

ORIGINAL ARTICLE

Evaluation of Electrocardiographic and Echocardiographic Findings In Patients Diagnosed with Polycythemia Vera and Essential Thrombocythemia

Polistemi Vera ve Esansiyel Trombositemi Tanısı Alan Hastalarda Elektrokardiyografik ve Ekokardiyografik Bulgularının Değerlendirilmesi

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ABSTRACT

Background/Aims: Polycythemia vera (PV) and essential thrombocythemia (ET) are chronic myeloproliferative diseases that can lead to various clinical outcomes, including arterial and venous thrombosis, pulmonary hypertension, and myocardial infarction. This study was designed to assess the cardiac effects of these diseases using electrocardiography and echocardiography. **Methods:** A total of 50 patients diagnosed with PV, 50 patients diagnosed with ET, and 50 healthy individuals forming the control group were enrolled in this study. Demographic information for all subjects was collected. Electrocardiography (ECG) recordings and standard transthoracic echocardiographic examinations were conducted for all patients and control subjects. Pulse wave velocity (PWV) measurements were assessed using a Holter blood pressure device. **Results:** In total, 50 PV patients, 50 ET patients, and 50 control group were included in the study. The demographic characteristics of the PV, ET and control groups were similar. The PR interval was significantly shorter in control subjects than in PV and ET patients ($p = 0.007$, $p = 0.024$). Although the measured values were within normal limits, diastolic posterior wall thickness was significantly lower in the control group compared to PV and ET patients ($p = 0.019$, $p = 0.009$). PWV was significantly higher in ET patients compared to the control group ($p = 0.012$). **Conclusion:** ECG parameters used to predict ventricular arrhythmias (QT, QTc, Tp-Te, Tp-Te/QT) and Pulmonary Artery Pressure showed no significant change, in opposition to existing literature. Nonetheless, similar to previous publications, PV and ET were found to negatively affect the diastolic function parameters on transthoracic echocardiography. While the aortic stiffness was significantly higher in ET patients compared to the control group, no significant difference was noted between PV patients and control subjects in terms of aortic stiffness.

Keywords: Echocardiography, Electrocardiography, Essential thrombocythemia, Polycythemia vera, Pulse Wave Velocity

Öz

Amaç: Polisitemi vera (PV) ve Esansiyel trombositemi (ET) kronik myeloproliferatif hastalıklardır. Myeloproliferatif seride artışla beraber arterial ve venöz trombozlar, pulmoner hipertansiyon, miyokard infarktüsü gibi çeşitli klinik sonuçlar oluşturabilmektedirler. Çalışmamızda bu hastalıkların kalp üzerine etkilerini elektrokardiyografi ve ekokardiyografi ile değerlendirme amaçlanmıştır.

Gereç ve Yöntem: Çalışmamıza PV tanılı 50 hasta ET tanılı 50 hasta ve kontrol grubu olarak sağlıklı 50 kişi alındı. Hasta demografik bilgilerine ilişkin veriler tüm deneklerde kaydedildi. Tüm hastalara ve kontrol grubuna elektrokardiyografi (EKG) kayıtları ve rutin transtorasik ekokardiyografik incelemeler yapıldı. Nabız dalga hızı (PWV), bir Holter kan basıncı cihazı ile değerlendirildi.

Bulgular: Çalışmaya toplam 50 PV hastası, 50 ET hastası ve 50 kontrol grubu dahil edildi. PV, ET ve kontrol gruplarının demografik özellikleri benzerdi. PR aralığı, kontrol olgularında PV ve ET hastalarına göre anlamlı olarak daha kısaydı ($p = 0.007$, $p = 0.024$). Ölçülen değerler normal sınırlarda olmasına rağmen kontrol grubunda diyastolik arka duvar kalınlığı PV ve ET hastalarına göre anlamlı olarak düşüktü ($p = 0.019$, $p = 0.009$). PWV, ET hastalarında kontrol grubuna göre anlamlı olarak yüksekti ($p = 0.012$).

Sonuç: Ventriküler aritmileri öngörmek için kullanılan EKG parametreleri (QT, QTc, Tp-Te, Tp-Te/QT) ve Pulmoner Arter Basıncı mevcut literatürün aksine anlamlı bir değişiklik göstermedi. Bununla birlikte, önceki yayınlara benzer şekilde, transtorasik ekokardiyografide PV ve ET'nin diyastolik fonksiyon parametrelerini olumsuz etkilediği bulundu. Aort sertliği ET hastalarında kontrol grubuna göre anlamlı olarak yüksek bulunurken, PV hastaları ile kontrol grubu arasında aort sertliği açısından anlamlı fark saptanmadı.

