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**Original Article**

# Effect of alcohol abuse on selected markers of inflammation, hemostasis, and endothelial function

**Short title:** Alcohol abuse and cardiovascular system

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## Abstract

**Background:** Alcohol consumption, even in moderate amounts, is associated with complex changes in blood biochemistry, involving abnormalities of many markers affecting cardiovascular risk.

**Methods:** A total of 100 patients with documented alcohol abuse were included in the study. Demographic data and information on alcohol consumption were collected using a standardized questionnaire. All patients underwent biochemical tests. The following parameters were evaluated: PAI-1, vWF, TNF-α, VCAM-1, adiponectin, fibrinogen, lipid profile, and hsCRP. The results were compared with a control group of 25 healthy subjects.

**Results:** A significant adverse effect of alcohol abuse was observed for markers such as PAI-1, TNF-α, VCAM-1, adiponectin, and fibrinogen. Moreover, most of the subjects showed elevated TC, LDL-C, and TG levels. There was a significant relationship between vWF and average daily alcohol consumption, a positive relationship between adiponectin levels and age, and between fibrinogen and the number of cigarettes smoked. No significant correlations were observed between the other markers and age, gender, place of residence, daily alcohol consumption, and total time of alcohol abuse.

**Conclusions:** Several abnormalities in most of the analyzed markers were observed in persons abusing alcohol, with no significant correlation with the daily amount of alcohol consumed and the total time of alcohol abuse, which may indicate permanent and irreversible damage to many tissues and organs as a result of chronic alcohol consumption. Further studies in this area with a larger group of patients are necessary to clarify the mechanisms leading to cardiovascular damage in the course of alcohol abuse.

**Keywords:** alcohol abuse, cardiovascular disease, cholesterol, endothelial function, inflammatory markers, hemostatic markers

## Introduction

Alcohol is considered the most health-threatening psychoactive agent worldwide and one of the major risk factors for many diseases, including cardiovascular diseases (CVD). In 2016, it accounted for as many as 19% of cardiac deaths worldwide, just after cancer and liver diseases [1]. The safe upper limit of alcohol consumption corresponds to about 100 grams of pure alcohol per week. The corresponding number of drinks depends on the serving size, as the standards vary among countries, and can be 8–14 g/drink [2]. Alcohol consumption above this limit is considered to be harmful and increases the risk of hypertension, hemorrhagic stroke, cardiac arrhythmias, and alcoholic cardiomyopathy, and reduces expected survival times [2–4].

The current data also challenge the previous concept that moderate alcohol consumption is generally associated with a lower risk of CVD. The protective effect of moderate alcohol consumption compared with non-use or abuse on CVD has not been confirmed, suggesting that the lowest risk of cardiovascular events is found among abstainers [2, 5].

In fact, high alcohol consumption leads to several abnormalities at the cellular and tissue level, including metabolic abnormalities, changes in blood coagulation, vascular endothelial function, and cell signaling, which result in impaired functioning of many systems and organs, including the cardiovascular system [4–6]. By affecting platelet levels, several coagulation factors, and plasminogen activator inhibitor type-1 (PAI-1), high ethanol levels are associated with reduced fibrinolysis and increased risk of thrombosis in CVD [6, 7]. By

damaging vascular endothelial cells and disrupting the production of several compounds, alcohol also plays a significant role in the pathogenesis of many diseases, including acute infections, cancer, and chronic inflammatory diseases, and it is involved in the pathogenesis of early atherosclerosis [8, 9].

Notably, ethanol is unique among toxins in that it disrupts almost all steps of lipid metabolism in the liver, which is why heavy drinkers tend to have higher concentrations of triglycerides (TG), total cholesterol (TC), and low-density cholesterol (LDL-C) compared to non-drinkers [10, 11]. Adiponectin is an important link between lipid metabolism, insulin resistance, type 2 diabetes, and atherosclerosis. Low alcohol consumption is clearly associated with increased blood levels of adiponectin in healthy individuals, and obese males and females with impaired glucose tolerance and type 2 diabetes, but these effects may vary depending on the type of alcohol consumed [12–14]. Unfortunately, data on adiponectin and heavy alcohol consumption are still sparse and inconclusive in the literature.

