doi:10.25143/prom-rsu_2023-03_dts

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GPx and MDA Oxidative Stress Markers and Severity of Depression as Predictives of Recurrent Stable Coronary Heart Disease

Summary of the Doctoral Thesis for obtaining a doctoral degree "Doctor of Science (*PhD*)"

Sector Group – Medical and Health Sciences
Sector – Clinical Medicine
Sub-Sector – Internal Diseases

Riga, 2023

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Defence of the Doctoral Thesis in Clinical Medicine will take place at the public session of the Promotion Council 23 January 2023 at 15.00 remotely via online platform Zoom

The Doctoral Thesis is available in RSU Library and on RSU website: https://www.rsu.lv/en/dissertations

Secretary of the Promotion Council:

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Abbreviations used in the Thesis

AD	Antidepressant
AI	Apoptosis index
AO	Antioxidant
BMI	Body mass index
CAD	Coronary artery disease
CHD	Coronary heart disease
CI	Confidence interval
CVD	Cardio-cerebrovascular diseases
D	Depression
GDS	Geriatric Depression Scale
GPx	Glutathione peroxidase
HPA	Hypothalamus–pituitary–adrenal axis
IV	Independent variable
KYN	Kynurenine
MDA	Malondialdehyde
MI	Myocardial infarction
NSTEMI	Non-ST elevation
OR	Odds ratio
OS	Oxidative stress
PSCHD	Primary stable coronary heart disease
ROS	Reactive oxygen species
RSCHD	Recurrent coronary heart disease
SD	Standard deviation
SCHD	Stable coronary heart disease
STEMI	Subsequent ST elevation
SSRIs	Selective serotonin reuptake inhibitors

TAC	Total antioxidant capacity
TRP	Tryptophan
WHO	World Health Organization

Introduction

Epidemiological data indicate that cardiovascular diseases (CVD) and depression (D) pose a huge global disease burden (GBD, 2016; Moraga, 2016).

D in cardiac disease is common, persistent, underrecognized, and deadly. The prevalence of D is, compared with the general population, significantly higher in patients with coronary heart disease (CHD) (Whooley&Wong, 2013).

Oxidative stress (OS) is defined by the imbalance between the production of reactive oxygen species (ROS) and the endogenous antioxidant mechanisms to counteract the effects of ROS or to repair the resulting damages (Antoniades et al., 2009). The common risk factors increase the production of OS and reduce AO defences, thereby promoting the occurrence and development of interacted ischemic CVD and D (Moylan et al., 2014; Maes et al., 2011). At the moment, there is insufficient evidence that routine screening of D in patients with stable coronary heart disease (SCHD) will ultimately help improve the patient's condition (Hasnain et al., 2011; WHO, 2017), which is why the study of the relationship between SCHD, D and OS is very important.

Aim of the study

The present study aimed to investigate changes in oxidative stress biomarker levels and its possible correlation with depression and recurrent stable coronary heart disease risks.

Objectives

1. To determine the prevalence and severity of D among patients with primary and recurrent SCHD.
2. To determine and compare OS marker MDA in patients with primary SCHD and recurrent SCHD.

3. To determine and compare OS marker GPx in patients with primary SCHD and recurrent SCHD.
4. To analyse correlations between MDA and severity of D in patients with primary and recurrent SCHD.
5. To analyse correlations between GPx and severity of D in patients with primary and recurrent SCHD.
6. To determine possible biomarkers as a risk factor for SCHD recurrence.

Hypothesis

Patients with recurrent SCHD and D would have a higher level of OS biomarkers than patients with primary SCHD without depression, which can be used in diagnostic tools for the risk of recurrence of SCHD in patients with D.

The novelty of the work

For the first time in Latvia, the relationship between primary hospitalization, rehospitalization, and its possible connection with D and OS markers was investigated. Also, before 2015 risk factor correlations between primary and recurrent SCHD, D, and OS markers (GPx and MDA) were not investigated.

The practical significance of the work

The current study can contribute to creating a better understanding of the relationship between OS, D, and CHD. Also, it can help to improve risk assessment strategies for CVD and D among patients with CHD, therefore reducing rehospitalization risks. Barriers to recognition of D include a lack of mental health expertise and training in cardiology practices, and many symptoms of D, such as fatigue, weight loss, poor appetite, or trouble sleeping, are easily

confused with physical disease. Therefore, the measurement of OS markers can be used as a diagnostic tool for D and the risk of recurrence in patients with CHD.

Oxidative stress markers can be used as a diagnostic tool for depression and recurrent cardiac events. There is a wide variety of different oxidative stress markers, and in this study two of them were investigated (MDA and GPx). Unlike GPx, results show contradictory data of MDA assessment in patients with coronary heart disease. Therefore, GPx could be used as a diagnostic tool for ≥45 years old patients to evaluate recurrent coronary heart disease risk. It is fast, informative and reliable, could be used by cardiologists, general practitioners, gerontologists, psychiatrists and other specialists, who are involved in coronary heart disease treatment. Identifying patients with high risk of recurrent coronary heart disease early allows better patient follow-up assessment and evaluate the need for antidepressant and/or antioxidant therapy.

1 Literature

1.1 Cardiovascular Disease

According to the World Health Organization data CVD is the number 1 cause of death globally, taking an estimated 17.9 million lives each year, an estimated 31 % of all deaths worldwide (WHO, 2017). In Latvia CVD was the most common cause of death – 54.6 % of all deaths, according to 2019 data (Ērglis et al., 2020).

"CVD is a group of diseases that include both the heart and blood vessels, thereby including CHD, coronary artery disease (CAD), stroke, hypertensive heart disease, inflammatory heart disease, rheumatic heart disease and other cardiovascular diseases" *(WHO, 2011).* CAD is usually used to refer to the pathologic process affecting the coronary arteries (usually atherosclerosis) whilst CHD includes the diagnoses of angina pectoris, myocardial infarction (MI) and silent myocardial ischemia. In turn, CHD mortality results from CAD (Sanchis-Gomar et al., 2016).

1.2 Depression and Cardiovascular Disease

Over the past 20 years, research has found that not only is D more common in cardiac patients than in the general population, but D is also a risk factor for cardiac morbidity and mortality, independent of traditional risk factors (Huffman et al., 2013). The authors concluded that D is an independent risk factor for CHD and is not related to other previously determined cardiac risk factors. This association persisted across all demographic groups in this well designed, case-control study (Khawaja et al., 2009). The prevalence of D is, compared with the general population, significantly higher in patients with CHD (Whooley&Wong, 2013). More than one fifth of all patients with CHD are

depressed (with the risk of D highest in the most severe CHD cases), and up to one third of them report elevated depressive symptoms. These are prevalence figures that are at least 4 times greater than in the general population (Hert&Detraux et al., 2018).