Anahtar Kelimeler: Ekokardiyografi, Elektrokardiyografi, Esansiyel trombositemi, Polisitemi vera, Pulse Wave Velosite

Introduction

Polycythemia vera (PV) is a chronic, clonal and progressive myeloproliferative disease characterized generally by leukocytosis, thrombocytosis and splenomegaly along with an increase in the erythroid cell line (1). Clinical symptoms appear as a result of increase in the erythrocyte volume. There is

an increased risk of bleeding and thrombosis in PV disease. Thrombosis is the most common complication and the leading cause of morbidity and mortality in PV (2,3). Thrombotic events of both arterial and venous circulation are notably prevalent. In addition, arterial ischemic complications, including myocardial

infarction (MI) have been suggested to be strongly correlated to the cardiovascular risk factors in patients with PV (4). Patients with PV are at increased risk of thrombosis (i.e., cerebrovascular event, MI, superficial thrombophlebitis, deep vein thrombosis, pulmonary embolism) and bleeding. In a large international study with PV patients as defined by the World Health Organization (WHO), 16% of patients were reported to have arterial thrombotic complications before or at the time of diagnosis while 7% of patients had venous thrombosis and 4% of patients had major bleeding (5). Emergence of pulmonary hypertension as a prominent complication shortening the survival time of patients, relates to vascular smooth muscle hyperplasia caused by growth factors released from activated platelets, and obstructions caused by megakaryocytes within the pulmonary circulation (6).

Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasia characterized by the continuous proliferation of megakaryocytes, resulting in increased circulatory platelet counts. The initial presentation involves megakaryocytic bone marrow hyperplasia, splenomegaly and thrombotic or hemorrhagic clinical findings. ET is characterized by microvascular symptoms and an increased risk of thrombohemorrhagic events (7). Although thrombotic complications are common, coronary artery occlusion and MI are rarely encountered. Most of the patients are asymptomatic at the time of diagnosis. In symptomatic patients, vasomotor symptoms appear as a cause of microvascular dysfunction, which may present as headache, dizziness, syncope, atypical chest pain, acral paresthesia, livedo reticularis, erythromelalgia and transient visual disturbances (8). Microvascular complications cause discomfort but are not life-threatening. Nevertheless, this assertion does not hold for thrombotic complications. In a prospective study, thrombotic complications were demonstrated to be the primary factor contributing to mortality and morbidity in 24% of ET patients who did not receive treatment for more than 27 months (9). Although thrombotic events usually affect the microvascular structure, larger venous thromboses such as stroke, transient ischemic attack, retinal vascular occlusions, pulmonary embolism, coronary artery ischemia, portal vein thrombosis and deep vein thrombosis may also occur (10,11). Hemorrhagic events are less commonly encountered than the thrombotic complications while the gastrointestinal tract is the major bleeding site. Minor skin and mucosal hemorrhages as well as the central nervous system hemorrhages may also occur.

Existing literature indicates that both PV and ET have unfavorable effects on the cardiovascular system. In this study, our primary objective was to assess the impact of these medical conditions on cardiac function utilizing electrocardiography and echocardiography methodologies.

Materials and Methods

A total of 100 hematology outpatients who were under routine follow-up with the diagnoses of PV (n=50) or ET (n=50), in accordance with the WHO diagnostic criteria, were included. Informed consent was obtained from all patients. This prospective study was conducted between May 11, 2021 and April 30, 2021 at hematology outpatient clinics of Necmettin Erbakan University, Meram Faculty of Medicine. A total of 50 healthy volunteers admitted to cardiology outpatient clinics of Meram Medical Faculty Hospital of Necmettin Erbakan University with various symptoms but had no abnormality on physical examination and laboratory findings constituted the control group.

