The relationship between venous insufficiency and serum magnesium level

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Abstract. ***Background***: Magnesium is the second most common cation in the cell. In addition to its role as a cofactor in many enzymatic pathways in physiological processes, it is necessary for the regular functioning of vascular smooth muscle cells. Magnesium deficiency has been associated with exacerbation of inflammation, which plays a role in the aetiopathogenesis of many diseases. ***Aim*:** To investigate the potential relationship between serum magnesium level and the development of chronic venous insufficiency by comparison with healthy individuals. ***Methods***: The study included 394 patients with venous insufficiency based on physical examination findings and colour Doppler ultrasonography, and 206 controls without venous insufficiency. Venous insufficiency was defined by colour Doppler as reflux lasting 0.5 seconds or more in superficial veins, and longer than one second in femoral and popliteal veins. Clinical, haematological and biochemical parameters, including serum magnesium level and indicators of inflammation, were compared between groups. ***Results:*** A total of 600 participants were included. There was no significant difference between the groups in terms of age and gender. In total, 187 (47.46%) patients with chronic venous insufficiency and 105 (50.97%) of the control group were male (p=0.414). The median age of the patients with chronic venous insufficiency was 48 (min-max: 41-49), and the median age of the control group was 49.00 (min-max: 45.00-60.25) (p=0.064). Serum magnesium level was found to be significantly lower in the group with chronic venous insufficiency compared to the control group; 1.90 mg/dL (min-max: 1.82-2) versus 2.1 mg/dL (min-max: 2-2.2) (p<0.001), respectively. ***Conclusion***: Low serum magnesium levels may pose a potential risk for the development of chronic venous insufficiency, which is common in the community.

Key words: venous insufficiency, inflammation, magnesium

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Venous insufficiency is a chronic progressive disease that is common in the adult population and can cause problems that can affect quality of life. Its prevalence in the adult population varies between 10% and 30% [1]. Venous insufficiency is an important health problem because it causes painful venous ulcers, resulting in loss of work and affects the quality of life of patients [2]. Many risk factors, such as advanced age, female gender, genetic predisposition, obesity, pregnancy, intra-abdominal cancers, and lifestyle, play a role in the aetiology of the disease [3, 4].

Increased inflammation plays a role in the aetiopathogenesis of venous insufficiency. In

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histological studies, it has been shown that collagen 1 and collagen 3 increase in endothelial cells in the venous vessel wall due to chronic inflammation, and loss of function in smooth muscle cells occurs as a result of impaired collagen-elastin balance. Venodilation develops as a result of histopathological changes in the vessel wall, and it is accepted that venous hypertension and valve insufficiency develop as a result of impaired venous return [5, 6].

Magnesium is the most common cation found in cells after potassium. It is an essential element for life that contributes to many enzymatic reactions. It plays a role in the regulation of smooth muscle tone through an antagonistic effect on calcium entry into vascular smooth muscle cells and calcium uptake from the sarcoplasmic reticulum [7].

Hypomagnesemia has been associated with increased inflammation in previous studies, and has been shown to play a role in the development of systemic inflammatory response syndrome, especially in patients hospitalized in the intensive care unit [8]. In a study investigating the relationship between magnesium level and inflammation, a negative correlation was found between magnesium level and hs-CRP level [9]. In our study, we aimed to investigate the relationship between serum magnesium levels and chronic venous insufficiency.

Methods

Our study included 394 patients who presented to cardiology and cardiovascular surgery outpatient clinics with leg pain, who were found to have venous insufficiency as a result of physical examination findings and colour Doppler ultrasonography. We also included 206 controls who did not have venous insufficiency based on their examinations between January 2016 and January 2020.

The study was carried out in accordance with the Principles of the Declaration of Helsinki, after approval of the Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (Date: 21.03.2022, Decision No: 2022-06-15). Patient information and laboratory tests were obtained by retrospectively scanning the hospital database (Sarus Hospital Information System) and patient files.

At the time of diagnosis, patients with malignancy, active infection, chronic inflammatory disease, patients taking oral contraceptives and hormone replacement therapy, immobile patients, patients who underwent surgery within the last three months, patients with a history of trauma within the last three months, patients with chronic kidney failure and chronic liver disease, pregnant women, patients under the age of 18, and patients using magnesium-containing drug supplements were not included in the study.