It is important to note that D increases all causes of cardiac mortality. For example, according to published data, patients with CVD and D are 2.8 times more likely to die within a year after MI than people without D (Khawaja et al., 2009). One of the factors influencing poor prognosis is the fact that patients with D have poor medication adherence, which directly affects the CVD treatment process. In addition, patients with D are more likely to have an unhealthy and sedentary lifestyle (Khawaja et al., 2009).

By collected data, depressive symptoms are diagnosed in less than 15 % of cases (Guck et al., 2001) and only 25 % of patients with CHD and severe D are diagnosed with psycho-emotional disorder and approximately only half of them receive adequate antidepressant (AD) therapy (Moryś et al., 2016). The diagnosis of D can be difficult in people with CVD as D symptoms such as fatigue and low energy are common in people with CVD and may also be a side effect of some drugs used to treat CVD such as beta blockers (Goodman et al., 2008; Carney&Freedland, 2008).

1.3 Cardiovascular Disease, Depression and Oxidative Stress

Oxidative stress as a concept appeared in 1985 and its definition was supplemented in 2007 and reads as follows: “oxidative stress is an imbalance between oxidants and antioxidants in favour of the oxidants, leading to a disruption of redox signalling and control and / or molecular damage” (Sies & Jones, 2007). Oxidative stress activates the immune inflammatory pathways (Liu et al., 2015; Moylan et al., 2014).

The hypothesis that inflammatory and OS are factors in both mood disorders and CHD seems to be growing stronger (Chauvet-Géliniera et al., 2013). Increased lipid peroxidation may be particularly relevant to depressive symptoms among patients with coronary artery disease (CAD) given the involvement of oxidative stress in that condition (Mazereeuw et al., 2017). Moreover, other researches confirm that the OS directly increases the risk of D in patients with CVD whereas it increases the risk of CVD in depressed people. In summary, the common risk factors increase the production of OS and reduce AO defences, thereby promoting the occurrence and development of interacted ischemic CVD and D (Lin et al., 2019). It has been shown that the depressed patients have elevated level of platelet adhesion and aggregation leading increased risk for cardiovascular events (Nezafati et al., 2015). OS can independently and directly affect stroke, CHD and D (Lin et al., 2019).

Several pieces of evidence have pointed to the involvement of altered tryptophan metabolism in inflammation and the development of mood disorders (Mattina et al., 2019). Higher levels of serum kynurenine compared with tryptophan (KYN/TRP ratio), have been demonstrated in CVD patients and provide evidence for altered kynurenine synthesis (Wirleitner et al., 2003). The KYN/TRPratio, as well as other kynurenine metabolites, are strongly associated with increased risk of poor outcomes following stroke (Brouns et al., 2010) and cardiovascular related mortality in the general population (Zuo et al., 2016). Furthermore, depressed coronary heart disease patients show greater serum (KYN/TRP) ratio compared with those without depression (Nikkheslat et al., 2015), suggesting that depression coupled with CVD leads to increased activation of the kynurenine pathway (Mattina et al., 2019). Activation of the kynurenine pathway following chronic inflammation is modified to increase the production of neurotoxic metabolites and release reactive oxygen species,

resulting in lipid peroxidation and neurodegenerative brain changes (Wang et al., 2015; Jeon&Kim, 2017).

Considering the negative cardiac and cognitive effects of persistent D in patients with CHD, adequate treatment with antidepressants is a clinically important need in the case of CHD Patients who respond to antidepressant therapy within the first year of treatment have shown to experience significantly lower rates of morbidity and mortality (Jiang, 2011). Several studies have shown that the new generation of antidepressants, in particular selective serotonin reuptake inhibitors, are well tolerated, have a satisfactory efficacy-tolerance profile and are easy to use in patients with cardiovascular disease (Chauvet-Géliniera et al., 2013). In addition, these molecules show clinical efficacy, acting on physio-pathological elements by improving endothelial function while reducing the concentration of inflammation markers (C-reactive protein, interleukin-6) (Pizzi et al., 2009). In the same way, a meta-analysis showed that selective serotonin reuptake inhibitors used in the wake of an acute coronary syndrome led to fewer rehospitalizations (Chauvet-Géliniera et al., 2013; Mazza et al., 2009).

There is increasing body of evidence supporting that D may be associated with changes in OS markers and that AD agents (especially long-term treatment) may increase AO defences. It is possible that augmentation of AO defences may be one of the mechanisms underlying the neuroprotective effects of ADs observed in the treatment of D (Celano&Huffman, 2011). The meta-analysis supports the facts that the serum total antioxidant capacity (TAC), paraoxonase and antioxidant levels are lower, and the serum free radical and oxidative damage product levels are higher than controls in depressed patients. Meanwhile, the antioxidant levels are increased and the oxidative damage product levels are decreased after antidepressant medication (Liu et al., 2015).

In fact, the use of SSRIs may prevent developing atherosclerotic plaques and also arterial thrombosis (Nezafati et al., 2015). Normalization of the levels of Reactive Oxygen species and AO activity after successful AD therapy (Cumurcu et al., 2009) suggests that OS mechanisms can be especially important in the study of pathophysiology and prognosis of D (Adifbair et al., 2016). Patients with heart failure, who respond to AD therapy within the first year of treatment have shown to experience significantly lower rates of morbidity and mortality (Jiang et al., 2011). Several lines of evidence indicate that different cardiovascular considerations should be inspected in patients who need to take AD medications (Yekehtaz et al., 2013).

1.4 Oxidative stress biomarkers – MDA and GPx

According to the literature, OS biomarkers can be analysed in cells and tissues, blood, urine, saliva, tears and synovial fluid samples (Armstrong&Stratton, 2016). Heart failure under both acute and chronic conditions is associated with increased levels of OS markers (e.g., MDA, glutathione peroxidase GPx). These findings suggest that CHD status may be determined by OS activity rather than the degree of coronary stenosis. Elevated concentrations of a variety of oxidative stress markers were linked with a more frequent occurrence of cardiac events (Vichova&Motovska, 2013).

One of the most important and extensively studied oxidants is MDA. In the field of modern biology to assess oxidative stress, MDA is an extensively utilized biomarker. MDA is one of the most commonly used indicators of lipid peroxidation (Del Rio et al., 2005), it can also be more resistant than other markers of the late stage (4-HNE, 8-ISO) of lipid peroxidation (Mazereeuw et al., 2017). The MDA molecule is stable and relatively inactive, compared with free radicals, however, it can not only significantly affect the stability and

function of cells, but can also be indirectly involved in the OS reaction (Voicehovskis, 2013). And being a marker of lipid peroxidation, the MDA level increases significantly with D (Frey et al., 2006). Results of the studies (Pezeshkian et al., 2001) showed that MDA levels increased significantly in heart diseases.

