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Research Article

Assessment of Oxidative Stress Levels and Total Oxidant and Antioxidant Status in Patients with Venous Insufficiency

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Abstract

Aim: There are variable treatment options for venous insufficiency depending on the origin of the various etiologic factors, the location, width, depth and infected area of the ulcer.In this study, we aimed to determine the oxidative stress load and to draw attention to the need for a multidisciplinary approach in the whole process as well as early diagnosis and treatment opportunities.

Material and Methods: This comparative observational study to investigate oxidative stress parameters in individuals with and without venous insufficiency. Effects of oxidative stress were investigated by serum 8-hydroxy-2' -deoxyguanosine Assay, Malondialdehit Assay, Total Antioxidant Status and Total Oxidant Status Assay tests using kits based on the enzyme-linked immunosorbent assay principle.

Results: A total of 68 individuals participated in the study, comprising 45.6% females and 54.4% males. No statistically significant differences were observed between the groups in terms of 8-hydroxy-2' -deoxyguanosine Assay, Total Oxidant Status Assay, Total Antioxidant Status, and Oxidative Stress Index Assay levels ($p = 0.417$, $p = 0.742$, $p = 0.210$, and $p = 0.416$, respectively). However, the Malondialdehit Assay level in the patient group (rank mean: 25.70) was significantly lower than that of the control group (rank mean: 38.10) ($p = 0.007$).

Conclusion: There are variations in the literature on oxidative stress markers levels in terms of mechanisms of action and outcomes. The varied results in the literature on oxidant and antioxidant mechanisms indicate that studies with much larger samples and analyses should be conducted on this subject.

Keywords: Antioxidant capacity, family medicine, oxidant capacity, oxidative stress, venous insufficiency.

INTRODUCTION

Venous insufficiency (VI) is a circulatory system disease in which venous return is impaired, with clinical symptoms such as pain, edema, varicose veins, skin changes and ulcers in the lower extremities. It is quite common in the community and seriously affects the quality of life.(1) Family medicine plays a key role in preventing complications of VI through both early diagnosis and long-term follow-up.(2)

The disease is among the increasingly common diseases all over the world. VI is a chronic disease that may be asymptomatic or may progress to a level that may require challenging treatments on the background of venous ulcers.The primary risk factors encompass a positive family history, increasing age, obesity, prolonged standing, smoking, a sedentary lifestyle, a history of lower extremity trauma, previous venous thrombosis, the presence of arteriovenous shunts, elevated estrogen exposure, and pregnancy (3).

Multidisciplinary coordination can be provided by the Family Medicine Specialist with information, counseling and follow-up of lifestyle changes to be made to the patient during the evaluation of VF risk factors, to predict possible complications in the process and to provide multidisciplinary coordination with consultation when necessary.(4)

The actions to be taken by the Family Medicine Specialist in primary, secondary and tertiary preventive medicine steps are listed as follows.

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Primary Prevention; Lifestyle adjustments such as avoiding prolonged standing can be recommended while combating obesity with the promotion of physical activity. Prevent the emergence of the disease by more closely following individuals who are registered in the population and have a positive family history . (5,6)

Secondary prevention: Identify varicose veins by recognizing the symptoms of VI and clinical examination, and ensure the use of compression stockings. Patients were classified according to the Clinical-Etiological-Anatomical-Pathophysiological (CEAP) system, which provides a standardized framework for assessing the severity and characteristics of chronic venous disorders. Contribute to early diagnosis and treatment by directing appropriate patients for evaluation with doppler ultrasound.(4,6)

Tertiary Prevention: Provide wound care and infection control in advanced cases with venous ulcer development. (2)

This disease, which is observed in 5-30% of the adult population, starts with a partial feeling of unhealthiness in people if it progresses from asymptomatic to symptomatic process, and as the symptoms progress, it brings problems on biopsychosocial and economic grounds. Due to the diversity of symptoms, the clinical reflections of the disease may start with leg tenderness, cosmetic problems and progress to processes such as venous claudication and even ulcerations that may involve the skin and subcutaneous tissues. Since the circulatory system cannot perform its functions effectively in patients with VI, the circulation of blood in the body will be impaired, leading to a decrease in the oxygen carrying capacity of venous blood and accumulation of metabolic wastes.(7)

Oxidative stress is caused by free radicals, mainly reactive oxygen species, that reduce antioxidant capacity through a number of biochemical mechanisms, leading to tissue and/or organ-level damage in the body. In patients with VI, increased oxidative stress can trigger conditions such as inflammation of the vessel walls, endothelial dysfunction and vascular occlusion. Antioxidants, the body's defense mechanisms against oxidative stress, neutralize free radicals. In the organism, the antioxidant defense system is in balance with free radicals formed in various ways. However, in cases where free radicals cannot be sufficiently cleared from the organism, they cause damage to DNA and damage products are formed.(8)

These damage-induced byproducts may contribute to the development of various metabolic disorders, aging, cancer, and even structural alterations in DNA, the genetic material. Among the well-established biomarkers of DNA damage is 8-hydroxy-2'-deoxyguanosine (8-OHdG).