The present study was designed to examine the effects of alcohol consumption above the harmful limit on a number of markers and factors, such as coagulation and fibrinolysis factors (plasma or serum levels of von Willebrand factor [vWF] antigen, PAI-1, fibrinogen, inflammatory factors (high-sensitivity C-reactive protein [hsCRP], tumor necrosis factor alpha [TNF-α]), adhesion molecules (vascular cellular adhesion molecule-1 [VCAM-1]), lipid metabolism parameters (TC, LDL-C, high-density cholesterol [HDL-C], TG), and a compound that affects lipid metabolism (adiponectin).

## Methods

### *Studied groups*

The study group included 100 patients with documented alcohol abuse according to ICD-10 codes F10.2, F10.3, and F10.4, who participated in an inpatient alcohol dependence treatment program at the Alcohol Dependence Treatment Unit at the Psychiatry Clinic in

Krakow from September 2018 to November 2019. None of the patients had a history of chronic diseases, including cardiovascular, respiratory, gastrointestinal, or metabolic diseases.

The control group included 25 healthy subjects with no history of chronic alcohol consumption.

The study followed the principles of the Declaration of Helsinki. All procedures involving human participants were performed in accordance with the ethical standards of the institutional and national research committee. The local Ethics Committee approved the study protocol. Written consent was obtained from all patients before being enrolled in the study.

***Questionnaire***

A standardized questionnaire was used to collect patient demographic data, information on chronic concomitant diseases, and cardiovascular risk factors. The same questionnaire was used to gather information on alcohol consumption (total duration of alcohol consumption and amount of alcohol consumed per day). The interviewer first explained to the participant that alcoholic beverages include all types of drinks containing alcohol, such as beer, wine, liqueur, gin, rum, vodka, cocktails, and other mixed drinks. The interviewer also explained that one drink (about 10 grams of pure ethanol) was considered equal to 330 ml of beer, 120 ml of wine, or 25 ml of vodka. Based on this information, the average daily alcohol consumption was divided into the following categories: 0 to 2 drinks, 3 to 5 drinks, 6 to 10 drinks, 11 to 20 drinks, and > 20 drinks per day. When assessing the total time of alcohol abuse, the following categories were adopted: < 1 year, 1 to 5 years, 5 to 10 years, 10 to 20 years, and > 20 years.

***Laboratory tests***

Fasting venous blood was drawn from the antecubital vein between 7:00 and 9:00 AM. Citrated blood (9:1 of 0.106 M sodium citrate) was centrifuged at 2500 g for 20 minutes at 20°C, while blood drawn into EDTA or serum tubes was centrifuged at 1600 g for 10 minutes at 4°C. All blood samples were stored at -80°C until analysis. Routine laboratory assays were used to determine the lipid profiles (TC, LDL-C*, HDL-C, TG), hsCRP, and fibrinogen.

Plasma fibrinogen concentration was assessed using the modified Clauss method with a BCS XP analyzer from Siemens Healthcare. The assessment of the lipid profile and hsCRP was performed using a Cobas c501 analyzer from Roche Diagnostics, employing the following methods:

TC: enzymatic method with esterase and cholesterol oxidase, and a calibrator with a value determined according to IDMS standardization;

HDL-C: direct method with synthetic polymer and detergent (SPD method - Daiichi);

LDL-C: enzymatic method with cholesterol esterase and cholesterol oxidase in the presence of surfactants;

TG: enzymatic method with glycerol-3-phosphate oxidase and $H_2O_2$ determination (with peroxidase);

hsCRP: latex-enhanced immunoturbidimetric method.

