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Hemorheological disturbances in patients with chronic form of atrial fibrillation

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Abstract
According to the World Health Organization (WHO), atrial fibrillation affects 1% of the World's population. Ischemic strokes and systemic thromboembolism are common complications of this rhythm disorder. Although the disease has been studied in various ways, hemorheological characteristics and their potential relationship with the progression of arrhythmias remain unclear. There are no physiological or pathophysiological processes at the microcirculation level, where hemorheology is important in terms of intensity and volume flow rate. When developing the research design, we accounted for these issues. The aim of the study was to identify the rheological characteristics in patients with chronic forms of atrial fibrillation, as well as to clarify the aspects of the interdependence between the severity of the disease and the rheological parameters.Thirty six patients with chronic forms of atrial fibrillation were examined. From the final processing of the material, the following results were obtained: the difference between patients with atrial fibrillation and the control group was reliable, with a confidence index of 1%. The results show that regardless of their course, all rheological characteristics in patients with atrial fibrillation are impaired.

Keywords: Hemorheology, erythrocyte aggregation, atrial fibrillation, blood flow

1. Introduction

Atrial fibrillation (AF) is the most common disease amongst other arrhythmias of the heart. According to current data, the prevalence of arrhythmia in adults ranges from 2% to 4% [1]. Morbidity in Georgia accounts for 0.9% of the population [2]. Recent research indicates that the risk of developing arrhythmia has increased. In Europe, for example, one out of every three people is at risk [3, 4, 5]. This contrasts with previous years when the figure for the 55-year-old age group was 1 in 4 [6]. Also, the prevalence of AF increases with age (Fig.1) [7].

Atrial fibrillation affects approximately six million Europeans, according to current data. With an increase in the average age of the population over the next 50 years, its prevalence is expected to increase 2.5 times [8]. Despite biomedicine's best efforts, the prevalence of atrial fibrillation and its associated morbidity and mortality is increasing globally [9, 10]. According to Framingham's studies, the risk of developing of the disease in men older than 40 is 26% and in women older than 40 is 23%. Eight percent of people older than 80 are diagnosed with atrial fibrillation. It's important to say that, the percentage of the count of atrial fibrillation in young people is increasing every year.

The quality of life of patients with atrial fibrillation is reduced regardless of other cardiovascular conditions and their age. Lack of coordination of atrial contractions contributes to blood coagulation and

the formation of blood clots, which leads to the creation of an embolism. Therefore, against the background of this rhythm disorder, it is common to develop ischemic strokes and systemic thromboembolism. 6-24% of patients with stroke are diagnosed with atrial fibrillation. Although atrial fibrillation does not belong to the group of life-threatening arrhythmias, it independently increases the risk of mortality in patients with a cardiac profile, and in the case of paroxysmal atrial fibrillation, it is life-threatening even in patients who still had not had a history of cardiogenic pathology.