In our study, Doppler ultrasonography examinations of both lower extremities were performed by the same radiologist using a 7.5-MHz linear probe on the Hitachi Hi Vision Preirus Ultrasonography device. Backflows lasting 0.5 seconds or longer in the superficial veins and longer than one second in the femoral and popliteal veins in the direction of venous flow with valsalva or distal compression were considered as venous insufficiency [10].

Glucose, creatine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), magnesium, total cholesterol, triglyceride, LDL (low-density lipoprotein) cholesterol and HDL (high-density lipoprotein) cholesterol tests of the patients were measured using the AU5800 Clinical Chemistry System (Beckman Coulter, INC, California, USA), and haematological parameters were measured with the XT-400Oi Hematology Analyzer (Symex, Kobe, Japan). The CRP/albumin ratio was calculated by dividing the serum CRP level by the serum albumin level, and the platelet/lymphocyte ratio (PLR) was calculated by dividing the platelet value in complete blood count by the lymphocyte value. The neutrophil/lymphocyte ratio (NLR) was calculated by dividing the neutrophil value in the complete blood count by the lymphocyte value, and the monocyte/HDL ratio was calculated by dividing the monocyte value in the complete blood count by the HDL value. The results of the group with venous insufficiency and the control group were compared statistically.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics version 22.0 (IBM Corp., USA) and MedCalc version 12.3.0.0. The Shapiro-Wilk test was used to test the normality of variables.

Continuous variables were presented as mean ± standard deviation for normally distributed variables; otherwise median (1st quartile - 3rd quartile) values were given. The independent samples t test or Mann-Whitney U-test was performed to compare two independent groups when the data were normally distributed and non-normal, respectively. Categorical variables were expressed by counts and percentages. Comparisons between the groups were performed with the Pearson chi-square test for categorical variables. Receiver operating characteristics (ROC) curve analysis was performed to evaluate the performance of diagnostic markers in discriminating venous insufficiency. The Youden J index was used to determine the optimal cut-off value. Risk factors were also evaluated with binary logistic regression analysis. $P<0.05$ considered statistically significant.

Results

The demographic and laboratory characteristics of the patients in our study are shown in *table 1*. A total of 600 individuals were included in the study: 394 patients with venous insufficiency and 206 controls without venous insufficiency. Of the patients included in the study, 48.67% (n=292) were male and 51.33% (n=308) were female. The median age of the patient group was 48 (min-max: 41-59), and the median age of the control group was 49 (min-max: 45-60). There was no statistically significant difference between the patient and control groups in terms of age (p=0.064) or gender (p=0.414).

Of the patients, 16.67% had diabetes mellitus (DM), 23.67% had hyperlipidaemia (HL), and 5.67% had a history of thyroid disease. Hypertension (32.3%) was found to be the most common comorbid disease. There was no significant difference between the patient and control groups in terms of diabetes mellitus (DM), hypertension (HT), hyperlipidaemia (HL) or thyroid disease (*table 2*).

Serum magnesium level (median: 1.90 mg/dL [min-max: 1.82-2.00] vs. 2.10 mg/dL [min-max: 2.00-2.20]), serum albumin level (median: 43.00 g/L [min-max: 40.00-44.93] vs. 44.00 g/L [min-max: 42.00-46.00]) and serum lymphocyte level (median: 2.20 [min-max: 1.80-2.67] vs. 2.45 [min-max: 1.98-2.90]) were significantly lower in the patient group than the healthy control group

Table 1. Demographic characteristics and laboratory findings of the study population.

Variable	Descriptive statistics (n=600)
Age (years)*	48.00 (42.00-59.00)
Gender***	
Male	292 (48.67)
Female	308 (51.33)
Diabetes mellitus n (%)***	100 (16.67)
Hypertension n (%)***	194 (32.33)
Hyperlipidaemia n (%)***	142 (23.67)
Thyroid disease n (%)***	34 (5.67)
Glucose (mg/dL)*	96.00 (89.00-108.00)
Creatine (mg/dL)*	0.74 (0.63-0.86)
AST (IU/L)*	19.00 (16.00-23.00)
ALT (IU/L)*	18.00 (13.25-24.00)
Total cholesterol (mg/dL)**	207.64±37.97
HDL (mg/dL)*	47.00 (41.00-56.00)
Triglyceride (mg/dL)*	130.00 (94.00-188.00)
LDL (mg/dL)*	124.00 (103.00-145.00)
Magnesium (mg/dL)*	1.99 (1.89-2.10)
Albumin (g/L)*	43.00 (41.00-45.00)
CRP (mg/L)*	2.70 (1.70-3.70)
Uric acid (mg/dL)*	4.90 (4.10-5.70)
WBC (10^3/μL)*	7.67 (6.35-9.02)
Haemoglobin (gr/L)*	13.80 (12.70-15.00)
Platelets (10^3/μL)*	242.00 (202.00-287.00)
RDW (%)*	13.20 (12.70-13.96)
MPV (fL)*	9.90 (9.20-10.70)
Neutrophils (10^3/μL)*	4.29 (3.44-5.38)
Lymphocytes (10^3/μL)*	2.29 (1.84-2.72)
Monocytes (10^3/μL)*	0.60 (0.49-0.73)
CRP/albumin ratio*	0.06 (0.04-0.09)
NLR*	1.88 (1.47-2.44)
PLR*	106.29 (84.88-133.51)
Monocyte / HDL ratio**	0.01 (0.01-0.02)