Important moment is that most potent antioxidant actions are mediated by enzymes, especially superoxide glutathione peroxidase (GPx) (Dhama et al., 2019). The main biological role of GPx in the body is protection against damage caused by free radicals and active forms of oxygen (Vaváková et al., 2015). The level of serum glutathione peroxidase is an excellent measure of the oxidative status of an individual and is most often employed in diagnostics (Dhama et al., 2019). The higher GPx activity could have been a compensatory mechanism for the excess production of free radicals in depressed patients (Liu et al., 2015).

Researches also reported increase of MDA and GPx levels in patients with coronary artery disease. GPx activation was significantly higher in patients with coronary artery disease than healthy controls (Kaya et al., 2012). It was found that serum GPx and MDA were significantly greater in CHD patients than in healthy controls (Cheraghi et al., 2019). Some other investigates have also reported increase of MDA and GPx levels in patients with CAD (Pezeshkian et al., 2001).

It has been demonstrated that AO enzyme activities are reduced in CHD, and this is linked to the increased disease risk. Many studies have indicated that free radical generation increases and AO defences decrease in response to increased OS in CHD patients. Activity levels of the AO enzymes GPx, and non-enzymatic AOs, are considered as predictors of CHD (Vichova&Motovska, 2013; Cheraghi et al., 2019).

2 Methods

It is a retrospective case-control study that was conducted to compare patients with PSCHD with patients who have RSCHD by determining oxidative markers levels and D signs and severity. No intervention was attempted to alter the course of the SCHD.

2.1 Study participants and research locale

It was decided to create two groups of patients – with PSCHD and RSCHD and compare them by OS marker levels and D symptoms and their severity. Re-evaluation of the same patients (who were diagnosed with PSCHD and subsequently hospitalized with RSCHD) was not performed due to various barriers.

2.2 Criteria for inclusion and exclusion of research participants

The inclusion and exclusion criteria for both groups were the same, with the only difference: for PSCHD patients – primary hospitalization due to first event of CHD, while for RSCHD –hospitalization due to recurrent event of CHD.

Inclusion criteria:

- patients with SCHD – by classification ICD-10: I20 Angina pectoris; I25 Chronic ischemic heart disease;
- patients are stable, with stable vital signs;
- age $\geq$ 45 years;
- non-smokers;
- not vegetarian;
- do not drink alcohol at least during the last 1 year;
- use prescribed drugs regularly.

Exclusion criteria:

- patients with diagnoses I21 Acute myocardial infarction; I22 Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction; I23 Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within 28 days); I24 Other acute ischemic heart diseases;
- unstable patients, patients in intensive care unit;
- age < 45 years;
- approved diabetes mellitus type 1 and 2;
- glucose tolerance disturbances;
- any acute illnesses;
- irregular usage of prescribed drugs;
- any F diagnosis;
- obesity (BMI ≥ 30).

Data on the regularity of medication use and adherence were obtained in the form of a self-report. People who drink alcohol, smoke, or have excluded meat from their diet, as well as patients with low medication adherence, were excluded from the study because these are confounding factors that potentially affect OS levels.

Patients were selected based on convenience, including all patients with PSCHD or RSCHD who met the study inclusion criteria over a certain period. Time period: from November 1, 2015, to July 15, 2017, until the required number of study participants was collected.

The sample size was calculated obtaining partial statistical data from the Latvian Centre of Cardiology in Pauls Stradiņš University Hospital. As a result, the sample size with 80 % statistical power was calculated – 86 study participants

in each group. It should be noted that the selection process in both groups was identical according to the set criteria. A total of 191 people were invited to participate in the study, and 17 patients refused to participate in the study. A total of 174 participants were enrolled in this study: 1) 86 in-patients with a RSCHD; 2) 88 in-patients with a PSCHD. There were no statistically significant differences between the two groups by gender and age (Chi-square test, $p = 0.1$ and $p = 0.2$, OR $p < 0.05$).

2.3 Research site

The study site was the Latvian Centre of Cardiology in Pauls Stradiņš University Hospital. It is important to mention, that patients were diagnosed by cardiologists of Latvian Centre of cardiology. The Latvian Centre of Cardiology provides a set of highly qualified third-level healthcare services in the field of cardiology (including CHD cases) to patients from all regions of Latvia.

2.4 Ethical aspects

All procedures complied with the ethical standards on human experimentation (World Medical Association Helsinki Declaration). The approval for this study was obtained from the Ethics Committee of Rīga Stradiņš University.

2.5 The course of the research

The primary selection of patients was done with the assistance of the Latvian Centre of Cardiology medical staff, their medical records were further examined, determining their diagnosis and comorbidities. In cases where the patient met the criteria, he / she was invited to participate in the study. If the

prospective study participant agreed, he / she was then interviewed. If the patient complied with inclusion criteria, he / she was asked to complete the Latvian version of the Geriatric Depression Scale questionnaire, and to submit to a blood test in the morning.

2.6 Investigation methods:

- Analysis of medical records – primary diagnosis, co-morbidity, and examination results, as well as BMI.
- Structured interview was conducted to make sure that the potential study participant met all the criteria of the study.
- Geriatric Depression Scale. The severity of depressive symptoms was assessed using the long 30-item form of the Geriatric Depression Scale (GDS), (Yesavage, 1982–1983), a valid Latvian version of GDS-LAT (Voicehovskis, 2013).
- Blood sample analysis. From each patient the blood samples were taken to measure OS parameters: MDA and GPx. MDA levels are determined using thiobarbituric acid reactive substance. Reference interval: 3.45–7.45 mmol/L (Armstrong&Browne, 1994; Armstrong, 1998; Boyum, 1966). GPx determination method: automatic spectrophotometric (Paglia, 1967). Reference interval: a) RSU Biochemistry lab.: 8530 ± 2352 U / L (average ± standard deviation (SD)); b) RANDOX: 7526 ± 3355 U / L (average ± SD).

2.7 Statistical analysis

Data were analysed using SPSS 23.0 officially licensed software**.** Statistical significance of the prevalence of dependent variables between the strata of independent variables was tested by using the Chi-square test. The

normal distribution of parametric variables was checked using the Kolmogorov-Smirnov test. T-test of ANOVA, Mann-Whitney U test and Kruskal-Wallis test were used. For the detection of correlations between parametric variables Spearman correlation analysis was used (correlation considered as weak if $r < 0.3$, mean, if r is ranged from 0.3–0.8 and as strong if $r > 0.8$). For multivariate analysis linear, binary, and multinomial logistic regressions were applied. Results are considered statistically significant if $p < 0.05$.