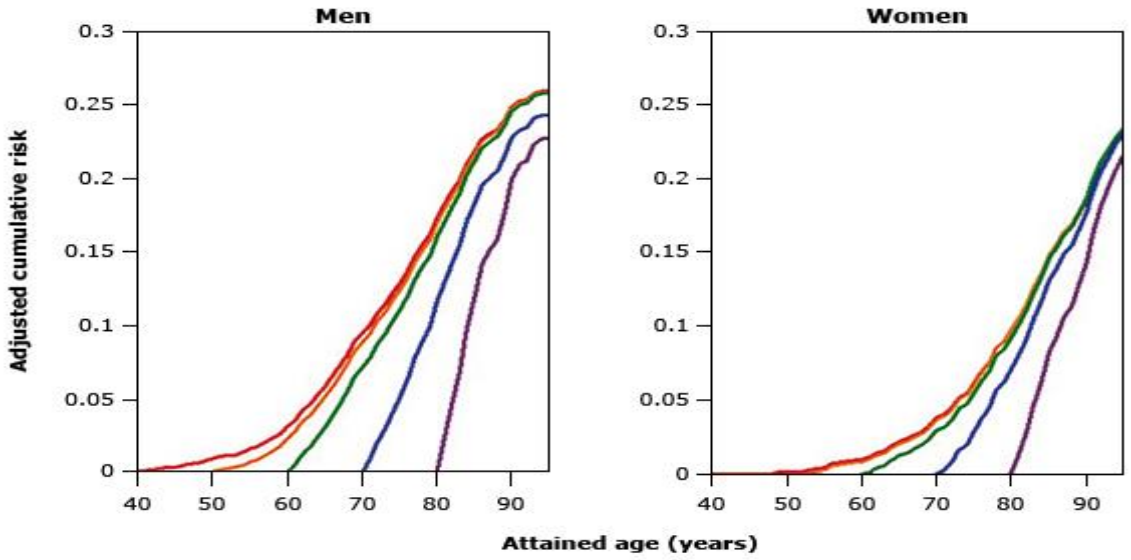

Fig.1. Dependence of the prevalence of AF on age in men and women [8]

There is some hypothesis that explains the pathogenesis of atrial fibrillation. They are all based on mechanisms based on local points and microwaves. However, none of them consider the role of hemodynamics and hemorheology in the formation of atrial fibrillation. The hemorheological state of the blood is not assessed during disease treatment; additionally, it is unknown how atrial fibrillation affects intracardiac macro and microcirculation [11]. There is no physiological or pathophysiological process that does not occur at the level of microcirculation, where hemorheology plays a critical role in terms of flow intensity and volume [12]. It is very important to study all the fundamental aspects and directions that will create new scientific data.

Despite significant advances in the detection and treatment of atrial fibrillation in recent years, this heart rhythm disorder remains a challenge for clinicians. Based on the standard management and treatment strategy for patients with atrial fibrillation, it is possible to conclude that antithrombotic therapy is administered against the backdrop of monitoring the coagulation system while the rheological state of the blood is not considered, neither during the initial diagnosis of the disease nor during the implementation of preventive measures [13].

They are all based on mechanisms based on local points and microwaves. But none of them consider the role of hemodynamics and hemorheology in the formation of atrial fibrillation. The hemorheological state of the blood is not assessed during disease treatment; additionally, it is unknown how atrial fibrillation affects intracardiac macro and microcirculation [1]. The determine of the effect of micro-and macro intracardiac blood flow is on the formation of atrial fibrillation is very important determine what the effect of micro-and macro intracardiac blood flow is on the formation of atrial fibrillation. All of them are based on local point and microwave-based mechanisms. But the hemorheological behavior of the blood is not evaluated during the treatment of the disease; moreover, it is not known how atrial fibrillation affects the intracardiac macro- and microcirculation [1]. Determining the effect of micro- and macro intracardiac blood flow on the formation of atrial fibrillation is very important to assess the effect of micro- and macro intracardial blood flow on the formation of atrial fibrillation.

Hemodynamic and hemorheological studies on atrial fibrillation will determine the pathogenesis of chronic forms of rhythm disorders.

The results of this study will allow us to pay attention to the hemorheological parameters as a

treatment target. It will reduce the number of patients diagnosed with atrial fibrillation. All the above is very important for fundamental and practical biomedicine because atrial fibrillation is the predictor of mortality [12]. Rheological studies during atrial fibrillation completely exclude their classification error. This research will give us an opportunity to personalize our patients' care. Also, this study has financial benefits as less money will be needed to be spent on atrial fibrillation in the future.

All this and the unfavorable epidemiological picture make this project very needy and this determined goal of our investigation. In the frame of this study, we focused to determine how hemodynamics and hemorheological parameters change in patients with chronic atrial fibrillation, as well as investigating various aspects of the relationship between disease severity and rheological parameters.

