International Journal of Cardiology 226 (2017) 34–37

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

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Reduced left ventricular strain is related to blood parameters in patients with polycythemia vera

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ARTICLE INFO

Article history:
Received 17 August 2016
Received in revised form 15 October 2016
Accepted 17 October 2016
Available online 18 October 2016

Keywords:
Polycythemia vera
Echocardiography
Global strain
Systolic function

Polycythemia vera (PV) is a chronic myeloproliferative neoplasm primarily characterized by erythrocytosis and often leukocytosis and/or thrombocytosis [1]. Thrombotic events are a major complication of the disease, accounting for 45% of all deaths [2]. In addition, a strong relationship has been observed between arterial ischemic complications and PV [3]. The high frequency of cardiovascular events in PV patients might not only be directly related to increased haematocrit values but also to elevated blood pressure and development of target organ damage [3,4]. In particular, assessment of the left ventricular (LV) morphology and function may uncover other mechanisms involved in the deleterious effect of PV on the cardiovascular system. However, data depicting this relationship is limited [5,6].

Therefore the aim of this study was to assess LV morphology and function in patients with PV including the evaluation of systolic function by global longitudinal, circumferential and radial strains (GLS, GCS and GRS, respectively) with the use of a new method – speckle tracking echocardiography (STE) – in relation to blood parameters.

Twenty-three consecutive patients with newly diagnosed PV and 23 age, gender and blood pressure values-matched control subjects were enrolled to our on-going study evaluating impact of PV on echocardiographic parameters. The diagnosis of PV was made according to World Health Organization (WHO) criteria [7]. At the time of the study none of the patients received therapy for PV (neither pharmacologic treatment nor phlebotomy). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. It was approved by the local Research Ethics Committee. Written informed consent was also obtained from each patient.

BP was measured in the sitting position after a 5 min rest. Ambulatory blood pressure monitoring (ABPM) was recorded using SpaceLabs 90207 or 90217 (Redmond, Washington, USA). Average 24-h systolic blood pressure (SBP), diastolic blood pressure (DBP) and average 24-h heart rate (HR) were analysed.

Transthoracic echocardiographic examination was performed using Vivid 7 (GE Medical System) with a 2.5 MHz transducer. Echocardiographic parameters were obtained from the average of three consecutive cardiac cycles. Left ventricular end-systolic and end-diastolic diameters, as well as interventricular septal and posterior wall thicknesses were measured according to the American Society of Echocardiography recommendations using the M-mode technique [8]. Left ventricular mass (LVM) was calculated using the formula proposed by Devereux. Left ventricular mass index (LVMI) was obtained by normalizing LVM to body surface area (BSA). LV systolic function was evaluated by ejection fraction (LVEF) using biplane Simpson's formula [8]. Systolic lateral and septal velocity (S′) was measured using tissue Doppler imaging. The complete analysis of the LV systolic function was assessed by speckle tracking echocardiography (STE). The global longitudinal (GLS), circumferential (GCS) and radial (GRS) strains were evaluated (frame rates ≥ 70 s^{-1}) using the 2D strain software. GLS was the average of the 17 segments from the apical views. (Fig. 1). GCS and GRS were the average of the 6 segments from the short-axis view (Fig. 2). Diastolic function was measured. Mitral inflow velocities were measured from the apical four-chamber view with the sample volume placed at the mitral valve leaflet tips. The transmitral early diastolic (E-wave) and atrial (A-wave) velocities were measured and the E/A ratio was calculated.

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http://dx.doi.org/10.1016/j.ijcard.2016.10.048
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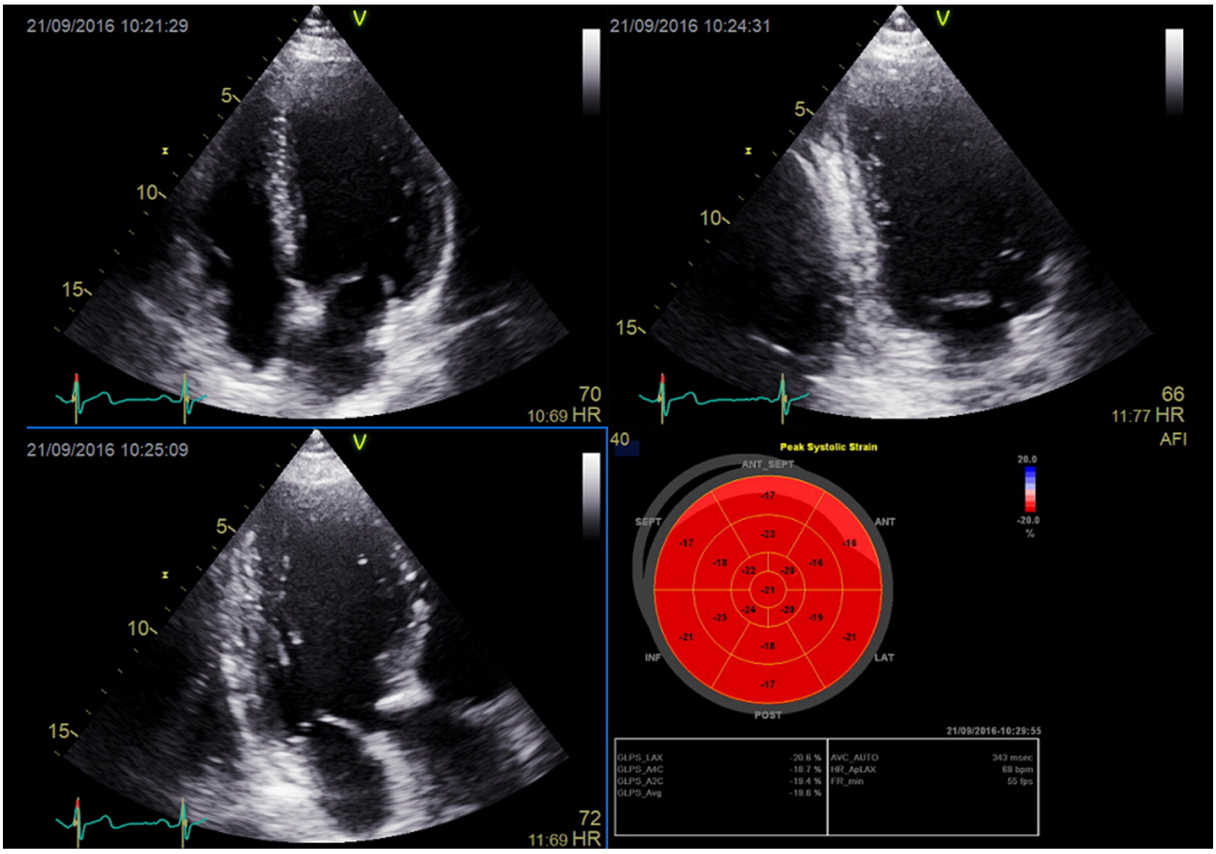