3 Results

3.1 Patient demographics

In the study there 174 responders participated – 49.4 % (n = 86) of them have experienced recurrent SCHD and 50.6 % (n = 88) of them formed a control group (patients of primary SCHD). There were no differences between the distribution of patients in the primary and the recurrent groups by gender and mean age. Half of the total sample (53.4 %) were males. The majority of the sample (83.9 %) had a high level of MDA and for the rest of them, the MDA level was considered normal (i.e., a low level of MDA was detected for none of the patients). For the majority of the patients (72.4 %) the GPx level was normal, for 17.8 % it was high, and for 9.8 % – low. Slightly more than half of the patients were experiencing a D (44.3 % – mild D and 6.9 % – severe D) (see Table 3.1).

Table 3.1

Description of the sample (total and stratified by SCHD status)

IV	Total		PSCHD		RSCHD		p*
	n	%	n	%	N	%	
Sex							
Male	93	53.4	43	48.9	50	58.1	0.22
Female	81	46.6	45	51.1	36	41.9	
Age							
81+	13	7.5	7	8.0	6	7.0	0.34
71–80	48	27.6	27	30.7	21	24.4	
61–70	71	40.8	30	34.1	41	47.7	
≤ 60	42	24.1	24	27.3	18	20.9	

Table 3.1 continued

IV	Total		Primary SCHD		Recurrent SCHD		p*
	n	%	n	%	N	%	
MDA							
Low	–	–	–	–	–	–	0.37
High	146	83.9	76	86.4	70	81.4	
Normal	28	16.1	12	13.6	16	18.6	
GPx							
Low	31	17.8	17	19.3	14	16.3	**0.003**
High	17	9.8	2	2.3	15	17.4	
Normal	126	72.4	69	78.4	57	66.3	
GDS							
Severe	12	6.9	6	6.8	6	7	0.65
Mild	77	44.3	36	40.9	41	47.7	
No	85	48.9	46	52.3	39	45.3	

* Statistically significant if $p < 0.05$

As can be seen in Table 3.1, groups of recurrent and primary SCHD did not differ according to any of the aforementioned variables except the GPx level – among patients of recurrent SCHD there was a lower proportion of individuals with a normal level of GPx when compared to primary SCHD patients (66.3 % and 78.4 % respectively) ($p = 0.003$).

3.2 MDA level

There was found a high MDA level in 146 patients and a normal MDA level in 28 patients in both groups together. In the primary SCHD group a high MDA level was in 76 (86.4 %) patients, in the recurrent SCHD group high MDA level was in 70 (81.4 %) patients. The mean score was slightly higher in the primary SCHD group, but, based on the binary logistic regression test, there was no statistically significant difference between the subgroups (p = 0.23). MDA indicators distribution depending on the deviation from the norm is shown in Table 3.1. The mean score, minimum, maximum indicators, and standard deviation are illustrated in Table 3.2.

Table 3.2

Factors associated with recurrent SCHD in univariate and multivariate analysis (if independent variables are nonparametric measures)

IV	PSCHD		RSCHD		OR*	95 % CI	p**	Adjusted OR*	95 % CI	p**
	n	%	n	%						
MDA										
High	76	52.1	70	47.9	0.69	0.31–1.56	0.37	0.53	0.22–1.27	0.15
Normal	12	42.9	16	57.1	1	–	–	1	–	–
GPx										
Low	17	54.8	14	45.2	1.00	0.45–2.20	0.99	0.96	0.42–2.19	0.92
High	2	11.8	15	88.2	**9.10**	**1.99–41.37**	**0.004**	**11.29**	**2.31–55.06**	**0.003**
Normal	69	54.8	57	45.2	1	–	–	1	–	–

Table 3.2 continued

IV	PSCHD		RSCHD		OR*	95 % CI	p**	Adjusted OR*	95 % CI	p**
	n	%	n	%						
GDS										
Severe	6	50.0	6	50.0	1.18	0.35–3.95	0.79	0.82	0.18–3.67	0.80
Mild	36	46.8	41	53.2	1.34	0.72–2.49	0.35	1.31	0.66–2.60	0.44
No	46	54.1	39	45.9	1	–	–	1	–	–

* OR – odds ratio; **Statistically significant if $p < 0.05$.

In the next part, GPx levels are analysed.

3.3 GPx level

There was found a high GPx level in 17 patients, a low level – in 31, and a normal level in 126 patients in both groups together. In primary SCHD group high GPx level was in 2 (2.3 %), patients, low – in 17 (19,35) and normal – in 69 (78.4 %) patients. In recurrent SCHD group high GPx level was found in 15 (17.4 %), patients, low – in 14 (16.3 %) and normal – in 57 (66.3 %) patients. The mean score was slightly higher in the recurrent SCHD group. Based on the binary logistic regression test, there was no statistically significant difference between the subgroups ($P = 0.06$). GPx indicators distribution depending on the deviation from the norm is shown in Table 3.1. The mean score, minimum, maximum, and standard deviation are illustrated in Table 3.2.

3.4 Depression prevalence and severity

Mild D was detected in 77 patients (44.3 %), and severe D – in 12 (6.9 %) in both groups together. In the primary SCHD group, severe D was detected in 6 (6.8 %) patients and mild D – in 36 (40.9 %) patients. In the recurrent SCHD group, severe D was detected in 6 (7 %) patients and mild D – in 41 (47.7 %) patients. No D was found in 46 (52.3 %) in the primary SCHD group and 39 (45.3 %) in the recurrent SCHD group. Based on the binary logistic regression test, there was no statistically significant difference between the subgroups ($p = 0.42$) by D prevalence and severity. GDS distribution depending are shown in Table 3.1. The mean score, minimum, maximum, and standard deviation of the GDS scale are illustrated in Table 3.2.

3.5 Correlation between OS markers

The correlation of OS factors (MDA and GPx indicators) was found to be positive and statistically significant but yet weak ($r = 0.18$, $p = 0.017$). The correlation of OS indicators in women with PSCHD was not statistically significant ($r = 0.12$, $p = 0.414$) and in men ($r = -0.11$, $p = 0.946$). On the contrary correlation of OS indicators in women with RSCHD was statistically significant, but low positive ($r = 0.39$, $p = 0.017$). The correlation of OS markers in men with RSCHD was not statistically significant ($r = 0.26$, $p = 0.06$).

3.6 Factors associated with the recurrent SCHD

When the independent variables are analysed as parametric values, it was found that the only factor statistically different between primary and recurrent SCHD patients, was GPx, i.e., among patients of recurrent SCHD mean GPx value is significantly higher than among patients of primary SCHD (8329.8 and 7474.5 U/g Hb respectively) ($p = 0.01$) (see Table 3.2).

