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КОРЕЛАЦИЯ НА ВЪТРЕСЪРДЕЧНИТЕ ХЕМОДИНАМИЧНИ ПОКАЗАТЕЛИ С ФАКТОРА НА ФОН ВИЛЕБРАНД – МАРКЕР ЗА ЕНДОТЕЛИАЛНА ДИСФУНКЦИЯ ПРИ ПАЦИЕНТИ С БОЛЕСТ НА КОРОНАРНИТЕ АРТЕРИИ, КОМБИНИРАНА С КОРОНАВИРУСНО ЗАБОЛЯВАНЕ (COVID-19)

В. Нетяженко¹, С. Мостовый¹, О. Сафонова²

¹Национален медицински университет "Богомолец" – Киев, Украйна

²Киевска градска клинична болница № 18 – Киев, Украйна

CORRELATION OF INTRACARDIAC HEMODYNAMICS INDICATORS WITH VON WILLEBRAND FACTOR – MARKER OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CORONARY ARTERY DISEASE COMBINED WITH CORONAVIRUS DISEASE (COVID-19)

V. Netiazhenko¹, S. Mostovyi¹, O. Safonova²

¹Bogomolets National Medical University – Kyiv, Ukraine

²Kyiv City Clinical Hospital No. 18 – Kyiv, Ukraine

Резюме.

Изследването има за цел да установи връзката между показателите и ролята на ендотелната дисфункция в патогенезата на различни състояния. Използван е методът на клинично наблюдение и са събрани данни като симптоми, медицинска история и лабораторни и инструментални изследвания. Проучването разкрива повишена активност на фактора на von Willebrand при повечето пациенти. При сравняване на групи пациенти в зависимост от наличието на съпътстващо коронавирусно заболяване е установено, че най-високото ниво на фактора на von Willebrand се наблюдава при пациенти с коронарна болест на сърцето в комбинация с коронавирусно заболяване, по-ниско ниво при лица само с коронавирусно заболяване и най-ниското ниво при пациенти с хронична коронарна болест на сърцето. Това показва корелация между нивото на фактора на von Willebrand и наличието на съпътстващо коронавирусно заболяване, което подчертава значението на съдовата ендотелна дисфункция в патогенезата на коронарната болест на сърцето. Установено е, че стойността на фактора на von Willebrand корелира с крайния диастолен размер на лявата камера както при пациенти с коронарна болест на сърцето, така и при пациенти с коронарна болест на сърцето в комбинация с коронавирусна болест. Това показва, че има силна връзка между фактора на von Willebrand и клиничната проява на коронарна болест на сърцето в комбинация с коронавирусна болест, което може да показва дисфункция на съдовия ендотел при тези пациенти.

Ключови думи:

исхемична болест на сърцето, COVID-19, лечение, ендотелно увреждане, възпалителни процеси

Адрес

Сергей Мостовый, Катедра по пропедевтика на вътрешните болести 1, Национален медицински университет

за кореспонденция:

"Богомолец", бул. Тарас Шевченко 13, 01601 Киев, Украйна, e-mail: serhii.mostov@gmail.com

Abstract.

The research aims to establish the relationship between indicators and the role of endothelial dysfunction in the pathogenesis of various conditions. The clinical observation method was used, and data such as symptoms, medical history, and laboratory and instrumental studies were collected. The study revealed an increased activity of von Willebrand factor (vWF) in the majority of patients. When comparing groups of patients depending on the presence of concomitant coronavirus disease, it was found that the highest level of vWF was observed in patients with coronary heart disease in combination with coronavirus disease, a lower level in patients with coronavirus disease alone, and the lowest level in patients with chronic coronary heart disease. This indicates a correlation between the level of vWF and the presence of concomitant coronavirus disease, which emphasises the importance of vascular endothelial dysfunction in the pathogenesis of coronary heart disease. It was found that the value of the vWF correlates with the left ventricular end-

diastolic size in both patients with coronary heart disease and patients with coronary heart disease in combination with coronavirus disease. This demonstrates that there is a strong association between vWF and the clinical manifestation of coronary heart disease in combination with coronavirus disease, which may indicate a dysfunction of the vascular endothelium in these patients.