While a certain balance between oxidant and antioxidant mechanisms is a physiological process, disruption of this balance will increase oxidative stress. This may cause difficulties in treatment. Venous hypertension, which will occur in patients with VI due to the effect of blood circulation, will accelerate the inflammation process as the oxygen in the blood becomes more reactive and increases the oxidant level in the blood.

Considering the pathophysiological mechanisms, oxidative stress and antioxidant capacity are open to new discoveries in the diagnosis and treatment process of patients with VI. By examining the effects of antioxidant and oxidant interactions on oxidative stress and cell death processes, it is thought to contribute to the development of treatment options for patients with VI by reducing oxidative stress levels or increasing antioxidant capacity. Oxidative stress contributes fundamentally to the pathogenesis of various chronic diseases—including cancer, cardiovascular disorders, neurodegenerative conditions, and autoimmune diseases—by inducing inflammatory responses through damage to cellular components.and antioxidant status on the clinical outcome of patients with VI.

This study aims to determine the importance of oxidative stress load in the development of VI disease and to emphasize the importance of preventive medicine and a multidisciplinary approach in order to increase both cost-effective and curative treatment options.

MATERIAL AND METHODS

Sample Size and Study Population

This study was designed as a comparative observational study to investigate oxidative stress parameters in individuals with and without venous insufficiency. The study comprised a total of 68 participants, including 33 patients diagnosed with venous insufficiency.and 35 healthy control subjects, based on the availability of eligible individuals and feasibility within the project's budget and timeline. All participants were recruited from outpatient clinics or hospital departments between February 1, 2023 and June 30,2023.

The inclusion criteria for the patient group required participants to be older than 18 years who have a confirmed diagnosis of venous insufficiency based on clinical and/or Doppler ultrasonographic findings, and providing written informed consent. The control group included age- and gender-matched individuals without any history or clinical evidence of venous insufficiency or other significant chronic illnesses.Exclusion criteria for both groups included death for any reason while the study is in progress Bleeding that will disrupt hemodynamics (such as hemorrhagic stroke, gastric bleeding) and ulcer patient whose treatment has ended.All participants voluntarily agreed to take part in the study, and data were collected during a single clinical visit for each individual.

Ethical Approval and Permissions

This study was approved by the Clinical Research Ethics Committee of Ordu University (Date/Decision No: 06.01.2023/13).

In addition, official permission to conduct the study and collect data was granted by the Ordu Provincial Directorate of Health (Date/Decision No: 31.01.2023/208319981).

Laboratory Tests:

Malondialdehit (MDA) Assay

Human malondialdehyde level was determined by ELISA (enzyme-linked immunosorbent assay) method. Malondialdehyde (MDA) levels were measured using a kit provided by Bioassay Technology Laboratory (BT Lab, Shanghai, China), following the manufacturer's instructions and protocols. Biotek Epoch 2 microplate reader was used for absorbance values (450 nm). Results were analyzed using Gen5 software.

Total Antioxidant Status and Total Oxidant Status Assay

To evaluate the impact of ART on total antioxidant and oxidant levels in Ishikawa endometrial cancer cells, the Rel Assay Total Antioxidant Status (TAS) and Total Oxidant Status (TOS) kits (Rel Assay Diagnostics, Gaziantep, Turkiye) were utilized. All procedures were performed in line with the manufacturer's protocol. Measurements of TAS and TOS were carried out using a Biotek Epoch 2 microplate reader in conjunction with Gen5 software. The calculation of TAS and TOS values was based on the following formula:

$$TOS = \frac{(\Delta Abs\ Sample)}{(\Delta Abs\ Standart)} \times Concentration\ of\ standart$$

$$TAS = \frac{(\Delta Abs\ H2O) - (\Delta Abs\ Sample)}{(\Delta Abs\ H2O) - (\Delta Abs\ Standart)}$$

