Clinical Hemorheology and Microcirculation xx (2021) x–xx
DOI 10.3233/CH-211105
IOS Press

An assessment of the hemorheological profile in patients with subclinical carotid atherosclerosis divided in relation to the number of cardiovascular risk factors and different degrees of insulin resistance

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Abstract. We present a cohort of 100 subjects [43 men and 57 women; median age 66.00(25)] who were tested using carotid ultrasound to identify subclinical carotid atherosclerosis (SCA). We have evaluated the behaviour of whole blood viscosity (WBV) at high (450 s^{-1}) and low (0.51 s^{-1}) shear rates, plasma viscosity (450^{-1}), hematocrit and mean erythrocyte aggregation. When compared to normal control subjects, using the Mann-Whitney test, we observed in SCA patients a significant increase in WBV only. The results were substantial after having divided the SCA subjects according to the cardiovascular risk factors (CRFs) and the degree of insulin resistance; the research was performed using two surrogate indexes such as TG/HDL-C and TyG. With the division carried out according to CRFs, employing the Kruskal-Wallis test, results show a significant increase in WBV (at high and low shear rates), in plasma viscosity, in erythrocyte aggregation and plasma fibrinogen level. Whereas by dividing them into the median of TG/HDL-C and TyG, we noticed a significant increase in WBV (at high and low shear rates) and in erythrocyte aggregation in the two groups with high TG/HDL-C ratio and with high TyG; having found an increased level of plasma fibrinogen in the latter. The data underlines the role of the main hemorheologic aspects in subclinical carotid atherosclerosis being closely correlated to the CRFs and different degrees of insulin resistance.

Keywords: Subclinical carotid atherosclerosis, hemorheological determinants, traditional cardiovascular risk factors, insuline-resistence, uric acid

1. Introduction

Subclinical atherosclerosis may be investigated through different approaches such as: the ultrasonographic study with ecocolordoppler, measurement of the ankle-brachial pressure index, the non-invasive evaluation of endothelial function, coronary calcium score and evaluation of the coronary artery with multidetector computed tomography [1].

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ISSN 1386-0291/$35.00

The identification of subclinical atherosclerosis is an early marker of vascular damage and expresses the susceptibility to develop atherosclerotic disease, regardless of the presence of one or more risk factors.

Many subjects, classified as at high risk by traditional assessment scales, have subclinical atherosclerosis [2]. Subjects with objective evidence of subclinical atherosclerosis have a higher risk of short- and long-term cardiovascular events than controls of the same age and sex. The early stages of atherosclerosis therefore become a key target for early diagnosis and satisfactory prognostic results. All risk factors are related to the presence of endothelial dysfunction and, at the same time, the hemorheological alterations play a role in the pathogenesis and progression of the disease, as well as the prognostic factors [3–5].

Fibrinogen, that is one of the most important determinants of plasma viscosity as it significantly influences erythrocyte aggregation [6]. Although, several studies have confirmed the role of plasma viscosity in the progression of cardiovascular diseases, plasma viscosity assessment has not always been used in clinical practice [7, 8].

Hemorheological alteration appears to be a risk factor for the development of cardiovascular disease through the effects on atherogenesis, thrombogenesis and tissue ischemia [5, 9, 10].

Several studies have demonstrated the relationship between blood viscosity alterations and the onset as well as progression of cardiovascular diseases [11]. Plasma hyperviscosity limits tissue perfusion in low-flow areas; it may be considered a marker of early atherosclerosis and a useful prognostic parameter in identifying subjects at risk of cardiovascular complications [10, 12].

Hemorheological parameters may be correlated with the degree of carotid stenosis in both symptomatic and asymptomatic subjects, without implications with such risk factors [13–17].

According to other authors, blood viscosity correlates with mean intimal thickening and reduced flow-mediated dilation [18]. A secondary hyperviscosity condition may be present in several metabolic and non-metabolic clinical disorders [19, 20]. Such observation would tend to complicate the analysis of the cause-effect relationship between hemorheological alteration and atherosclerosis [21].

Taking into account the aforementioned considerations, we have examined some determinants of the hemorheologic profile in a group of subjects with subclinical carotid atherosclerosis (SCA). Subsequently, we divided them into two different subgroups in relation to the number of cardiovascular risk factors and in relation to the different degrees of insulin resistance.