2. Methods

Thirty-six patients with chronic forms of atrial fibrillation (16 women 16 and 20 men, the average age of patients 65±10) were examined. Pathology that may be present: coronary artery disease (CAD), arterial hypertension, chronic heart failure, stage I-II (NIHA). Two large groups were distinguished: patients with heart rhythm disorders and the control group. The study participants were divided into subgroups based on the American College of Cardiology and the European Association of Cardiology's Society of atrial fibrillation. Patients with rhythm disorders were divided into two subgroups: Group I: Patients with persistent form (n=14, man-8, women-6); Group II: Patients with the permanent form of arrhythmias (n=22, man-14, women-8). This study included healthy individuals with an average age of 65, which constituted the control group (n=20, 12 men and 8 women). These individuals had no pathology, were not on any medications at the time, and had a normal electrocardiogram. The following studies were conducted to diagnose several forms of rhythm disorders: electrocardiogram (ECG), echocardiography (EQO), and the index of erythrocytes' aggregability, deformability, and plasma viscosity to evaluate the blood rheological parameters. Furthermore, the "Georgian technique" method was used to study the erythrocyte aggregability index. This new innovative method was created by Georgian scientists in Georgia and is known in the world as direct, numeral and exact [13, 14]. The erythrocyte aggregation index allows us to quantity erythrocyte aggregation, which is lacking in other methods currently available. It is the percentage ratio of the area of aggregated erythrocytes in the field of view to the total area of erythrocytes. A textural analysis system can be used to perform this analysis (Tas-Plus, Leitz, Germany). We chose the methodology described above because it is innovative, modern, and primarily created and processed in Georgia. This method is modern and widely acknowledged as the best in the world [15,16]. The erythrocyte deformability index (nucleopore membrane filter method) [17], was determined by the filtration method. It is based on the variation of the erythrocyte exit rate in a porous filter (the smallest capillary lumen is 5 μm) under constant pressure conditions (10 cm of Hg). A capillary viscometer was used to measure plasma viscosity at 37°C. The final plasma viscosity value is the average of multiple viscometer measurements of plasma viscosity. Ivane Beritashvili Center of Experimental Biomedicine Laboratory of rheology and diagnostic-analytical services investigated the rheological properties. The data were statistically processed using the SPSS program.

3. Results

Erythrocyte aggregation is consistently impaired in individuals with permanent and persistent forms of atrial fibrillation. The maximum mean value was recorded in the group with the permanent form of arrhythmia. Erythrocyte membrane deformability was also impaired in both groups compared to the control group; the maximum rate was also found in patients with a permanent form of arrhythmia. Moreover, the maximum value of plasma viscosity was observed in patients with the persistent form. The mean values of the erythrocyte aggregation index were compared with the erythrocyte deformability and plasma viscosity of each group; differences between patients with atrial fibrillation and those in the control group were reliable, with a confidence index of 1%.

It was discovered that erythrocyte aggregation is consistently impaired in people with permanent and persistent atrial fibrillation **(**see Table 1).

Table 1
Rheological profile in the patients groups with chronic and with atrial fibrillation (AF) and in the control group

Forms of AF	Persistent (n=14)	Permanent (n=22)	Control (n=20)
Sex Ratio (M/F)	8/6	14/8	12/8
Age (years)	65±10	65±10	65±10
EAI/%	39.76±13.84*	41.47±10.4**	25.61±1.29***
EDI/%	2.18±0.45*	2.18±0.92**	2.09±0.25***
VpI, mPa.s	1.17±0.84*	1.2±0.69**	1.09±0.35***

Values are expressed as mean ±sd. AF-atrial fibrillation. EAI-index of erythrocytes aggregability EDI-index of erythrocytes deformability, VpI-plasma viscosity; Statistically different from control group *p <0.01, **p<0.03, ***p<0.01; statistically different from Perm. and persist. form *p<0.01, **p<0.04, ***p<0.02.

As shown in Table 1, the average indicator of the erythrocyte aggregability index is disturbed in both permanent and persistent atrial fibrillation.