Data on patient demographics (age, gender), height, weight, waist circumference, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded in each patient. All patients had 12-lead electrocardiography (ECG) recordings and routine transthoracic echocardiographic examinations. Pulse wave velocity (PWV) was evaluated with a Holter blood pressure device (24/h PWA monitor). The inclusion criteria were defined as having PV and ET diagnosis according to the WHO criteria, giving consent for the study, having an EF \geq 50 and presence of normal sinus rhythm. Patients younger than 18 years of age, pregnant women, patients with EF < 50, and those with a history of known cardiovascular disease, secondary polycythemia, and reactive thrombocytosis were excluded from the study.

Electrocardiographic Evaluation

The 12-lead ECG recordings were made in the supine position, after 5 minutes of rest by using a "Nihon Kohden, Tokyo" device at a paper speed of 25 mm/sec. An ECG with at least 10 analyzable leads was considered suitable for evaluation. Heart rate (beats/min), maximum P wave duration (ms), minimum P wave duration (ms), PR interval (ms), RR interval (ms), QRS duration (ms), QT interval (ms), corrected QT interval (ms), Tp-e interval (ms), cardiac electrophysiological balance index (ICEB) and Tp-e/QT were the parameters analyzed.

Echocardiographic Evaluation

All echocardiographic examinations were performed in the left lateral decubitus position using the Philips Epiq 7 device (Philips Healthcare Systems, USA) by a cardiologists blinded to clinical status of the patients. Echocardiographic examinations were performed in accordance with the criteria of the American Society of Echocardiography; parasternal long axis, short axis, apical 4-chamber and 2-chamber images were examined using M-mode, continuous wave (CW), pulse wave (PW) Doppler and tissue Doppler examinations.

Assessment of Aortic Stiffness

The measurement of pulse wave velocity (PWV), as an indirect indicator of aortic stiffness, was performed by using Mobil-O-Graph PWA monitor device (Stolberg/Germany) present in the cardiology clinic. In each patient, three separate measurements were performed using an appropriately sized upper arm cuff device and after a resting period for at least 5 minutes. The average of three measurements obtained from device recordings was considered the final PWV.

Statistical analysis

Statistical analysis was made using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY). Kolmogorov-Smirnov test was used for distribution analysis of continuous numerical variables. As descriptive variables, mean \pm standard deviation (SD) was used for data with normal distribution, and median (min-max) was used for the non-normally distributed data. Inter-group comparisons were performed by using one-way analysis of variance (ANOVA) for normally distributed variables. Post-hoc analysis was made using Tukey (for homogeneous variances) and Tamhane's T2 (for non-homogeneous variances) tests. Kruskal Wallis test was used for analysis of non-normally distributed variables with use of Bonferroni corrected Mann-Whitney U test for pairwise comparisons. Categorical variables were expressed as percentages (%). $p < 0.05$ was considered statistically significant.

Results

The median (min-max) age of subjects was 57 (18 - 75) years in the PV group (n=50, 35 males,), 56.5 (20 - 78) years in the ET group (n = 50, 17 males) and 51 (32 - 70) years in the control group (n = 50, 21 males). The demographic characteristics and vital signs in PV, ET and control groups are shown in Table 1. No significant difference was noted between PV, ET and control groups in terms of age, weight, heart rate, SBP, DBP and MAP.

Table 1. Demographic Characteristics and Vital signs

	PV	ET	Control Group	p
Age (year)	57 (18 - 75)	56.50 (20 - 78)	51 (32-70)	0.164
Height (cm)	170 (148-187)	165 (141-181)	165(151-183)	0.024 ^a
Weight (kg)	81.60 \pm 13.9	77.34 \pm 14.69	78.14 \pm 12.52	0.261
Waist Circumference (cm)	104.22 \pm 11.94	101.26 \pm 13.23	96.94 \pm 10.55	0.011 ^b
Pulse (beats/min)	86.22 \pm 12.45	81.68 \pm 12.71	81.08 \pm 11.98	0.080
Systolic Blood Pressure (mmHg)	132(101-213)	131(92-191)	125(99-165)	0.942
Diastolic Blood Pressure (mmHg)	86.64 \pm 13.78	86.04 \pm 13.63	84.50 \pm 11.39	0.697
Mean Arterial Pressure (mmHg)	107.70 \pm 15.96	108.50 \pm 15.69	104.18 \pm 11.08	0.284

a Kruskal Wallis Test

b One-way analysis of variance (ANOVA)