The mean age was slightly higher among patients of primary SCHD as well as the median MDA, whereas the median GDS value was higher among patients with recurrent SCHD. But, as has been mentioned already before, these tendencies cannot be considered statistically significant. The multivariate analysis has not changed the conclusion. After the adjustment, the only factor significantly associated with the recurrent status of SCHD was GPx ($p = 0.008$). But as regards the measure of OR – the increase in GPx per unit is making so small changes in OR that it was not detectable within two decimal figures. This was the reason why in the further data analysis the parametric measures were categorized and analysed as nonparametric variables.

There is a tendency for the odds of recurrent SCHD to be higher among males, older patients, and persons with mild D. Interestingly that the odds of recurrent SCHD are lower among patients with high levels of MDA. But these observations are not statistically significant in univariate, or multivariate analyses. The only factor showing stable and statistically significant association with recurrent SCHD is GPx level, i.e., in multivariate analysis independently from other factors high levels of GPx are associated with 11.29 times higher odds of having recurrent SCHD status ($p = 0.003$).

3.7 Factors associated with the D

Patients with present D were experiencing both – high levels of MDA and GPx – more often than responders with no D (11.2 % and 8.2 % respectively). But this trend cannot be considered statistically significant ($p = 0.51$). And vice versa – among patients with simultaneously high levels of MDA and GPx the prevalence of D is higher than among patients with normal levels of MDA and GPx or with high or low levels of just one of the indicators (58.8 % and 50.3 % respectively). And the level of statistical significance of the

mentioned observation is surely the same, i.e., not reaching the level of significance (p = 0.51) (see Table 3.3).

Table 3.3

Prevalence of high levels of MDA and GPx simultaneously in relation to the presence of D

Status of D	High both – MDA and GPx		Normal MDA and GPx or high one of them		Total	
	n	%	n	%	n	%
Present	10	11.2	79	88.8	89	100.0
Absent	7	8.2	78	91.8	85	100.0

And vice versa – among patients with simultaneously high levels of MDA and GPx the prevalence of depression is higher than among patients with normal levels of MDA and GPx or with high or low levels of just one of the indicators (58.8 % and 50.3 % respectively). And the level of statistical significance of the mentioned observation is surely the same, i.e., not reaching the level of significance (p = 0.51) (Table 3.4).

Table 3.4

Prevalence of D according to the status of simultaneously high levels of MDA and GPx

Status of D	High both – MDA and GPx		Normal MDA and GPx or high one of them	
	n	%	n	%
Present	10	58.8	79	50.3
Absent	7	41.2	78	49.7
Total	17	100.0	157	100.0

If the measures of the severity of depression (GDS) and levels of OS are analysed as parametric variables, there a slightly negative correlation can be observed between GDS and MDA ($r = -0.035$) and a slightly positive correlation between GDS and GPx ($r = 0.087$). So, both of the correlations have to be considered as weak. And both of them are lacking statistical significance ($p = 0.65$ and $p = 0.25$ respectively).

When the dependent and independent variables are analysed as nonparametric ones, it can be seen from the univariate analysis that there is a tendency that higher odds of severe or mild depression there are for people of older age, for those having high levels of GPx and for people with the recurrent status of SCHD. Whereas odds are lower among males, people with high levels of MDA, and low levels of GPx. But it must be underlined that all the mentioned associations are not statistically significant. The only significant association was found between severe depression and age over 81 years (vs 60 or fewer years OR 18.67; $p = 0.006$) and mild depression and age group "71–80 years" (vs 60 or fewer years OR 4.51; $p = 0.001$) (see Table 3.5).

Table 3.5

Factors associated with severity of D in univariate analysis

IV	Severe D		Mild D		No D		OR (severe vs no D)	95 % CI	p	OR (mild vs no D)	95 % CI	p
	n	%	n	%	n	%						
	12	**6.9**	**77**	**44.3**	**85**	**48.8**						
Sex												
Male	5	5.4	40	43.0	48	51.6	0.55	0.16–1.88	0.34	0.83	0.45–1.55	0.56
Female	7	8.6	37	45.7	37	45.7	1	–	–	1	–	–
Age												
81+	4	30.8	6	46.2	3	23.1	**18.67**	**2.35–148.43**	**0.006**	4.67	1.00–21.81	0.05
71–80	4	8.3	29	60.4	15	31.3	3.73	0.61–22.80	0.15	**4.51**	**1.80–11.32**	**0.001**
61–70	2	2.8	30	42.3	39	54.9	0.72	0.10–5.41	0.75	1.80	0.79–4.10	0.17
≤ 60	2	4.8	12	28.6	28	66.7	1	–	–	1	–	–
MDA												
High	8	5.5	63	43.2	75	51.4	0.27	0.07–1.05	0.06	0.60	0.25–1.44	0.25
Normal	4	14.3	14	50.0	10	35.7	1	–	–	1	–	–

Table 3.5 continued

IV	Severe D		Mild D		No D		OR (severe vs no D)	95 % CI	p	OR (mild vs no D)	95 % CI	p
	n	%	n	%	n	%						
	12	**6.9**	**77**	**44.3**	**85**	**48.8**						
GPx												
Low	1	3.2	13	41.9	17	54.8	0.45	0.05–3.84	0.46	0.82	0.37–1.84	0.63
High	3	17.6	7	41.2	7	41.2	3.27	0.70–15.25	0.13	1.07	0.35–3.24	0.91
Normal	8	6.3	57	45.2	61	48.4	1	–	–	1	–	–
SCHD												
RSCHD	6	7.0	41	47.7	39	45.3	1.18	0.35–3.95	0.79	1.34	0.72–2.49	0.35
PSCHD	6	6.8	36	40.9	46	52.3	1	–	–	1	–	–

After the adjustment (see Table 3.6) the association between older age and severe or mild depression became stronger. Thus, it can be concluded that the age of 81 years or older increases the odds of severe depression 38.01 times (p = 0.003) (when compared to people of the age 60 years or less) and increases the odds of mild depression 5.54 times (p = 0.04). And the age of 71–80 years increases the odds of mild depression 4.63 times when compared to younger patients.