Key words: coronary heart disease, COVID-19, treatment, endothelial damage, inflammatory processes

Address for correspondence: Serhii Mostovyi, Department of Propaedeutics of Internal Medicine No. 1, Bogomolets National Medical University, 13 Taras Shevchenko Blvd., 01601 Kyiv, Ukraine; e-mail: serhii.mostov@gmail.com

INTRODUCTION

Studying the relationship between COVID-19 and coronary heart disease (CHD) can improve CHD treatment and reveal intracardiac hemodynamic and von Willebrand factor (vWF) changes. Exploring the relationship between endothelial dysfunction and thrombosis risk is crucial. This helps identify high-risk CHD patients and implement preventive measures by improving understanding of the causes of thrombotic complications and endothelial dysfunction in COVID-19 patients. CHD and COVID-19 research improve patient care and reduces mortality and disability by improving treatment, risk assessment, and prevention.

Various factors affect blood flow and blood vessel health in CHD patients, especially during COVID-19, complicating direct connections. Diversifying samples is essential for representative results. Reliable, practical results require careful study design, methodology, and execution. These issues improve diagnosis and treatment of COVID-19's cardiac effects. Results improve prognosis, complications, and patient care.

COVID-19 can cause thrombosis and endothelial dysfunction, according to V. Yu. Dobrianska [1]. The study of the relationship between these complications calls into question the best ways to manage them and requires more research and treatment strategies. L. M. Sursaeva suggests that treatment effects, lack of a control group, patient variations, environmental conditions, lifestyles, and physical activity may distort study results [2]. M. P. Galkevich states that intracardiac haemodynamics includes blood pressure, circulating blood volume, and blood flow velocity [3]. Intracardiac haemodynamics and the vWF, a marker of endothelial dysfunction, are linked, suggesting vascular dysfunction and cardiac complications.

L. V. Tsuglevich says this research is crucial to understanding COVID-19-related coronary artery disease [4]. This can identify new risk markers, improve diagnostic and treatment strategies, and improve patient outcome prediction. According to I. F. Belenichev, studying intracardiac haemodynamics and vWF may lead to new therapeutic approaches [5]. It may suggest target mechanisms for treating and developing new drugs to improve endothelial function and cardiovascular health in this patient population. Evidence of changes in these parameters in COVID-19 patients with coro-

nary artery disease may affect the development or use of new or existing drugs to improve endothelial function and cardiovascular health. Z. I. Litovkina showed that studying this topic will help identify high-risk patients and prescribe prevention and treatment [6]. This is essential for disease prognosis and complication reduction. Understanding risk factors and patient characteristics allows doctors to create personalised cardiovascular disease prevention and treatment plans to lower risk and improve quality of life.

MATERIAL AND METHODS

The study used such methods as polymerase chain reaction (PCR), multislice computed tomography (MCT), coronary angiography (CAG), static method, and transthoracic echocardiography. Firstly, a sample of 80 people was taken and divided into 3 groups. In the beginning, 80 participants were divided into three groups: G1 (CHD), G2 (CHD with COVID-19), and G3 (no CHD). A control group (CG) of 35 healthy volunteers without SARS-CoV-2 infection or COVID-19 vaccination was created for comparison. CG participants had upper respiratory tract samples PCRed to exclude asymptomatic carriers of SARS-CoV-2. SARS-CoV-2 RNA was extracted from the patient's upper respiratory tract. These included saliva, nasal secretions, and airway prints. After extracting RNA, RNA polymerase enzyme, and primers were added to a reaction mixture. High temperatures denature SARS-CoV-2 double-stranded RNA. Lowering the temperature allowed primers to bind to SARS-CoV-2 RNA complementary sequences. To replicate SARS-CoV-2 RNA, RNA polymerase was used to synthesise new nucleotides based on its complementary sequences. Denaturation, anelination, and extension are repeated several times. Each cycle adds RNA to the reaction mixture. Gel electrophoresis or special detection devices can detect amplified SARS-CoV-2 RNA after PCR cycles.

