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ORIGINAL ARTICLE

Impaired Blood Rheology in Pulmonary Arterial Hypertension

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Background Understanding of the pathophysiologic manifestations of pulmonary arterial hypertension (PAH) is still evolving. The aims of the present study were to determine the alterations in blood rheology, and to investigate the relationship between those alterations and laboratory parameters in PAH.

Methods The study included 21 consecutive treatment-naive patients with PAH and 32 age and sex-matched healthy controls. Patients were categorised in class II (n = 6), class III (n = 13), and class IV (n = 2). All subjects underwent right-heart catheterisation. Erythrocyte deformability and aggregation were measured by an ektacytometer.

Results Haemodynamic variables were as follows: the mean right atrial pressure: 9.94 ± 5.76 mmHg; the average pulmonary vascular resistance: 5.66 ± 3 WU; Fick cardiac index: 4.15 ± 2.75 l/min/m^2; and mixed venous O_2 saturation: 64.59 ± 12.53%. The average 6-minute walk distance was 351.09 ± 133.08 m. Erythrocyte deformability measured at 0.95, 3.00, and 5.33 Pa was significantly lower, erythrocyte aggregation index (AI) was higher, and aggregation half-time (t1/2) was lower in PAH. AI and fibrinogen were positively correlated with NT pro-BNP (AI-NT pro-BNP: r = 0.579; fibrinogen-NT pro-BNP: r = 0.591). t1/2 was negatively correlated with NT pro-BNP (t1/2-NT pro-BNP: r = −0.648).

Conclusions The increase in erythrocyte aggregation and the decrease in deformability may theoretically increase the flow resistance and may be of haemodynamic significance. The association between erythrocyte aggregation and NT pro-BNP may indicate that erythrocyte aggregation increases with disease progression. These alterations contribute to the understanding of the pathophysiology and could serve as markers of disease presence.

Keywords Blood rheology • Erythrocyte deformability • Erythrocyte aggregation • Pulmonary arterial hypertension

Introduction

Pulmonary arterial hypertension (PAH) is a life threatening multifactorial disorder characterised by pulmonary vasoconstriction and aberrant proliferation of smooth muscle cells, leading to increased pulmonary vascular resistance [1]. Understanding of the pathobiology of PAH is still evolving. Although there has been significant progress in the treatment of this disease over the last two decades, the number of drugs that are proven to improve outcomes is still limited [2]. Therefore, disease management remains unsatisfactory and prognosis is still poor for many patients. More efficient

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treatment strategies are urgently needed to further improve outcomes for the majority of patients. In microcirculation, rheological characteristics of blood (i.e., erythrocyte deformability and aggregation, plasma viscosity) are the major determinants of resistance to flow and their alterations are known to impair microcirculatory blood flow [3–5]. It has been demonstrated that erythrocyte aggregation was associated with an increase in peripheral resistance in hypertensive subjects [6] and it may affect the resistance either directly or indirectly via altered endothelial function [7]. Rheological parameters are reported to be altered in a variety of vascular diseases: increased erythrocyte aggregation in atherosclerotic cardiovascular disease [8]; increased erythrocyte aggregation and decreased erythrocyte deformability in acute ischaemic stroke [9] and heart failure [10]; increased plasma viscosity in acute myocardial infarction [11]. Recently, it has been demonstrated that erythrocyte stiffening plays a key role in altering pulmonary vascular haemodynamics [12] and elevated low-shear blood viscosity is associated with negative haemodynamic perturbations in a passive univentricular pulmonary circulation [13]. The hypothesis of the present study was that rheological properties of blood might be altered in the presence of PAH. Hence, the aims of the present study were to determine the alterations in blood rheology (erythrocyte aggregation and deformability), and to investigate the relationship between those alterations and laboratory parameters in PAH.

Parts of the results of this study have been previously reported in form of abstracts [14,15].

