrial EMD as the time interval from the onset of atrial electrical activity (P wave on surface ECG) to the onset of mechanical atrial contraction (late diastolic A wave) in TDI. All values were averaged over three successive strokes. We called atrial EMD 'PA lateral' when measured from the lateral mitral annulus; called 'PA septal' when measured from the septal mitral annulus; and 'PA tricuspid' when measured from the right ventricle tricuspid annulus. Then, we calculated inter-atrial EMD (difference between PA lateral and PA tricuspid), intra-atrial EMD (difference between PA septal and PA tricuspid), and left-atrial EMD (difference between PA lateral and PA septal).

We randomly selected a total of 20 participants, 10 from the patient group and 10 from the control group, to evaluate the intra-observer variation. We replicated the measurements under the same baseline conditions. Then, we found intra-observer variability to be 4% for lateral PA, 4.4% for septal PA, and 5.1% for tricuspid PA, respectively.

Statistical Analysis

We run all statistical analyses using the Statistical Package for the Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). The distribution of the data was checked using the Kolmogorov-Smirnov test. While the Independent Samples T-Test was used to compare normally distributed quantitative variables, we ran the Mann-Whitney U test to compare quantitative variables showing a nonnormal distribution. We performed the univariate analysis of categorical variables using the χ^2 test. Continuous variables were shown as mean \pm SD, whereas categorical variables were given as percentages. We presented medians and interquartile ranges for the variables not normally distributed. A 2-tailed probability value of <0.05 was considered significant.

RESULTS

We presented baseline characteristics and the laboratory findings of the patients and controls in **Table 1**.

There was no significant difference between the patient and the control groups by baseline characteristics (age, sex, hypertension). Considering laboratory findings, we found neutrophil count, neutrophil/lymphocyte ratio (NLR) levels, and high-sensitivity C-reactive protein (hs-CRP) levels to be significantly higher in the patient group (6 ± 1.4 vs. 4.5 ± 2.3 , $p=0.001$; 3.5 ± 1.4 vs. 2.5 ± 1.9 , $p=0.024$; 6.2 ± 1.9 mg/dl vs. 4.1 ± 1.3 mg/dl, $p<0.001$, respectively).

Table 1. Comparison of baseline laboratory measurements among the study groups

Variables	CONTROL (n=38)	VITILIGO (n=38)	P-value
Age (years)	39,6±8.9	40.7±12.1	0.699
Male/female	14/24	10/22	0.460
HT	9	10	0.380
SBP, mmHg	121.2±9	119±10.3	0.335
DBP, mmHg	74.3±6.6	72.8±7.5	0.795
Heart rate	77.7±8.1	76.4±9.1	0.534
Glucose (mg/dl)	98.8±17.2	102.8±19.8	0.349
Creatinine (mg/dl)	0.83±0.1	0.92±0.3	0.103
AST (U/L)	21.1±5.1	23.3±7.8	0.361
ALT (U/L)	21.2±8.8	24.5±9.2	0.333
WBC (x 10 ³ /μL)	8.7±3.6	8.8±3.5	0.158
Neutrophil (x 10 ³ /μL)	4.5±2.3	6±1.4	0.001
Lymphocyte (x 10 ³ /μL)	2±0.4	1.84±0.4	0.201
NLR	2.5±1.9	3.5±1.4	0.024
Hemoglobin (g/L)	14.4±1.5	14.9±1.2	0.158
Platelet (x 10 ³ /mm ³)	256.3±71.6	258.6±60.4	0.881
Hs CRP	4.1±1.3	6.2±1.9	<0.001

Data are expressed as mean±standard deviation for normally distributed data and percentage (%) for categorical variables, WBC: White Blood Cell, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, NLR: neutrophil to lymphocyte ratio, AST: Aspartate aminotransferase, ALT: Alanine transaminase

Table 2 shows echocardiographic and atrial electromechanical time parameters. Accordingly, we could not find a significant difference between the groups by left ventricular systolic and diastolic diameters, left atrial diameter and area, ventricular septum, posterior wall thickness, and left ventricular ejection fractions. Regarding the cardiovascular function parameters of the LV, there was no statistically significant difference between the groups.

Table 2. Echocardiography characteristics of the study population

Variables	CONTROL (n=38)	VITILIGO (n=38)	P-value
LA Diameter, cm	3.38±0.27	3.42±0.26	0.470
LA area, cm ²	21.5±2.2	21.7±1.8	0.679
LVDD, cm	4.66±0.4	4.68±0.4	0.805
LVESD, cm	3±0.4	3.1±0.3	0.601
IVSD, cm	1.06±0.11	1.07±0.14	0.706
PWD, cm	1.02±0.09	1.05±0.13	0.217
LVEF, %	67.3±5.9	65.1±5	0.079
PA Lateral, ms	58,3±12.5	69.1±9	<0.001
PA Septum, ms	45.1±9	54.4±6.5	<0.001
PA Tricuspid, ms	34.1±9.2	36.7±5.4	0.145
PA Lateral-PA Tricuspid (Inter-atrial delay)	24.2±10.8	36.3±8.5	<0.001
Pa Septal – PA Tricuspid (Intra-atrial delay)	10.9±5.8	18.1±8.3	<0.001
PA Lateral- PA Septal (Left-atrial delay)	13.2±7.2	15.3±6.9	0.330
Mitral E velocity	7.3±1.1	7.5±1.3	0.617
Mitral A velocity	5.8±1.6	6.1±1.4	0.492
DT, ms	180.4±37.2	188.2±35.4	0.817
IVRT, ms			
(S') cm/s	11.8±2.8	11.6±3.2	0.742
(E') cm/s	13.1±2.8	13±3.1	0.887
(A') cm/s	10.1±2.2	10.2±2.6	0.831

LA=Left atrium; LVDD=LV end-diastolic dimension; LVSD=LV end-systolic dimension; IVSD=interventricular septum thickness; PWD=posterior wall thickness; LVEF=LV ejection fraction; DT=deceleration time; IVRT=isovolumic relaxation time; Inter-atrial delay: PA lateral-PA tricuspid; Intra-atrial delay: PA septum-PA tricuspid; Left-atrial delay: PA lateral-PA septum; S': systolic velocity from the mitral annulus; E': early diastolic velocity from the mitral annulus; A': late diastolic velocity from the mitral annulus.

Although we found the PA lateral and PA septum values to be significantly prolonged in the vitiligo group compared to the control group, there was no difference between the groups in the PA tricuspid values (69.1±9 vs. 58.3±12.5, p<0.001; 54.4±6.5 vs. 45.1±9, p<0.001; 36.7±5.4 vs. 34.1±9.2, p=0.145, respectively). In addition, inter-atrial and intra-atrial EMD were significantly higher in the vitiligo group compared to the control group (36.3±8.5 vs. 24.2±10.8, p<0.001; 18.1±8.3 vs. 10.9±5.8, p<0.001, respectively). Finally, left atrial EMD was higher in the vitiligo group, but we could not reach a significant difference between the groups (15.3±6.9 vs. 13.2±7.2, p=0.33).

DISCUSSION

This is the first study showing that intra-atrial and inter-atrial conduction times were prolonged in vitiligo patients. In our study, CRP and NLR levels were found to be significantly higher in the vitiligo patients compared to the control group.

Vitiligo pathogenesis includes cellular defects within melanocytes and autoimmunity targeting these cells. Melanocytes are found in adipose tissue, the eyes, the inner ear, and leptomeninges, as well as in the skin.^{11,12} Some studies claimed that melanocytes both exert anti-inflammatory effects and act as an antioxidant system.¹² We found vitiligo patients to have increased levels of interferon-α (IFN-α) (proinflammatory) but decreased levels of interleukin-10 (IL-10) (anti-inflammatory) compared to controls, which supports the idea that inflammation may increase in vitiligo patients.⁴ Previous studies documented that the levels of homovanillic acid and vanillylmandelic acid were higher in the urine of vitiligo patients. Mental and physical stress, which is considered to intensify the pathogenesis of vitiligo, can cause vasoconstriction, hypoxia, and catecholamine discharge, leading to excessive production of oxygen radicals that destroy melanocytes and, at the same time, further increasing catecholamine secretion by stimulating the hypothalamic-pituitary-adrenal axis.^{4,13}

Solak et al.¹⁴ and Demirbaş et al.¹⁵ found higher CRP and NLR levels in vitiligo patients and reported a relationship between inflammation level and severity of the disorder. Grimes et al.¹⁶ discovered increased tissue necrosis factor-alpha (TNF-α), and interferon-γ in vitiligo patients. In our study, we revealed that the patient group had higher CRP and NLR levels than the control group, in line with the studies mentioned above.

Non-invasive measurement of atrial EMD with TDI, as an alternative to invasive electrophysiological measurements, is considered successful in evaluating the risk of AF.⁷ Cui et al.¹⁷ showed that the atrial conduction delay measured by TDI was significantly prolonged in patients with paroxysmal AF compared to the control group. Roshanalli et al.¹⁸ reported that atrial electromechanical interval is a predictor of AF developing after coronary artery bypass grafting and that preoperative amiodarone administration decreases the incidence of postoperative AF in patients with prolonged atrial electromechanical interval. Previous studies proved that atrial EMD is prolonged in many clinical disorders, such as diabetes mellitus, psoriasis, and inflammatory bowel disease.¹⁹⁻²² In addition, the incidence of AF in these diseases is significantly higher compared to the normal population. As a result, atrial EMD is prolonged in paroxysmal AF and considered a predictor of incipient AF.²³ Our research showed

that intra-atrial and inter-atrial EMD, a method that predicts the chance of developing AF in the future, lasted a lot longer in people with vitiligo compared to healthy controls.

AF has a rather complex pathophysiology, and the mechanisms promoting AF have not been completely elucidated. These mechanisms are thought to depend on remodeling mechanisms (electrical, structural, and autonomic) that allow the initiation and maintenance of AF (sympathetic activity in AF). The substantial evidence from various animal models suggests that autonomic dysfunction, namely increased sympathetic activity and, thus, autonomic remodeling, have an impact on AF.^{24,25} It was previously concluded that increased sympathetic activity leads to heterogeneous changes in atrial refractoriness, reinforcing the reentrant wave.^{26,27}

It has long been known that inflammation is an integral part of the pathogenesis of AF. Patients suffering from inflammation due to myocardial infarction, acute myopericarditis, chronic rheumatic heart disease, or cardiac surgery have increased AF rates. Some inflammatory markers, including many of the interleukins (IL-2, IL-6, and IL-8), as well as CRP, TNF- α , and monocyte chemoattractant protein-1 (MCP-1), are associated with a predisposition to AF.^{28,29} Inflammatory interaction in atrial cardiomyocytes causes changes in the effective refractory period, conduction slowdown, hypertrophy, and fibrosis.³⁰ In line with the findings in this study, Solak et al.¹⁴ previously showed that systemic inflammation increases in AF. Although we did not evaluate sympathetic activation, considering the previous results, it is reasonable to accept that the patients in our study had elevated catecholamines. Our study found that the longer intra-atrial and inter-atrial EMD in people with vitiligo compared to controls may have been caused by inflammation and atrial remodeling because of sympathetic hyperactivity.