*Median (1st quartile-3rd quartile)
**Mean±standard deviation
***n (%)
ALT: alanine aminotransferase; AST: aspartate aminotransferase; CRP: C-reactive protein; MPV: mean platelet volume; RDW: red cell distribution width; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; LDL: low-density lipoprotein; HDL: high-density lipoprotein, WBC: white blood count.

Table 2. Comparison between demographic characteristics and laboratory findings and venous insufficiency and the control group.

	Venous insufficiency group (*n*=394)	Control group (*n*=206)	*p* value
Age (years)*	48.00 (41.00-59.00)	49.00 (45.00-60.25)	0.064
Gender***			
Male	187 (47.46)	105 (50.97)	0.414
Female	207 (52.54)	101 (49.03)	
Diabetes mellitus *n* (%)***	62 (15.74)	38 (18.45)	0.398
Hypertension *n* (%)***	126 (31.98)	68 (33.01)	0.798
Hyperlipidaemia *n* (%)***	94 (23.86)	48 (23.30)	0.879
Thyroid disease *n* (%)***	22 (5.58)	12 (5.83)	0.903
Glucose (mg/dL)*	97.50 (89.00-107.25)	95.00 (89.00-110.00)	0.574
Creatine (mg/dL)*	0.73 (0.64-0.83)	0.76 (0.63-0.90)	0.191
AST (IU/L)*	19.00 (16.00-23.00)	19.00 (16.00-23.00)	0.784
ALT (IU/L)*	18.00 (13.75-24.00)	19.00 (13.00-25.00)	0.626
Total cholesterol (mg/dL)***	208.11±37.60	206.74±38.73	0.676
HDL (mg/dL)*	47.50 (41.75-56.00)	45.00 (39.00-56.00)	0.072
Triglyceride (mg/dL)*	133.00 (93.00-187.25)	123.00 (96.50-192.25)	0.916
LDL (mg/dL)*	123 (103.00-144.25)	127 (101.00-146.00)	0.916
Magnesium (mg/dL)*	1.90 (1.82-2.00)	2.10 (2.00-2.20)	<0.001
Albumin (g/L)*	43.00 (40.00-44.93)	44.00 (42.00-46.00)	<0.001
CRP (mg/L)*	3.00 (2.00-4.00)	2.00 (1.18-2.90)	<0.001
Uric acid (mg/dL)*	5.00 (4.22-5.72)	4.66 (3.90-5.61)	0.010
WBC (10^3/μL)*	7.63 (6.30-9.12)	7.75 (6.50-8.79)	0.918
Haemoglobin (gr/L)*	13.80 (12.68-14.80)	14.00 (12.80-15.00)	0.599
Platelets (10^3/μL)*	241 (202.00-286.25)	246 (202.00-287.25)	0.764
RDW (%)*	13.20 (12.70-14.00)	13.00 (12.60-13.80)	0.056
MPV (fL)*	10.00 (9.20-10.70)	9.85 (9.00-10.50)	0.117
Neutrophils (10^3/μL)*	4.31 (3.44-5.43)	4.28 (3.50-5.16)	0.330
Lymphocytes (10^3/μL)*	2.20 (1.80-2.67)	2.45 (1.98-2.90)	<0.001
Monocytes (10^3/μL)*	0.60 (0.48-0.74)	0.60 (0.50-0.70)	0.482
CRP/albumin ratio*	0.07 (0.05-0.10)	0.05 (0.03-0.07)	<0.001
NLR*	2.00 (1.51-2.53)	1.77 (1.41-2.14)	<0.001
PLR*	109.01 (87.59-137.53)	101.29 (79.13-128.02)	0.007
Monocyte / HDL ratio*	0.01 (0.01-0.02)	0.01 (0.01-0.02)	0.933

*Median (1st quartile-3rd quartile)
**Mean±standard deviation
***n (%)
ALT: alanine aminotransferase; AST: aspartate aminotransferase; CRP: C-reactive protein; MPV: mean platelet volume; RDW: red cell distribution width; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; LDL: low-density lipoprotein; HDL: high-density lipoprotein; WBC: white blood count.