Plasma or serum levels of vWF antigen, PAI-1, VCAM-1, TNF-α, and adiponectin were assayed in duplicates by ELISAs (all from Biorbyt Ltd, Cambridge, UK) according to the manufacturer's instructions by investigators blinded to the sample origin. The inter-assay coefficients of variation were < 7%.

*All patients in the study group were classified as low cardiovascular risk based on the physical examination, and the target LDL-C concentration was < 3.0 mmol [2].

### *Statistical analysis*

The R statistical package version 4.0.2 was used for the analysis. Categorical variables were presented as numbers and percentages — n (%), and continuous variables were presented as median, interquartile range (IQR), and ranges. In all analyses, differences for which the test probability, i.e., the p-value, was lower than the accepted significance level of $\alpha = 0.05$ were considered statistically significant.

The statistical significance of the differences in the values of numerical variables between the 2 groups was tested using the U-Mann-Whitney test, and in the case of a larger number of groups, the Kruskal-Wallis test (with Dunn's post hoc test and the Bonferroni correction for multiple testing). The existence of monotonic relations between variables was verified using Spearman's rank correlation coefficient.

## Results

The study group included 100 asymptomatic patients with a history of chronic alcohol abuse, with a median age of 44 (range 25–73) years. Detailed characteristics of the study group are presented in Table 1. The control group consisted of 25 patients with a median age of 47 (range 29–56) years, with no history of alcohol abuse and no concomitant chronic diseases. Most subjects in the control group were men (72%). There were no statistically significant differences between the study group and the control group with regard to age (44 vs. 47 years; $p = 0.6125$) and sex (79% vs. 72% males; $p = 0.6293$).

Table 2 shows the results of the basic laboratory tests of the 100 patients in the study group, such as lipid profile and hsCRP. Significant percentages exceeding the normal range

were observed for most tests. No statistically significant relations were observed between the analyzed tests and the average daily alcohol consumption or total duration of alcohol abuse in the study group, as shown in Tables S1–S2 (supplementary material).

Table 3 shows a detailed comparison of the evaluated markers in the study and control groups. Statistically significant differences were obtained for PAI-1, TNF-α, VCAM-1, adiponectin, and fibrinogen. No significant relationships were observed between the studied markers and the sex, place of residence, or smoking status of the patients in the study group. A statistically significant relationship was found only between age and adiponectin levels — Spearman's rank correlation coefficient indicated a weak, positive relationship between these variables. In addition, a significant correlation was observed between the number of cigarettes smoked per day and fibrinogen levels — Spearman's rank correlation coefficient indicated a weak positive relationship between these variables, as shown in Table 4.

Analyzing the relationship of the assessed markers with the average daily number of consumed alcohol units, a statistically significant relationship was observed only for vWF. The value of this factor increased with the amount of alcohol consumed per day up to the level of about 6–10 units. Above 20 units of alcohol per day, the value of vWF began to decrease, assuming the shape of an inverted U curve (Table 5). No statistically significant relationships between the studied markers and the total duration of alcohol abuse were observed in the study group, as shown in Table 6.

**Discussion**

In the presented study, the impact of alcohol consumption above the harmful limit on several markers and factors was analyzed, such as coagulation and fibrinolysis factors (vWF, PAI-1, fibrinogen), inflammatory factors (hsCRP, TNF-α), adhesion molecules (VCAM-1),

lipid metabolism parameters, and adiponectin. A significant adverse effect of alcohol abuse was observed for markers such as PAI-1, TNF-α, VCAM-1, adiponectin and fibrinogen. Moreover, most of the subjects showed elevated TC, LDL-C, and TG levels. There was a significant relationship between vWF and average daily alcohol consumption, a positive relationship between adiponectin levels and age, and between fibrinogen and number of cigarettes smoked. No significant correlations were observed between the other markers and age, gender, place of residence, daily alcohol consumption, and total time of alcohol abuse.