Even though our research was not a follow-up study, we concluded that intra-atrial and inter-atrial EMD, techniques that predict cardiac arrhythmias, were significantly prolonged in patients with vitiligo. Considering the relevant literature, it is not wrong to assert that vitiligo patients are at risk for AF.

Study Limitations

The present study bears some limitations. First, it was difficult for us to predict how long participants had been suffering from the disorder. Secondly, the sample size was relatively small. Besides, we evaluated atrial EMD, a helpful marker for AF development, but this is not a follow-up study. Thus, we did not directly investigate AF development. The last limitation is that, unfortunately, we could not perform Holter monitoring to detect AF and other atrial arrhythmias. Overall, further studies need to consider examining the variables over a longer time period and including more participants.

CONCLUSION

As the European Society of Cardiology emphasizes in its latest AF guidelines, it is critical to identify and manage risk factors and comorbidities that predispose to AF prior to the development of atrial remodeling and fibrosis. Identifying individuals with vitiligo who have a higher risk of developing AF in the community may facilitate early AF detection. Therefore, we consider the results of this study to be clinically significant.

ETHICAL DECLARATIONS

Ethics Committee Approval: The approval of the ethics committee, Kayseri City Training and Research Hospital, dated 07.01.2021 and numbered 2021/253 was obtained before the study, and it was conducted in accordance with the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Determination of cardiovascular risks in adult individuals and assessment of the level of knowledge of cardiovascular risk factors

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Cite this article: Keleşoğlu Ş, Şafak ED, Keleşoğlu A. Determination of cardiovascular risks in adult individuals and assessment of the level of knowledge of cardiovascular risk factors. *J Cardiol Cardiovasc Surg.* 2023;1(4):71-76.

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Received: 25/12/2023

Accepted: 19/12/2023

Published: 29/12/2023

ABSTRACT

Aims: In the last century, the negative effects of factors such as nutrition, intense work tempo and stress on cardiovascular health have been increasing. The importance of preventive health services is increasing and policies are being developed to increase quality. In Family Medicine practice, calculating the cardiovascular diseases (CVD) risk that adult patients who do not have complaints about the cardiovascular system may experience in the coming years becomes important in this sense. Therefore, in this study, we aimed to calculate the ten-year risk of fatal cardiovascular events by the Systematic Coronary Risk Evaluation (SCORE) risk scoring in apparently cardiovascularly healthy individuals presenting to a family medicine outpatient clinic and to plan treatment according to the results. We also aim to evaluate the awareness of CVD risk factors in these individuals by using the Cardiovascular Disease Risk Factors Knowledge Level (CARRF-KL), whose reliability and efficacy have been shown in various previous studies.

Methods: 122 voluntary individuals between the ages of 40-80 were recruited to a family medicine polyclinic for any reason (43 males, 79 females). Participants' awareness was assessed by the CARRF-KL and the 10-year cardiovascular disease risk by the SCORE risk score.

Results: When the participants' SCORE risk averages were examined, 32.8% were low risk, 50.8% middle risk, 10.7% high risk and 5.7% very high risk group. When systolic blood pressure (SBP) levels according to the SCORE risk distribution were evaluated, in 7 patients with a very high risk distribution and the SBP value was higher than 130 mmHg, 2 of which were in the range of 130-139 mmHg, and 5 of them were above 140 mmHg. There was a statistically significant correlation between total cholesterol and low-density lipoprotein cholesterol levels and SCORE risk score distribution of lipid profile distributions of participants ($p<0.05$). This relationship was not detected in high-density lipoprotein cholesterol and triglyceride levels. The mean scores of the men in the study group on the CARRF-KL scale were 24.83, while the women were 24.31 and there was no difference between the gender. When the CARRF-KL scale mean scores were compared with the SCORE risk score distribution, no significant difference was found between the groups ($F=1.026$, $p=0.384$).

Conclusion: Our study suggests that SCORE risk assessment in cardiovascular disease is an easy assessment that can routinely be performed in family medicine outpatient clinics. It is possible that cardiovascular diseases can be detected and prevented in advance by the spread of clinical measures such as SCORE and risk measures such as CARRF-KL.

Keywords: Cardiovascular disease, risk factors, knowledge level, SCORE, CARRF-KL

INTRODUCTION

Cardiovascular diseases (CVD) are the most important cause of morbidity and mortality in our country as well as worldwide.^{1,2} Especially in the last century, more and more adverse effects on cardiovascular health have been observed over time due to factors such as diet, busy work schedules, stress, etc.³⁻⁵ In order to reduce such adverse effects, policies are tried to be produced by official institutions in our country and around the world.

In order to prevent and reduce the prevalence of CVDs, risk management has taken its place among the most prioritized issues. The quality of preventive health services

is increasing in our country as well as in the whole world. In fact, the protection and improvement of cardiovascular health are in an important position within these services that gather many different functions together.

In Family Medicine practice, the calculation of the CVD risk that adult patients without complaints related to the cardiovascular system may experience in the following years constitutes one of the most important pillars of the principle of protection and promotion of cardiovascular health.⁶ However, a practical and economical scale should be used for such a risk calculation. One of the scales widely used for this purpose all over the world is the Systematic Coronary Risk Evaluation (SCORE) Risk Scale.⁷

Therefore, in this study, we aimed to calculate the ten-year risk of fatal cardiovascular events by SCORE risk scoring in apparently cardiovascularly healthy individuals presenting to a family medicine outpatient clinic and to plan treatment according to the results. We also aim to evaluate the awareness of CVD risk factors in these individuals by using the Cardiovascular Disease Risk Factors Knowledge Level (CARRF-KL) Scale, whose reliability and efficacy have been shown in various previous studies.⁸

METHODS

Ethics

The approval of Clinical Research Ethics Committee of Erciyes University, dated 20.07.2017 and numbered 01/2017-47 was obtained before the study, and it was conducted in accordance with the Declaration of Helsinki.

Sample

The study included 122 adult volunteers aged 40-80 years who applied to Erciyes University Family Medicine outpatient clinic for any reason between July 2017 and December 2017. Sociodemographic characteristics such as age, gender, educational status, and smoking status were questioned. Glucose, hemoglobin A1C (HbA1C), blood urea nitrogen (BUN), creatinine (Cre), high-density lipoprotein cholesterol (HDL), triglyceride (TG), low-density lipoprotein cholesterol (LDL), and total cholesterol levels were also measured. The data obtained were calculated with the SCORE risk scale, and the 10-year CVD mortality risk of the patients was determined. Exclusion criteria were cerebrovascular disorder, chronic kidney disease, diabetes mellitus, peripheral artery disease and CVD.

SCORE Risk Scale

Patients' age, gender, smoking status, systolic blood pressure (SBP), total cholesterol values, and 10-year CVD mortality risks from the SCORE risk scale table were classified as low risk, intermediate risk, high risk, and very high risk. The calculated risk was classified as low risk if <1%, intermediate risk if between 1-5%, high risk if ≥5-10%, and very high risk if ≥10%.

CARRF-KL Scale

A validated and reliable cardiovascular disease risk factor knowledge level scale was used to measure the level of knowledge about CVD risk factors in adults. The first four items in the scale were related to the characteristics and preventability of CVDs and the age factor, while 15 items asked about risk factors (items 5, 6, 9-12, 14, 18-20, 23-25, 27, 28) and 9 items (items 7, 8, 13, 15, 16, 17, 21, 22, 26) asked about the result of change in risk behaviors.⁸ Individuals were asked to answer the questions as 'yes', 'no', and 'don't know', and 1 point was given for each correct answer. The 28 questions on the scale were evaluated as a total score without subdividing them into subgroups.

Statistical Analysis

The SPSS 22.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and numerical measurements were summarized by interpreting the mean, standard deviation (minimum and maximum where

necessary), and significance level. Since the sample size was over 30, the assumption that numerical measurements were normally distributed was accepted. In cases where the dependent variable was continuous and the independent variable was categorical, an ANOVA and an independent sample t-test were performed. In ANOVA tests, the Tukey test, one of the post-hoc tests, was used to determine from which group the significant differences originated. In cases where the dependent and independent variables were categorized, a chi-square test was performed and tabulated. The reliability of the SCORE Risk Scale on the selected sample was tested with Cronbach's alpha, and the reliability value was found to be 0.84. The statistical significance level (p) was taken as <0.05 in all tests.

RESULTS

Of the study group, 49 (40.2%) were male and 73 (59.8%) were female. The mean age was 50.16 ± 9.09 years (range 40-79). 62.3% of the participants were under 50 years of age, 23.7% were between 51 and 60 years of age, 9.8% were between 61 and 70 years of age, and 4% were in the 71 and over age group.

The mean values of cardiovascular disease risk factors are given in the **Table 1**. The mean systolic blood pressure (SBP) was 128.13 mmHg, and the mean DBP was 79.86 mmHg. A total of 37 patients (30.3%) had blood pressure levels above 140/90 mmHg at admission. The mean total cholesterol and TG levels were 204.15 ± 42.08 mg/dl and 171.66 ± 123.39 mg/dl, respectively. The mean LDL cholesterol was 119.68 ± 36.69 mg/dl, and the mean HDL cholesterol was 49.68 ± 13.49 mg/dl.

Table 1. Average values of cardiovascular disease risk

Variables	Mean \pm SD
HbA1C (%)	5.35 \pm 0.42
Glucose (mg/dl)	94.89 \pm 12.16
Total cholesterol (mg/dl)	204.15 \pm 42.80
Triglyceride (mg/dl)	171.66 \pm 123.39
Low-density lipoprotein (mg/dl)	119.68 \pm 36.69
High-density lipoprotein (mg/dl)	49.68 \pm 13.49
Blood urea nitrogen (mmol/L)	13.04 \pm 3.16
Creatinine (mg/dl)	0.84 \pm 0.58
Systolic blood pressure (mmHg)	128.13 \pm 16.27
Diastolic blood pressure (mmHg)	79.86 \pm 11.15

According to the SCORE risk scoring system, 40 (32.8%), 62 (50.8%), 13 (10.7%), and 7 (5.7%) participants had a low, moderate, high, and very high 10-year risk of death due to CVD, respectively. SCORE risk scale averages are given in **Figure 1**.

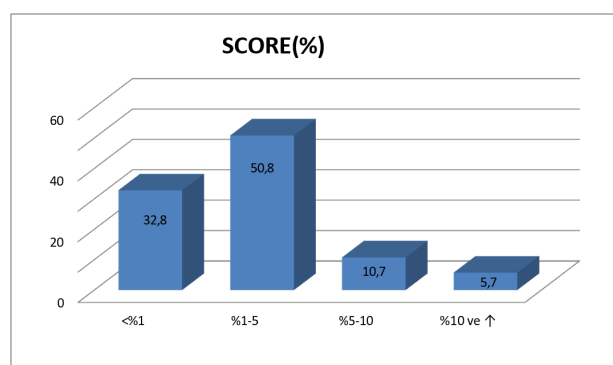


Figure 1. SCORE risk scale averages

When a comparison was made according to gender in the study, it was found that men had significantly higher HbA1C (p=0.021), triglyceride level (p=0.001), BUN (p=0.0001) and creatine (p:0.001) values but significantly lower HDL (p:0.0001) values than women. There was no difference between genders in glucose, total cholesterol, LDL levels, or SBP and DBP (**Table 2**).