(p<0.001 for each). Serum uric acid level (median: 5.00 mg/dL [min-max: 4.22-5.72] vs. 4.66 mg/dL [min-max: 3.90-5.61]; p=0.010) and serum C-reactive protein (CRP) (median: 3.00 mg/L [min-max: 2.00-4.00] vs. 2.00 mg/L [min-max: 1.18-2.90]; p<0.001) were significantly higher in the patient group than the healthy control group. There was no significant difference between the groups with regards to other laboratory parameters. The CRP/albumin ratio (p<0.001), NLR (p<0.001) and PLR (p=0.007) were significantly higher in the patient group than in the healthy control group. There was no statistically significant difference between the two groups in terms of monocyte/HDL ratio (p=0.933) (*table 2*).

ROC analysis was performed to evaluate the value of magnesium, CRP, albumin, uric acid, lymphocyte, CRP/albumin ratio, NLR, PLR and monocyte/HDL ratio in predicting venous insufficiency. The optimal cut-off value for magnesium was 1.97 mg/dL, and the sensitivity and specificity corresponding to this cut-off value were 66.50 and 85.92, respectively (area under the curve=0.825, p<0.001) (*table 3*).

In univariate analyses, variables with significant differences between the groups were included in the model, and binary logistic regression analysis was performed. Numerical variables were categorized according to the optimal cut-off points obtained from the ROC analysis, and were included in the model as binary variables. Accordingly, magnesium (≤1.97/>1.97), CRP/Alb (>0.06/≤0.06), uric acid (>4.5/≤4.5), NLR (>1.96/≤1.96), and PLR (>82.19/≤82.19) variants were included. The model was shown to be significant (Omnibus test: p<0.001, Hosmer and Lemeshow test: p=0.419). Magnesium ≤1.97 increased the risk of venous insufficiency 13.752-fold compared to a value of >1.97 (p<0.001). The risk of venous insufficiency was 2.418-fold higher in patients with CRP/albumin ratio >0.06 compared to those with ≤0.06 (p<0.001). The risk of venous insufficiency was 1.698-fold higher in patients with uric acid level >4.5 than in

Table 3. Results of the ROC analysis.

Variables	AUC	*p* value	Cut-off	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV
Magnesium	0.825	<0.001	≤1.97	66.50 (61.6 - 71.1)	85.92 (80.4 - 90.4)	90.0 (86.0 - 93.2)	57.3 (51.6 - 62.9)
CRP	0.674	<0.001	>2.6	60.15 (55.1 - 65.0)	66.99 (60.1 - 73.4)	77.7 (72.6 - 82.3)	46.8 (41.0 - 52.7)
Albumin	0.603	<0.001	≤43.7	62.18 (57.2 - 67.0)	56.31 (49.2 - 63.2)	73.1 (68.0 - 77.8)	43.8 (37.7 - 50.0)
Uric acid	0.564	0,012	>4.5	67.51 (62.6 - 72.1)	47.09 (40.1 - 54.1)	70.9 (66.1 - 75.5)	43.1 (36.5 - 49.9)
CRP/albumin ratio	0.681	<0.001	>0.06	54.82 (49.8 - 59.8)	72.33 (65.7 - 78.3)	79.1 (73.8 - 83.8)	45.6 (40.1 - 51.1)
Lymphocytes	0.592	<0.001	≤2.38	61.68 (56.7 - 66.5)	55.34 (48.3 - 62.3)	72.5 (67.4 - 77.3)	43.0 (37.0 - 49.2)
NLR	0.593	<0.001	>1.96	52.03 (47.0 - 57.1)	66.50 (59.6 - 72.9)	74.8 (69.2 - 79.9)	42.0 (36.6 - 47.6)
PLR	0.567	0.007	>82.19	82.74 (78.6 - 86.3)	28.64 (22.6 - 35.3)	68.9 (64.5 - 73.1)	46.5 (37.5 - 55.6)
Monocyte / HDL ratio	0.519	0.374	-	-	-	-	-

AUC: area under the ROC curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; CRP: C-reactive protein; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; HDL: high-density lipoprotein.