2. Subjects

This group included 100 subjects (43 men and 57 women, median age 66.00 (25.00) years) with subclinical carotid atherosclerosis (SCA). This vascular condition was demonstrated effecting a carotid ultrasound examination. The common carotid artery, the bifurcation and the internal carotid artery have been examined bilaterally with a linear 7.5 MHz ultrasound probe using an Esaote MyLab 25 and following standard hospital procedures. The carotid atherosclerotic plaques, unilateral in 43 and bilateral in 57 subjects, were all of fibrocalcific type with no implications in terms of the hemodynamic profile. In all the SCA subjects was examined also the ankle-brachial index being less than 0.90 in 3 subjects, and they resulted to be asymptomatic for peripheral arterial disease. The subject group involved in the study had no evidence of clinically significant cardiovascular diseases by history, physical examination, ECG, echocardiogram, or chest x-ray. The SCA subject group got later divided according to the number of cardiovascular risk factors (hypercholesterolemia - 73%, arterial hypertension - 66%, family history of cardiovascular disease - 65%, smoker or ex-smoker - 52%, metabolic syndrome - 33%, obesity - 28%, diabetes mellitus - 15%) into two subgroups. 43 of them had 1 to 2 cardiovascular risk factors (CRF) and 57 had 3 to 5 CRFs. The same group was divided into different

Table 1
Medians (IQR) and ranges of anthropometric and laboratory parameters in the whole group of SCA subjects

	Median (IQR)	range
Age (years)	66 (25)	45–83
BMI (Kg/m^2)	28.08 (5.68)	17.99–43.25
WC (cm)	96.50 (16)	67–125
Fasting blood glucose (mg/dl)	94.5 (17)	77–237
Total cholesterol (mg/dl)	199.5 (53.7)	108–338
HDL cholesterol (mg/dl)	50.5 (15)	22–103
LDL cholesterol (mg/dl)	122.2 (40.2)	51.4–246.8
Triglycerides (mg/dl)	102 (62.55)	44–309
Uric acid (mg/dl)	4.50 (1.175)	1.10–7.70
CRP (mg/l)	2.9 (2.5)	0.3–9.5
N/L ratio	1.856 (0.935)	0.624–5.243
Fibrinogen (mg/dl)	305 (36.8)	199–518
SBP (mmHg)	130 (20)	100–160
DBP (mmHg)	80 (10)	60–100

IQR = interquartile range; SCA = subclinical carotid atherosclerosis; BMI = body mass index; WC = waist circumference; CRP = C-reactive protein; N/L = neutrophil/lymphocyte; SBP = systolic blood pressure; DBP = diastolic blood pressure.

subgroups according to their TyG parameters. Such further division was carried out according to their triglycerides/HDL-cholesterol (TG/HDL-C) ratio and to their logarithm of the product of triglycerides and fasting plasma glucose level (TyG index). Both these related parameters are considered markers of insulin resistance [22]. The SCA group was divided into those with a low and high TG/HDL-C ratio and those with a low and high TyG index according to their median value respectively.

Medians, IQR and range of age, anthropometric parameters, glucometabolic patterns, lipid profile and blood pressure values for the SCA subject group are shown in Table 1.

The control group consisted of 31 subjects (13 men and 18 women; median age 42; interquartile ranges 21) selected among the hospital staff who were free from disease.

3. Methods

Venous blood samples were collected by venous puncture in the morning from the antecubital vein of fasting subjects and immediately transferred to anticoagulated glass tubes for the evaluation of the following parameters:

- Whole blood viscosity (WBV) at the shear rate of 450 s^{-1}, by using the cone-on-plate viscometer Well-Brookfield DV III Ultra (Brookfield, Middleboro, MA, USA);
- Whole blood viscosity (WBV) at the shear rate of 0.51 s^{-1} employing a viscometer Contraves LS30 (proRheo GmbH, Althengstett, Germany);
- Plasma viscosity (PV) at the shear rate of 450 s^{-1}, by using the cone-on-plate viscometer Wells-Brookfield DV III Ultra (Brookfeld Middleboro, MA, USA);
- Hematocrit (Ht), obtained by using a micromethod technique.
- Mean erythrocyte aggregation by using the Myrenne aggregometer MA-1 (Myrenne Gmbh, Roetgen, Germany).