Table 3.6

Factors associated with severity of D in multivariate analysis

IV	aOR (severe vs no D)	95 % CI	p	aOR (mild vs no D)	95 % CI	p
Age						
81+	**38.01**	**3.35–431.96**	**0.003**	**5.43**	**1.10–26.77**	**0.04**
71–80	5.89	0.72–48.40	0.10	**4.63**	**1.80–11.92**	**0.002**
61–70	0.69	0.08–5.82	0.73	1,75	0.75–4.09	0.19
≤ 60	1	–	–	1	–	–
MDA						
High	**0.16**	**0.03–0.82**	**0.03**	0.60	0.23–1.53	0.28
Normal	1	–	–	1	–	–
GPx						
Low	0.19	0.02–1.95	0.16	0.67	0.28–1.63	0.38
High	**11.69**	**1.60–85.46**	**0.02**	1.66	0.52–5.27	0.39
Normal	1	–	–	1	–	–

Also, both indicators of oxidative stress are showing statistically significant associations with severe depression. High GPx levels are increasing the odds of severe depression 11.69 times (p = 0.02) independently from other factors (including SCHD status). Whereas high levels of MDA are decreasing the odds of severe depression more than six times (OR 0.16; p = 0.03). The rest of the factors (sex and the status of SCHD) are not showing significant associations with D.

3.8 Factors associated with the RSCHD in relation to the presence of D

If only people with D were analysed (n = 89), the findings remained the same as for the total sample – the only factor significantly increasing the odds of experiencing recurrent SCHD was the high level of GPx (OR 12.76; p = 0.03). As regards the other factors – there was a tendency that higher odds of experiencing recurrent SCHD for males and people aged 61–71 (compared to the younger ones). People with high levels of MDA are having almost 40 % lower odds of experiencing recurrent SCHD. But the mentioned tendencies cannot be considered statistically significant (see Table 3.7).

Table 3.7

Factors associated with recurrent SCHD in univariate and multivariate analysis among patients with D

IV	PSCHD		RSCHD		OR*	95 % CI	p**	Adjusted OR*	95 % CI	p**
	n	%	n	%						
MDA										
High	34	47.9	37	52.1	0.87	0.31–2.46	0.79	0.64	0.21–1.97	0.44
Normal	8	44.4	10	55.6	1	–	–	1	–	–

Table 3.7 continued

IV	PSCHD		RSCHD		OR*	95 % CI	p**	Adjusted OR*	95 % CI	p**
	n	%	n	%						
GPx										
Low	5	35.7	9	64.3	2.23	0.68–7.40	0.19	3.04	0.80–11.60	0.10
High	1	10.0	9	90.0	**11.18**	**1.34–93.37**	**0.03**	**12.76**	**1.34–121.84**	**0.03**
Normal	36	55.4	29	44.6	1	–	–	1	–	–

* OR – odds ratio; ** Statistically significant if $p < 0.05$

Further – by switching the D and SCHD from being the dependent variables to being independent ones (and making markers of oxidative stress the dependent variables), it can be concluded that high levels of GPx are more frequent among patients of recurrent SCHD regardless of the status of depression whereas the low levels of GPx are more prevalent among primary SCHD patients with no depression. These tendencies seem to be statistically significant ($p = 0.02$). When the four strata of depression and SCHD status are further compared pairwise, it is concluded that the high levels of GPx are significantly more frequent within the group "depression and recurrent SCHD" (19.1 %) than within the groups "no depression and primary SCHD" (2.2 %; $p = 0.03$) or within the group "depression and primary SCHD" (2.4 %; $p = 0.03$). The rest of the pairwise combinations are not statistically significant (see Table 3.8).

Table 3.8

Prevalence of high levels of GPx in relation to the presence of D and recurrent SCHD

Status of depression in relation to SCHD	Low GPx		High GPx		Normal GPx	
	n	%	n	%	n	%
Depression + recurrent SCHD	9	19.1	9	19.1*^	29	61.7
Depression + primary SCHD	5	11.9	1	2.4^	36	85.7
No depression + recurrent SCHD	5	12.8	6	15.4	28	71.8
No depression + primary SCHD	12	26.1	1	2.2*	33	71.7

* p = 0.03, ^p = 0.03

The same observations are present for high levels of both – MDA and GPx. They are more frequent among patients of recurrent SCHD regardless of the status of depression. And the observation can be considered statistically significant (p = 0.006). But when the four strata are further compared pairwise, it is concluded that the high levels of MDA and GPX are significantly more frequent within the group "depression and recurrent SCHD" (19.1 %) than within the groups "no depression and primary SCHD" (2.2 %; p = 0.03) or within the group "depression and primary SCHD" (2.4 %; p = 0.04) (see Table 3.9).

Table 3.9

Prevalence of simultaneously high levels of MDA and GPx in relation to the presence of D and recurrent SCHD

Status of D in relation to SCHD	High both – MDA and GPx		Normal MDA and GPx or high one of them	
	n	%	n	%
D + recurrent SCHD*^	9	19.1	38	80.9
D + primary SCHD^	1	2.4	41	97.6
No D + recurrent SCHD	6	15.4	33	84.6
No D + primary SCHD*	1	2.2	45	97.8

* $p = 0.03$, ^$p = 0.04$, statistically significant if $p < 0.05$

Tables 3.10 and 3.11 show that the frequency of recurrent SCHD is the highest within the groups with high levels of GPx regardless of the presence of depression when compared to the strata with normal or low levels of GPx. And this tendency is statistically significant ($p = 0.006$). Analyzing the strata pairwise it is concluded that the prevalence of recurrent SCHD is significantly higher among patients with depression and high levels of GPx (90.0 %) when compared to people with no depression and normal or low levels of GPx (42.3 %; $p = 0.02$) or patients with depression but normal or low levels of GPx (48.1 %; $p = 0.04$) (Table 3.10).

The levels of MDA are not giving any additional impact on the relationship between the status of depression in combination with levels of GPx and the status of SCHD.

Table 3.10

Prevalence of simultaneously high levels of MDA and GPx in relation to the presence of D and recurrent SCHD

Status of depression and GPx	Recurrent SCHD		Primary SCHD	
	n	%	n	%
Depression + high GPx*^	9	90.0	1	10.0
No depression + high GPx	6	85.7	1	14.3
Depression + normal or low GPx^	38	48.1	41	51.9
No depression + normal or low GPx*	33	42.3	45	57.7

* p = 0.02, ^p = 0.04

The conclusions are identical to the ones described above for the combination of the D and GPx alone (see Table 3.11).

Table 3.11

Prevalence of high levels of MDA in relation to the presence of D and recurrent SCHD

Status of depression, MDA and GPx	RSCHD		PSCHD	
	n	%	n	%
D + high MDA + high GPx	9	90.0	1	10.0
No D + high MDA + high GPx	6	85.7	1	14.3
D + normal MDA + normal or low GPx	38	48.1	41	51.9
No D + normal MDA + normal or low GPx	33	42.3	45	57.7

* p = 0.02, ^p = 0.04

When the levels of MDA and GPx are analysed as parametric variables, it can be seen that the mean value of MDA is the highest among patients with no

depression and primary SCHD (11.04, SD 3.05) and the lowest among people with no depression and recurrent SCHD (9.68, SD 2.40). But the differences in mean MDA among the four strata of depression and SCHD status are not statistically significant (p = 0.40).