Patients had MCT scans of their lungs using X-rays, processed with computer algorithms for 3D lung imaging and lesion assessment related to COVID-19, including inflammation, pneumonic lesions, or masses. Coronary angiography involved injecting a contrast agent into coronary arteries, visualizing their condition

and potential lesions. X-rays were used to record arterial conditions for detecting chronic coronary heart disease. Doctors analysed the images to confirm coronary artery disease. Transthoracic echocardiography followed American Society of Echocardiography (ASE) recommendations, assessing cardiac chamber remodelling and left ventricular function, both systolic and diastolic.

MCT scans were performed using X-rays and computer algorithms for 3D lung imaging and COVID-19 lesion assessment, including inflammation, pneumonic lesions, and masses. Coronary angiography injected contrast into coronary arteries to detect lesions. X-rays recorded arterial conditions for chronic CHD detection. Physicians confirmed coronary artery disease from the images. Transthoracic echocardiography assessed cardiac chamber remodelling and systolic and diastolic left ventricular function per ASE guidelines.

Blood clotting requires the glycoprotein vWF in the bloodstream. Erik von Willebrand discovered vWF, a protein that plays many vital roles in the circulatory system. VWF helps platelets attach to injured blood vessel linings in the early stages of blood clot formation. It also transports Factor VIII, a coagulation factor, preventing degradation and extending its lifespan. VWF helps platelets adhere to the damaged vessel's endothelium, strengthening blood clots. Besides clotting, vWF protects endothelial cells, which line blood vessels, ensuring optimal vascular performance. VWF disruptions can cause bleeding disorders like von Willebrand Disease or abnormal blood clotting. This shows how important von Willebrand Factor is in balancing bleeding and clotting. VvWF reference limits determine this vital blood glycoprotein's normal and abnormal levels. Normal vWF levels vary by lab and assay. VWF levels are typically expressed as a percentage of normal plasma pool, 50-150%. Levels below 50% suggest von Willebrand disease, while above 150% may indicate endothelial dysfunction or other pathologies. These levels must be interpreted in light of patient profiles and clinical findings.

RESULTS

The complex relationship between CHD and COVID-19 is the focus of this study. This study seeks to better understand this correlation to improve treatment, identify risk factors, and develop preventive measures for affected individuals. This study aims to understand how these two diseases affect intracardiac blood flow and vWF levels. It also examines patients with both conditions' increased blood clot risk and vessel inner lining damage. This research should help develop effective treatments for COVID-19 and coronary heart disease patients. Additionally, it will detect high-risk

patients quickly, allowing for timely intervention to manage their conditions and prevent complications.

The study examined intracardiac hemodynamics and endothelial dysfunction marker vWF in CHD and COVID-19 patients. It looked for links between endothelial dysfunction marker vWF and hemodynamic parameters in CHD and COVID-19. Central hemodynamics blood pressure, heart rate, minute blood volume, and intracardiac systolic and diastolic function—are vital cardiovascular indicators. Hemodynamic parameters reveal the cardiovascular system in CHD, where heart blood supply is compromised. VWF increases the risk of blood clots and cardiovascular complications due to endothelial dysfunction. As vWF helps blood clot, its level can indicate endothelial dysfunction.

The study found vWF-intracardiac hemodynamic correlations. High vWF values increased blood pressure, heart rate, and vascular resistance and cardiac workload. Patients with both coronary artery disease and COVID-19 had higher vWF levels than those with only one, suggesting an interaction between these diseases and endothelial dysfunction. COVID-19 increases vWF by worsening endothelial dysfunction. The link between intracardiac hemodynamics, vWF, and endothelial dysfunction in coronary artery disease patients, especially in COVID-19, is significant.