Table 2
Medians (IQR) of rheological parameters in control subjects and the whole group of SCA subjects

	Control subjects ($n = 31$)	SCA ($n = 100$)
WBV 450 sec^{-1} (mPa·s)	3.090 (0.7)	3.350 (0.68) ***
WBV 0.51 sec^{-1} (mPa·s)	24.22 (6.37)	24.36 (7.4)
PV 450 sec^{-1} (mPa·s)	1.230 (0.08)	1.260 (0.1)
Ht (%)	42.00 (6.00)	40.00 (3.00)
MEA	11.60 (2.70)	12.60 (3.20)

***$p < 0.001$ (Mann-Whitney test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

4. Statistical analysis

The statistical difference between control group and the SCA subject group was analysed according to the Mann-Whitney test. The correlation coefficients between hemorheological determinants and the other parameters were examined using the Spearman test. The Mann-Whitney test was also employed to analyse the differences in hemorheological parameters between each subgroup of SCA subjects. The statistical differences among normal controls and each subgroup of SCA subjects was examined using the Kruskal-Wallis test.

5. Results

When we compared the SCA subject group to the control group, we found an increase in whole blood viscosity (WBV) at high shear rate only; no variation in fact was evident in WBV at low shear rate, plasma viscosity, hematocrit and mean erythrocyte aggregation (Table 2). Afterwards, by employing the Spearman test we examined the correlation coefficients among the determinants of the hemorheological pattern with insulin resistance indexes (TG/HDL-C ratio and TyG), with anthropometric parameters (BMI and waist circumference) and with metabolic and inflammation markers (uric acid, fibrinogen, C-reactive protein and neutrophil/lymphocyte ratio). From this preliminary analysis emerges that both parameters reflecting insulin resistance are correlated to the WBV, at high and low shear rates, as well as both anthropometric parameters are correlated to the plasma viscosity while among the metabolic and inflammation markers only the uric acid is correlated, at low significance degree, with all the hemorheological determinants (Table 3).

By comparing the control group to the SCA subject group divided by the number of cardiovascular risk factors (CRFs) we have observed, using the Kruskal-Wallis test, that WBV at high shear rate, plasma viscosity and erythrocyte aggregation had increased in SCA subjects with 3-5 CRFs, while no variation was found in WBV at low shear rate and hematocrit (Table 4). The Mann-Whitney test was used to compare the subgroup of SCA subjects presenting 1-2 CRFs with those presenting 3-5 CRFs. We noticed an increase in WBV at high shear rate, plasma viscosity, hematocrit and fibrinogen in SCA subjects with 3-5 CRFs; with this subdivision no statistical variation was observed in WBV at low shear rate and in erythrocyte aggregation (Table 5).

When we compared the control group with the SCA subjects, who were divided according to their median of TG/HDL-C ratio, we found by employing the Kruskal-Wallis test an increase in WBV at high and low shear rates in the SCA subject subgroup with high TG/HDL-C ratio, although no alterations in plasma viscosity and hematocrit (Table 6) were present. Using the Mann-Whitney test,

Table 3

Correlation coefficients between hemorheological parameters and A) indices of insulin resistance, B) anthropometric indices, C) metabolic and inflammation indices

vs	WBV 450 sec^{-1}	WBV 0.51 sec^{-1}	PV	Ht	MEA
A)					
TG/HDL	0.2793**	0.2191*	0.1259	0.1237	0.1701
TyG	0.2269*	0.2470*	0.1062	0.0925	0.2557*
B)					
BMI	0.1644	0.1099	0.2822**	0.06617	0.1138
WC	0.1448	0.06776	0.3401***	0.06505	0.08480
C)					
Uric acid	0.2213*	0.2147*	0.2617**	0.2422*	0.2463*
Fibrinogen	0.1093	0.0705	0.1114	0.0340	–0.0559
CRP	–0.0050	–0.0072	–0.0182	0.0298	–0.1512
N/L ratio	0.0131	–0.0576	–0.1079	–0.0020	–0.0931

*$p < 0.05$; **$p < 0.01$ (Spearma1n test). WBV = whole blood viscosity; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation; BMI = body mass index; WC = waist circumference; CRP = C-reactive protein; N/L = neutrophil/lymphocyte.