Methods

Study Design, Haemodynamics, Inclusion and Exclusion Criteria

The study design was prospective and included 21 consecutive treatment-naive patients with PAH and 32 age and sex-matched healthy controls. All patients were recruited from a cardiology out-patient clinic. The control group, which was comprised of 32 age- and sex-matched healthy participants who presented to a medical out-patient clinic for routine annual physicals, was chosen in a consecutive manner without exclusion criteria. World Health Organization (WHO) class (a modification of the New York Heart Association [NYHA] functional class) was used. Determination of all patients' functional class (FC) was performed by two trained physicians. In case of a discrepancy, a third physician was consulted. The diagnosis of PAH was set by right-heart catheterisation (RHC), exhibiting a mean pulmonary artery pressure (mPAP) of 25 mmHg or greater at rest and a pulmonary artery wedge pressure (PAWP) or left ventricular end-diastolic pressure [LVEDP] of 15 mmHg or less at normal or reduced cardiac output, according to the 2009 guidelines [16], or a mPAP $\geq$25 mmHg, a PAWP $\leq$15 mmHg, and a pulmonary vascular resistance (PVR) >3 WU, according to the 2015 guidelines [2].

Exclusion criteria were the presence of pulmonary hypertension due to left heart disease, lung diseases and/or hypoxia, pulmonary hypertension with unclear and/or multifactorial mechanisms, pregnancy or lactation, current or past smoking, regular use of alcohol, any systemic inflammatory condition, major systemic or psychiatric disorder, and use of any medication with potential confounding effects on blood rheology. In addition, patients with unrepaired congenital heart defects, chronic thromboembolic pulmonary hypertension (operable or inoperable), and who were hypoxic on room air or desaturated on a 6-minute hall walk (6MHW), were excluded. The study protocol was approved by the Medical Ethics Committee of the participating university (the registry number 60116787-020/65509) and the study was conducted in accordance with the Declaration of Helsinki. All subjects provided written informed consent.

The subjects' body weight was recorded in kilograms (kg) and their height was measured in metres (m). All subjects performed a 6MHW and underwent right-heart catheterisation to confirm the diagnosis and to assess haemodynamics. Transthoracic echocardiography was performed on all participants as an initial test. In order to rule out heart failure with preserved ejection fraction, all subjects with multiple risk factors for diastolic dysfunction underwent left heart catheterisation.

Catheterisation

Right-heart catheterisation was performed antegrade through either the inferior vena cava or superior vena cava. Percutaneous entry was achieved through the femoral and internal jugular veins. A Swan–Ganz catheter was used for haemodynamic measurements. Right atrial, right ventricular, pulmonary artery, and pulmonary capillary wedge pressures were measured. Blood samples for oximetry were obtained from the superior vena cava and pulmonary artery in all patients. Pulmonary vascular resistance was calculated using the following formula: PVR = mPAP – PAWP/pulmonary flow (Qp). Qp (L/min) was calculated using Fick's equation [17]. The Judkins technique was used for left-heart catheterisation and coronary arteriography when indicated. Left ventricular end-diastolic pressure was obtained by advancing a pigtail catheter into the left ventricle when necessary.

Samples and Measurements

After 8 hours of fasting, 10 mL of venous blood samples were drawn by venipuncture into standard EDTA-containing tubes (1.5 mg/mL). Samples were appropriately transferred to the Physiology Laboratory and haemorheological tests were performed within 3 hours in accordance with the "new guidelines for hemorheological laboratory techniques" [18]. Haematological parameters were determined by an electronic haematology analyser (Siemens ADVIA® 2120i System, Siemens Healthcare Diagnostics, Japan). Immunoglobulin (Ig) levels were measured using colorimetric method (Roche Cobas 8000, Roche Hitachi Moduler, Mannheim, Germany). Blood samples treated with sodium citrate

were analysed for plasma fibrinogen concentration using a fully automated coagulometer [Beckman COULTER Acl top 700, Instrumentation Laboratory (USA)].