Oxidative Stress Index Assay

The Oxidative Stress Index (OSI) serves as a measure of oxidative stress levels and is a unitless parameter calculated by taking the ratio of TOS to TAS. To facilitate this calculation, TAS was initially converted from mmol Trolox equivalents per liter to μmol Trolox equivalents per liter. (9)

$$OSI = \left[\frac{TOS(\mu molH2O2\ equivalents/L)}{TAS(\mu molTrolox\ equivalents/L)} \right] \times 100$$

8-hydroxy-2' -deoxyguanosine Assay

Human 8-Hydroxy-2 Deoxyguanosine (8-OHdG) biomarker, which indicates DNA damage caused by oxidative stress, was determined by ELISA method. 8-OHdG (Bioassay Technology Laboratory, BT Lab, Shanghai, China) determination was carried out by following BT Lab (Shanghai, China) kit and protocols. Biotek Epoch 2 microplate reader was used for absorbance values (450 nm). Results were analyzed using Gen5 software.

Statistical Analysis

The distribution of numerical variables was examined using the Shapiro–Wilk test, and the equality of variances across groups was tested with Levene's test. Descriptive statistics for numerical data included the mean, standard deviation (SD), median, and range (minimum–maximum), while categorical variables were summarized using frequencies (n) and percentages (%). A significance level of 0.05 (α) was adopted for all statistical tests. Data analysis was performed using IBM SPSS Statistics for Windows, version 30.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The study included a total of 68 participants, comprising 45.6% females and 54.4% males. The overall mean age was 63.59 ± 13.83 years (range: 41–96; median: 63.0). The patient group consisted of 33 individuals, with males representing the majority (51.5%), while the control group included 35 individuals, also predominantly male (57.1%). The Chi-square test revealed no statistically significant difference in gender distribution between the groups ($p = 0.641$). Likewise, the independent samples t-test indicated no significant difference in mean age between the groups ($p = 0.965$). (Table 1). When the distribution of comorbidities in the patient and control groups was analyzed, hypertension ranked first with 66.7% in the patient group and 40% in the control group. The second most common comorbidity was diabetes in both groups. The comorbidity status of the patients included in the study is given in Table 2. Table 3 shows whether the participants were on any treatment.

Descriptive statistics and comparative results for 8-OHdG, TOS (μmol/L), TAS (μmol Trolox Equiv./L), OSI, and MDA variables are presented in Table 4. No statistically significant differences were detected between the groups regarding 8-OHdG, TOS, TAS, and OSI ($p = 0.417$, $p = 0.742$, $p = 0.210$, and $p = 0.416$, respectively). However, the MDA level in the patient group (rank mean: 25.70) was significantly lower compared to the control group (rank mean: 38.10) ($p = 0.007$).

The correlations between high density lipoprotein (HDL) and 8-OHdG, TOS, TAS, OSI and MDA are shown in Table 5. HDL showed no significant correlation with any of our study variables in the patient group ($p>0.05$), whereas a moderately significant negative correlation was found with TAS in the control group ($r=-0.402$; $p=0.034$).

Comparison of 8-OHdG, TOS, TAS, OSI and MDA in patients with and without coronary artery disease (CAD) is shown in Table 6, and comparison of 8-OHdG, TOS, TAS, OSI and MDA in patients with and without heart failure (HF) is shown in Table 7.

Table 1. Age and gender distribution of patients according to groups

		n	%	p	Mean	SD	Median	Min-Max	p
Patient Group	Female	16	48.5	0.641[a]	62.00	11.50	62.00	43-87	0.965[b]
	Male	17	51.5		64.94	16.40	64.00	41-96	
	Total	33	100.00		63.52	14.09	63.0	41-96	
Control Group	Female	15	42.9		61.67	15.22	62.00	41-87	
	Male	20	57.1		65.33	12.67	63.50	44-93	
	Total	35	100.00		63.67	13.79	63.0	41-93	
Total	Female	31	45.6		61.84	13.20	62.0	41-87	
	Male	37	54.4		65.14	14.38	64.0	41-96	
	Total	68	100.00		63.59	13.83	63.0	41-96	

SD: Standard Deviation; [a]: Pearson's chi-square test; [b]: Independent samples t-test

Table 2. Distribution of comorbidities (e.g., hypertension, diabetes mellitus, hyperlipidemia) by study groups