Table 2. Significance of cardiovascular risk factors according to gender variable

Variables	Male (n=49) Mean	Female (n=73) Mean	Total Mean	F	P-value
HbA1C (%)	5.46	5.28	5.35	0.328	0.021*
Glucose (mg/dl)	97.2	93.34	94.8	7.138	0.086
Total Cholesterol (mg/dl)	204.61	203.84	204.22	0.061	0.924
Triglyceride(mg/dl)	217.91	140.61	171.6	10.86	0.001*
Low-density lipoprotein(mg/dl)	117.78	120.96	119.37	0.003	0.64
High-density lipoprotein (mg/dl)	43.15	54.06	49.6	0.254	0.0001*
Blood urea nitrogen (mmol/l)	14.55	12.02	13.04	0.1	0.0001*
Creatinine (mg/dl)	1.06	0.69	0.84	3.233	0.001*
Systolic Blood Pressure (mmHg)	131.24	126.05	128.13	0.115	0.084
Diastolic Blood Pressure (mmHg)	81.97	78,45	79.86	1.045	0.087

*p<0.05

Table 3. Distribution of study parameters according to SCORE risk distribution

Variables	SCORE risk %				P
	<1 (n=40)	>1- <5 (n=62)	>5-<10 (n=13)	% 10 ve üzeri (n=7)	
Gender					
Female	33 (82.5)	31 (50.0)	6 (46.2)	3 (42.9)	0.003*
Male	7 (17.5)	31 (50.0)	7 (53.8)	4 (57.1)	
Marital status					
Married	36 (90.0)	53 (85.5)	13 (100.0)	7 (100.0)	0.503
Single	4 (10.0)	9 (14.5)	0 (0.0)	0 (0.0)	
Education status					
Illiterate	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)	0.780
Primary school	9 (22.5)	14 (22.6)	3 (23.1)	3 (42.9)	
Middle school	1 (2.5)	5 (8.1)	0 (0.0)	0 (0.0)	
High school	11 (27.5)	13 (21.0)	4 (30.8)	3 (42.9)	
University	19 (47.5)	29 (46.8)	6 (46.2)	1 (14.3)	
Smoking					
Yes	3 (7.5) ^a	29 (46.8)	2 (15.4)	1 (14.3)	0.001*
No	37 (92.5) ^a	33 (53.2)	11 (84.6)	6 (85.7)	
Systolic blood pressure (mmHg)					
<130	30	31	5	0	0.0001*
130-139	10	11	3	2	
>140	0	20	5	5	
Diastolic blood pressure (mmHg)					
<85	35	38	9	4	0.177
85-89	2	10	2	1	
>90	3	14	2	2	

*p<0.05

Among the study group, 71.3% (n=87) were non-smokers, and 28.7% n=(35) were smokers. Of the study group, 0.8% were illiterate, 23.8% were in primary school, 4.9% were in middle school, 25.4% were in high school, and 45.2% were university students. Of the participants, 89.3% (n=109) were married,

and 10.7% (n=13) were single. When the relationship between SCORE risk distribution and study parameters was examined, it was found that being married/single and being literate were not associated with SCORE risk score distribution. When the smoking status of the participants was examined in detail, it was found to be significantly associated with the SCORE risk score distribution. When all participants were divided into three groups according to SBP and DBP values, when the relationships between the SCORE risk score distribution and the SCORE risk score distribution of the participants classified according to their blood pressure values were examined, a statistically significant relationship was found between SBP stages and score risk score distribution and blood pressure, while this relationship was not observed in DBP stages (**Table 3**).

Fasting blood glucose value distribution was not associated with SCORE risk score distribution. However, there was a statistically significant relationship between total cholesterol, LDL levels, and SCORE risk score distribution. This relationship was not found in HDL and TG levels (**Table 4**).

Table 4. Distribution of laboratory findings according to SCORE risk distribution

Variables	Score Risk Values				P	
	<%1 (n=40)	>1- <5 (n=62)	>5-<10 (n=13)	>%10 (n=7)		
Fasting blood glukose(mg/dl)	<100	32	48	8	4	0.362
	>100	8	14	5	3	
Total Cholesterol (mg/dl)	<190	21	23	2	1	0.045*
	>190	19	39	11	6	
Low-density lipoprotein (mg/dl)	<115	25	34	2	3	0.027*
	>115	15	28	11	4	
High-density lipoprotein (mg/dl)	Male<40	5	17	3	2	0.097
	Male>40	2	14	4	2	
	Female<45	8	7	2	0	
	Female>45	25	24	4	3	
Triglyceride (mg/dl)	<150	22	33	4	2	0.276
	>150	18	29	9	5	

*p<0.05

There was no significant difference (p=0.147) when the mean scores (24.83) of the men in the study group on the CARRF-KL Scale were compared with the mean scores (24.31) of the women. When the study was analyzed according to age, it was observed that the average of the scores obtained from the CARRF-KL scale by the group under 50 years of age was 24.43, the average of the scores obtained by the group between 51-60 years of age was 24.74, the average of the group between 61-70 years of age was 23.90, and the average of the group between 71 and over was 24, and the difference between the averages was not significant (F=0.853, p=0.682). It was observed that the CARRF-KL scale did not show a significant variation between genders, smoking, and age. Illiterate people scored 23, primary school graduates 23.58, secondary school graduates 23.66, high school graduates 24.22, and university graduates 25.30 on average. It was observed that the difference between the averages was significant (F=5.173, p=0.001) (**Table 5**).

Table 5. Evaluation of the CARRF-KL Scale according to its variables

Variables		n	Ort	P
Gender	Male	49	24.83	0.147
	Female	73	24.31	
Smoking	Yes	35	24.28	0.392
	No	87	24.62	
Marital status	204.61	203.84	204.22	0.075
	Married	109	24.63	
Age	Under 50	76	24.43	0.682
	51-60	29	24.74	
	61-70	12	23.9	
	71 and over	5	24	
Education status	Illiterate	1	23	0.001*
	Primary school	29	23.58	
	Middle school	6	23.66	
	High school	31	24.22	
	University	55	25.3	
Tukey (education status)	Primary school	55-29	1.72	0.0001*
	High school	55-31	1.08	0.045*
Presence of heart disease in the family	Primary school	55-29	1.72	0.013
	High school	55-31	1.08	

*p<0.05

When the mean values of the CARRF-KL scale were compared with the SCORE risk score distribution, it was observed that there was no significant difference between the groups (F=1.026, p=0.384) (Table 6).

Table 6. Distribution relationship between CARRF-KL scale and SCORE risk score

	SCORE	n	%	F	P
CARRF-KL Scale	<1%	40	32.8	1.026	0.384
	1-5%	62	50.8		
	5-10%	13	10.7		
	10% and above	7	5.7		

DISCUSSION

In our study, it was observed that the level of knowledge and awareness about CVD was higher in the study group compared to previous studies. By increasing the level of awareness, the emergence of chronic diseases such as CVD can be prevented or at least delayed. In patients, the rate of progression of the disease can be slowed down, and the survival period can be prolonged. Our study showed that with the application of SCORE risk scoring, it will be possible to increase the number of patients diagnosed and the number of patients treated. For this purpose, it would be an important step to install risk scoring on the follow-up screens of primary care physicians.

Health professionals working in primary care have important responsibilities in preventing CVD or other chronic diseases, identifying risky individuals and directing them to early diagnosis and treatment, and reducing possible complications by raising awareness in the community, educating individuals, providing healthy living habits, and ensuring their compliance with treatment when they become ill. Primary prevention is very important in CVD, which are among the most common diseases of our day and one of the leading causes of death worldwide, and therefore

early diagnosis and treatment are extremely important.^{9,10} In addition, most acute cardiovascular events occur in a clinically asymptomatic patient population. Today, despite the recent emphasis on primary treatment approaches for prevention in CVD management, it has still not reached the desired level.

One of the most recent and widely accepted guidelines, the European Guidelines for Cardiovascular Disease Prevention in Clinical Practice, recommends the use of the SCORE system based on prospective data from a diverse and large European population. CVD risk scores such as the SCORE assess the risk of developing CVD and the risk of death from CVD in apparently healthy subjects, i.e., those with no clinical or pre-clinical symptoms. In our study, we used the SCORE risk scale because it is in the form of easy-to-understand colored tables and is easier to calculate than other risk factors, thus causing less time loss in outpatient clinic conditions. Indeed, in previous studies, it was found that the SCORE risk score was associated with tomographically measured coronary calcium score and intravascular ultrasonographically assessed coronary plaque burden.¹¹⁻¹³

When SCORE risk scoring factors were analyzed one by one, total cholesterol values were found to be compatible with WHO values.¹⁴ In addition, the values in Istanbul, one of the cities where the Turkish Adult Risk Factor (TEKHARF) study was conducted, were close to our values.¹⁵ Again, as a result of the TEK HARF study, it was shown that the values of TG in our society are high when compared to other countries, and it is said that this high level is more pronounced, especially in men.¹⁵ In our study, although TG values were higher in men, we did not find a statistically significant relationship between high TG and SCORE risk scoring. When HDL was evaluated, 53% of men and 23.2% of women were included in this group when HDL < 45 mg/dl in women and < 40 mg/dl in men, according to SCORE Scoring. The fact that the desired values in HDL levels could not be reached both in our study and in other studies may be explained by the fact that genetic factors that directly affect HDL, such as causing hyperinsulinism, abdominal obesity, atherosclerosis, and hypertriglyceridemia, have not been sufficiently progressed in the primary detection or treatment of these conditions, and that exercise, which is perhaps the most important non-drug treatment for lowering HDL in Turkish people, has not been sufficiently introduced into our lives.¹⁵⁻¹⁷ It is noteworthy that the rate of smoking in our study group showed a decrease compared to the results of the TEK HARF study.^{15,18} In the study conducted by Akoğlu et al.¹⁸, it was found that 52.3% of the patients had never smoked, 27.5% had smoked, and 20.2% had smoked before and quit. In the Framingham Heart Study, every 10 mmHg increase SBP increased the risk of fatal and non-fatal CVD by 16%, including both sexes. In our study, the prevalence of hypertension at presentation (>140/90 mmHg) among the participants was found to be 30.3%. Although it is higher than the study by Sözmen et al.¹⁹, it is compatible with the prevalence of hypertension obtained in the Turkish Hypertension Prevalence Study and the study by Lamm et al.^{20,21} When all risk factors were evaluated, most participants in our study (n=102, 83.6%) were in the low and intermediate risk groups. We attributed the fact that most of the participants in our study were in the low and intermediate risk groups to the low risk profile of the participants, that is, the absence of CVD risk factors.

The CARRF-KL scale, whose reliability and validity have

been proven in the Turkish population, is used to determine the knowledge level of the participants about the risk of developing CVD.²² Al Hamarneh et al.²³ and Jafary et al.²⁴ also reported that individuals with a family history of heart disease had a higher level of knowledge. In studies conducted by Thanavaro et al.²⁵, Frijling et al.²⁶, and Al Hamarneh et al.²³, it was found that the mean CARRF-KL score increased as the level of education increased. However, in Sözmen et al.¹⁹ study, it was found to be inversely proportional to educational status. In our study, in line with the literature, we found that the participants' education level and the presence of a family history of heart disease were associated with the CARRF-KL scale score. The effect of educational status on the increase in the CARRF-KL scale score is obvious, but the effect of the presence of a family history of CAD may be explained by increased awareness of the disease and thus increased awareness of potential risk factors.