Table 1 lists study group clinical characteristics. No significant age differences existed between patient groups. All groups had similar gender, body weight, and smoking status. Hypertension was common in G1 and G2, but rare in G3. Type 2 diabetes was more common in CHD patients (G1 and G2) than in G3. The CHD groups had similar rates of acute myocardial infarction (AMI) and CAG. G2 and G3 had similar COVID-19 lung damage severity. MDCT showed 9 G3 patients had CT2 lung lesions, 12 CT3, and 4 CT4. In G2, 10 patients had CT2 lung lesions, 10 CT3, and 5 CT4.

ECG results showed ventricular extrasystole in G1 (CHD) at 19%, G2 (CHD+COVID-19) at 55%, and Group 3 (COVID-19) at 35%, with no statistical significance ($p=0.085$). Rates of atrial extrasystole, left bundle branch block, and first-degree atrioventricular block were similar among groups. Clinical factors, including AMI and CABG history, were compared. Groups 2 and 3 had higher hypertension rates than Group 1 (p -values < 0.001). Group 1 had a higher T2DM diagnosis frequency compared to Group 3 ($p=0.05$). In summary, ECG data suggest a correlation between intracardiac hemodynamics and vWF in CAD patients with COVID-19 (Table 2).

Echocardiography showed structural changes in the left heart, right ventricle, and left ventricular dysfunction in study patients. Compared to the control group, they had higher pulmonary artery systolic pressure (PASP) values. The third group (COVID-19 without CHD) main-

Table 1. Demographic data, anthropometric parameters and clinical features

Indicators	Control n = 35	Patient groups			p (Group 1 vs Group 2)	p (Group 1 vs Group 3)	p (Group 2 vs Group 3)
		Group 1 (CHD), n = 30	Group 2 (CHD+COVID-19), n = 25	Group 3 (COVID-19), n = 25			
Age, years	48.6 ± 17.3	52.4 ± 19.1*	60.4 ± 9.9*	51.1 ± 18.7	NS	NS	NS
Males, n	28	15	21	20	NS	NZ	NZ
Body mass index, kg/m ²	24.2 ± 6.9	23.8 ± 8.4	27.2 ± 5.1	23.8 ± 8.4	ND	ND	ND
Hypertension, n	-	25	23	10	ND	< 0.001	< 0.001
CD2	-	6	11	3	NS	0.05	0.05
HM, n	-	13	8	-	NS	-	-
CAG	-	14	19	-	NS	-	-
Willebrand factor		155	183	120			

Note: p1-2 – statistical significance of the difference between group 1 and group 2; p1-3 – statistically significant differences between group 1 and group 3; p2-3 – statistically significant differences between group 2 and group 3; ND – statistically significant difference is not significant; * – statistically significant difference is significant (p < 0.05) compared to control.

Table 2. Von Willebrand factor levels by patient group

Patient Group	n	Von Willebrand Factor Level	p-value vs CAD group
CAD	30	155 ± 59%	-
CAD + COVID-19	25	193 ± 62%	p < 0.01
COVID-149	25	± 120%	p < 0.05

tained left ventricular ejection fraction (LVEF). However, transthoracic echocardiography showed more severe dilation and impaired left ventricular systolic function in CAD patients in Groups 1 and 2 than in the control and third groups. Meanwhile, patients with combined coronary heart disease and COVID-19 (group 2) had greater left ventricular dilation than those without coronavirus disease (G1). Compared to cases where both conditions manifest themselves separately, patients with combined CHD and COVID-19 had more pronounced dilation and slightly worse systolic function of the left ventricle, the most pronounced dilation of the right ventricle, and a more pronounced increase in STA (Table 3).