Erythrocyte Deformability Measurements

Erythrocyte deformability was determined under various fluid shear stresses by laser diffraction analysis using an ektacytometer (Laser-assisted optical rotational cell analyzer [LORCA], RR Mechatronics, Hoorn, The Netherlands). The main advantage of this up-to-date laser technique is its reproducibility and accuracy. The system has been described elsewhere in detail [19]. Briefly, a low Hct suspension of erythrocyte in an isotonic viscous medium (4% polyvinylpyrrolidone 360 solution; MW 360 kD; Sigma P 5288; St. Louis, MI, USA) was sheared in a Couette system composed of a glass cup and a precisely fitting bob, with a gap of 0.3 mm between the cylinders. A laser beam was directed through the sheared sample, and the diffraction pattern produced by the deformed cells was analysed by a microcomputer. On the basis of the geometry of the elliptical diffraction pattern, elongation index (EI) was calculated as $EI = (L - W)/(L + W)$, where L and W are the length and width of the diffraction pattern, respectively. EI values were determined for nine shear stresses between 0.3 and 30 pascal (Pa) and similar patterns of erythrocyte deformability alterations were obtained between groups at all stress levels. All measurements were carried out at 37 °C.

Erythrocyte Aggregation Measurements

Erythrocyte aggregation was also determined by LORCA as described elsewhere [19]. The measurement method is based on the detection of laser back-scattering from the sheared (disaggregated), then unsheared (aggregating) blood, performed in a computer-assisted system at 37 °C. Backscattering data were evaluated by a computer, and the aggregation index (AI) and aggregation half time (t1/2) were calculated on the basis that there is less light backscattered from aggregating red cells. Aggregation measurements were obtained using erythrocytes in autologous plasma adjusted to 40% Hct. Blood was fully oxygenated before the measurements.

Statistical Analysis

Statistical analysis was performed using SPSS v.21.0 for Windows (SPSS Inc., Armonk, NY, USA). Shapiro–Wilk's test was used to investigate normal distribution. Continuous and categorical data were shown as means ± SD and percentages, respectively. When parametric test assumptions were met, Independent Samples t test was used to compare the differences between groups. Mann-Whitney U test was used if the assumptions were not met. Categorical data were compared using the chi-square test. Spearman correlation analysis was performed to investigate the relationship between continuous variables. The level of statistical significance was set at $p \leq 0.05$.

A power analysis was performed before study initiation. Based on a previous study's effect size being 0.87 [20], which was determined for AI, we chose an effect size value of 0.80 to estimate a sample size for the present study and we found that a total number of 42 participants (21 patients and 21 controls) would result in 80% power with 95% confidence. We included 53 participants (21 patients and 32 controls) in the present study. The power analysis performed after the study showed that our results reached 87% power with 95% confidence when examined for AI.