Electrocardiographic Parameters: There was no significant difference between PV, ET and control groups in terms of electrocardiographic parameters including QRS, QT, QTc, P max and QT/QRS. Although the three groups showed significant differences in other electrocardiographic parameters, the values in each group were within the normal limits. Heart rate was significantly higher in the PV group than in the control group ($p = 0.003$). The PR interval was significantly shorter in the control group than in PV and ET patients ($p = 0.007$ and $p = 0.024$, respectively). The RR interval was significantly shorter in the PV group compared to ET and control groups ($p = 0.025$ and $p < 0.001$, respectively). QT - V6 was significantly higher in the control group compared to PV patients ($p < 0.001$). QT-V1 was significantly lower in the PV group compared with ET and control groups ($p = 0.007$ and $p = 0.001$, respectively). Pmin was significantly lower in PV patients compared to ET patients and the control group ($p = 0.015$ and $p = 0.002$, respectively). The control group had significantly higher Tp-Te ($p = 0.001$ and $p < 0.001$, respectively) and Tp-Te/QT ($p = 0.023$ and $p < 0.001$, respectively) than the PV and ET patients. Electrocardiographic parameters of the study groups are shown in Table 2.

Table 2. Electrocardiographic Parameters

	PV	ET	Control Group	p
Heart rate (bpm)	80.46 \pm 13.64	76.08 \pm 11.60	72.42 \pm 10.58	0.004 ^a
PR interval (ms)	159(118-204)	160(112-200)	145(100-200)	0.016 ^b
RR interval (ms)	734(440-1000)	790(520-1100)	840(600-1080)	0.001 ^b
QRS (ms)	90(68-142)	90(64-134)	100(80-120)	0.248
QT (ms)	369.64 \pm 28.21	380.04 \pm 29.38	382.58 \pm 28.07	0.059
QTc (ms)	423.4(391.3-504.2)	420.5(366.6-519)	419.8(350.7-475)	0.423
QT-V1 (ms)	360(280-444)	380(300-480)	380(320-440)	0.002 ^b
QT-V6 (ms)	360(280-440)	360(320-460)	380(300-460)	0.002 ^b
P max (ms)	110(80-140)	100(80-130)	120(80-140)	0.347
P min (ms)	62.5(40-86)	75(60-90)	80(60-90)	0.004 ^b
Tp-Te (ms)	84(60-120)	80(60-140)	100(60-140)	<0.001 ^b
Tp-Te/QT	0.239 \pm 0.048	0.224 \pm 0.50	0.266 \pm 0.049	<0.001 ^a
QT/QRS	4.04 \pm 0.54	4.24 \pm 0.57	4.08 \pm 0.61	0.180

a One-way analysis of variance (ANOVA),

b Kruskal Wallis Test

Echocardiographic and Aortic Stiffness Parameters

The comparison of the echocardiographic and aortic stiffness parameters of the PV, ET and control groups showed no significant difference in LA diameter, LV end-systolic diameter, LV end-diastolic diameter, LV-EF, IVS thickness, aortic velocity, systolic PAP, Lateral S, Lateral A, Septal E, Septal A, RV E, TAPSE and MAPSE parameters (Table 3).