Scalzi et al.²⁷ found that age was an important determinant of risk awareness, and awareness was better in younger patients. In another study by Antsoy et al.²⁸, the CARRF-KL scale score was reported to be higher in women. According to another study by Sözmen et al.¹⁹, the level of knowledge increased with increasing age, being married, and working in an income-generating job. The results of CARRF-KL, which were found to be different as a result of all these studies, suggest that awareness, contrary to what is known, shows variability in participants away from classical information. In addition, the higher rates in our study compared to previous studies can be explained by the increased awareness activities in both visual and written media over the years, especially the warning labels on cigarette packs, such as the warning labels on cigarette packs made by the relevant associations on risk factors such as hypertension and smoking.

Study Limitations

The number of patients was limited. The fact that it was only a single city and a single center may prevent the results from being generalized to the entire population. Test-retest reliability and convergent validity, which should be considered in future studies, were not evaluated in this study. The non-probability convenience sampling method introduces selection bias. Individuals included in the study may be either less knowledgeable or more knowledgeable than the general population. Therefore, it may differ from the actual knowledge situation of the public. Calculating a knowledge score based on correct answers to a set of questions is somewhat arbitrary and may not capture the different weights that may be given to different questions. However, we think this score provides a fair estimate of the individual's level of knowledge.

CONCLUSION

In order to measure awareness of cardiovascular risk factors, up-to-date epidemiologic data systems should be established. For this purpose, it was concluded that it would be beneficial to determine the risk scales after identifying the individuals with CVD risk factors among the individuals applying to primary health care institutions, to increase the information about cardiovascular risk factors, and to increase the practices to increase awareness. The risk resulting from the combination of risk factors is greater than the risk resulting from their individual presence. Our study showed

that the number of patients diagnosed and the number of patients treated can be increased by applying the SCORE risk scoring recommended by ESC and TKD. For this purpose, it would be an important step to install risk scoring on the follow-up screens of primary care physicians.

ETHICAL DECLARATIONS

Ethics Committee Approval: The approval of Clinical Researches Ethics Committee of Erciyes University, dated 20.07.2017 and numbered 01/2017-47 was obtained before the study, and it was conducted in accordance with the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Evaluation of right ventricle functions in acute pulmonary thromboembolism using tissue Doppler imaging

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Cite this article: Yılmaz Y, Sirkeci MT, Keleşoğlu Ş, Oğuzhan A. Evaluation of right ventricle functions in acute pulmonary thromboembolism using tissue doppler imaging. *J Cardiol Cardiovasc Surg.* 2023;1(4):77-81.

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Received: 30/11/2023

Accepted: 26/12/2023

Published: 29/12/2023

ABSTRACT

Aims: Right ventricular (RV) systolic and diastolic functions are impaired in a significant proportion of patients with acute pulmonary thromboembolism (PTE). In these cases, knowledge of RV function is of great importance both in the diagnosis and in the choice of treatment. Our aim was to evaluate RV systolic and diastolic functions by standard pulse Doppler and tissue Doppler imaging (TDI) in normotensive patients with PTE without hemodynamic disturbances.

Methods: A total of 48 subjects, including 28 acute PTE patients (14 M, 14 F) with a mean age of 41 ± 13 years and 20 healthy subjects (10 M, 10 F) with a mean age of 40 ± 9 years, were included in our study. At the level of the tricuspid and mitral valve cusps, pulse Doppler echocardiography evaluated diastolic filling parameters. With the TDI technique, the diastolic function of the RV lateral wall and septum were analyzed in segments in the apical four-cavity image. Diastolic early and late velocities (e' , a'), e'/a' ratio, $e'dt$, isovolumetric relaxation time (IVRT), systolic velocity (s'), and systolic duration (s' duration) were evaluated by TDI.

Results: Among the RV standard Doppler parameters, a significant decrease in E velocity and E/A ratio and a significant increase in A velocity were observed compared to the control group ($p=0.042$; $p=0.002$; $p=0.001$, respectively). A non-significant prolongation in $E'dt$ was detected. RV ejection fraction was significantly lower in PTE patients compared to the control group (51.1% vs. 69.7%) ($p=0.001$). TDI was used to look at the RV systolic function, and it was found that all segments had higher systolic (Sa-m) velocities than the control group. However, systolic velocities in patients with DHB in the RV were found to be lower in the annular regions and RV-free walls. Increased s' velocities were observed in annular regions and RV-free walls. However, no statistical significance was found in s' velocity values.

Conclusion: RV systolic and diastolic functions may be impaired in normotensive patients with PTE without hemodynamic disturbances.

Keywords: Acute pulmonary embolism, tissue Doppler Imaging, right ventricular diastolic function

INTRODUCTION

Acute pulmonary thromboembolism (PTE) is not always an easily diagnosed disease due to its non-specific clinical manifestations. Since the right ventricle (RV) is affected in a significant proportion of PTE cases, knowledge of RV systolic and diastolic function is of great importance in diagnosis, selection of treatment, and prediction of prognosis.¹⁻⁶

Echocardiography is widely used in the evaluation of RV function. Because the RV has a trabecular structure and complex geometry, two-dimensional echocardiographic images are sometimes inadequate and make evaluation more difficult.⁷

Although invasive methods are considered the gold standard for the evaluation of RV diastolic function, a practical and noninvasive method such as echocardiographic examination is also widely used.⁸ It has become an

increasingly widely used method because it is noninvasive, harmless, inexpensive, easily applicable, and reproducible.⁹ Diastolic function assessment by pulse wave Doppler echocardiography has limitations because it is affected by some factors, such as systolic loading conditions.⁹

Tissue Doppler Imaging (TDI) can overcome various limitations of the conventional pulse wave Doppler method.^{9,10} There are several studies evaluating RV systolic and diastolic functions by TDI in normal subjects and different pathologic conditions.¹¹⁻¹³ Evaluation of RV functions by TDI in patients with PTE may provide additional information about the severity of PTE and guide both diagnosis and treatment.

The aim of our study was to evaluate RV systolic and diastolic functions by standard pulse Doppler and TDI in normotensive patients with PTE without hemodynamic disturbances.

METHODS

After institutional approval, this thesis study was conducted in the echocardiography laboratory of the cardiology outpatient clinic, Erciyes University, Faculty of Medicine, between November 2001 and September 2002. The study was conducted as a prospective, cross-sectional and single-centered study. The study looked at 48 people: 28 with acute PTE (14 men and 14 women) with an average age of 41 ± 13 years, and 20 healthy people (10 men and 10 women) with an average age of 40 ± 9 years. They were all hospitalized in the chest diseases service and the gynecology and obstetrics service and were sent to the echocardiography laboratory for transthoracic echocardiography before or during the diagnosis.

Diagnosis

- High probability on V/Q scintigraphy + high clinical suspicion and/or DVT detected on lower extremity venous Doppler,
- Moderate probability + high clinical suspicion on V/Q scintigraphy and/or DVT detected on lower extremity venous Doppler,
- Patients with PTE findings on spiral thorax CT + high clinical suspicion and/or DVT detected on a lower extremity venous Doppler were considered as PTE.

Exclusion criteria: Patients with poor echocardiographic image quality, Patients with clinical onset of PTE of more than seven days, Patients with acute disease leading to hemodynamic disturbance, Patients with arrhythmia (rhythm other than sinus rhythm), Patients with severe valvular disease (moderate to severe stenosis and insufficiency), patients with artificial valves, Patients with a previous myocardial infarction or coronary bypass surgery, Patients with a known history of CAD or findings compatible with CAD on ECG, patients with regional wall motion abnormality in the left V on echocardiography, patients with right V wall thickness over 6 mm, patients with COPD, chronic renal failure, diabetes mellitus, history of alcohol and drug use, patients with psychiatric illness, patients with hypertension (blood pressure $>140/90$ mmHg), patients over 65 years of age.

Echocardiographic Examination

The procedure was done with a Vingmed System V (Vingmed GE System 5, Horten, Norway) echocardiography device with a 2.5 MHz transducer while the patients were breathing normally and lying on their left side with their legs bent over them. This was done after five minutes of rest. Two-dimensional, M-mode, pulse wave Doppler, color Doppler, and pulse wave tissue Doppler examinations were performed through standard windows as recommended by the American Society of Echocardiography. Heart rate and blood pressure (BP) were measured every five minutes during the procedure.

M-Mode, 2-Dimensional, Color Doppler and Standard Doppler Echocardiographic Examinations

Simpson's method was used for RV EF measurement in apical four-cavity imaging. Areas were calculated by determining endocardial border tracings at end-diastole and end-systole. On apical four-chamber imaging, RV and LV widths were measured from the basal septum to the

widest part of the LV and RV lateral wall endocardium at the end of diastole. The RV wall motion abnormality was assessed as previously recommended.⁴ Measurement of diastolic indices for the RV was performed as for the LV. The measurements were performed during the apnea period after deep expiration, as recommended by Zoghbi et al.¹⁴ Pulmonary flow velocity and pulmonary flow acceleration time (PACT) (m/sec) were measured. Pulmonary artery pressure was also calculated as previously described by Mahan et al.¹⁵

Tissue Doppler Echocardiographic Examination

Recordings were obtained using pulsed-wave tissue Doppler format with apical four-cavity imaging for long-axis velocities and short-axis imaging for circular velocities. Long-axis velocities were obtained by placing the pulse wave sample volume (5mm) at the tricuspid lateral annulus, free wall mid- and apical regions, and septal annulus, mid- and apical regions. All Doppler measurements were performed by taking the mean values of five consecutive cardiac cycles during calm respiration. From these images, the systolic (s') wave velocity, early (e'), and late (a') diastolic wave velocities of the annulus were measured. From the time intervals of these waves, e'deseleration time (e'dt), isovolumetric relaxation (IVRT), and duration of the systolic wave (s'duration) were measured. For s' duration, the time between the beginning and end of the s' wave was measured. For IVRT measured by tissue Doppler, the time between the end of the s' wave and the beginning of the e'wave was measured.

Statistical Analysis

Statistical analyses were performed using the "SPSS 10.0 for Windows" software package. Numerical data were given as the mean \pm standard deviation. Pearson's method of bivariate correlation analysis was used to analyze the relationships between variables. An independent T test (unpaired T test) was used for the comparison of two independent groups, and an ANOVA test (Tukey test for post hoc comparisons) was used for the comparison of three independent groups. The error level α was taken as 0.05. Values with a $P < 0.05$ were considered significant.

RESULTS

A total of 48 individuals, including 28 patients (14 M; 14 F) with a mean age of 41 ± 13 years and 20 controls (10 M; 10 F) with a mean age of 40 ± 9 years, were included in the study. The baseline clinical characteristics of the acute PTE and control groups are shown in **Table 1**.