		Patient Group		Control Group	
		n	%	n	%
Diyabetes	None	18	56.3	22	62.9
	Yes	14	43.8	13	37.1
Hypertension	None	11	33.3	21	60.0
	Yes	22	66.7	14	40.0
COPD	None	30	90.9	34	97.1
	Yes	3	9.1	1	2.9
Asthma	None	29	87.9	32	91.4
	Yes	4	12.1	3	8.6
Canser	None	32	97.0	34	97.1
	Yes	1	3.0	1	2.9
CKD	None	33	100.0	31	88.6
	Yes	0	0.0	4	11.4
Atrial Fibrilation	None	32	97.0	33	97.1
	Yes	1	3.0	1	2.9
Hyperlipidemia	None	26	78.8	31	88.6
	Yes	7	21.2	4	11.4
Demantia	None	30	90.9	31	88.6
	Yes	3	9.1	4	11.4
CAD	None	27	81.8	32	91.4
	Yes	6	18.2	3	8.6
HF	None	26	78.8	32	91.4
	Yes	7	21.2	3	8.6
Obesity	None	33	100.0	35	100.0
	Yes	0	0.0	0	0.0
CVD	None	32	97.0	35	100.0
	Yes	1	3.0	0	0.0
Parkinson's	None	32	97.0	35	100.0
	Yes	1	3.0	0	0.0
Hypotiroidism	None	29	87.9	30	85.7
	Yes	4	12.1	5	14.3

COPD: Chronic obstructive pulmonary disease CKD: Chronic Kidney Disease
CAD: Coronary Artery Disease HF: Hearth Failure CVD: Cerebro Vascular Disease

Table 3. Treatment profiles (e.g., hypertension, diabetes mellitus, etc.) of participants by group

		Patient Group		Control Group	
		n	%	n	%
Anti HT	None	13	39.4	16	53.3
	Yes	20	60.6	14	46.7
Anti DM	None	25	75.8	23	76.7
	Yes	8	24.2	7	23.3
Vildagliptine	Non	32	97.0	30	100.0
	Yes	1	3.0	0	0.0
Antiagregan	None	14	43.8	20	66.7
	Yes	18	56.3	10	33.3
Anticoagulant	None	27	81.8	27	90.0
	Yes	6	18.2	3	10.0
Levothyroxine	None	28	84.8	25	83.3
	Yes	5	15.2	5	16.7
Insulin (SC use)	None	29	87.9	27	90.0
	Yes	4	12.1	3	10.0
Anti HL	None	29	87.9	26	86.7
	Yes	4	12.1	4	13.3

Table 4. Treatment profiles (e.g., hypertension, diabetes mellitus, etc.) of participants by group

	Groups	n	Mean	SD	p
8-OHdG	Patient	33	55.436	2.840	0.417[a]
	Control	31	56.077	3.433	
TOS (μmol/L)	Patient	33	8.981(MR:33.24)	2.751	0.747[b]
	Control	31	9.117(MR:31.71)	6.128	
TAS (μmol Trolox Equiv./L)	Patient	33	821.875	270.082	0.210[a]
	Control	31	737.155	264.591	
OSI	Patient	33	1.285	0.752	0.416[a]
	Control	31	1.560	1.765	
MDA	Patient	33	9.683(MR:25.70)	8.130	0.007[b]
	Control	29	18.878(MR:38.10)	14.764	

SD: Standard Deviation; MR: Mean Rank; [a]: Independent samples t-test; [b]: Mann-Whitney U test

Table 5. Correlations Between HDL and oxidative stress biomarkers

	Patient Group (n=33)		Control Group (n=31)	
	r	p	r	p
8-OHdG	-0.254	0.154	0.059	0.767
T0S(μmol/L)	-0.085	0.639	-0.081	0.682
TAS(μmol Trolox Equiv./L)	-0.250	0.160	-0.402	0.034
OSI	0.177	0.323	0.096	0.628
MDA	0.098	0.587	0.103	0.617

r: Spearman's rho correlation coefficient

Table 6. Comparison of oxidative stress biomarkers in individuals with and without CAD