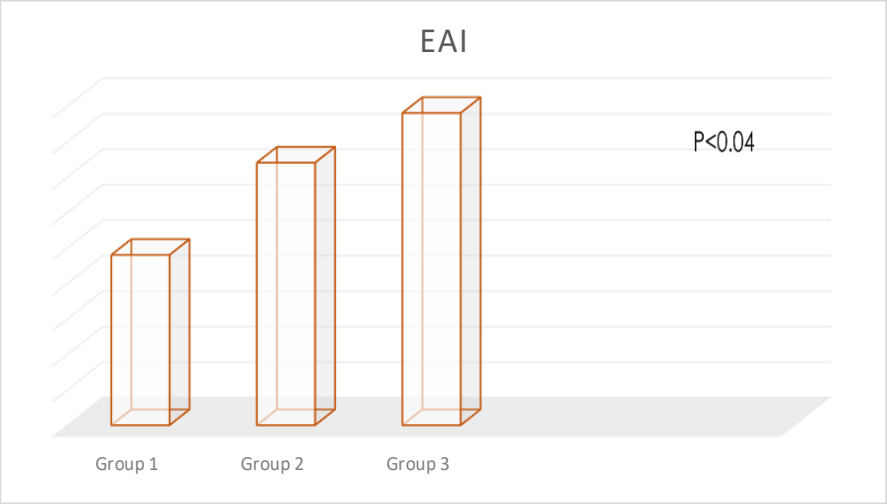

Fig. 2. Average values of the erythrocyte aggregability index: Group I-Control; Group II -persistent, Group III-permanent form of AF

The maximum average value is fixed in the subgroup of the permanent form of rhythm disturbance; this indicator is 93%, which is nearly twice the average value of the control group's erythrocyte aggregability index (see Fig. 2). When compared to the control group, erythrocyte membrane deformability is also reduced in both subgroups. The maximum rate of this parameter is also seen in patients with a permanent form of arrhythmia, and it is 33% (0.8) higher than in the control group of the healthy population (see Fig. 3). In patients with a persistent form of the maximum plasma viscosity is fixed at 39% higher than normal (see Fig. 4). We obtained the following results from the final processing of the material: the difference between the patients with atrial fibrillation and the control group was reliable, with a confidence index of 1%. As a result, regardless of their course, patients with atrial fibrillation have all their rheological characteristics impaired.

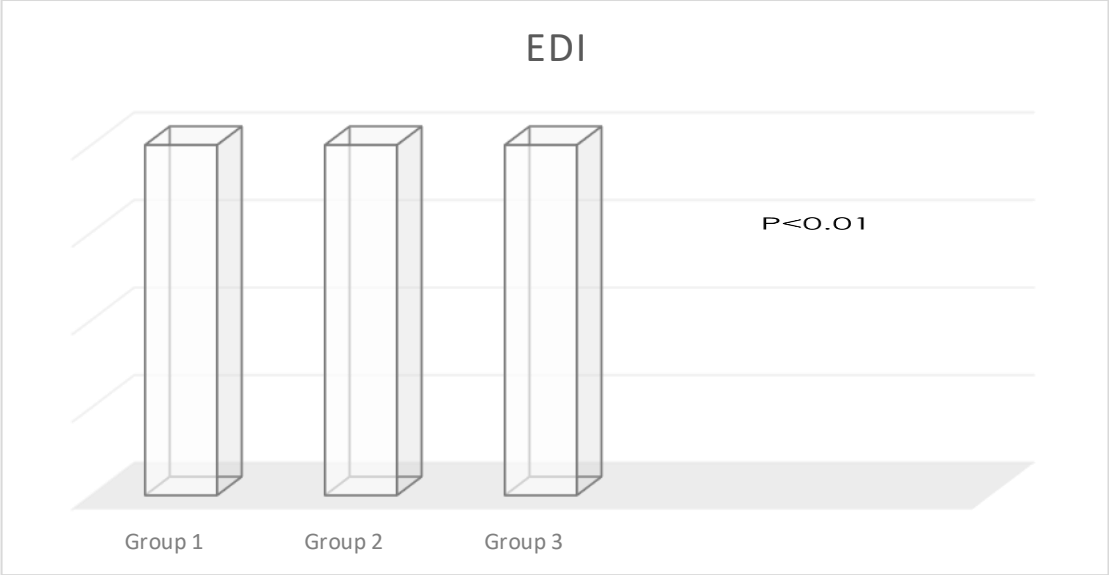

Fig. 3. Average values of the erythrocyte deformability index: Group I-Control; Group II –persistent, Group III-permanent form of AF