	Patient Group n=28	Control Group n=20	p value
Age (years)	41 ± 13 (19-65)	40 ± 9 (25-60)	NS
Gender			
Male	14 (37 \pm 3)	10 (38 \pm 2)	NS
Female	14 (43 \pm 3)	10 (42 \pm 3)	NS
Systolic Blood Pressure (mmHg)	121 ± 14	123 ± 11	NS
Diastolic Blood Pressure (mmHg)	68 ± 12	74 ± 10	NS
Average Blood Pressure (mmHg)	86 ± 11	90 ± 10	NS
Pulse (beats/min)	86 ± 10	75 ± 8	0.001*
Hemoglobin (g/dl):	13.1 ± 2.4	12.8 ± 2	NS
Blood glucose (mg/dl)	106 ± 59	99 ± 48	NS
Creatinine (mg/dl)	1.0 ± 0.2	0.8 ± 0.2	NS

* Statistically significant; NS; not statistically significant

While the pulse rate was significantly higher in the patient group (p=0.001), other variables were similar in both groups. Information about the underlying clinical conditions is detailed in **Table 2**.

Table 2. General characteristics of PTE patients

Risk factors for PTE	%, n
DVT	%53.5 (15)
Previous trauma/surgery	%57 (16)
Birth control pill use (n=14)	%7.14 (1)
Diseases related to hemostasis	%7.14 (2)
Symptoms	
Presyncope	%14
Side pain	%96
Palpitation	%61
Dyspnea	%96
hemoptysis	%29
Average symptom duration	4.2 ± 1.8 days
ECG findings	
Sinus rhythm: %	%100 (28)
Sinus tachycardia: (heart rate 90/min □)	%54 (15)
Incomplete or complete right bundle branch block: %	%25 (7)
Right axle deviation: %	%14 (4)
SIQ3T3 pattern: %	%25 (7)
V1-3 abnormal repolarization: %	%14 (4)
Normal ECG (heart rate 90)	%25 (7)

RV EF measured by Simpson’s method was significantly lower in the PTE group compared to the control group (51.1% vs. 69.7%), (p=0.001). There was a significant increase in the RV end-diastolic diameter obtained in the apical four-window image in the PTE group compared to the control group (p=0.003). This increase was greater in patients with RV wall motion abnormalities (50.6 mm vs. 39.5 mm). PAB values calculated from PAcT were also significantly increased in the patient group compared to the control group (p=0.014).

When RV standard pulse Doppler parameters obtained through the tricuspid valve were analyzed, a significant decrease in E-wave velocity was found in the patient group (p=0.042). The wave velocity was also significantly increased (p=0.002). The E/A value obtained by comparing the ratio of these two waves to each other showed a significant decrease in the patient group (p=0.001). Standard pulse Doppler flow parameters obtained from transtricuspid flow in the PTE and control groups are shown in **Table 3**.

Table 3. Transtricuspid diastolic flow patterns with standard pulse Doppler Echocardiography

Triküspid	Patient	Control Group n=20	p value
E	0.52 ± 0.09	0.57 ± 0.07	0.042*
A	0.53 ± 0.15	0.42 ± 0.06	0.002*
E/A	1.07 ± 0.38	1.38 ± 0.15	0.001*
Edt	175 ± 81	149 ± 52	0.21

* Statistically significant

The results obtained by the tissue Doppler method in the patient and control groups are shown in **Table 4**. In patients with PTE, s’ wave velocity increased in the lateral and septal annulus, but this increase was not statistically significant (p=0.805, p=0.265, respectively). e’ values were significant in the lateral annulus (p=0.023), septal annulus (p=0.129), and e’ values decreased in the PTE group, but this decrease

was not statistically significant. In the patient group, lateral annulus and septal annulus were statistically significant in a’ values (p=0.023, p=0.047, respectively). Although there was a decrease in e’/a’ ratios in the patient group, it was not statistically significant (p >0.05). The s’ durations of the segments were found to be significantly shorter in the PTE group compared to the control group in the lateral and septal segments (p=0.001). IVRT values were prolonged in both annuli, but not statistically significant (p>0.05).

Table 4. Right Ventricular Septal and Lateral Annulus tissue Doppler echocardiography findings

	Patient n=28	Control n=20	p	
RV lateral annulus	s’	0.138 ± 0.036	0.136 ± 0.027	0.805
	e’	0.123 ± 0.045	0.151 ± 0.035	0.023*
	a’	0.159 ± 0.07	0.129 ± 0.02	0.038*
	e’/a’	0.98 ± 0.61	1.170 ± 0.31	0.111
	e’dt	136.0 ± 42.1	120.7 ± 57.1	0.315
	s’ time	241.8 ± 34	287.5 ± 35.6	0.001*
RV septal annulus	IRT	57 ± 27	52.7 ± 31.7	0.624
	s’	0.0925 ± 0.026	0.0855 ± 0.1	0.265
	e’	0.101 ± 0.035	0.113 ± 0.020	0.129
	a’	0.110 ± 0.04	0.09 ± 0.017	0.047
	e’/a’	1.06 ± 0.62	1.26 ± 0.32	0.089
	Edt	127.5 ± 39.4	121.78 ± 47.9	0.066
	s’ time	240.7 ± 41.2	291.5 ± 28.7	0.001*
	IRT	63.1 ± 43.1	62.5 ± 34.0	0.956

RV; Right ventricle DT; Deceleration time IRT; Isovolumetric relaxation time

DISCUSSION

In our study, we demonstrated that systolic and diastolic functions were affected in PTE patients with normal blood pressure, even if hemodynamic deterioration was not observed. We evaluated these results in accordance with the literature.

Many changes in lung and heart function occur in PTE. Pulmonary vascular resistance and RV afterload increase with occlusion of the pulmonary arteries and the release of vasoconstrictor factors. In a significant proportion of PTE cases, RV function deteriorates in direct proportion to the severity of the embolism, with a reported rate of 50% in some series.^{6,16,17} The presence of signs of right ventricular overload in PTE is associated with a poor prognosis, and the evaluation of RV function is very important.¹⁻⁶ Pulse wave Doppler echocardiography has been used for many years as a noninvasive test for the evaluation of diastolic function.^{8,9} However, this method has some limitations and is affected by heart rate changes and different loading conditions, and may normalize with the progression of diastolic dysfunction.⁹ Previous studies have reported that RV dysfunction was not observed in approximately 40% of normotensive patients presenting with acute PTE.^{4,18} Impaired RV function and hemodynamic instability were reported to be the most decisive findings in in-hospital mortality, with a mortality rate of 25%.^{4,19,20} Goldhaber et al. reported that RV hypokinesia was observed in approximately half of the patients with PTE.¹⁸ In our study, we found RV hypokinesia less frequently, which may be due to the fact that we excluded patients with underlying cardiac and pulmonary disease, so RV systolic dysfunction may have been observed less frequently. We also found significant RV diastolic dysfunction in the patient group.

Although hemodynamically unstable RV dysfunction is associated with increased mortality, PTE cases with RV dysfunction evaluated by echocardiography alone have not been found to have increased mortality.²¹ However, TDI RV myocardial velocities predict an increased risk of death up to 1 year after the event. TDI has been shown to be a very useful technique for quantitative assessment of LV diastolic and systolic function and is more sensitive for the early detection of functional myocardial abnormalities.¹¹

We obtained similar findings in our patients with acute increases in RV afterload. Several mechanisms may be involved in the deterioration of RV diastolic function; RV function may be impaired directly due to the amount of increase in RV afterload. At the same time, RV ischemia, which is thought to occur due to the increase in arterial load, may affect diastolic functions. They have shown that pressure load has an important role in RV diastolic dysfunction.²² They reported that early diastolic RV relaxation was significantly impaired in acute pressure overload due to RV dilatation and hypoxia and that this prolongation in relaxation was less in patients with chronic pressure overload than in acute cases.

A lot of things can go wrong when trying to figure out how well the RV is working, including the patient's age and heart rate, the LV's ejection fraction, and things that have to do with the Doppler scan.^{5,6} A study by Caso et al.¹³ looked at COPD patients who fit this model. They found that the RV lateral annulus TDI e'/a' ratio was low and IVRT was significantly higher with or without pulmonary hypertension. As an indicator of RV diastolic dysfunction, we observed decreased RV lateral wall TDI e' velocities and e'/a' ratio, increased a' velocities, and prolonged IVRT intervals.

We think that TDI, as a new method that can relatively overcome the limitations of standard pulse Doppler, can be used as a suitable method for the evaluation of patients with PTE. In our study, we observed that systolic and diastolic functions were affected in PTE patients with normal blood pressure, even if hemodynamic deterioration was not observed.

Limitations

This study has some limitations. First of all, relatively few patients were included, and it was a single-center, retrospective study. Patients' echocardiography was performed only during the first hospitalization to the hospital. Follow-up echocardiographies were not performed in the hospital and after discharge. Examinations such as Strain Echocardiography and magnetic resonance imaging, which are relatively new imaging methods, were not performed on the patients in our study group. We could not include the drugs used in the study population in the analyses. Pulmonary angiography was not used as the gold standard in the diagnosis of PTE. Coronary artery disease could not be excluded angiographically. Simpson's method, which we use for RV ejection fraction, may not be as accurate as the gold standard method of invasive measurements. The presence of trabeculations and the inability to clearly select the RV endocardium may have impacted our two-dimensional echocardiographic measurements. The difficulty in obtaining measurements from apical regions with TDI may have affected our results.

CONCLUSION

As a result, cardiovascular autonomic neuropathy (CAN) is a common and severe complication of diabetes that can lead to hemodynamic instability during anesthesia. HRV is a new test that is more sensitive than the standard reflex test and detects cardiac autonomic dysfunction earlier. In this study, the hemodynamic effects during anesthesia induction and intubation were compared between type 2 diabetic and nondiabetic patients. Etomidate administration resulted in minimal hemodynamic changes while maintaining hemodynamic stability by preserving sympathetic outflow and autonomic reflexes in diabetic patients. The study concluded that etomidate may be a suitable option for anesthesia induction in diabetic patients with CAN. Furthermore, we feel that HRV evaluated at rest may not be adequate for detecting autonomic neuropathy in some instances.

ETHICAL DECLARATIONS

Ethics Committee Approval: "Evaluation of right ventricle functions in acute pulmonary thromboembolism using Tissue Doppler Imaging" was derived from the thesis study conducted in 2001. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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


Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Evaluation of the risk of sudden cardiac death in obstructive sleep apnea syndrome patients with Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio

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Cite this article: Dişyapar MK, Keleşoğlu Ş, Yetkin NA, Özdemir F, Yılmaz Y. Evaluation of the risk of sudden cardiac death in obstructive sleep apnea syndrome patients with Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio. *J Cardiol Cardiovasc Surg.* 2023;1(4):82-85.

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Received: 13/12/2023

Accepted: 28/12/2023

Published: 29/12/2023

ABSTRACT

Aims: Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by recurrent collapse of the upper airway during sleep. OSAS is associated with an increased risk of cardiovascular morbidity and mortality. Tpeak to Tend (Tp-e) interval, the Tp-e interval/QT interval (Tp-e/QT) ratio, and the Tp-e interval/corrected QT interval (Tp-e/QTc) ratio, are associated with ventricular arrhythmias and sudden cardiac death in various disease groups. We aimed to investigate the relationship between changes in the new arrhythmia markers Tp-e interval, Tp-e/QT and Tp-e/QTc ratios in OSAS patients.