Table 4

Medians (IQR) of rheological parameters in control subjects and in SCA subjects subdivided according to the number of RFs

	Control subjects ($n = 31$)	SCA with 1-2 RFs ($n = 43$)	SCA with 3-5 RFs ($n = 57$)	K-W statistic
WBV 450 sec^{-1} (mPa·s)	3.090 (0.7)	3.150 (0.66)	3.600 (0.66)	16.86***
WBV 0.51 sec^{-1} (mPa·s)	24.22 (6.37)	24.22 (6.93)	25.50 (8.79)	3.765
PV 450 sec^{-1} (mPa·s)	1.230 (0.08)	1.22 (0.10)	1.28 (0.095)	11.39**
Ht (%)	42.00 (6.00)	40.00 (3.00)	41.00 (4.00)	5.919
MEA	11.60 (2.70)	11.60 (3.20)	13.00 (2.87)	7.631*

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ (Kruskal-Wallis test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; RFs = risk factors; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

Table 5

Medians (IQR) of rheological parameters in SCA subjects subdivided according to the number of RFs

	SCA with 1-2 RFs ($n = 43$)	SCA with 3-5 RFs ($n = 57$)
WBV 450 sec^{-1} (mPa·s)	3.150 (0.66)	3.600 (0.66)**
WBV 0.51 sec^{-1} (mPa·s)	24.22 (6.93)	25.50 (8.79)
PV 450 sec^{-1} (mPa·s)	1.22 (0.10)	1.28 (0.095)**
Ht (%)	40.00 (3.00)	41.00 (4.00)*
MEA	11.60 (3.20)	13.00 (2.87)
Fibrinogen (mg/dl)	301 (33)	310 (34)*

*$p < 0.05$; **$p < 0.01$ (Mann-Whitney test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; RFs = risk factors; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

Table 6
Medians (IQR) of rheological parameters in control subjects and in SCA subjects subdivided according to the median of TG/HDL ratio

	Control subjects ($n=31$)	SCA with low TG/HDL ($n=50$)	SCA with high TG/HDL ($n=50$)	K-W statistic
WBV 450 sec^{-1} (mPa·s)	3.090 (0.7)	3.170 (0.63)	3.605 (0.587)	17.27***
WBV 0.51 sec^{-1} (mPa·s)	24.22 (6.37)	23.07 (6.84)	26.77 (8.07)	9.657**
PV 450 sec^{-1} (mPa·s)	1.230 (0.08)	1.260 (0.10)	1.255 (0.112)	3.684
Ht (%)	42.00 (6.00)	40.00 (4.00)	41.00 (4.00)	3.282
MEA	11.60 (2.70)	12.16 (2.60)	13.35 (3.74)	7.057*

*$p<0.05$; **$p<0.01$; ***$p<0.001$ (Kruskal-Wallis test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; TG = triglycerides; HDL = high density lipoprotein cholesterol; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

Table 7
Medians (IQR) of rheological parameters in SCA subjects subdivided according to the median of TG/HDL ratio

	SCA with low TG/HDL ($n=50$)	SCA with high TG/HDL ($n=50$)
WBV 450 sec^{-1} (mPa·s)	3.170 (0.63)	3.605 (0.587)**
WBV 0.51 sec^{-1} (mPa·s)	23.07 (6.84)	26.77 (8.07)**
PV 450 sec^{-1} (mPa·s)	1.260 (0.10)	1.255 (0.112)
Ht (%)	40.00 (4.00)	41.00 (4.00)
MEA	12.16 (2.60)	13.35 (3.74)
Fibrinogen (mg/dl)	305 (32)	308.5 (51.7)

**$p<0.01$ (Mann-Whitney test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; TG = triglycerides; HDL = high density lipoprotein cholesterol; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

we compared the SCA subject group with low and high TG/HDL-C ratio and observed that in those with high TG/HDL-C ratio there was a significant increase in WBV at two shear rates only (Table 7).

The Kruskal-Wallis test was used to compare the control group to the SCA subject group who were divided according to the median of TyG index and we noticed an increase in WBV at high and low shear rates and in fibrinogen in the SCA subject subgroup with high TyG index (Table 8). Making use of the Mann-Whitney test and comparing SCA subjects with low and high TyG index we found a rise in WBV viscosity at both shear rates and fibrinogen in those with high TyG index (Table 9).

6. Discussion

In the SCA subject group, there is a significant rise in WBV at high shear rate; in the same survey no variation was observed with regard to the other hemorheological determinants. Even if only at high shear rate, the behaviour of WBV was predictable in subjects with SCA.