Out of the 80 patients studied, 72 showed increased vWF activity, with average values higher than those in the control group. The levels varied among patient groups based on the presence of COVID-19. Patients with both CHD and COVID-19 had the highest levels, followed by patients with COVID-19 alone, and the lowest levels were in patients with chronic CHD. This correlation underscores the significance of vascular endothelial dysfunction in CHD development. The vWF level correlated with the size of the left ventricle during the diastolic phase in patients with CHD and in those with CHD and COVID-19. This indicates a close link between the vWF and clinical manifestations of CHD in patients with COVID-19, reflecting vascular endothelial dysfunction.

The exact mechanism by which vWF increases the risk of adverse events in CHD combined with COVID-19 remains unknown. It might result from heightened endothelial damage in CHD, leading to spontaneous thrombus formation and elevated vWF levels. Additionally, the vWF's role in platelet adhesion and aggregation during coagulation may heighten the risk of thrombus formation in patients with existing vascular damage, contributing to plaque destabilization and recurrent myocardial infarction. It's also possible that ischemic coronary syndromes involve the activation of various cells like platelets, monocytes, and macrophages, making the analysis of these processes more complex [7, 8].

Endothelial dysfunction and coagulation system changes result from increased vWF. Inflammation and oxidative stress impact intravascular endothelial function. Endothelium-produced NO and other substances regulate vascular tone and prepare blood vessels for flow. Endothelial dysfunction alters intravascular conditions. Both hyperlipidemia and hyperglycemia affect blood vessels. Hyperlipidemia forms vessel wall fatty plaques, while hyperglycemia inflames the endothelium [9]. Endothelial cells produce vWF in response to these intravascular changes. Blood clots, platelet dislocation, thrombosis, and cardiovascular risk can result from high vWF. Hyperglycaemia, dyslipidemia, and endothelial dysfunction activate the vWF, causing blood clots and cardiovascular risk.

Table 3. Myocardium structural and functional evaluation using echocardiography data from groups 1-3 and the control group.

Indicators	Control n = 35	Patient groups			p (Group 1 vs Group 2)	p (Group 1 vs Group 3)	p (Group 2 vs Group 3)
		Group 1 (CHD), n = 30	Group 2 (CHD+COVID-19), n = 25	Group 3 (COVID-19), n = 25			
Anterior-posterior size of the left atrium, cm	3.59 ± 0.07	4.22 ± 0.2*	4.55 ± 0.42*	3.71 ± 0.42	NS	< 0.001	< 0.001
The ratio of the anterior-posterior size of the left atrium to the diameter of the aortic root, units	1.01 ± 0.06	1.11 ± 0.12*	1.28 ± 0.11*	1.18 ± 0.17*	NS	< 0.01	NS
Diastolic ventricular septal thickness, cm	0.89 ± 0.01	1.01 ± 0.08*	1.05 ± 0.1*	0.92 ± 0.11*	NS	NS	< 0.001
The thickness of the left ventricular posterior wall in diastole, cm	0.88 ± 0.02	1.02 ± 0.08*	1.04 ± 0.09*	0.94 ± 0.1*	NS	NS	<0.01
Left ventricular myocardial mass indexed by body surface area, g/m ²	81 ± 8	117 ± 12*	137 ± 12*	89 ± 10	NS	< 0.001	< 0.001
End-diastolic left ventricular size, ml	120 ± 23	179 ± 33*	209 ± 21*	126 ± 21	< 0.001	< 0.001	< 0.001
Left ventricular ejection fraction, %	68.8 ± 2.9	47.8 ± 4.6*	46.4 ± 12.1*	55.5 ± 10.1*	NS	< 0.001	< 0.001
The ratio of diastolic transmitral flow velocity, units	1.41 ± 0.07	0.84 ± 0.41*	1 ± 0.29*	1.1 ± 0.18*	NS	NS	NS
Left ventricular isovolumic relaxation time, ms	80 ± 12	91 ± 17*	94 ± 11*	76 ± 14	NS	< 0.01	< 0.01
Slowing of early diastolic filling of the left ventricle, ms	168 ± 14	201 ± 14*	199 ± 18*	180 ± 25	NS	< 0.001	NS
Anterior-posterior size of the right ventricle, cm	2.11 ± 0.05	2.93 ± 0.24*	3.5 ± 0.44*	3.06 ± 0.54*	< 0.001	NS	NS
Right ventricular wall thickness, cm	0.37 ± 0.1	0.34 ± 0.1	0.54 ± 0.07*	0.46 ± 0.15*	< 0.001	NS	NS
Systolic pulmonary artery pressure, mm Hg	24.8 ± 3.6	28.8 ± 6.5*	39.2 ± 7.1*	36.6 ± 7.6*	< 0.001	< 0.001	NS
von Willebrand factor, %	83 ± 22	154 ± 59*	193 ± 62*	162 ± 56*	< 0.01	< 0.01	NS
Level of N-terminal fragment of brain natriuretic peptide precursor, pg/ml	97 ± 26	708 ± 122*	921 ± 142*	173 ± 51*	< 0.01	< 0.01	< 0.01
C-reactive protein level, mg/l	4.08 ± 1.75	7.68 ± 0.3*	14.1 ± 10.24*	12.2 ± 7.19*	< 0.01	< 0.01	NS