Results

Clinical and laboratory characteristics of 53 subjects are shown in Table 1. In total, 18 female and 3 male PAH patients were enrolled into this study. The mean age was 59 ± 9 years. Fourteen (14) patients were in WHO FC II, six were in WHO FC III, and one was in ambulatory WHO FC IV. Two (2) patients had PAH associated with congenital heart disease (repaired), 10 patients had idiopathic PAH, nine patients had PAH associated with scleroderma. Haemodynamic variables were as follows: the mean right atrial pressure (mRAP): 9.94 ± 5.76 mmHg; the average pulmonary vascular resistance (PVR): 5.66 ± 3 WU; Fick cardiac index (CI): 4.15 ± 2.75 l/min/m^2; and mixed venous O_2 saturation (Svo_2): 64.59 ± 12.53%. The average 6MHW distance was 351.09 ± 133.08 m. Haemoglobin (Hb), haematocrit (Hct), erythrocyte count, mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) of patients were significantly lower ($p = 0.0001$, $p = 0.0001$, $p = 0.006$, $p = 0.012$, $p = 0.0001$, respectively). Erythrocyte distribution width (RDW) and Ig G levels were significantly higher in PAH patients ($p = 0.0001$, $p = 0.033$, respectively). Erythrocyte deformability (i.e., EI) of the groups was measured at nine shear stresses between 0.3 and 30.0 Pa. EI and erythrocyte aggregation parameters (i.e., AI, t1/2) are shown in Table 2. EI values of PAH patients at three shear stresses (0.95, 3.00 and 5.33 Pa) were significantly lower than controls ($p = 0.045$, $p = 0.046$ and $p = 0.050$, respectively). AI values of PAH patients were significantly higher and their $t^1/_2$ values were lower than controls ($p = 0.0001$ and $p = 0.0001$ respectively). AI and fibrinogen were positively correlated with N-terminal pro–brain natriuretic peptide (NT pro-BNP) ($r = 0.579$, $p = 0.012$, $r = 0.543$, $p = 0.006$, respectively). $t^1/_2$ was negatively correlated with NT pro-BNP ($r = -0.648$, $p = 0.004$) (Figure 1). There were no significant associations between haemodynamic data and rheological measurements. No significant associations were noted between erythrocyte deformability or aggregation and laboratory parameters, including 6MWD.

Discussion

The main findings of this study are: (1) erythrocyte deformability was decreased; (2) erythrocyte aggregation was increased in patients with PAH; and (3) erythrocyte aggregation was associated with NT pro-BNP. These findings indicate that impaired rheology could theoretically increase the flow resistance through the pulmonary vascular system and could be of haemodynamic significance in patients with PAH.

Table 1 Baseline clinical, haemodynamic, and laboratory characteristics of subjects (n = 53).

		Control group (n = 32)	Pulmonary arterial hypertension (PH) (n = 21)	P
Age (years)		57.28 ± 11.22	59 ± 9	0.312
Gender (F/M)		20/12 (%62,5/%37,5)	18/3 (%85,7/%14,3)	0.067
Hb (g/dl)		13.98 ± 1.87	11.69 ± 1.96	0.0001*
Hct (%)		42.15 ± 5.22	36.87 ± 5.52	0.0001*
RBC (m/μL)		4.86 ± 0.53	4.35 ± 0.9	0.006*
MCV (fL)		86.72 ± 5.67	86.41 ± 10.84	0.148
MCH (pg)		28.78 ± 2.32	27.4 ± 4.15	0.012*
MCHC (g/dl)		33.17 ± 1.09	31.65 ± 1.64	0.0001*
RDW (%)		13.35 ± 1.16	16.26 ± 2.64	0.0001*
WBC (K/uL)		7.41 ± 1.81	6.36 ± 2.2	0.063
Plt (K/uL)		249.5 ± 63.06	231.14 ± 52.6	0.275
Fibrinogen (mg/dL)		310.53 ± 87.57	341.16 ± 84.95	0.228
IG M (mg/dL)		97.66 ± 49.38	123.08 ± 92.05	0.592
IG G (mg/dL)		1047.83 ± 205.35	1198.61 ± 266.81	0.033*
IG A (mg/dL)		245.38 ± 121.55	301.74 ± 169.18	0.216
6 min walking distance (m)		–	351.09 ± 133.08	–
WHO functional class	2	–	6 (%28.6)	–
	3		13 (%61.9)	
	4		2 (%9.5)	
Aetiology of PAH, n (%)				
Idiopathic PAH		–	10	–
APAH – CTD		–	9	–
APAH – CHD, repaired		–	2	–
Pulmonary haemodynamics				
Mean RAP (mm Hg)		–	9.94 ± 5.76	–
Mean PVR (WU)		–	5.66 ± 3	–
Fick Cardiac Index (L/min/m^2)			4.15 ± 2.75	–
mVO_2 (%)		–	64.59 ± 12.53	–
NT pro-BNP (pg/mL)			567.06 ± 587.2	–

Values are given as percentages or means ± SD.