Methods: The study looked at 45 people with OSAS (32 men) over the age of 18 and 43 healthy people (27 men) who were diagnosed with OSAS through polysomnography in a sleep lab. Tp-e interval, Tp-e/QT and Tp-e/QTc ratios were calculated on the ECG.

Results: The QT interval was shorter in the patient group than in the control group, in contrast to the QTc interval, which was comparable between groups ($p = 0.006$ and 0.810 in the patient and control groups, respectively). The Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio were significantly higher in OSAS patients included in the patient group compared to those included in the control group ($p < 0.01$ in total).

Conclusion: The Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were prolonged in OSAS patients. These findings suggest that OSAS patients may be predisposed to severe ventricular arrhythmias.

Keywords: Obstructive sleep apnea syndrome, Tp-e interval, Tp-e/QT ratio, Tp-e/QTc ratio, sudden cardiac death

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by recurrent collapse of the upper airway during sleep. OSAS affects 2% of middle-aged women and 4% of men. Polysomnography is the gold standard diagnostic method using the number of apneas and hypopneas per hour of sleep, and the apnea-hypopnea index (AHI) is the way to measure this. The incidence increases with age and weight gain. OSAS is associated with an increased risk of cardiovascular morbidity and mortality.¹ It is also clearly associated with heart failure, atrial fibrillation (AF), coronary disease, and stroke.^{2,3}

Arrhythmias such as sinus node dysfunction (sick sinus syndrome), atrioventricular block, AF, ventricular ectopy, and even ventricular tachycardia and sudden cardiac death have been reported in OSAS. The most common ventricular arrhythmia in OSAS is ventricular ectopic activity (VEA),

and severe arrhythmias such as ventricular tachycardia are also seen.⁴⁻⁶ The development of ventricular arrhythmias has also been claimed to be related to the severity of OSAS and oxygen desaturation.^{4,7} Patients with ventricular arrhythmias are less likely to have respiratory system disease, and there is a close relationship between sudden cardiac death and AHI.⁷

Assessment of ventricular recovery and repolarization dispersion on the electrocardiogram (ECG) are useful markers for future ventricular arrhythmias. Certain markers of ventricular repolarization, such as the QT interval and T-wave alternans, have been shown to be useful in predicting arrhythmias.⁸ Recent studies have shown that the ratio of new indices, such as the Tpeak to Trend (Tp-e) interval, the Tp-e interval/QT interval (Tp-e/QT) ratio, and the Tp-e interval/corrected QT interval (Tp-e/QTc) ratio, are associated with ventricular arrhythmias and sudden cardiac death in various disease groups.⁹

In this study, we aimed to investigate the relationship between changes in the new arrhythmia markers Tp-e interval, Tp-e/QT and Tp-e/QTc ratios in OSAS patients.

METHODS

The study was carried out with the permission of Ethical Committee of Kayseri City Training and Research Hospital (Date:12.12.2023, Decision No: 957). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study looked at 45 people with OSAS (32 men) over the age of 18 and 43 healthy people (27 men) who were diagnosed with OSAS through polysomnography in a sleep lab, had an Apnea-Hypopnea Index (AHI) >5, and had not been treated before. Medical history, laboratory results, and echocardiographic information were obtained from medical history records. The control group consisted of age- and gender-matched patients with no suspected respiratory system disease based on medical history, physical examination, and echocardiography findings.

The exclusion criteria were uninterpretable ECGs (left bundle branch block, presence of pacemaker, U waves and negative T waves on prewarning ECGs), hypertrophic cardiomyopathy, severe valvular disease, coronary artery disease, hypothyroidism and hyperthyroidism, hypokalemia and hyperkalemia, hypomagnesemia and hypermagnesemia, creatinine clearance (CrCl) <60 ml/min, and body mass index (BMI) >30 kg/m². None of the enrolled patients were taking any medication affecting the QT interval. Written informed consent and local ethics committee approval were obtained from all patients.

Sleep Test

Polysomnographic evaluation was performed in the sleep laboratory by continuous monitoring and analysis of ECG, electroencephalogram, electromyogram, pulse oximetry, electrooculogram, nasal airflow, snoring, leg movements, thoracic and abdominal movements, and body position. Polysomnographic records were evaluated by computer-assisted manual scoring according to the criteria of the American Academy of Sleep Medicine by physicians experienced in sleep disorders and polysomnography. OSAS was defined as the number of apneic and hypopneic events per hour during sleep.¹⁰ Apnea was defined as the absence of airflow for at least 10 seconds. Hypopnea was defined as the reduction of airflow with 4% oxygen desaturation lasting at least 10 seconds with subsequent arousal.

Electrocardiogram Analysis

All standard 12-lead ECGs were performed in the supine position and at rest using an ECG device (Philips brand) standardized to 1 mV/cm and 25 mm/s paper speed. All ECGs were scanned and transferred to personal computers. ECGs were magnified 5-fold and measured using an electronic caliper (Cardio Calipers software version 3.3; Iconico.com, Philadelphia, PA, USA) for the necessary measurements. To reduce inaccurate measurements, two cardiologists performed ECG assessments while being blind to clinical information.

The Tp-e interval was defined as the distance between the peak of the T wave and the end of the T wave. All Tp-e intervals were measured using the best available T wave and

generally using lead V5. When the V5 lead was not available for analysis, the V4 or V6 lead was used.

The QT interval was found by measuring the distance from the start of the QRS complex to the end of the T wave in lead V6, which is the best way to see the transmural axis of the left ventricle. Heart rate was then taken into account using the Bazett method. formula, i.e., QTc = QT/√R-R (R-R interval). Calculating Tp-e/QT and Tp-e/QTc ratios involved dividing Tp-e by QT and Tp-e by QTc, respectively. Intraobserver and interobserver coefficients of variation were less than 5%.

Echocardiography

Patients and healthy volunteers underwent conventional echocardiographic examination with an M4S-RS (1.5-3.6 MHz) cardiac transducer and Vingmed System 5 (General Electronic Horten, Norway) echocardiograph. Left ventricular diastolic (LVIDd) and systolic (LVIDs) diameters, interventricular septum (IVSWT), and posterior wall (LVPWT) diastolic thicknesses were measured in the parasternal long axis with M-mode echocardiography according to the standards set by the American Echocardiography Association. The ejection fraction was calculated using the Teichholz formula.

Statistical Analysis

Statistical analyses were performed using the SPSS Statistical software package for Windows version 21.0 (SPSS Inc., Chicago, IL, USA). The distributional characteristics of the data were determined using the Kolmogorov-Smirnov test. Independent samples t-test was used for parametric scale variables. Mann-Whitney U test was used for nonparametric scale variables. The χ^2 (chi-square) test was used for the univariate analysis of categorical variables. Variables were expressed as mean \pm SD (standard deviation); categorical variables were expressed as percentages. A probability value of $p < 0.05$ was considered to be significant, and two-tailed p values were used for all statistical analyses.

RESULTS

Baseline clinical and demographic characteristics of the study groups are presented in **Table 1**. There were no statistically significant differences between the patient and control groups in terms of gender, age, smoking status, diabetes, and hypertension ($p > 0.05$). Systolic blood pressure was slightly elevated, and BMI was high in the patient group.

Table 1. Baseline characteristics of the study populations

	OSAS (n=45)	Control (n=43)	p
Age (years)	49±9	51±4	NS
Gender (male/female)	32/13	27/16	NS
Systolic blood pressure (mmHg)	120±12	110±6	<0.05
Diastolic blood pressure (mmHg)	80±7	70±8	NS
Stature (cm)	168±8	168±8	NS
Weight (kg)	84±15	70±7	<0.001
Body mass index (kg/m ²)	29±6	24±2	<0.001

OSAS; Obstructive Sleep Apnea Syndrome NS; not statistically significant

Independent samples t-test was used for parametric scale variables. Variables were expressed as mean \pm SD (standard deviation); categorical variables were expressed as percentages.

The ECG parameters of the groups are shown in **Table 2**. Heart rate and QRS duration were similar between the groups ($p = 0.344$ and 0.220 in the patient and control groups, respectively). The QT interval was shorter in the patient group than in the control group, in contrast to the QTc interval, which was comparable between groups ($p = 0.006$ and 0.810 in the patient and control groups, respectively). The Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio were significantly higher in OSAS patients included in the patient group compared to those included in the control group ($p < 0.01$ in total).

Table 2. Electrocardiographic characteristics of the study population

Variables	Control group (45)	OSAS (43)	P
Heart rate (beat/min)	79.3±7.6	81.7±9.7	.017
QT (ms)	387.2±18.3	390.2±19.6	.280
QTc (ms)	424.1±12.9	403.6±10.8	<0.001
Tp-e (ms)	73.1±5.2	85.8±6.8	<0.001
TPe/QTc ratio (ms)	0.172±0.1	0.212±0.2	<0.001
TPe/QT ratio (ms)	0.188±0.2	0.219±0.2	<0.001

QTc; corrected QT interval, Tp-e; Tpeak to Tend interval, Tp-e/QT; Tp-e interval/QT interval ratio, Tpe/QTc; Tp-e interval/corrected QT interval ratio
The χ^2 (chi-square) test was used for the univariate analysis of categorical variables. Variables were expressed as mean \pm SD (standard deviation); categorical variables were expressed as percentages.

DISCUSSION

The most important result of our study is that the Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were prolonged in OSAS patients. These findings suggest that OSAS patients may be predisposed to severe ventricular arrhythmias.

The association between OSAS and cardiovascular disease has long been recognized and has been clearly demonstrated in hypertension as well as heart failure, atrial fibrillation (AF), coronary disease, and stroke.⁷ The hypoxemia, hypercapnia, intrathoracic pressure fluctuations, reoxygenation, and arousals that occur in OSAS affect many tissues, including the cardiovascular system.^{2,3,11} As a result, vasoconstriction, tachycardia, and acute blood pressure elevations due to sympathetic activation may occur. These mechanisms have direct cardiotoxic effects, including increased left ventricular wall stress, decreased cardiac variability, increased afterload, acute diastolic dysfunction, left atrial stress, left atrial enlargement, hypercoagulability, oxidative stress, and endothelial dysfunction.⁷ Myocardial cells are overstimulated, and cardiac arrhythmias occur.

Three different cell types have been identified electrophysiologically in the ventricle: endocardial, epicardial, and myocardial M cells.^{12,13} The peak of the T wave indicates epicardial repolarization, while the end of the T wave has been shown to overlap with repolarization of M cells; hence, the Tp-e interval is the duration of the transmural distribution of repolarization.¹⁴ There is an association between Tp-e and life-threatening arrhythmic events, and therefore Tp-e helps to predict the risk of developing arrhythmias.¹⁵⁻¹⁹ However, QT and Tp-e intervals vary greatly between individuals, and the Tp-e interval is affected by changes in heart rate. Therefore, regardless of Tp-e interval values, the Tp-e/QT ratio is thought to be more consistent across individuals and heart rates.⁹

Several studies have shown that OSAS is associated with an increased risk of ventricular arrhythmias and sudden cardiac death.^{5,20,21} Gami et al.²² 15-year follow-up study

by Gami et al.²²: SCD is a significant and increased risk among individuals suffering from sleep apnea. Barta et al.²³ reported that QT dispersion and QTc dispersion were not increased during the nocturnal period. Baumert et al.²⁴ showed that OSAS is associated with changes in QT interval variability during sleep. Sökmen et al.²⁵, Kilicarlan et al.²⁶, and Karacop et al.²⁷ found that Tp-e, Tpe/QT ratio, and Tp-e/QTc ratio were prolonged in OSAS patients. In our study, QT and QTc intervals were not different between the study and control groups. However, we found that other indicators of ventricular repolarization (i.e., Tp-e, Tpe/QT ratio, and Tp-e/QTc ratio) were increased in patients with OSAS. These results are consistent with the literature. However, we did not evaluate the clinical severity of our patients. Therefore, we could not evaluate the correlation with the severity of hypoxia or AHI. However, we still think that it predicts cardiac augmentations.