Table 3. Echocardiographic and Aortic Stiffness Parameters

	PV	ET	Control Group	P
LA diameter (cm)	3.5(2.2-4.7)	3.2(2.2-4.5)	3.5(2.5-3.9)	0.099
LV end-systolic diameter (cm)	2.5(1.5-3.9)	2.5(1.8-3.5)	2.5(2-3.3)	0.232
LV end-diastolic diameter (cm)	4.6(3.5-5.4)	4.5(4-5.3)	4.5(4-5)	0.450
LV-EF (%)	61.49±1.24	61.50±1.01	61.91±1.27	0.132
IVS thickness (mm) (Diastolic)	1(0.8-1.5)	1.1(0.9-1.5)	1(0.9-1.5)	0.291
Posterior Wall thickness (mm) (Diastolic)	1(0.8-1.3)	1(0.9-1.4)	0.9(0.9-1.2)	0.017 ^a
Mitral E wave velocity (cm/s)	60(45-110)	70(40-116)	80(50-132)	0.019 ^a
Mitral A wave velocity (cm/s)	81.54±19.04	78.76±19.85	70.74±18.44	0.015 ^b
Aortic diameter (cm)	2.6(2.2-3.3)	2.5(2-3.4)	2.7(2-3.3)	0.011 ^a
Aortic velocity (cm/s)	138.5(100-190)	131.5(100-200)	129(95-165)	0.840
Pulmonary velocity (cm/s)	85(65-125)	93(60-140)	80(70-120)	0.012 ^a
Systolic PAB (mmHg)	27(23-42)	27.5(22-41)	27(22-40)	0.864
Lateral S (cm/s)	10(5-16.8)	10(6-14.7)	9.65(5-17)	0.564
Lateral E (cm/s)	8.45(4-16)	9.5(5-18)	11(5-18)	0.001 ^a
Lateral A (cm/s)	11(5-18)	12(6-16)	10.1(5-17)	0.082
Septal S (cm/s)	9(5-14)	9(4-14)	8(6-16)	0.011 ^a
Septal E (cm/s)	8(5-18)	8.6(4-17)	8.7(5-14)	0.395
Septal A (cm/s)	11.25(5-15)	10(7-18)	10(6-18)	0.712
RV S (cm/s)	14(9.4-24)	14(8-21)	12.9(10-20)	<0.001 ^a
RV E (cm/s)	11(6-18.2)	12(7.5-19)	11(6-22)	0.278
RV A (cm/s)	17(8-30)	16(7.2-24)	15(7-35)	0.027 ^a
TAPSE (cm)	2.25(1.8-3.3)	2.25(1.6-3)	2.3(1.9-3)	0.075
MAPSE (cm)	1.6(1.2-2.1)	1.7(1.3-2.2)	1.7(1.3-2.5)	0.107
PWV (m/s)	8.22±1.82	8.59±1.94	7.64±1.15	0.019 ^b

^a Kruskal Wallis Test

^b One-way analysis of variance (ANOVA)

Although the measured values were within normal limits, diastolic posterior wall thickness was significantly lower in the control group compared to PV and ET patients ($p=0.019$ and $p=0.009$, respectively). Mitral E wave velocity was significantly higher in the control group compared to PV patients ($p=0.005$). Mitral A wave velocity was higher in PV patients than the control group ($p<0.001$). Aortic diameter was significantly higher in the control group compared to ET patients ($p=0.003$). Also, pulmonary velocity was significantly lower in the control group compared to ET patients ($p=0.003$). Lateral E was significantly lower in PV patients compared to ET patients and the control group ($p=0.017$ and $p<0.001$, respectively). In the control group, both septal S ($p=0.018$ and $p=0.007$, respectively) and RV S ($p<0.001$ and $p=0.001$, respectively) values were significantly lower than the values recorded in the PV and ET groups. RV A was significantly lower in the control group than in the PV group ($p=0.008$).

PWV was significantly higher in ET patients compared to the control group ($p=0.012$). Echocardiographic and aortic stiffness parameters are shown in Table 3.

Discussion

In previous studies, increase in blood viscosity was considered likely to be associated with increased cardiovascular mortality and morbidity. In a study by Skretteberg et al., elevated hematocrit levels were reported as an independent risk factor for increased long-term cardiovascular mortality in males with a high erythrocyte sedimentation rate (12). Similarly, Cho et al. demonstrated that increases in blood viscosity led to microvascular dysfunction (13). In addition, Çetin et al. reported that high blood viscosity was associated with worse coronary collateral circulation development in patients with chronic total occlusion of coronary artery (14). The increased viscosity not only contributes to increased cardiovascular mortality and morbidity but is also known to play a role in the pathogenesis, progression, and prognosis of various life-threatening disorders such as stroke, transient ischemic attack, diabetes mellitus, and renal problems. (15). Also, in a study by Caimi et al., hyperviscosity was reported to be associated with atrial fibrillation (16).

Following the evidence regarding the relation of the deterioration in blood rheology with the diseases such as cardiovascular diseases, hypertension and dyslipidemia, the underlying causes have been investigated. The increase in blood viscosity caused by the increase in hematocrit levels is considered likely to affect the tissue oxygenation directly. Increased erythrocyte count would facilitate platelet adhesion and cause endothelial accumulation, thereby increasing the risk of thrombotic complications (17). Besides, high hematocrit accelerates atherosclerosis by increasing serum lipid levels resulting in accumulation of plasma proteins and platelets in subendothelial tissue (12).