Abbreviations: APAH, associated pulmonary arterial hypertension; CHD, congenital heart disease; CTD, connective tissue disease; CTEPH, chronic thromboembolic pulmonary hypertension; RAP, right atrial pressure; PVR, pulmonary vascular resistance; WHO, World Health Organization; Hb, haemoglobin; Hct, haematocrit; RBC, red blood cell count; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; RDW, red blood cell distribution width; WBC, white blood cell count; Plt, platelet count; IG M immunoglobulin M; IG G, immunoglobulin G; IG A, immunoglobulin A.

*$p \leq 0.05$, the difference from controls.

Pulmonary arterial hypertension comprises a highly heterogeneous group of life-threatening lung diseases. To date, the actual mechanisms that contribute to the development of PAH are still not well characterised. In this study, we showed that erythrocyte deformability was reduced in patients with PAH. This is in line with a previous study by Persson et al. [21], who measured erythrocyte deformability using a different non-computerised technique, a filtrometer. However, we measured it using LORCA, which is an up-to-date device to measure erythrocyte aggregation and deformability, with a good reproducibility in consecutive measurements. We noted that erythrocyte deformability was lower at shear stresses of 0.95, 3.00 and 5.33 Pa.

In PAH, the pathologic lesions involve mainly the distal pulmonary arteries (<500 μm in diameter) [1]. Presumably, within the distal pulmonary vasculature, one would observe shear stress anywhere between 2.00 to 3.00 Pa as this range has also been used previously [22]. In addition, we measured erythrocyte aggregation index (AI) and found that it was increased in PAH patients. AI is an important parameter to investigate erythrocyte aggregation, because the overall aggregation behaviour of the suspension is described by it. AI is the ratio of the area above the syllectogram curve (Area A) to the total area (Area A + Area B) over a time period of 10 seconds.

The increment observed in AI of aggregation is consistent with the decrement in $t^1/_2$ and indicates that erythrocyte

Table 2 Haemorheological parameters of the study population.

	Controls (n = 32)		Patients with PAH (n = 21)		P
	Mean ± Std. Dev	Med (min–max)	Mean ± Std. Dev	Med (min–max)	
Erythrocyte deformability (EI) measured (Pa)					
0.30	0.05 ± 0.03	0.04 (0.01– 0.12)	0.04 ± 0.04	0.04 (0.01–0.17)	0.423
0.53	0.09 ± 0.05	0.08 (0.02–0.2)	0.07 ± 0.05	0.05 (0.04–0.27)	0.17
0.95	0.17 ± 0.08	0.18 (0.03–0.37)	0.14 ± 0.07	0.13 (0.06–0.37)	0.045*
1.69	0.28 ± 0.1	0.3 (0.08–0.49)	0.24 ± 0.07	0.24 (0.13–0.45)	0.081
3.00	0.38 ± 0.08	0.4 (0.18–0.49)	0.34 ± 0.06	0.35 (0.23–0.51)	0.046*
5.33	0.46 ± 0.07	0.48 (0.28–0.55)	0.44 ± 0.05	0.45 (0.34–0.55)	0.05*
9.49	0.53 ± 0.05	0.54 (0.39–0.6)	0.51 ± 0.04	0.51 (0.43–0.59)	0.112
16.87	0.58 ± 0.04	0.59 (0.47–0.64)	0.57 ± 0.03	0.57 (0.51—0.63)	0.206
30.00	0.62 ± 0.04	0.63 (0.53–0.68)	0.61 ± 0.03	0.61 (0.56–0.67)	0.206
Erythrocyte aggregation values					
AI (%)	65.65 ± 14.58	68.88 (0.8–81.96)	74.8 ± 5.79	74.6 (58.52–85.35)	0.0001*
t $^{1}/_{2}$ (sn)	1.86 ± 0.69	1.71 (0.73–4.16)	1.24 ± 0.47	1.18 (0.43–2.71)	0.0001*

Values are given as means ± SD.