Whereas for the mean values of GPx the conclusion is the opposite – the mean level is the highest among people with no depression but recurrent SCHD (8458.36, SD 1949.61) and the lowest among patients with no depression and primary SCHD (7011.76, SD 1882.16). I.e., both groups of recurrent SCHD have the highest mean values of GPx regardless of the status of depression. And these observations are statistically significant (p = 0.008). Further comparing the mean GPx between strata of the status of D and SCHD it has been found that the mean level of GPx is significantly lower among patients with no depression and primary SCHD when compared to the people with no depression but recurrent SCHD (p = 0.001), among patients with depression and primary SCHD (p = 0.009) and people with depression and recurrent SCHD (p = 0.01). Further cross-tabulation analysis can be seen in Table 3.12.

Table 3.12

Prevalence and odds of recurrent SCHD stratified by the presence of D and the level of GPx

Dependent variables	OR (95 % CI)	p
D, low GPx	2.12	0.22
D, high GPx	**10.61**	**0.03**
D, normal GPx	0.95	0.89
No D, low GPx	0.49	0.23
No D, high GPx	7.07	0.08
No D, normal GPx	1	–

The cross-tabulation analysis revealed that the group “D + high GPx” had 10.6 times higher chances of recurrent SHCD compared to the “no D + normal GPx” group (Table 3.12.).

4 Discussion

As mentioned above, the present study aimed to investigate the relationships between OS level, the prevalence of D, and the risk of recurrent SCHD. The hypothesis was that in recurrent SCHD patients and D would be a higher level of OS than in patients with primary SCHD without D.

4.1 Prevalence of D

The result of the research revealed that the prevalence of D was in 51.2 % of all patients, which is in accordance with previous research. Basing on the literature, between 31–45 % of patients with coronary heart disease (CHD), including those with stable coronary artery disease, unstable angina, or myocardial infarction (MI), suffer from clinically significant depressive symptoms (Celano&Huffman, 2011).

By our expectations in the recurrent SCHD patients' the prevalence of D was higher (47,7 % in the primary group and 54,7 % in the recurrent group), though the difference between primary and recurrent patients was not statistically significant ($p = 0,44$). Multivariate logistic regression results indicated that as the D indicators increase by 1 unit, the chances of recurrent SCHD increase 1.04 times or 4 %, but it was not statistically significant.

The small difference between groups could be explained by 1) the presence of D a long time before primary hospitalization, not only after the cardiac event; 2) all the patients were enrolled in the research before hospital discharge, which means sometimes after 7–10 days of treatment and adherence to sleep and nutrition. In a study of hospitalized patients with a variety of cardiac conditions, those who met the criteria for clinical depression during admission had improvement in adherence (to diet, exercise, and medication) if their D improved following hospitalization. This suggests that reduced adherence to key

secondary prevention behaviours in depressed cardiac patients may be modifiable with the treatment of the depressive symptoms (Bauer et al., 2012)

4.2 OS level

There were analysed two markers of OS: were MDA – lipid peroxidation product, which shows OS level, and antioxidant(AO) enzyme GPx – a marker of the body's defence against OS.

In most of all patients was found high MDA level (in 146 patients, or 83,9 %) from 174, which is similar to the literature. Results of the studies of Pezeshkian et al (2001). Showed that MDA levels increased significantly in heart diseases. Some other investigations have also reported an increase in MDA and GPx levels in patients with CAD (Armstrong, 1998). Despite our expectations, in the primary SCHD group, the MDA level was slightly higher, though there was no statistically significant difference between the subgroups. Moreover, cross-tabulation analysis indicates that a higher MDA level was in a patient with primary SCHD without depression (in 91,3 % of patients). Though there were no statistically significant differences between subgroups ($p = 0,38$), this tendency could be taken into account.

In turn, the GPx level was significantly higher in the recurrent SCHD subgroup ($p = 0,01$). Multivariate analysis showed that a higher GPx level 11.29–fold increased the risk of SCHD. Kaya et al. (2012), also reported an increase in MDA and GPx levels in patients with coronary artery disease. GPx enzyme activation was significantly higher in patients with coronary artery disease than in healthy controls (Kaya et al., 2012). As well the result of the present research revealed that in patients with recurrent SCHD is a slightly lower GPx level than in patients with primary SCHD. It has been demonstrated that AO enzyme activities are reduced in CHD, and this is linked to increased disease risk. Many

studies have indicated that free radical generation increases and AO defences decrease in response to increased OS in CHD patients. Activity levels of the AO enzymes GPx, and non-enzymatic AO, are considered predictors of CHD (Cheraghi et al., 2019).

The discrepancies – higher MDA levels in patients with primary SCHD – can be explained by several factors. First, OS may be an early causative factor in CVD pathology rather than a late consequence (Vaváková et al., 2017) and OS and inflammation develop long before the onset of the first symptoms. We could suppose that OS in recurrent SCHD patients was longer than in the primary, but activation of AO enzymes partially compensated for high OS level. The fact that GPx level was higher in patients with recurrent SHCD, which means antioxidative system defence activation, could confirm this assumption. Second, the use of beta-blockers. All of both groups' patients took beta-blocker therapy during hospitalization. Previous research found that treatment with beta-blockers such as metoprolol, carvedilol, and bisoprolol reduces the levels of OS (Nakamura et al., 2011; Kukin et al., 2011). Unfortunately, in the present study we did not have information on the use of beta-blockers before hospitalization. We could assume that patients with recurrent SCHD used beta blockers longer than patients with primary SCHD – a long time before hospitalization. The longer beta-blocker use could explain lower MDA levels in the recurrent SCHD group. Third, we did not have data on psychoactive drug use or psychological support of the patients before they were enrolled in the study or other factors that could affect the MDA level.

An interesting finding in the present research was the cross-tabulation analysis indicated that both OS markers (MDA and GPx) together were significantly higher in the recurrent SCHD subgroup, and compared pairwise, it was found that the high levels of MDA and GPx are significantly more frequent within the group "D and recurrent SCHD" than within the groups "no D and

primary SCHD" ($p = 0.03$) or within the group "depression and primary SCHD" ($p = 0.04$). Analyzing the strata pairwise it was found that the prevalence of recurrent SCHD is significantly higher among patients with depression and high levels of GPx (90.0 %) when compared to people without depression and normal or low levels of GPx ($p = 0.02$) or patients with depression but normal or low levels of GPx ($p = 0.04$). Moreover, as it's the group "D + high GPx" had 10.6 times higher chances of recurrent SHCD compared to the "no D + normal GPx" group. Hence, we can suppose that OS indeed is a risk factor for SCHD recurrence, especially in patients with D. Although the division into groups of combinations entailed a small number of people in each subgroup, we suggest taking these findings into account in further studies. As mentioned above, these only in-patients before discharge were included in the study, who already observed a certain sleep regimen and diet, and received appropriate treatment and care, which could reduce the symptoms of both depression and OS. That could explain the small number of patients with both depression and OS in each primary and recurrent SCHD subgroup.