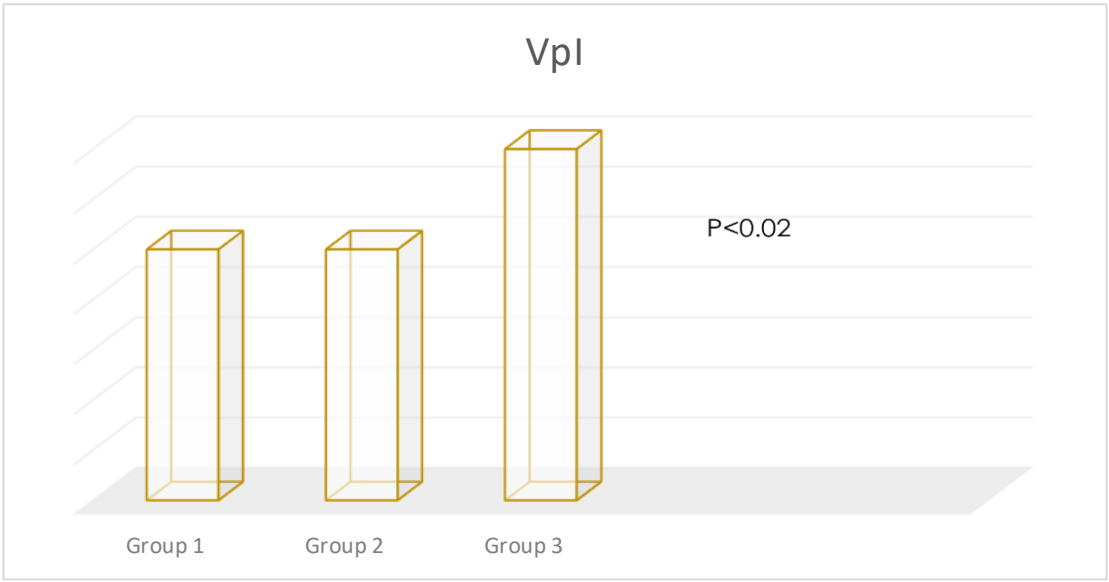

Fig. 4. Average values of the plasma viscosity: Group I - Control; Group II - persistent, Group III- a permanent form of AF

The results of this study were as follows: Group I (patients with a persistent form of atrial fibrillation) index of erythrocyte aggregability was 39.76±13.84%, erythrocytes deformability was 2.18±0.45 %, and the plasma viscosity - 1.17±0.84 mPa.s. Group II (patients with the permanent form of atrial fibrillation) index of erythrocytes aggregability was 41.47±10.4%, erythrocytes deformability was 2.18± 0.92% and the plasma viscosity was 1.2 ±0.69 mPa.s. Additionally, the control group had an index of erythrocyte aggregation of 25.61 1.29%, erythrocyte deformability was 2.09± 0.25%, and plasma viscosity was 1.09±0.35 mPa.s. Erythrocyte aggregation is consistently impaired in individuals with permanent and persistent forms of atrial fibrillation. The maximum mean value was recorded in the group with the permanent form of arrhythmia. Erythrocyte membrane deformability was also impaired in both groups compared to the control group; the maximum rate was also found in patients with a permanent form of arrhythmia. Moreover, the maximum value of plasma viscosity was observed in patients with the persistent form. The mean values of the erythrocyte aggregation index were compared with the erythrocyte deformability and plasma viscosity of each

group; differences between patients with atrial fibrillation and those in the control group were reliable, with a confidence index of 1% mPa.s.

4. Discussion

We assessed rheological parameters in patients with atrial fibrillation for the first time. As is well known, optimal perfusion is required for the proper functioning of the myocardium, as well as any other tissue, which is unthinkable without the normal interaction of hemorheological and hemodynamic factors.