Over the years, the role of blood viscosity in this specific vascular area and also its role in the pathophysiology of atherothrombosis has been examined and discussed by several authors [12–14, 16, 23–27]. As it is known, the vascular geometry and in particular the presence of curves, bifurcations and

Table 8
Medians (IQR) of rheological parameters in control subjects and in SCA subjects subdivided according to the median of TyG index

	Control subjects ($n = 31$)	SCA with low TyG ($n = 50$)	SCA with high TyG ($n = 50$)	K-W statistic
WBV 450 sec^{-1} (mPa·s)	3.090 (0.7)	3.170 (0.74)	3.590 (0.547)	15.64***
WBV 0.51 sec^{-1} (mPa·s)	24.22 (6.37)	23.86 (6.60)	26.77 (9.00)	7.123*
PV 450 sec^{-1} (mPa·s)	1.230 (0.08)	1.250 (0.10)	1.275 (0.112)	3.933
Ht (%)	42.00 (6.00)	40.00 (3.00)	40.00 (4.00)	1.946
MEA	11.60 (2.70)	12.10 (2.60)	13.20 (3.74)	6.453*

*$p < 0.05$; ***$p < 0.001$ (Kruskal-Wallis test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

Table 9
Medians (IQR) of rheological parameters in SCA subjects subdivided according to the median of TyG index

	SCA with low TyG ($n = 50$)	SCA with high TyG ($n = 50$)
WBV 450 sec^{-1} (mPa·s)	3.170 (0.74)	3.590 (0.547)*
WBV 0.51 sec^{-1} (mPa·s)	23.86 (6.60)	26.77 (9.00)*
PV 450 sec^{-1} (mPa·s)	1.250 (0.10)	1.275 (0.112)
Ht (%)	40.00 (3.00)	40.00 (4.00)
MEA	12.10 (2.60)	13.20 (3.74)
Fibrinogen (mg/dl)	304 (30)	310 (57.5)*

*$p < 0.05$ (Mann-Whitney test). IQR = interquartile range; SCA = subclinical carotid atherosclerosis; WBV = whole blood viscosity; mPa = milliPascal; PV = plasma viscosity; Ht = haematocrit; MEA = mean erythrocyte aggregation.

stenosis modifies the district hemodynamic profile, and this sudden variation affects wall shear stress and consequently blood viscosity. In this regard, many papers have analysed the role of the modified shear stress in the pathogenesis of atherosclerosis [28]. In vascular bifurcations and in particular in those of the carotid artery [29], there is a remarkable flow recirculation which slows down the blood flow and consequently the shear stress while it increases blood viscosity. Blood viscosity at low shear is especially correlated to the erythrocyte aggregation that depends, apart from the intrinsic erythrocyte characteristics, also by the concentration of plasma protein levels and especially by fibrinogen.

Recently, Sloop's [30] studies have resulted in the elaboration of the hemorheological-hemodynamic theory of atherogenesis, which has been useful to explain the first stages of atherothrombosis.

An interesting starting point emerges from the analysis of correlations among the two indexes reflecting insulin resistance, anthropometric parameters and metabolic and inflammation markers with the main hemorheological determinants.

In the SCA subject group, the indexes of insulin resistance are significantly correlated to the WBV, at high and low shear rates, while no correlation was found with plasma viscosity and hematocrit; a positive correlation was observed instead between TyG index and mean erythrocyte aggregation. Subsequently, in the course of the discussion, we have examined the influence of the insulin resistance on blood viscosity and vice versa.

Going on to examining the correlations in the SCA subject group, interesting are the data concerning BMI and WC with plasma viscosity. Up to now, other researchers [31] had discovered a positive correlation between WC and plasma viscosity in patients with metabolic syndrome (MS) while others [32] in MS subjects have found a positive correlation between WC with WBV but not with plasma viscosity. Others [33] have observed a positive correlation between BMI and plasma viscosity.

Keeping in mind the abovementioned, the data observed by us in the SCA subject group seems to confirm such findings, although in our survey there were 33 subjects who suffered with metabolic syndrome and 28 subjects were obese.

The only significant correlation concerned the uric acid with all the hemorheological determinants. A positive correlation between uric acid and WBV has been described in healthy adults living on mountains [34] while in subjects with abdominal obesity [35] no relationship has been found between uric acid and plasma viscosity. Others [36] have described a positive correlation between uric acid and hematocrit in subjects with untreated borderline hypertension and in patients with established hypertension. In the SCA subject group we have found a positive correlation between uric acid and mean erythrocyte aggregation. To this regard, some researchers [37], in experimental models, have demonstrated that the uric acid increases erythrocyte aggregation. Such hemorheological phenomenon may be mainly attributed to the uric acid, and in particular to urate anions, i.e., the reduction of the zeta potential facilitates aggregation [30]. In fact, the interaction of the erythrocyte surface charge and the plasma ions cause the dimension of the ion cloud and the electric potential at the border of this cloud is the zeta potential [30].