		Without CAD					With CAD					p*
		n	Mean	SD	Median	MR	n	Mean	SD	Median	MR	
Patient Group	8-OHdG	27	55.48	2.83	55.10	17.11	6	55.25	3.15	55.79	16.50	0.910
	T0S	27	9.01	2.91	8.82	17.20	6	8.83	2.09	8.38	16.08	0.803
	TAS	27	843.39	271.20	849.03	17.78	6	725.07	265.76	711.91	13.50	0.348
	OSI	27	1.27	0.80	1.00	16.19	6	1.36	0.51	1.39	20.67	0.324
	MDA	27	9.12	8.10	7.09	16.41	6	12.23	8.53	12.82	19.67	0.479
Control Group	8-OHdG	28	56.36	2.65	56.22	16.32	3	53.45	8.40	54.91	13.00	0.590
	T0S	28	9.14	6.44	8.87	15.93	3	8.89	1.60	8.72	16.67	0.925
	TAS	28	751.93	246.90	729.92	16.04	3	599.26	442.26	847.65	15.67	0.975
	OSI	28	1.30	0.91	1.19	15.71	3	3.98	5.07	1.25	18.67	0.635
	MDA	26	19.06	15.32	14.55	14.88	3	17.26	10.70	16.77	16.00	0.866
Total	8-OHdG	55	55.93	2.75	56.07	33.05	9	54.65	4.97	54.91	29.11	0.556
	T0S	55	9.08	4.98	8.82	32.56	9	8.85	1.83	8.46	32.11	0.946
	TAS	55	796.83	260.81	799.17	33.20	9	683.13	311.44	810.25	28.22	0.457
	OSI	55	1.29	0.85	1.02	31.56	9	2.23	2.88	1.38	38.22	0.320
	MDA	53	14.00	13.07	10.76	31.04	9	13.91	8.97	16.77	34.22	0.624

*SD: Standard Deviation; MR: Mean Rank; *: Mann-Whitney U test*

Table 7. Comparison of oxidative stress biomarkers in individuals with and without HF

		Without HF					With HF					p*
		n	Mean	SD	Median	MR	n	Mean	SD	Median	MR	
Patient Group	8-OHdG	26	55.53	2.96	55.51	17.40	7	55.08	2.50	54.68	15.50	0.644
	T0S	26	9.19	2.56	8.77	17.73	7	8.20	3.50	8.46	14.29	0.402
	TAS	26	853.67	288.37	873.96	18.54	7	703.80	147.99	788.09	11.29	0.078
	OSI	26	1.30	0.81	1.02	16.88	7	1.22	0.56	1.10	17.43	0.895
	MDA	26	9.72	7.75	8.07	17.38	7	9.55	10.11	6.02	15.57	0.660
Control Group	8-OHdG	28	56.59	2.72	56.22	16.82	3	51.29	6.25	52.85	8.33	0.124
	T0S	28	8.81	6.27	8.74	15.39	3	11.95	4.29	12.56	21.67	0.256
	TAS	28	730.91	277.54	718.84	15.64	3	795.48	67.94	799.17	19.33	0.504
	OSI	28	1.56	1.85	1.14	15.71	3	1.54	0.67	1.57	18.67	0.593
	MDA	27	19.02	14.99	15.66	15.11	2	16.95	15.89	16.95	13.50	0.796
Total	8-OHdG	54	56.08	2.86	56.13	34.19	10	53.94	4.02	54.21	23.35	0.091
	T0S	54	9.00	4.81	8.74	32.36	10	9.32	3.94	8.79	33.25	0.890
	TAS	54	790.01	286.88	818.56	33.40	10	731.30	132.62	789.47	27.65	0.370
	OSI	54	1.44	1.44	1.03	32.15	10	1.31	0.57	1.24	34.40	0.725
	MDA	53	14.46	12.78	10.81	32.32	9	11.19	10.91	6.02	26.67	0.385

*SD: Standard Deviation; MR: Mean Rank; *: Mann-Whitney U test*

DISCUSSION

Understanding the association between venous insufficiency and oxidative stress, as well as identifying at-risk populations, is of critical importance. Demographic characteristics and lifestyle factors may be determinant in the development and severity of the disease. Lifestyle factors may be difficult to determine objectively due to personal variation. When demographic characteristics are examined, in addition to the study in the literature, which was observed 36.14 times more frequently in women, in the study by Evans et al, VF was found to be 9% in men and 7% in women.(10,11) A study carried out in France reported venous symptoms in 51.3% of women and 20.4% of men (5). Another large-scale study involving 40,095 adults in Poland, predominantly female, found the prevalence of varicose veins to be nearly equal between men and women (12). In a multicenter study conducted in our country on VI

risk factors, 63% of the VI patient group consisted of women. (13) Our study observed no significant gender differences between the patient and control groups. According to all these results, the reason for the different results regarding gender may be due to the variability in the sample sizes of the studies and differences in ethnicity.