High alcohol consumption has been associated with decreased fibrinolysis and enhanced thrombosis risk in CVD [6]. Heavy drinking, especially in the evening, has been shown to cause acute inhibition of fibrinolysis that persists into the morning hours, which may accelerate atherosclerosis and increase the risk of thrombotic coronary events. This explains the higher risk of death from cardiovascular causes in persons who abuse alcohol [7].

In the present study, the PAI-1 and fibrinogen levels were significantly higher in the group of persons who abuse alcohol compared to the control group. A significant correlation between the fibrinogen blood concentration and the number of cigarettes smoked per day was also detected. Similar observations are described in the literature [6, 7, 15]. For example, in a study by Mennen et al. [15], the authors observed a strong correlation between alcohol consumption and plasma fibrinogen levels: fibrinogen levels were higher in heavy drinkers (> 60 g of alcohol per day) as well as non-drinkers. Moreover, smoking was also positively associated with the plasma fibrinogen concentration.

The level of the vWF was also evaluated in the present study, and its value did not differ significantly between the study and control groups. It has been shown that elevated plasma vWF levels correlate with organ failure and the length of survival in hospital in cases of severe alcoholic hepatitis (AH) [16, 17]. The lack of significant differences in vWF levels

between the 2 groups in this study was probably because the subjects were persons without diagnosed chronic diseases, including liver abnormalities.

Because atherosclerosis is considered an inflammatory disease, and ethanol may play a role in modulating the inflammatory response [18–20], the present study evaluated parameters such as TNF-α, hsCRP, as well as the already mentioned fibrinogen and vWF, which belong to acute phase proteins. In the presented study, no significant relationships in hsCRP levels were determined between the examined groups, but a significant difference in TNF-α levels was observed, with higher values in the alcohol-abusing group.

In their study, Gonzalez-Quintela et al. [21] showed that serum TNF-α levels are elevated in alcoholics regardless of the common TNF gene polymorphisms. In a Spanish study [22], the authors assessed the plasma levels of soluble TNF-α receptors 1 and 2 (sTNFR1 and sTNFR2), which were significantly higher in patients with cirrhosis compared to those with existing liver disease but without cirrhosis and those without liver disease, in both alcoholics and non-alcoholics. The TNF-α system was shown to become activated in patients with cirrhosis regardless of the etiology, which indicates the need for further research in this area.

In our study, VCAM-1 levels were analyzed, and we found them to be significantly elevated in the study group compared to the control group. Importantly, the concentration of this molecule did not depend on any of the analyzed variables, which may be indicative of varying degrees of persistent vascular endothelial dysfunction and persistently high serum VCAM-1 levels in response to long-term exposure to a toxic agent – alcohol. In a study by Xia et al. [23], the levels of soluble forms of endothelial cell activation markers (including sICAM-1 and sVCAM-1) were shown to be highly elevated in patients with AH, and alcohol abstinence did not completely reverse these abnormalities. Similar results were obtained in a study by Di Gennaro et al. [16], which demonstrated that severe alcoholism, even despite

long-term abstinence, is associated with persistent vascular endothelial dysfunction and multiple metabolic abnormalities with an unfavorable cardiovascular profile.

The observation indicating abnormalities in the lipid profile of most subjects in our study is also highly significant. In the abundant literature on this issue, many studies show a similar dose-response relationship between alcohol and blood lipids. Most of the data concern the relation between HDL-C and apolipoprotein-AI, but heavy drinkers usually demonstrate higher plasma levels of TG, TC, and LDL-C compared to non-drinkers [10, 11, 24]. For example, a cross-sectional study conducted in China revealed that heavy drinking (> 30 g per day) led to a harmful effect of increased TG and TC [25]. In another study, by Kwon et al. [26], it was found that high-risk drinking was associated with a higher risk of hypertriglyceridemia and elevated LDL-C levels in both sexes, as well as lower HDL-C levels.