Limitations

The main limitations of our study are that the number of patients in our study group, prolonged Tpe, Tpe/QTc ratio were relatively small to see if OSAS patients develop ventricular arrhythmias and were not followed up by rhythm Holter and clinically for possible future ventricular arrhythmias. Our control group patients did not undergo sleep testing, which may have led to inaccurate results. OSAS patients were not grouped according to disease severity; further studies including OSAS patients more proportional to disease severity may reveal different results. We also did not evaluate the relationship between AHI and ventricular repolarization parameters.

CONCLUSION

Our results show that new ECG markers may provide more information about arrhythmic risk in OSAS patients than baseline ECGs. The pathologic state of OSAS in the cardiovascular system appears to have the potential to cause arrhythmogenic effects.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ethical Committee of Kayseri City Training and Research Hospital (Date:12.12.2023, Decision No: 957). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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New electrocardiographic parameters and risk of atrial arrhythmias in INOCA patients

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Cite this article: Keleşoğlu Ş, Yılmaz Y. New electrocardiographic parameters and risk of atrial arrhythmias in INOCA patients. *J Cardiol Cardiovasc Surg.* 2023;1(4):86-89.

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Received: 27/11/2023

Accepted: 28/12/2023

Published: 29/12/2023

ABSTRACT

Aims: Ischemia with no obstructive arteries (INOCA) is a clinical condition in which symptoms and signs of coronary artery disease are present, but coronary angiography does not show severe vessel narrowing. Atrial fibrillation (AF) is a common arrhythmia in cardiology practice, with an increasing prevalence with age and concomitant heart disease. P-wave dispersion (PWD) is an electrocardiographic (ECG) parameter defined as the difference between the maximum and minimum P-wave duration. There is an increasing number of studies showing an association between PWD and cardiovascular events. In this study, we aimed to evaluate the risk of AF in INOCA patients by detecting PWD, a new ECG parameter.

Methods: The study included 51 INOCA patients and 36 healthy subjects as a control group. The groups were compared in terms of demographic characteristics, laboratory findings, echocardiography, and ECG findings. The difference between the longest P wave (Pmax) and the shortest P wave (Pmin) was considered as PWD (PWD=Pmax-Pmin).

Results: When the patient group was compared with the control group, no difference was detected in terms of demographic characteristics or laboratory findings. When compared with the control group, Pmax duration and Pd values were significantly longer in the patient group compared to the control group (Pmax durations 112.7±7.09 ms and 98.1±5.5 ms, respectively, p<0.001; Pd durations 43.0±9.4 ms and 31.4±12.4 ms, respectively, p<0.001). On the other hand, Pmin durations did not differ significantly between the groups (p>0.05).

Conclusion: We observed that PWD was higher in INOCA patients compared to controls, and our results suggest that INOCA patients are at risk for AF.

Keywords: Ischemia with no obstructive arteries, P-wave dispersion, atrial fibrillation

INTRODUCTION

Ischemia with no obstructive arteries (INOCA) is a clinical condition with clinically stable symptoms and signs of ischemic heart disease despite normal or near-normal coronary arteries in angiography. The incidence of this syndrome, which was included in the Cardiology Guidelines for the first time in 2021, has been reported to be between 50-65% in women and 17-32% in men.¹⁻³ Approximately 30% of patients with coronary artery disease (CAD) have concomitant atrial fibrillation (AF).⁴ AF independently increases the risk of death by 39% in patients with stable CAD. Patients with stable CAD and concomitant AF have almost twice the risk of stroke compared with patients with stable CAD without AF.⁵

AF, which is the most common rhythm disorder in clinical practice, is of critical importance because of the hemodynamic disturbances and thromboembolic events it brings with it.⁶ Although the mechanisms causing AF are not fully understood, many risk factors, including age, hypertension (HT), CAD, cerebrovascular disease, and

diabetes mellitus (DM), are thought to play a role in the development of AF.⁷ Moreover, accumulating evidence has shown that myocardial damage and ischemia, inflammation and inflammatory factors, the autonomic nervous system, and oxidative stress play an important role in the pathogenesis of AF.⁸⁻¹¹

P-wave dispersion (PWD), defined as the difference between the maximum and minimum P-wave duration on surface electrocardiography (ECG), is a new ECG marker associated with the inhomogeneous and discontinuous propagation of sinus impulses.¹² The correlation between the presence of inter- and intra-atrial conduction abnormalities and the induction of paroxysmal AF (PAF) is well documented.¹³ Estimating the likelihood of patients developing PAF can guide the clinician in the management and stratification of patients at a higher risk of developing AF.

To our knowledge, cardiac evaluation using PWD has not been previously performed in INOCA patients. Therefore, we aimed to investigate whether AF can be predicted by evaluating PWD in these patients.

METHODS

The study was carried out with the permission of Ethical Committee of Faculty of Medicine of Erciyes University (Date:16.12.2020, Decision No: 2020-35). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients aged 18-85 years who presented to the Erciyes University Faculty of Medicine outpatient clinic with chest pain and/or exertional dyspnea due to ischemia, underwent coronary angiography, and did not have obstructive epicardial CAD on coronary angiography (coronary artery stenosis ratio $\geq 50\%$ and/or fractional flow reserve < 0.8) were included in the study. The study was conducted between November 2019 and November 2023 and included 51 INOCA patients. Thirty-six demographically similar patients without ischemic chest pain who underwent a stress test for any reason and had a negative stress test were considered the control group.

All patients underwent a detailed history, physical examination, 12-lead ECG, complete blood count, and serum biochemistry tests. A detailed transthoracic echocardiographic (ECHO) examination was performed in all patients. No atrial or ventricular conduction abnormality was detected on ECGs in the patient group or the control group. In addition, none of the patients included in the study had a history of PAF. Patients with a history of ischemic heart disease, patients without sinus rhythm and with pacemakers, patients with segmental or global wall motion abnormalities, patients with moderate to severe valvular heart disease, and patients with structural heart disease, endocrine neoplasms, parathyroid cancer, patients with thyroid cancer or hyperparathyroidism, renal failure, hypertrophic cardiomyopathy, hypokalemia and hyperkalemia, hypomagnesemia and hypermagnesemia, creatinine clearance (CrCl) < 60 ml/min, body mass index (BMI) < 30 kg/m², and severe comorbidities were excluded.

Electrocardiogram Analysis

All standard 12-lead ECGs were obtained in the supine position and at rest using an ECG device (Philips brand) standardized to 1 mV/cm and 25 mm/s paper speed. All ECGs were scanned and transferred to personal computers. ECGs were magnified 5-fold and measured using an electronic caliper (Cardio Calipers software version 3.3; Iconico.com, Philadelphia, PA, USA) for the necessary measurements.

The starting point of the P wave was considered the intersection of the isoelectric line and the P wave, and the endpoint of the P wave was considered the intersection of the isoelectric line and the terminal point of the P wave. The maximum P wave (Pmax) duration was considered to be the longest atrial conduction time. The difference between the longest P wave (Pmax) and the shortest P wave (Pmin) was considered PWD (PWD=Pmax-Pmin). All calculations were evaluated by two cardiologists who were blinded to the clinical characteristics of the patients.

Echocardiography

Patients and healthy volunteers underwent conventional ECHO imaging with an M4S-RS (1.5-3.6 MHz) cardiac transducer and Vingmed System 7 (General Electronic Horten, Norway) ECHO. Left ventricular diastolic (LVIDd) and systolic (LVIDs) diameters, interventricular septum (IVSWT), and posterior wall (LVPWT) diastolic thicknesses

were measured in the parasternal long axis with M-mode ECHO according to the standards defined by the American Medical Association. The ejection fraction on ECHO was calculated using the Teichholz formula.¹⁴

Statistical Analysis

Statistical analyses were performed using SPSS Statistics software package version 21.0 (SPSS Inc., Chicago, IL, USA) for Windows. The distribution characteristics of the data were determined by using the Kolmogorov-Smirnov test. Independent samples A t-test was used for parametric scale variables. Mann-Whitney the U test was used for nonparametric scale variables. The χ^2 (chi-squared) test was used for univariate analysis of the categorical variables. The variables were reported as means \pm SD (standard deviation), whereas the categorical variables were reported as percentages. Correlation analyses were performed using Pearson and Spearman coefficients of correlation. A probability value of $p < 0.05$ was considered to be significant, and two-tailed p values were used for all statistical analyses.

RESULTS

The baseline characteristics of the patient and control groups are given in **Table 1**. There was no statistically significant difference between the two groups in terms of demographic and clinical parameters, such as age, gender, presence of HT, presence of DM, smoking status, and baseline blood parameters ($p > 0.05$). The ECHO parameters of the patient and control groups are shown in **Table 1**. There was no statistically significant difference between the two groups in terms of the ECHO parameters. Heart rate and PR intervals were similar in both groups.

Table 1. Baseline clinical, demographic and echocardiographic features of the study groups

Variables	Control Group (n=36)	INOCA Group	p value
Age (years)	52.7 \pm 11.2	51.4 \pm 7.4	0.742
Male/female	25/11	37/14	0.655
HT	7 (%19.4)	11 (%21.6)	0.439
DM	3 (%8.3)	6 (%11.8)	0.772
Smoke	4 (%11.7)	7 (%16.2)	0.645
Systolic blood pressure, mm Hg	119.4 \pm 15.2	121.3 \pm 10.9	0.712
Diastolic blood pressure, mm Hg	71.28 \pm 10.3	69.9 \pm 9.7	0.385
Glucose (mg/dL)	89.4 \pm 9.3	92.1 \pm 11.3	0.225
Creatinine (mg/dL)	1.0 \pm 2.1	0.9 \pm 1.9	0.298
Total cholesterol	185.7 \pm 33.2	191.1 \pm 42.4	0.743
HDL	42.9 \pm 11.5	39.5 \pm 9.4	0.199
LDL	116.2 \pm 31.5	121.65 \pm 48.7	0.941
TG	165.7 \pm 70.6	155.4 \pm 66.9	0.445
AST (U/L)	23.6 \pm 8.4	20.9 \pm 6.9	0.813
ALT (U/L)	21.4 \pm 8.1	23.0 \pm 8.3	0.221
WBC (10 ³ /uL)	8.3 \pm 2.1	7.55 \pm 2.5	0.673
Hemoglobin (g/l)	13.1 \pm 0.9	15.2 \pm 1.9	0.334
Platelet (/mm ³)	280.8 \pm 61.5	253.5 \pm 81.5	0.568
LVEF	65.1 \pm 4.7	58.6 \pm 2.9	0.378
LVEDD (cm)	4.1 \pm 0.8	4.4 \pm 2.2	0.509
LVESD (cm)	3.4 \pm 0.5	3.55 \pm 2.3	0.692
IVSD (cm)	0.9 \pm 0.4	1.0 \pm 0.3	0.436
PWD (cm)	.9 \pm 0.7	1.1 \pm 0.3	0.591

Data are expressed as mean \pm standard deviation for normally distributed data and percentage (%) for categorical variables. DM: Diabetes Mellitus, HT: Hypertension, HDL: High density lipoprotein, LDL: low density lipoprotein, TG: Triglyceride, WBC: White Blood Cell, LVEDD: Left Ventricular End Diastole Diameter, LVESD: Left Ventricular End Systole Diameter, IVSD: Interventricular Septal Diameter, PWD: Posterior Wall Diameter, LVEF: Left Ventricular Ejection Fraction

Pmax duration and Pd values of the patient group were significantly longer than those of the control group (Pmax durations 112.7±7.09 ms and 98.1±5.5 ms, respectively, $p<0.001$; Pd durations 43.0±9.4 ms and 31.4±12.4 ms, respectively, $p<0.001$; **Table 2**). On the other hand, Pmin times did not differ significantly between the groups ($p>0.05$).