Abbreviations: AI, aggregation index, EI, elongation index, Pa, pascal, t $^{1}/_{2}$: aggregation half time; PAH, pulmonary arterial hypertension.

*$p \leq 0.05$, the difference from controls.

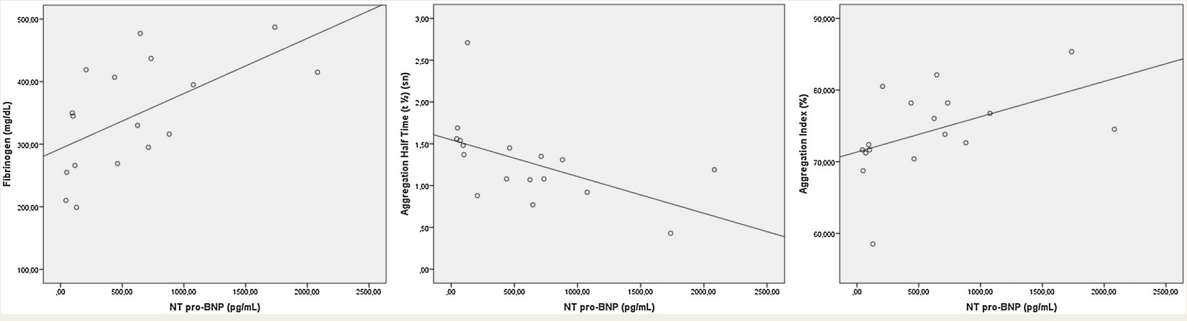

Figure 1 Correlation between NT pro-BNP and Fibrinogen, and erythrocyte aggregation values.

aggregation is elevated. Erythrocyte aggregation and deformability are the main components of haemorheology [23], whose flow characteristics are one of the determinants of oxygen delivery to tissues. In microcirculation, erythrocytes must collapse to pass through narrow capillaries; hence, erythrocyte deformability and aggregation are major determinants of resistance to flow [24]. The physiological importance of erythrocyte aggregation, which is the reversible adhesion of adjacent erythrocytes in circulation, is due to its tendency to increase the blood viscosity in low shear flow and to disturb the passage in capillary circulation [25]. Therefore, decreased erythrocyte deformability and increased erythrocyte aggregation in patients with PAH might further compromise pulmonary haemodynamics and could thereby worsen the clinical status of PAH patients.

Plasma proteins (fibrinogen and immunoglobulins), the erythrocyte morphology, and mechanical properties of erythrocytes, which depend on proper metabolic conditions and the presence of a normal homeostasis in their microenvironment, are known to be the most important determinants of erythrocyte aggregation [25,26]. No significant difference in fibrinogen levels was noted between the groups in this study, indicating that the augmentation observed in erythrocyte aggregation may not be explained by alteration of plasma fibrinogen levels. However, we identified significant differences in Hb, Hct, erythrocyte count, MCH, MCHC, RDW, and Ig G values. The finding that Ig G values were increased in PAH patients is consistent with a previous study [27], where increased Ig G values might at least partly contribute to increased erythrocyte aggregation in PAH patients. In contrast to the finding that an increase in MCHC may result in a lower erythrocyte deformability by enhancing intracellular viscosity [28], we observed a lower MCHC in PAH, which may be associated with the decreases in the other haematological parameters, i.e., Hb, Hct, and erythrocyte. Thus, decreased deformability may not be explained by MCHC changes. Mattar et al. recently reported that there was no correlation between haematological

parameters and PAH in patients with chronic myeloproliferative disorders [29], which are associated with PAH, have been included in group 5, for which the aetiology is unclear and/or multifactorial. Such patients were excluded from the current study. Impaired deformability also shortens erythrocyte life span, which may be related with the increase observed in RDW [30]. We also excluded patients who were hypoxic at baseline or became hypoxic with exercise (6MHW); therefore, the observed rheologic alterations could be related to the underlying PAH substrate.