In our study, we also found significantly higher levels of adiponectin in the study group compared to the control group, with the highest levels observed in the group of persons consuming up to 2 drinks per day and the lowest in those consuming > 20 units of alcohol per day. In contrast, a significant relation was found between adiponectin levels and age. As other studies have shown, this may be related to the higher accumulation of fat in the elderly, with fat being an important source of adiponectin and pro-inflammatory cytokines [27].

## Conclusions

In the present study, abnormal trends were observed for most (except for vWF) of the markers analyzed in alcohol abusers, with no significant correlation with daily alcohol consumption (except for vWF levels) or total duration of alcohol abuse. No significant correlation was observed for most markers with variables, such as age, sex, place of residence, and smoking. The absence of the above correlations may be the result of irreversible damage to many

tissues and organs in chronic drinkers who consume alcoholic beverages above the harmful limit, which at this stage does not depend on further increases or decreases in ethanol intake. Further studies in this direction on a larger group of patients, taking into account additional factors such as the type of alcohol consumed, are therefore necessary to clarify the mechanisms leading to cardiovascular damage in the course of alcohol abuse.

**Conflict of interest:** None declared.

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**Table 1**. Characteristics of the study group

| Variable | | Overall (n = 100) |
|---|---|---|
| Age, y, median (IQR) | | 44 (36.75–52.0) |
| Male gender | | 79 |
| Smoking | | 81 |
| Place of residence | Town | 52 |
| | Village | 48 |
| Number of cigarettes smoked during the day | N | 81 |
| | Median (IQR) | 20 (15–20) |
| | Range | 1–40 |
| Portions of consumed alcohol/per day | 0–2 drinks | 2 |
| | 3–5 drinks | 6 |
| | 6–10 drinks | 14 |
| | 11–20 drinks | 27 |
| | > 20 drinks | 51 |
| Time of alcohol abuse | < 1 year | 12 |
| | 1–5 years | 28 |

| | | |
|---|---|---|
| | 5–10 years | 24 |
| | 10–20 years | 17 |
| | > 20 years | 18 |
| | No data | 1 |

Data are presented as the percentage of patients unless otherwise indicated. IQR — interquartile range

**Table 2.** Results of basic laboratory tests (lipid profile, hsCRP) in the study group

| Variable | Parameter | Overall (n = 100) | Category |
|---|---|---|---|
| TC, mmol/l (Norm: 3.0–5.0 mmol/l) | Median (IQR) | 5.09 (4.42–5.6) | Above norm: 53% (n = 53)<br>Norm: 47% (n = 47)<br>Below norm: 0% (n = 0) |
| | Range | 3.31–8.24 | |
| HDL-C, mmol/l (Norm: ≥ 1.0 mmol/l in men; ≥ 1.2 mmol/l in women) | Median (IQR) | 1.14 (0.96–1.38) | Norm: 65% (n = 65)<br>Out of norm: 35% (n = 35) |
| | Range | 0.52–2.61 | |
| LDL-C, mmol/l (Norm: < 3.0 mmol/l) | Median (IQR) | 3.43 (2.82–3.98) | Norm: 33% (n = 33)<br>Out of norm: 67% (n = 67) |
| | Range | 2.01–6.71 | |
| TG, mmol/l (Norm: < 1.7 mmol/l) | Median (IQR) | 2.22 (1.43–3.17) | Norm: 34% (n = 34)<br>Out of norm: 66% (n = 66) |
| | Range | 0.64–8.54 | |
| hsCRP, mg/l (Norm: < 3.0 mmol/l) | Median (IQR) | 1.43 (0.74–2.5) | Norm: 77% (n = 77)<br>Out of norm: 23% (n = 23) |
| | Range | 0.15–58 | |

HDL-C — high-density cholesterol; hsCRP — high-sensitivity C-reactive protein; IQR — interquartile range; LDL-C — low-density cholesterol; TC — total cholesterol; TG — triglycerides