Fig. 1. Measurement of global longitudinal strain from 17 segments from the apical views using the speckle tracking echocardiography method.

Isovolumic relaxation time (IVRT) and deceleration time of the E velocity (DT) were obtained. Myocardial velocities were measured from the septal and lateral mitral annulus. The early diastolic velocity (E′) was measured and the E/E′ ratio was calculated.

All data was expressed as the mean ± standard deviation and frequency as a percentage. Differences between the parametric variables of the two groups were assessed by Student's *t*-test. The linear association between parametric variables was assessed by Pearson's correlation analysis and partial correlation allowing controlling for the effects of additional variables analysis. All statistical analyses were performed with the commercially available computer software PASW Statistics 18 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

All 23 patients with PV (10 F, 13 M; mean age 61.8 ± 8.4 years) [PV group] and 23 control subjects (10 F, 13 M, mean age 60.7 ± 5.0) [control group] were analysed. Acquired mutations in JAK2V617F were found in 22 patients with PV. The baseline characteristics of the PV and control groups are shown in Table 1. There were no significant differences in age, gender, BMI, and blood pressure between analysed groups, however, known duration of hypertension was shorter in the PV group. There were no differences in the number of antihypertensive drugs between analysed groups. Haemoglobin (Hb) and haematocrit (Hct) were significantly higher in the PV group compared to the control group.

Data of the echocardiographic study was presented in Table 2. There were no differences in LVMI between analysed groups and in systolic function assessed by EF. However, GLS, GCS and GRS were significantly lower in the PV group compared to the control group. Out of the parameters describing diastolic function only IVRT was significantly longer in the PV group. The difference in IVRT between patients with PV and controls remained significant when adjusted for blood pressure levels and heart rate. GLS significantly correlated with Hb ($\beta = -0.488$, $p < 0.0001$) and Hct ($\beta = 0.408$, $p = 0.001$). GCS significantly correlated with Hb ($\beta = -0.537$, $p = 0.005$). These correlations remained significant after correcting for age and BP levels. There were no correlations between GLS, GCS, GRS, IVRT and 24-h SBP, DBP, and 24-h HR. IVRT correlated with RBC ($\beta = -0.463$, $p = 0.05$). There were no significant correlations between Hb, Hct and GRS, EF, IVRT, E-wave, A-wave, E/A, DT, and E/E′.

The major findings of our study are changes of systolic function in PV based on the evaluation of GLS, GCS and GRS. The novelty of our findings is that impairment of systolic function was significantly associated with haematocrit and haemoglobin levels. There are several possible explanations for our observations.

It should be noted that primary PV is characterized by hyperviscosity, which is associated with an increase of total plasma volume and reduced O_2 saturation of the erythrocytes [9]. Therefore, hyperviscosity may result in an increased myocardial workload and tissue ischemia, which in turn may lead to reduce left ventricular systolic function. Early systolic changes may not influence ejection fraction (EF) and should be assessed by more sensitive methods, such as speckle tracking echocardiography, which allows local or global longitudinal, circumferential and radial fibres strain measurement [10,11].

More in detail, in our study GLS, GCS and GRS were significantly lower in PV groups compared to the control group. Haemoglobin and haematocrit correlated also with the degree of LV systolic impairment, which may suggest the influence of hyperviscosity on systolic function.

High Hct level is another potential mechanism which may lead to elevated afterload because of increased peripheral resistance [9]. Both elevated afterload and increased peripheral resistance may lead to a high rate of hypertension in the PV group, which is considered as one of the most consistent features of PV [12]. In our study we confirmed a high prevalence of arterial hypertension (76%). It is of note that GLS and GCS correlated with blood parameters independently of arterial blood pressure.

LVMI may also be related to reduced strain parameters. However, in the presented study there were no statistically significant differences in

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