To the best of our knowledge, this report provides the first evidence of altered blood rheology in PAH, which is characterised by occlusive vascular remodelling. The mechanisms that give rise to PAH are poorly understood, but believed to entail the combination of multiple risk factors. Potential roles of endothelial cell dysfunction and high shear stress have been suggested [22]. In this study, erythrocyte deformability was significantly reduced, particularly at higher shear stresses. Together with increased aggregation, this alteration could further impair microcirculation. Altered erythrocyte deformability and aggregation have been reported in other disease states [6–11] and in an animal model Schreier et al. [12] demonstrated that chemically stiffened erythrocytes increased mPAP, PVR, and wave reflections. However, we did not observe any association between erythrocyte deformability and haemodynamics in our patients. Cheng et al. [13] found that blood viscosity has a strong and significant association with pulmonary blood flow and PVR in univentricular circulations where low-shear non-pulsatile blood flow is present in the pulmonary arterial tree. However, they did not observe elevated erythrocyte aggregation in univentricular circulations. We were not able to study plasma viscosity due to technical problems. We found that AI, t1/2, and fibrinogen were associated with NT pro-BNP. AI and fibrinogen were positively correlated with NT pro-BNP, and t1/2 was negatively correlated with NT pro-BNP. These findings indicate that erythrocyte aggregation might increase as the disease progresses. Previous studies have demonstrated the prognostic value of using all available single and repeated measurements of NT–pro-BNP, which is a recognised prognostic marker of right heart failure and death in PAH [31]. The association between plasma NT-proBNP and erythrocyte aggregation could reflect the degree of increased right ventricular wall stress and subsequent deterioration in erythrocyte aggregation.

Study Limitations

Our study had some limitations. We determined CI by Fick technique alone. Distribution of patients among functional classes was also not balanced. Therefore, we could not assess the effect of PAH severity on haemorheological variables. Due to technical problems we had during the study, we were not able to determine plasma viscosity. Pulmonary arterial hypertension studies have traditionally enrolled patients from group 1 (PAH) of the PH classification, a heterogenous group of disorders having similar pathobiology [1]. This study also included patients with idiopathic PAH, associated PAH-scleroderma, and associated PAH-congenital heart disease (repaired); therefore, our results may not be applicable to one particular disease. However, we excluded patients with unrepaired congenital defects and CTEPH patients (both operated and inoperable ones) to have rather homogenous cohort at least based on pathophysiology. We would have liked to study rheological parameters only in men or women due to the potential confounding effects of hormonal changes. In this study, there were no gender differences in rheology among PAH patients, which is in line with the previous works: Overall erythrocyte deformability did not differ between male and female athletes [32]; there were no significant differences between donor age and sex groups [33]; no statistically significant differences in erythrocyte deformability or relaxation time were observed between male and female erythrocytes at any storage time [34]. In addition, in this study, the difference between the proportions of male and female in the groups did not reach a statistical significance (Table 1). This study included PAH patients who had less severe disease status compared to other cohorts [35], which could be explained by the facts that our patients were Caucasian, out-patient with less severe disease (mostly WHO FC II), and we determined PVR and CI by Fick technique alone. We did not find any predictor of survival among rheological parameters; however, our sample size and event number were too small for a reliable survival analysis. Larger sized studies with higher event rates are needed if those parameters could be useful as markers of disease prognosis.

Conclusions

We have demonstrated that erythrocyte aggregation is increased, erythrocyte deformability is decreased, and erythrocyte aggregation is associated with NT pro-BNP in patients with PAH. Impaired haemorheological parameters may theoretically increase the flow resistance through the distal pulmonary vasculature and may be of haemodynamic significance. These alterations may contribute to the current understanding of the pathophysiology and may represent markers of disease presence.

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Disclosure

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Conflicts of Interest

None.

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