**Table 3.** Comparison of the results of the tested markers in the study and control groups

| Variable | Parameter | Study group | Control group | P-value |
|---|---|---|---|---|
| vWF, pg/ml | N | 100 | 25 | 0.0812 |
| | Median (IQR) | 895.05 (697.83–1070.0) | 795.13 (722.8–893.6) | |
| PAI-1, ng/ml | N | 96 | 25 | < 0.001 |
| | Median (IQR) | 20.19 (14.5–27.01) | 13.29 (10.23–15.42) | |
| TNF-α, pg/ml | N | 96 | 25 | < 0.001 |
| | Median (IQR) | 7.76 (3.91–11.51) | 1.8 (1.2–2.5) | |
| VCAM-1, ng/ml | N | 100 | 25 | < 0.001 |
| | Median (IQR) | 572.77 (474.25–617.58) | 327.89 (321.64–344.63) | |
| Adiponectin, µg/ml | N | 100 | 25 | < 0.001 |
| | Median (IQR) | 17.52 (15.1–19.21) | 8.53 (6.94–9.97) | |

| Variable | Parameter | Study group | Control group | P-value |
|---|---|---|---|---|
| Fibrinogen, g/l | N | 100 | 25 | < 0.001 |
| | Median (IQR) | 3.6 (3.0–4.13) | 2.54 (2.43–2.72) | |

IQR — interquartile range; PAI-1 — plasminogen activator inhibitor 1; TNF-α — tumor necrosis factor alpha; VCAM-1 — vascular cellular adhesion molecule-1; vWF — von Willebrand factor

**Table 4.** Results for the studied markers in relation to age and number of cigarettes smoked per day in the study group — Spearman's correlation matrix

| | Age, years | Number of cigarettes smoked per day |
|---|---|---|
| vWF, pg/ml (n = 100) | –0.200 (p = 0.079) | 0.045 (p = 0.699) |
| PAI-1, ng/ml (n = 96) | –0.010 (p = 0.933) | 0.110 (p = 0.337) |
| TNF-α, pg/ml (n = 96) | –0.114 (p = 0.320) | 0.019 (p = 0.869) |
| VCAM-1, ng/ml (n = 100) | 0.006 (p = 0.958) | -0.123 (p = 0.284) |
| Adiponectin, µg/ml (n = 100) | 0.362 (p = 0.001) | 0.171 (p = 0.135) |
| Fibrinogen, g/l (n = 100) | 0.174 (p = 0.127) | 0.301 (p = 0.007) |

PAI-1 — plasminogen activator inhibitor 1; TNF-α — tumor necrosis factor alpha; VCAM-1 — vascular cellular adhesion molecule-1; vWF — von Willebrand factor

**Table 5.** Comparison of the results of the studied markers according to the average daily number of units of alcohol consumed in the study group

| Variable | Parameter | 0–2 drinks | 3–5 drinks | 6–10 drinks | 11–20 drinks | > 20 drinks | P-value |
|---|---|---|---|---|---|---|---|
| vWF, pg/ml | N | 2 | 6 | 14 | 27 | 51 | 0.0319 |
| | Median (IQR) | 714.32 (670.7–757.93) | 847.73 (678.74–958.31) | 993.12 (816.81–1161.05) | 993.12 (817.64–1116.3) | 832.48 (657.06–971.76) | |
| PAI-1, ng/ml | N | 2 | 6 | 13 | 25 | 50 | 0.578 |
| | Median (IQR) | 21.12 (20.13–22.11) | 19.67 (15.39–24.35) | 16.03 (12.46–22.12) | 21.91 (18.36–27.42) | 19.21 (14.53–29.78) | |
| TNF-α, pg/ml | N | 2 | 6 | 13 | 25 | 50 | 0.2154 |
| | Median (IQR) | 7.18 (5.029.35) | 9.32 (6.59–13.73) | 9.51 (8.22–15.95) | 4.98 (2.16–9.26) | 7.22 (3.91–11.24) | |
| VCAM-1, ng/ml | N | 2 | 6 | 14 | 27 | 51 | 0.188 |
| | Median (IQR) | 541.42 (517.15–565.7) | 552.55 (437.59–736.01) | 506.25 (413.27–567.04) | 572.23 (507.53–612.66) | 599.51 (486.28–631.7) | |
| Adiponectin, µg/ml | N | 2 | 6 | 14 | 27 | 51 | 0.2356 |
| | Median (IQR) | 18.7 (18.26–19.13) | 18.3 (17.11–19.55) | 18.14 (16.17–19.73) | 17.96 (17.04–19.25) | 16.68 (12.36–18.8) | |
| Fibrinogen, g/l | N | 2 | 6 | 14 | 27 | 51 | 0.9702 |
| | Median (IQR) | 3.41 (3.28–3.53) | 3.64 (3.47–3.99) | 3.66 (3.25–3.95) | 3.7 (3.06–4.26) | 3.51 (2.91–4.22) | |