The hemorheological profile results to be majorly altered in the group with 3-5 CRFs, besides a remarkable increase in WBV at high shear rate and a rise in plasma viscosity and in the mean erythrocyte aggregation. Such results became evident after having observed the results obtained from the comparison between normal control and SCA subjects, who have been divided according to the number of cardiovascular risk factors (CRFs), and also after having compared the two SCA subject groups. By comparing exclusively, the two SCA subject groups, also the values of the plasma fibrinogen and of the hematocrit are significantly higher in those with 3-5 CRFs.

The division based on the number of CRFs present in our cohort of SCA subjects indicates distinctly how the hemorheological profile is dependent on the amount of these traditional CRFs. Each of these CRFs influence the hemorheological profile or at least any of its determinants.

To this regard, in fact, many authors have examined the complex role carried out by the plasma lipid pattern on the hemorheological profile [38–40] and others have examined the way in which the arterial hypertension might influence the hemorheologic profile or any of its determinants [41–44].

In our cohort of SCA subjects, 52 were smokers or ex-smokers and some authors [45, 46] have demonstrated not only the dose-effect correlation between smoking and hemorheological profile, but also how the abstention from smoking normalizes the hemorheological determinants.

Also, subjects with metabolic syndrome (MS) present an alteration of the hemorheological profile, an aspect which has been fully studied. Considering that the subjects included in this survey seem to exhibit a cardiovascular or cardiometabolic clustering as judged by the percentage of CRFs discovered in each of these subjects. The hemorheological alteration in this metabolic condition, up to now, has been observed by many authors [47, 48]. It is interesting to underscore how some researchers [49] have ascertained that WBV at high shear rate increased in relation to the number of MS main components, while others [50] have demonstrated that the variation that correlated with the number of MS components regarded not only WBV (corrected for hematocrit) but also plasma viscosity, erythrocyte aggregation and fibrinogen levels.

Among the traditional CRFs, the one which has been less represented among the cases of SCA, is surely the diabetic disease, in fact, only in 15 subjects with such metabolic disorder were diagnosed.

Diabetes mellitus is characterized by an impairment of the hemorheological profile, as reported by several authors [51, 52].

Recently, particular attention has been addressed to the examination of the hemorheologic profile also in prediabetes condition [53], considering that the prediabetes seems associated with subclinical carotid atherosclerosis [54]. Interesting are the observations concerning the role of the hemoglobin A1c level on the erythrocyte deformability and blood viscosity [55] but also as a predictor of carotid artery plaques [56].

Between SCA subjects with 1-2 CRFs and those with 3-5 CRFs there is also a significant variation, even if at low significance degree, of the plasma fibrinogen level. Plasma fibrinogen plays its role in atherothrombosis through different mechanisms and it is also a marker of clinical and subclinical carotid atherosclerosis [57–59]. To date, many researchers have also ascertained that in several clinical disorders the plasma fibrinogen level results to be associated with the number of CRFs [60].

In our cohort of SCA subjects, attractive are the values obtained from the division carried out according to the parameters reflecting the insulin resistance (TG/HDL-C and TyG). To examine the trend of the hemorheologic profile with regard to these two parameters, it is necessary to consider the positive relationships between TG/HDL-C and TyG with WBV and for TyG also with mean erythrocyte aggregation. Moreover, many authors have demonstrated a negative correlation between insulin sensitivity and blood viscosity and a positive relationship between insulin resistance and blood viscosity [61, 62]; and this data seems to confirm previous literature. The same confirmation concerns also the positive relationship between TyG and erythrocyte aggregation [63]. Differently from what has been found previously by us, in a small group of MS patients [64], no correlation had been noticed between TG/HDL-C and TyG with plasma viscosity.

In this cohort of subjects with asymptomatic carotid plaques, the behaviour of some hemorheologic determinants is closely influenced by insulin resistance, and these observations, also including the influence on fibrinogen, were underlined previously by different researchers [65].

In conclusion, in subjects with subclinical carotid atherosclerosis the hemorheologic determinants and in particular whole blood viscosity, at high and low shear rates, and mean erythrocyte aggregation seem to depend on the number of cardiovascular risk factors and the different degrees of insulin resistance, such data was explored by employing two surrogate indexes.

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