Bleeding and predisposition to thrombosis, the most important causes of mortality and morbidity in myeloproliferative diseases, can be seen in approximately 50% of PV and ET patients (18,19). Thrombotic complications of both arterial and venous systems are likely to occur in these patients (20). In fact, thrombotic complications were reported to develop more commonly in PV patients than in ET patients while the hyperviscosity caused by increased erythrocyte count was considered more important than the platelet count in the development of thrombotic complications (21). Other studies investigating the pathophysiology of hypercoagulability and predisposition to thrombosis, which are common in myeloproliferative diseases, have also revealed that chronic endothelial damage, blood hyperviscosity, platelet activation and hypoxemia are the underlying mechanisms of thrombotic complications (22,23).

Prolonged myocardial repolarization duration is an important indicator of susceptibility to ventricular arrhythmias and can be assessed on electrocardiography using the calculations for QT, QTc, QT dispersion parameters (24). In addition, Tp-Te, which shows the time from the peak to the end of the T wave, is a unique parameter that shows the ventricular transmural repo-

larization distribution (25,26). Moreover, Tp-Te has been shown to be associated with cardiovascular mortality independent of QT and QTc (26). Tp-Te/QT is a similar parameter that can be used to predict ventricular arrhythmias (27). The duration of the P wave, which shows atrial depolarization in electrocardiography, also provides clinically significant information about the susceptibility to atrial arrhythmias (especially atrial fibrillation) (28). There are various studies in the literature examining the electrocardiographic changes in myeloproliferative diseases. In a study by Kayrak et al., P wave measurements and ventricular repolarization parameters (QT, QTc, Tp-Te, Tp-Te/QT) were significantly higher in PV patients compared to age- and gender-matched healthy controls, possibly increasing the predisposition to atrial and ventricular arrhythmias (29). In another study, Krishnamoorthy et al. showed that the frequency of atrial fibrillation was significantly higher in PV patients than in the general population (30). There is no study in the literature showing the effect of ET on electrocardiography. In our study, we aimed to examine the effect of PV and ET on electrocardiography and echocardiography parameters. In our study, QT and QTc were not found statistically different from the control group in PV and ET patients whereas Tp-Te, Tp-Te/QT, Pmin values were significantly lower than the control group, contrary to the existing literature. The differences between our findings and those from previous studies may be explained by the fact that patients with cardiovascular disease risk factors (i.e., diabetes mellitus, smoking history, family history, silent ischemia), which may adversely affect the microvascular circulation and alter myocardial electrical activity, were not excluded from the study, and the relatively small sample size of the present study.

Assessment of the change in echocardiographic parameters in myeloproliferative diseases was another important consideration in the current study. As a result of our study, the mitral E wave was found significantly lower in the PV group compared to the control group, while the mitral A wave was significantly higher than the control group. The mitral E wave, which was formed just after the mitral valve opening in the early diastole phase by the free flow of blood accumulated in the left atrium through the mitral valve, begins to decrease gradually in diastolic dysfunction where the compliance of the left ventricle decreases. In the last stage of diastole, the mitral A wave, which is formed by left atrial contraction, increases relatively. In the present study, tissue Doppler parameters related to diastolic functions (lateral E, septal S, and RV S) differed significantly between control and patient (PV and ET) groups, in accordance with the diastolic dysfunction in the latter. In this regard, our findings seem to indicate the likelihood of PV patients to develop predisposition to left ventricular diastolic dysfunction notably. In a study by Osama et al. hyperviscosity caused by PV and ET was reported to affect the left ventricular diastolic functions negatively (31). In another study, Kayrak et al. evaluated left and right ventricular performances in PV patients using the tissue Doppler

method and found that RV A was significantly higher in PV patients compared to the control group (32). Similarly, in our study, RV A was significantly higher in the PV group than in the control group.

In our study, the effect of myeloproliferative diseases on aortic stiffness was also examined. The increase in aortic stiffness, which is a characteristic finding of aging, is directly related to classical cardiovascular disease risk factors (33). Vlachopoulos et al. showed that aortic stiffness is an independent predictor of vascular diseases mortality and morbidity (34). There is no study in the literature showing the relation between aortic stiffness and PV and ET. In our study, aortic stiffness was found significantly higher in ET patients compared to the control group while no significant difference was found between PV patients and the control group.