The role of hemorheological and hemodynamic factors is very important in the development of cardiovascular disease and in all pathological problems which are going with vessel disorders [18-26]. Whatever the mechanism of blood flow disorders in various pathology with different etiological signs, rheological disorders play a definite role in the violation of blood structure [27, 28, 29].

The treatment principle for any disease is based on influencing the etiopathogenic ring; in the case of arrhythmias, in particular, depending on the forms of current in the conditions of atrial fibrillation, special attention is paid to structural and functional changes of the atrial myocardium, which lead to electrophysiological changes, which conditions are created for the detection and maintenance of atrial fibrillation; The findings of our study suggest that hemorheological system disorders are the foundation for the development of the pathological processes described above. As a result, the severity of atrial fibrillation that has developed against this background was determined. Increased erythrocyte aggregation causes an increase in peripheral resistance, which, in the presence of unsystematic arrhythmic contractility, aggravates the systolic and diastolic dysfunction of the left ventricle, creating favourable conditions for the maintenance of atrial fibrillation. Cardiac rhythm disorders have a certain relationship with normal microcirculation, the transport of oxygen and energy substances, and the balance of energy extraction-utilization processes. Rheological changes and their role during myocardial infarction as a factor involved in the mechanism of thrombosis formation are investigated. Our findings suggest the presence of rheological changes in the chronic course of atrial fibrillation. For the first time, we have established a relationship between the course of arrhythmia and negative changes in rheological parameters. As a result, patients with atrial fibrillation have all rheological characteristics impaired, as expected. Our findings show that the ability of erythrocytes to aggregate, a powerful determinant of rheological changes, increases progressively as the severity of the clinical manifestation of the disease increases; the already increased thrombogenic potential of blood is enhanced by the increased ability of erythrocytes to aggregate. The fact that rheological disorders deteriorate with disease progression is highlighted. For example, the changes that occur during the persistent form of arrhythmia deepen over time.

Everything points to the existence of a close relationship between rheological changes and the processes occurring in the cardiovascular system. The findings suggest that erythrocyte aggregation is a critical factor in the progression of atrial fibrillation and requires constant monitoring, both in the manifestations of individual forms of the disease and in terms of prevention. Furthermore, the „Georgian technique" method we used allows us to obtain quantitative data and objectify it. Through retrospective observation of patients, we will be able to reveal regularities in the course of the disease. Rheological parameters were initially evaluated in patients with chronic atrial fibrillation and a correlation was found between the severity of the disease and rheological characteristics. Rheological disorders are exacerbated as the disease progresses, changing from the persistent to the permanent form of atrial fibrillation. During atrial fibrillation, blood thrombogenic potential is raised due to increasing erythrocyte aggregation and plasma viscosity. This indicates a close relationship between changes in rheological parameters and ongoing processes in the cardiovascular system. Increased rheological parameters are risk factors for arrhythmia and contribute to the disease's rapid progression. The obtained data concludes that erythrocyte aggregation is a vital factor during arrhythmia and requires permanent monitoring of manifestation as well as prevention of the disease. Furthermore, the „Georgian technique"method used allows us to obtain quantitative data and objectify it. This will allow retrospective observation of the patterns of disease progression in patients. Moreover, extensive scientific work and clinical research are required to choose an accurate disease management strategy, highlighting the fascinating and current issues of biomedical direction. Rheological studies during pulsatile arrhythmia completely rule out classification errors [30-37]. The algorithm for choosing treatment tactics will be simplified and the effectiveness of treatment will improve. This is critical for applied cardiology because it allows us to personalize patients, as recommended by the European Union

H2020.

5. Conclusion

It can be concluded that the aggregation of erythrocytes is one of the most important factors for the progression of atrial fibrillation and requires constant monitoring both for the manifestations of individual forms of the disease and from the point of view of prevention. Thus, erythrocyte aggregation is the determinant of blood flow in ventricular arrhythmia.

Rheological studies in pulsatile arrhythmias contribute to the correct classification of the disease, which contributes to the appointment of effective treatment and personalization of patients.

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