Table 4. Logistic regression analysis.

Variables	*p* value	OR	95% CI for OR	
			Lower	Upper
Magnesium (RC: >1.97 mg/dL)	<0.001	13.752	8.471	22.327
CRP/albumin ratio (RC: ≤0.06)	<0.001	2.791	1.825	4.270
Uric acid (RC: ≤4.5 mg/dL)	0.016	1.698	1.105	2.610
Neutrophil-lymphocyte ratio (RC: ≤1.96)	0.002	2.061	1.316	3.228
Platelet-lymphocyte ratio (RC: ≤82.19)	0.027	1.829	1.071	3.123

RC: reference category; OR: odds ratio; CI: confidence interval.

patients with ≤4.5 (p=0.016). The risk of venous insufficiency was 2.061-fold higher in patients with NLR >1.96 than in patients with ≤1.96 (p=0.002). Finally, the risk of venous insufficiency was 1.829-fold higher in patients with PLR >82.19 compared to those with ≤82.19 (p=0.027) (*table 4*).

Discussion

The main finding of our study is that the serum magnesium level in patients with venous insufficiency was lower than that in the control group with similar age and gender characteristics, and the CRP/albumin ratio, NLR and PLR were higher compared to the control group.

Chronic venous insufficiency has a wide spectrum of symptoms that can progress from asymptomatic telangiectasias to painful venous ulcers. It is an important health problem that can affect the quality of life due to complications [11], and is predicted to affect approximately 40% of the general population [12].

Venous insufficiency is a multifactorial disease. Morphological studies in patients with chronic venous insufficiency have shown that inflammation plays a role in the pathophysiology of the disease. Venous hypertension and valvular incompetence leading to shear stress trigger endothelial activation. A dysfunctional endothelium perpetuates the inflammatory cascade. As a result of chronic inflammation, the release of intercellular adhesion molecule-1 (ICAM-1) and other adhesion molecules, which increase the uptake of leukocytes to the endothelial surface, increases, and as a result of the activation of matrix metalloproteinases, extracellular matrix destruction occurs in the venous media and adventitia [13, 14]. Collagen I and collagen III synthesis increases in the venous wall structure and an imbalance occurs in the collagen/elastin level. With the resulting endothelial damage and structural changes in smooth muscle cells, a decrease in vascular tone and venodilation occurs. It is accepted that venous hypertension and venous valve insufficiency develop as a result of venodilation [14, 15].

C-reactive protein (CRP) is an acute phase protein that is not affected by age or gender; it is synthesized in the liver under IL-6 control and has been used as a strong marker of inflammation for many years. The relationship between high serum CRP level and increased cardiovascular events and prognosis has been shown in many studies [16, 17]. CRP induces the expression of adhesion molecules such as E-selectin, vascular adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) on the endothelial cell surface, thus facilitating leukocyte adhesion, causing endothelial damage [18]. Albumin is the major protein of the plasma, synthesized in the liver. It is an acute-phase reactant and its serum level decreases with inflammation [19]. Studies have shown that there is a relationship between low albumin levels and mortality [20, 21]. The ratio of CRP/albumin, which is used as a new inflammation parameter, is thought to be more related to severity of inflammation relative to albumin or CRP alone [22]. In our study, in accordance with the literature, in patients with venous insufficiency (the pathogenesis of which involves inflammation), serum CRP levels and CRP/albumin ratios (indicators of inflammation) were found to be significantly higher than in the control group and albumin levels were found to be lower in the patient group.

The PLR is an inexpensive and easily applicable marker that has recently been used to assess chronic inflammation. There are studies showing that it is more effective in demonstrating inflammation compared to the NLR [23, 24]. PLR has been associated with poor prognosis in many diseases such as diabetes, kidney disease, and cancer [25]. In addition, increased PLR has been shown to be associated with mortality in cardiovascular diseases, similar to the NLR [26, 27]. In the studies of Oylumlu *et al*., including 587 patients with acute coronary syndrome, the PLR was found to be superior to the NLR in demonstrating in-hospital mortality [28]. In our study, PLR, which is an indicator of inflammation, was found to be higher in the venous insufficiency group than in the control group.