In conclusion, our findings related to the effects of myeloproliferative diseases PV and ET on electrocardiography and transthoracic echocardiography, ECG parameters used to predict ventricular arrhythmias (QT, QTc, Tp-Te, Tp-Te/QT) and PAP were not significant in opposition to the existing literature. Similar to previous publications, PV and ET were determined to have adverse effects on diastolic function parameters in transthoracic echocardiography. While aortic stiffness was significantly higher in ET patients compared to the control group, no difference was found in PV patients compared to the control group. Our findings regarding the unfavorable effects of myeloproliferative diseases on the cardiovascular system need to be justified by further larger scale prospective randomized studies.

Conflict of Interest

The authors declare that there are no relevant financial or non-financial competing interests to report.

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None.

Author Contributions

Bahattin Engin Kaya: Materials, Writing article, Design, Literature Review, Critical review, Sinan Demircioğlu: Supervision, Writing article, Design, Literature Review Critical review. Atakan Tekinalp: Analysis, Ahmet Lütfi Sertdemir: Conception. Mustafa Çağrı Ergün: Writing article, Design, data collection and/or processing. Ali Kürşat Tuna: Data collection and/or processing. Şerif Ahmet Kandemir: Data collection and/or processing, Abdullah İçli: Analysis and/or interpretation, control/supervision. Özcan Çeneli: Critical review. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that there are no relevant financial or non-financial competing interests to report.

Informed consent

Informed consent was obtained from all individual participants included in the study.

This prospective study was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and in full accordance with local Good Clinical Practice, and approved by the Necmettin Erbakan University Meram Faculty of Medicine Ethics Committee (Date of Approval: 08/05/2020; Reference number/Protocol No: 2020/2498).