Table 2. Electrocardiographic Characteristics of the study population

Variables	Control Group (N=36)	INOCA Group	p value
Heart rate (min)	82.7±11.2	86.25±3.2	0.109
PR interval (ms)	144 ± 9	142 ± 5	0.798
P Max(ms)	98.1±5.5	112.7±8.9	p<0.001
P Min (ms)	66.2±8.1	68.1±6.6	0.235
PD (ms)	31.4±12.4	43.0±9.4	p<0.001

Pmax = maximum P-wave duration; Pmin = minimum P-wave duration; Pd = P-wave dispersion, Min = Minute, ms = millisecond

DISCUSSION

In this study, PWD on a 12-lead superficial ECG was found to be significantly higher in INOCA patients. To the best of our knowledge, this is the first study in the literature.

In INOCA, the risk of developing myocardial infarction, cardiovascular death, stroke, and heart failure may increase up to 10-fold compared to the normal population.^{15,16} If accompanied by DM and HT, the mortality rate increases even more.¹⁵ Some studies have claimed that patients with INOCA have a worse quality of life, more limited physical activity, and a higher frequency of angina compared to patients with stable CAD.¹⁶ These patients require more frequent hospitalization and more frequent angiography.

PWD is a new ECG marker associated with the heterogeneous and discontinuous propagation of sinus impulses. Moreover, the association between the presence of intra-atrial conduction abnormalities and the induction of PAF is well documented.¹⁷⁻¹⁹ PWD has also been found to be associated with carotid atherosclerosis.²⁰ PWD has also been shown to increase the coronary slow flow phenomenon.²¹ PWD has been reported to be significantly associated with left ventricular diastolic dysfunction.²² Tukek et al.²³ showed that a shorter minimum P wave duration was associated with PAF in patients with an increased left atrial diameter. Dilaveris et al.²⁴ reported that shorter P-wave duration was an independent predictor of extensive AF. Haşimi et al.²⁵ showed that a shorter minimum P-wave duration was an important determinant of AF in patients undergoing coronary artery bypass surgery. Altun et al.²⁶ showed that PWD was longer in patients with Syndrome X compared to the normal population. Ariyarajah et al.²⁷ showed a significant relationship between increased P-wave duration (prolonged atrial depolarization) and AF recurrence in myocardial infarction patients without ST elevation. In our study, we found an increase in PWD. This increase in PWD may be a determinant of the possible development of AF in INOCA.

The pathophysiology of AF development in INOCA patients may be quite complex. However, the following mechanisms can be speculated as the causes: first, the atrial blood supply is reduced in the coronary arteries, even at the microvascular level, and atrial reentry mechanisms are accelerated.^{28,29} Second, atrial pressure increases as a result of atrial ischemia and causes atrial changes (compression ischemia) due to stretching of the atrial walls, leading to

natriuretic peptide release.³⁰⁻³⁴ Third, inflammation occurs in the atrium with ischemia and plays an important role in the development of AF with increased inflammatory response and oxidative stress.³⁵⁻³⁹ Another one suggests that increased sympathetic activity in CAD leads to heterogeneous changes in atrial refractoriness, causing reentrant waves and having an effect on the development of AF.^{40,41}

CONCLUSION

Although our study was not a follow-up study, we observed that PWD, a technique to predict cardiac arrhythmias, was significantly longer in INOCA patients. Our results suggest that INOCA patients are at risk for AF. Identifying individuals with INOCA who are at higher risk of developing AF may facilitate early detection of AF. Therefore, we believe that the results of this study are clinically relevant.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ethical Committee of Faculty of Medicine of Erciyes University (Date:16.12.2020, Decision No: 2020-35). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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A patient with J-point elevation and AV complete block presenting with recurrent syncope attacks

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Cite this article: Sakallı S, Polat E, Dondurmacı E, Karaburan Ö. A patient with J-point elevation and AV complete block presenting with recurrent syncope attacks. *J Cardiol Cardiovasc Surg.* 2023;1(4):90-91.

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Received: 14/09/2023

Accepted: 19/11/2023

Published: 29/12/2023

Abstract

J point elevation, although mostly benign, has a spectrum that can lead to arrhythmias and can be mortal enough to cause sudden cardiac death. The arrhythmias seen in patients are frequently ventricular arrhythmias. In the literature, there are very few cases of complete atrio-ventricular block with J point elevation. Here, we present a case with J point elevation with syncope attacks and complete AV complete block.

Keywords: J point elevation, atrio-ventricular block, ventricular tachycardia

INTRODUCTION

The junction of the QRS and ST segment on the electrocardiogram (ECG) is called the J point. This region refers to the region where repolarization begins.¹ J point elevation is defined as an elevation of ≥ 0.1 mV in 2 consecutive leads on ECG.²

The association of patients with J point elevation with ventricular tachycardia and ventricular fibrillation is frequently emphasized in guidelines and case reports, and here we will discuss a case of J point elevation associated with AV complete block.

CASE

A 55-year-old man with no known medical history presents to the emergency department with an attack of syncope at work. Heart rate was 52/min, electrocardiogram showed J point elevation in D2, D3, aVF, V5, V6. Echocardiography showed normal left ventricular systolic function with no pathologic findings. Troponin value was within normal limits.

The patient was evaluated by neurology to determine the etiology of syncope and no pathology was observed. Neurologic causes were excluded and the patient was hospitalized in the intensive care unit for cardiac rhythm monitoring.

In the intensive care unit follow-up, AV complete block was observed on the monitor and atropine 1 mg was administered and sinus rhythm was provided in **Figure 1**. Since AV complete block was observed in the monitor recordings, coronary angiography was performed to exclude acute coronary occlusion in the etiology. Coronary angiography showed plaque in the coronary arteries.

Implantable cardioverter defibrillator (ICD) implantation was recommended to the patient with J point elevation on ECG and AV complete block ECG recording. The patient refused ICD implantation and was discharged voluntarily.

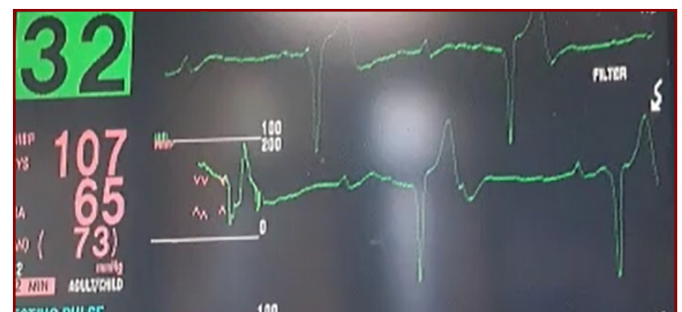


Figure 1. AV complete block on the monitor ECG

One week after discharge, the patient presented to the emergency department with a syncope attack again. The patient had a heart rate of 62/min, sinus rhythm, and J point elevation in D2, D3, aVF, V5, V6 on ECG in **Figure 2**.

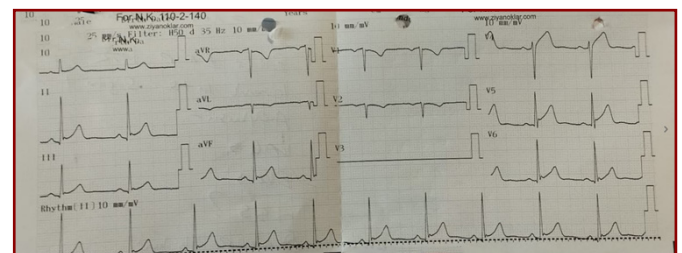


Figure 2. J point elevation in D2, D3, aVF, V5, V6 on ECG

ICD implantation was recommended instead of pacemaker implantation in the patient who had previously documented AV complete block due to the presence of J point on ECG and the knowledge that J point elevation may lead to arrhythmic events in the future. The patient accepted ICD implantation and ICD was implanted.

The patient presented to the emergency room 10 months after ICD implantation with the complaint of ICD shock. Battery analysis of the patient revealed ICD shock due to ventricular tachycardia.

DISCUSSION

J point elevation, also known as J wave syndrome or early repolarization, is a syndrome with a spectrum that may be a benign finding on ECG or may cause a mortal clinical condition such as sudden cardiac death.¹

While J point elevation is a benign condition usually seen in healthy people and athletes, studies have shown that some J point elevations can lead to ventricular arrhythmias.¹ In the studies, it has been observed that the localization lead of the elevation, morphology of elevation, and the height of the elevation may be associated with arrhythmia. The arrhythmogenicity of elevation in the inferior leads as the localization lead was observed to be higher.³ Early repolarization with slurring or notching morphology was observed to be more arrhythmic.⁴ A J-wave height >0.2 mV is also not considered benign.¹

According to the 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death, ICD implantation is recommended as class I for patients returning from cardiac arrest in J point elevation with malignant characteristics.⁵ Patients in electrical storm with isoproterenol or quinidine are recommended an ICD as Class 2a. An implantable loop recorder (ILR) as Class 2a or an ICD as Class 2b is recommended for patients with high-risk early repolarization disease or a family history of unexpected sudden death at an early age or a family history of early repolarization syndrome.⁵

Our patient was an AV complete block patient with recurrent syncope attacks and was planned to be implanted with a pacemaker if J point elevation was not seen on ECG. However, since J point elevation was seen in the inferior and lateral leads on ECG, the patient was implanted with an ICD. The fact that the patient developed ventricular tachycardia 10 months later reminds us once again that ECGs of patients who will be implanted with a pacemaker for block should be carefully examined for early repolarization syndrome.

CONCLUSION

In patients with J point elevation, we should not only focus on ventricular tachycardia and ventricular fibrillation, but we should also be careful about atrioventricular block. Likewise, in patients presenting with complete AV block, we should also look at the ECG for early repolarization before directly indicating a pacemaker, and if there is evidence of early repolarization on the ECG, we should choose a pacemaker/ICD according to the guideline algorithms.

ETHICAL DECLARATIONS

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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

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

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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