Increasing inflammation changes the NLR in patients with venous insufficiency. Proteolytic and hydrolytic enzymes and free oxygen radicals secreted by increased neutrophils secondary to the inflammatory process cause damage to the venous valve endothelium. In addition, lymphocytes undergoing apoptosis with inflammation increase the level of inflammatory cytokines and increase the development of endothelial damage. The NLR is widely used as a simple, fast and inexpensive inflammatory marker [29, 30]. It has been studied in many inflammatory diseases, and its relationship with the development of atherosclerosis and adverse cardiovascular events has been shown [31, 32]. In a study conducted in patients with venous insufficiency, it was reported that the NLR is an independent predictor of venous insufficiency and is an important marker in determining the severity of the disease [33]. In our study, the NLR, a simple inflammatory marker, was found to be higher in the group with venous insufficiency. Although there are not many studies in the literature on this subject, a high NLR is associated with venous insufficiency as an indicator of inflammation that plays a role in every stage of endothelial damage.

Monocytes cause the secretion of proinflammatory cytokines and increase in number under oxidative stress during the inflammatory process. HDL both inhibits the oxidation of LDL cholesterol and exerts anti-inflammatory and antioxidative effects by inhibiting the expression of adhesion molecules on the endothelial surface [34]. The monocyte/HDL ratio is accepted as an inflammatory marker, which is a new determinant of mortality and morbidity in many diseases, including cardiovascular diseases [35]. In a study investigating the relationship between saphenous vein graft patency and monocyte/HDL ratio, no significant correlation was found with saphenous vein graft patency [36]. We could not find any study in the literature investigating the relationship between venous insufficiency and monocyte/HDL ratio. Moreover, in our study, we were unable to determine a statistically significant difference between the patient and control group.

Magnesium is the second most common cation in cells. It acts as a cofactor in more than 300 enzymatic pathways, including nucleic acid synthesis [37]. Magnesium is an element with anti-inflammatory properties that plays a role in many steps of the immune system. Its effect on inflammation has been studied for many years. In studies on animal models, it has been shown that a low magnesium level causes an increase in leukocyte activation, excessive free radicals and the release of proinflammatory cytokines [38, 39]. An increase in nuclear factor-kappa B and IL-1α levels have been demonstrated in endothelial cells as a result of exposure to low extracellular magnesium. The increase in these two factors enhances oxidative stress in endothelial cells, leading to upregulation of some cytokines and growth factors that cause damage [40]. In a study of diabetic patients over 65 years of age, a correlation between increased magnesium intake and endothelial function was investigated, revealing aa significant improvement in endothelial function and an increase in exercise tolerance as a result of magnesium supplementation [41].

Findings from epidemiological studies show that there is a negative correlation between magnesium and CRP levels. In a cross-sectional study examining adults over the age of 17, the CRP level was shown to decrease by 22% in the group that took 50-mg daily supplements, and it was emphasized that taking magnesium supplements to reduce inflammation may be beneficial [42]. In a cross-sectional study of 657 female patients aged 43-69 years, Song *et al*. found that the CRP level was 24% lower and the E-selectin level 14% lower in the group consuming high-dose magnesium [43]. In our study, magnesium levels were found to be significantly lower in patients with venous insufficiency compared to the control group.

Limitations

The most important limitation of our study is that it was retrospective and consisted of a relatively small number of patient groups. In addition, since serum magnesium levels can be affected by diet and alcohol, the magnesium level measured in clinical practice may not always provide information about total magnesium. Moreover, most of the magnesium in the body is in the intracellular space, and only 1% is in the extracellular space**.** In our study, patients were not divided into subgroups according to the degree of venous insufficiency, and a relationship between magnesium level and the degree of venous insufficiency was not investigated. Many patients had either diabetes mellitus, hypertension or hyperlipidaemia. These diseases are widely known to have adverse effects on the metabolic balance of magnesemia. However, the study was based on a real-life setting and many patients in daily practice have some of these comorbidities together with venous insufficiency. In addition, there was no significant difference between the patient group and control group in terms of comorbidities such as diabetes mellitus, hypertension or hyperlipidaemia. Finally, another limitation is that the drugs of the study population were not noted, as certain therapies may affect magnesemia.

Conclusion

Studies have revealed a key role for magnesium in the inflammatory network. Magnesium deficiency increases inflammation and adversely affects the prognosis of cardiovascular diseases. Further extensive research is needed on the role of magnesium supplementation in preventing the occurrence and/or progression of chronic venous insufficiency.

Disclosure

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