References

- Spivak JL, Barosi G, Tognoni G, Barbui T, Finazzi G, Marchioli R, et al. Chronic myeloproliferative disorders. Hematology / the Education Program of the American Society of Hematology. American Society of Hematology. Education Program. 2003.
- Demircioglu S, Budancamanak S, Dogan A. Can Serum B12 Level Be Used As An Effective Differential Criterion in Differential Diagnosis of Primary and Secondary Polycythemia. Selçuk Tıp Dergisi. 2020 Mar 1;1(36):22-6.
- Gökgöz Z, Özdemirkıran F, Cömert M, Saydam G. Kronik Miyeloproliferatif Neoplazi Tanılı 114 Hastanın İncelemesi. Selçuk Tıp Dergisi. 2014;30(4):169-71.
- Watson K V., Key N. Vascular complications of essential thrombocythemia: a link to cardiovascular risk factors. Br J Haematol. 1993;198-203.
- Tefferi A, Rumi E, Finazzi G, Gisslinger H, Vannucchi AM, Rodeghiero F, et al. Survival and prognosis among 1545 patients with contemporary polycythemia vera: An international study. Leukemia. 2013;
- Vianello F, Battisti A, Cella G, Marchetti M, Falanga A. Defining the thrombotic risk in patients with myeloproliferative neoplasms. TheScientificWorldJournal. 2011.
- Elliott MA, Tefferi A. Thrombosis and haemorrhage in polycythemia vera and essential thrombocythemia. British Journal of Haematology. 2005. p. 275-90.
- Besses C, Cervantes F, Pereira A, Florensa L, Solé F, Hernández-Boluda JC, et al. Major vascular complications in essential thrombocythemia: A study of the predictive factors in a series of 148 patients. Leukemia. 1999;
- Cortelazzo S, Finazzi G, Ruggeri M, Vestri O, Galli M, Rodeghiero F, et al. Hydroxyurea for Patients with Essential Thrombocythemia and a High Risk of Thrombosis. New England Journal of Medicine. 1995;
- Gao W, Shen W, Luo X, Shi H, Jiang X, Pan J. ST-segment elevation myocardial infarction in patient with essential thrombocythemia without associated risk. Int J Cardiol. 2015;
- Barbui T, Finazzi G, De Gaetano G, Marchioli R, Tognoni G, Patrono C, et al. Polycythemia vera: The natural history of 1213 patients followed for 20 years. Ann Intern Med. 1995;
- Skretteberg PT, Bodegård J, Kjeldsen SE, Erikssen G, Thaulow E, Sandvik L, et al. Interaction between inflammation and blood viscosity predicts cardiovascular mortality. Scandinavian Cardiovascular Journal. 2010;
- Cho Y II, Cho DJ. Hemorheology and microvascular disorders. Korean Circulation Journal. 2011.
- Cetin MS, Cetin EHO, Balci KG, Aydin S, Ediboglu E, Bayraktar MF, et al. The association between whole blood viscosity and coronary collateral circulation in patients with chronic total occlusion. Korean Circ J. 2016;
- Li RY, Cao ZG, Li Y, Wang RT. Increased whole blood viscosity is associated with silent cerebral infarction. Clin Hemorheol Microcirc. 2015;
- Caimi G, Messina L, Alfano R, Canincir B, Fabbiano A, Cammarata AM, et al. Haemorheological profile in subjects with nonvalvular atrial fibrillation. Clin Hemorheol Microcirc. 1999;
- Naghedi-Baghdar H, Nazari SM, Taghipour A, Nematy M, Shokri S, Mehri MR, et al. Effect of diet on blood viscosity in healthy humans: a systematic review. Electron Physician. 2018;
- Schafer AI. Bleeding and thrombosis in the myeloproliferative disorders. Blood. 1984.
- Bellucci S, Janvier M, Tobelem G, Flandrin G, Charpak Y, Berger R, et al. Essential thrombocythemia. Clinical evolutionary and biological data. Cancer. 1986;
- Hoffman R SM. Hematology: Basic Principles and Practice. Ann Intern Med. 1991;
- Rossi C, Randi ML, Zerbinati P, Rinaldi V, Girolami A. Acute coronary disease in essential thrombocythemia and polycythemia vera. J Intern Med. 1998;
- Arellano-Rodrigo E, Alvarez-Larrán A, Reverter JC, Villamor N, Colomer D, Cervantes F. Increased platelet and leukocyte activation as contributing mechanisms for thrombosis in essential thrombocythemia and correlation with the JAK2 mutational status. Haematologica. 2006;
- Falanga A, Marchetti M, Vignoli A, Balducci D, Barbui T. Leukocyte-platelet interaction in patients with essential thrombocythemia and polycythemia vera. Exp Hematol. 2005;
- Antzelevitch C. Heterogeneity and cardiac arrhythmias: An overview. Heart Rhythm. 2007;
- Okutucu S, Karakulak UN, Aksoy H, Sabanoglu C, Hekimsoy V, Sahiner L, et al. Prolonged Tp-e interval and Tp-e/QT correlates well with modified Rodnan skin severity score in patients with systemic sclerosis. Cardiol J. 2016;
- Yan GX, Martin J. Electrocardiographic T wave: A symbol of transmural dispersion of repolarization in the ventricles. Journal of Cardiovascular Electrophysiology. 2003.
- Gupta P, Patel C, Patel H, Narayanaswamy S, Malhotra B, Green JT, et al. Tp-e/QT ratio as an index of arrhythmogenesis. J Electrocardiol. 2008;
- Dilaveris PE, Gialafos EJ, Sideris SK, Theopistou AM, Andrikopoulos GK, Kyriakidis M, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J. 1998;
- Kayrak M, Acar K, Gul EE, Abdulhalikov T, Bağlıcaklıoğlu M, Sonmez O, et al. Electrocardiographic findings in patients with polycythemia vera. Int J Med Sci. 2011;
- Krishnamoorthy P, Kalla A, Gopalakrishnan A, Mittal V, Garg J, Patel NC, et al. Polycythemia vera is associated with increased atrial fibrillation compared to the general population: Results from the national inpatient sample database. Circulation. 2016;
- Ibrahim, Osama A, Muhamad R. Abdel Hameed MMF. Diastolic Dysfunction in Patients with Myeloproliferative Neoplasms. The Journal of the Egyptian Society of Haematology & Research. 2014;10(1).
- Kayrak M, Acar K, Gul EE, Bağlıcaklıoğlu M, Kaya Z, Sonmez O, et al. Assessment of left ventricular myocardial performance by tissue doppler echocardiography in patients with polycythemia vera. Echocardiography. 2011;
- Sethi S, Rivera O, Oliveros R, Chilton R. Aortic stiffness: Pathophysiology, clinical implications, and approach to treatment. Integrated Blood Pressure Control. 2014.
- Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of Cardiovascular Events and All-Cause Mortality With Arterial Stiffness. A Systematic Review and Meta-Analysis. J Am Coll Cardiol. 2010;