Several studies have demonstrated elevated plasma MDA concentrations in patients with venous insufficiency (VI). For instance, Budzyń et al. reported significantly higher MDA levels in VI patients compared to controls (14), and Condezo-Hoyos et al. similarly found increased MDA levels in the varicose vein (VF) patient group (15). These findings suggest that elevated MDA is a marker of oxidative stress in VI patients. However, in our study, MDA levels in the patient group were significantly lower than those observed in the control group.There may be several reasons for this difference between the studies. First of all, differences in lifestyle between the samples may have caused this result. In addition, the VI disease stage in the patient group in our study may be at an earlier stage compared to other studies or compensation may have been provided by improving the antioxidant defense system with antioxidant mechanisms such as superoxide dismutase and glutathione, which were not evaluated in our study.

In the study of Menteşe et al. TOS and OSI levels increased, while no difference was observed in TAS levels.(16) Saribal et al. found an increase in some oxidative enzyme activities in varicose vein patients, while no change was observed in others.(17) The analysis revealed no significant intergroup differences in oxidative stress indicators, including 8-OHdG, total oxidant status (TOS), total antioxidant status (TAS), and the oxidative stress index (OSI).This suggests that the effect of VI on oxidative biomarkers may vary between individuals. We think that the reason for this variability is that enzymatic antioxidant levels increase in the initial stages of vascular pathologies and try to balance the ROS load in accordance with the literature.(18) Condezo-Hoyos et al. used the global oxidative stress index in their study. Accordingly, they found a weak increase in OSI in patients with in the early course of VI and attributed this to the effect of compensatory defense.(15)

Among antihypertensive agents, ACE inhibitors have tissue protective properties by increasing antioxidant capacity with an increase in bradykinin.(19) Over a 12-week period, Zofenopril controlled the participants' blood pressure and significantly decreased MDA levels.(20) Anithypertensive drugs suppress oxidative stress by decreasing NADPH oxidase activity, reducing ROS production and scavenging free radicals in some molecules in both experimental and human studies. (21) Consequently, clinically decreasing values can be detected in oxidative stress markers such as OSI, MDA. The most common chronic disease in our study was HT and therefore the most commonly used drug group was antihypertensives. Although subgroups in this drug group were not examined by us, the fact that all groups had similar characteristics may be related to the fact that our data on oxidant and antioxidant capacities were measured at these levels in our study.

Within the patient group, no significant associations were found between high-density lipoprotein (HDL) levels and the measured variables, suggesting that oxidative homeostasis may be compromised due to the presence of other chronic comorbidities. Feng et al. found that HDL antioxidant capacity was significantly decreased in diabetic patients.(22) The significant negative correlation that we found at a moderate level with TAS (μmol Trolox Equiv./L) in the control group may be due to the antioxidant effect of HDL itself. Because HDL levels that neutralize lipid hydroperoxides and inhibit low density lipoprotein (LDL) oxidation and reduce the need for antioxidant production may have caused TAS to remain low.(23)

When we evaluate these different results reported in the literature for antioxidant and oxidant parameters together, our study makes an important contribution to the literature on the biochemical traces of VI. The observed differences across studies may be influenced by factors such as the disease stages of the patient groups, ethnic variability, the medications administered, sample size, and discrepancies in sample collection and analytical methodologies. In addition, in our study, only the medical ingredients used by the patients were questioned and whether they used any food supplements containing anti-oxidants was not questioned. Although this is one of the limitations of our study, if there are participants using supplements in the patient group, the results of our study may have been affected by this situation.

Limitation

The small sample size of our study, the stage of the disease was not recorded in the patient group, and the use of food supplements was not questioned, which may have affected the results of our study. Another limitation of our study is that we did not specifically account for comorbidities in elderly patients, which are known to contribute to increased oxidative stress. However, we attempted to minimize the confounding effect of age by matching the control group according to the age distribution of the patient group.

CONCLUSION

There are variations between the mechanisms of action and the results of oxidative stress markers such as MDA, 8-OHdG, TOS, TAS and OSI levels in the literature. The concordance and discrepancies of the results of our study with the literature are discussed. Accordingly, low or non-variable results were obtained among oxidative stress markers. We believe that this is due to the limitations mentioned above In the future, we plan to conduct new studies with larger sample sizes in which the existing limitations are eliminated. The varied results in the literature on oxidant and antioxidant mechanisms indicate the need for studies with much larger samples and analyses. The fact that VI disease, which has a high prevalence globally, has not yet been fully prevented despite all preventive medicine measures, makes cost-ineffective treatment modal-

ities effective on health policy regulators. With a wide range of studies, it will be possible to organize cost-effective health policies with the use of anti-oxidant food supplements and / or new preventive medicine modalities to be developed.

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