There is a need to add that it's the first research comparing OS and depression in primary and recurrent patients with SCHD. Previous studies compared OS levels in CHD patients and healthy controls. Cheraghi et al (2019), found that serum GPx and MDA were significantly greater in CHD patients than in healthy controls (Cheraghi et al., 2019). Moreover, other researches confirm that the OS directly increases the risk of depression in patients with cardiovascular diseases, whereas it increases the risk of cardiovascular diseases in depressed people. In summary, the common risk factors increase the production of OS and reduce antioxidant defences, thereby promoting the occurrence and development of interacted ischemic CVD and depression (Lin et al., 2019)

Depression, a frequently occurring disease, has a bidirectional relationship with ischemic CVD and partially shares common risk factors (such as obesity and diabetes) and mechanisms (such as inflammation and OS) with CVD, providing a new direction for future research. Based on the literature on patients with CVD, D is often chronic and recurrent. Among patients with CVD hospitalized for acute cardiac events and found to meet criteria for D during or shortly after admission, approximately 50–70 % had ongoing depressive symptoms that preceded their cardiac event. This finding is consistent with literature that describes persistent D in patients with stable CAD. Depressed patients with unstable CAD appear to be at even greater risk for poor cardiac outcomes. OS can independently and directly affect stroke, CHD, and D. Furthermore, OS acts as a link between ischemic CVD and D. (Lin et al., 2019) Several lines of evidence indicate that different cardiovascular considerations should be inspected in patients who need to take AD medications (Yekehtaz et al., 2013). There is an increasing body of evidence supporting that D may be associated with changes in OS markers and that AD agents (especially long-term treatment) may increase AO defences. Augmentation of AO defences may be one of the mechanisms underlying the neuroprotective effects of Ads observed in the treatment of D (Celano&Huffman, 2011). It has been shown that depressed patients have elevated levels of platelet adhesion and aggregation leading to increased risk for cardiovascular events. The use of SSRIs may prevent the development of atherosclerotic plaques and also arterial thrombosis (Nezafati et al., 2015). Patients, who respond to AD therapy within the first year of treatment have been shown to experience significantly lower rates of morbidity and mortality (Yekehtaz et al., 2013).

Further research is necessary to fully understand underlying processes in terms of OS and D, that provoke recurrence of CHD events. In summary, there is a need to find effective therapies to control CVD and D. When D screening is

paired with a management protocol or system of care (e.g., a care management program) to treat D in persons with CVD, there has been consistent evidence for improved patient outcomes (including, in some studies, improved adherence, reduced cardiac symptoms, reduced cardiac events and improved blood pressure and lipids). Patients who meet the full criteria for D should be treated, whether cardiac events are recent or remote (Celano&Huffman, 2011). OS directly increases the risk of D in patients with CVD, whereas it increases the risk of CVD in depressed people. The common risk factors increase the production of OS and reduce AO defences, thereby promoting the occurrence and development of interacted ischemic CVD and D (Lin et al., 2019).

4.3 Limitations of the study:

1. There were rather heterogenous groups by age and gender in both groups, which could influence the results. MDA appears to be sensitive to both gender and age. It is significantly lower and shows a greater age dependence in women than in men. The age-dependent slope of the steady state concentration is maximal at the age between 50 and 55 years, indicating that it may be attributed to the change of metabolism in the postmenopausal period. Interestingly, total glutathione decreased with age simultaneously with the increase in MDA (Pinchuk et al., 2019).
2. In the current study, there were not take into account patients' anthropometric data, only persons with BMI > 30 were excluded, based on the literature, there was no clear association between obesity and systemic OS in subjects with BMI add less than 30 kg/m^2 (Ito et al., 2019).

3. In the present research, the authors could not exclude other factors that affect D and / or OS in patients in relation to SCHD recurrence (dietary intake, substance use disorder, chronic somatic disorder, difficult life events no relationships, no family, poor social life, lower socioeconomic status, etc.)

Conclusions

1. More than a half of patients were experiencing mild or severe depression symptoms with higher rates among patients with recurrent stable coronary heart disease.
2. Majority of patients had high levels of MDA with higher rates in patients with primary stable coronary heart disease.
3. GPx level was normal in the majority of patients, but the elevated level was more common among patients with recurrent stable coronary heart disease.
4. MDA level was slightly higher in the primary stable coronary heart disease group without depression. Therefore, increased MDA level is a risk factor for stable coronary heart disease in general but it does not link to depression severity and recurrence of stable coronary heart disease.
5. GPx level was significantly higher in depressed patients with recurrent stable coronary heart disease compared to patients without depression and to patients with primary stable coronary heart disease. Patients with both high GPx and depression had 10.6 times higher chances of recurrent stable coronary heart disease compared to those with normal GPx and without depression.
6. According to the findings of the study we suppose that a high level of GPx is a risk factor for SCHD recurrence, especially in patients with D.

Practical recommendations

1. It is extremely important to measure depression levels in all patients with SCHD.
2. It is important to develop a multidisciplinary approach in SCHD patient treatment, combined with liaison psychiatry.
3. According to available literature data and research results patients with primary and recurrent events of SCHD differ biochemically by OS markers, therefore it is important to analyse the necessity to revise treatment options and combinations, for example, antidepressant and / or AO use in each case individually. We might suggest timely use antidepressants can reduce the risk of rehospitalization and increase expenses connected with treatment.
4. As GPx is a more significant marker of the risk of depression and recurrence of stable coronary heart disease, it is important to implement GPx in diagnostics at an early stage of SCHD.

Publications and thesis

Publications:

1. Ivaščenko, T, Voicehovskis, V, Kalējs, O, Voicehovska, J, Šķesters, A, Pahomova, N and Lejnieks, A. 2022. "Depression and Oxidative Stress Interaction in Stable Coronary Heart Disease" Proceedings of the Latvian Academy of Sciences. Section B. Natural, Exact, and Applied Sciences., vol.76, no.2, 181–187. https://doi.org/10.2478/prolas-2022-0028
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Conferences:

1. RSU international research conference on medical and health care sciences, poster presentation “GPx, MDA, depression and risk of recurrence of stable coronary heart disease”. 24.03.2021.
2. RSU international research conference on medical and health care sciences, poster presentation “Atrial fibrillation patient health-related quality of life change over 6- and 12-months depending on the used oral anticoagulant type”. 24.03.2021.

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