IQR — interquartile range; PAI-1 — plasminogen activator inhibitor 1; TNF-α — tumor necrosis factor alpha; VCAM-1 — vascular cellular adhesion molecule-1; vWF — von Willebrand factor

**Table 6.** Comparison of the results of the studied markers according to the total duration of alcohol abuse in the study group

| Variable | Parameter | < 1 year | 1–5 years | 5–10 years | 10–20 years | > 20 years | P-value |
|---|---|---|---|---|---|---|---|
| vWF, pg/ml | N | 12 | 28 | 24 | 17 | 19 | 0.4511 |
| | Median (IQR) | 863.07 (622.15 – 979.28) | 985.64 (812.11 – 1111.73) | 777.18 (664.98 – 1224.25) | 871.3 (774.94 – 951.95) | 857.74 (717.9–967.87) | |
| PAI-1, ng/ml | N | 12 | 25 | 24 | 17 | 18 | 0.7383 |
| | Median (IQR) | 20.59 (18.62–27.17) | 21.91 (14.5–26.51) | 19.21 (15.61–28.17) | 17.19 (12.46–30.85) | 23.1 (12.21–25.65) | |
| TNF-α, pg/ml | N | 12 | 25 | 24 | 17 | 18 | 0.2442 |
| | Median (IQR) | 8.22 (1.6–15.39) | 9.26 (3.91–12.62) | 8.22 (3.91–12.62) | 7.13 (6.05–10.41) | 3.91 (1.81–9.31) | |
| VCAM-1, | N | 12 | 28 | 24 | 17 | 19 | 0.871 |

| Variable | Parameter | < 1 year | 1–5 years | 5–10 years | 10–20 years | > 20 years | P-value |
|---|---|---|---|---|---|---|---|
| ng/ml | Median (IQR) | 525.33 (450.28 –593.4) | 576.83 (486.14 – 687.28) | 565.28 (497.77 – 610.66) | 524.11 (447.6– 614.81) | 596.51 (472.72 – 617.53) | 6 |
| Adiponectin, µg/ml | N | 12 | 28 | 24 | 17 | 19 | 0.0926 |
| | Median (IQR) | 16.64 (15.39– 17.92) | 18.33 (16.79– 19.42) | 16.04 (10.83– 18.22) | 17.9 (13.5– 18.35) | 18.23 (16.33– 19.73) | |
| Fibrinogen, g/l | N | 12 | 28 | 24 | 17 | 19 | 0.0697 |
| | Median (IQR) | 3.3 (3.01– 3.62) | 3.58 (3.13– 3.86) | 3.87 (3.36– 4.24) | 3.18 (2.84– 3.87) | 4.12 (3.29– 4.63) | |

IQR — interquartile range; PAI-1 — plasminogen activator inhibitor 1; TNF-α — tumor necrosis factor alpha; VCAM-1 — vascular cellular adhesion molecule-1; vWF — von Willebrand factor