Note: p1-2 – the statistical significance of the difference between group 1 and group; p1-3 – statistically significant differences between group 1 and group 3; p2-3 – statistical significance of the differences between groups 2 and 3; ND – statistically significant difference is not significant; * – statistically significant difference is significant ($p < 0.05$) compared to the control.

DISCUSSION

COVID-19 patients with coronary artery disease had lower cardiac output, limiting organ oxygenation and function. Infection, inflammation, and oxidative stress contribute to COVID-19 cardiovascular dysfunction. To diagnose, treat, and prevent COVID-19, we must understand these changes. Viscosity, blood volume, and vascular wall condition increase vascular resistance, causing hypertension. Infection response and sympathetic nervous system activation may cause high blood pressure and atherosclerosis in COVID-19 patients with coronary artery disease [10, 11].

High blood pressure strains the heart and lowers cardiac output due to vascular resistance. Patients with COVID-19 and coronary artery disease must have el-

evated blood pressure checked. Medications, lifestyle changes, and vascular resistance and heart function interventions can detect and treat hypertension. COVID-19 can cause tachycardia in CHD patients by altering autonomic nervous system regulation [12]. Sympathetic and parasympathetic nerves regulate heart rhythm and other functions. The sympathetic system increases heart rate and contractions, while the parasympathetic decreases them. Covid-19 can affect heart rate through direct heart muscle effects, inflammation, or infection-triggered sympathetic nervous system activation [13, 14].

High heart rates harm coronary heart patients. This increase in heart rate reduces heart muscle oxygen supply by increasing oxygen consumption. Arrhythmias, such as rapid or irregular heartbeats, can

be dangerous for people with coronary heart disease. Some factors can raise heart rate, but autonomic nervous system changes are linked to it in COVID-19 patients with CHD. The heart needs potassium, sodium, and calcium to function properly. COVID-19 can affect heart rhythm with electrolyte imbalance. A lack of oxygen can also raise heart rate [15-17].

Elevated activity of vWF can lead to the activation of platelet coagulation and the formation of blood clots. This poses a significant risk for patients with coronary heart disease, who are already predisposed to thrombosis due to the presence of atherosclerotic lesions in their blood vessels. If a blood clot develops in the vessels supplying the heart, it can result in a heart attack. Similarly, if a blood clot obstructs a vessel in the brain, it can lead to a stroke. These complications are particularly hazardous for individuals with coronary artery disease, as their heart vessels may already have sclerosis and be susceptible to blood clot formation [18, 19].

Active inflammation and high vWF levels indicate vascular endothelium damage and impaired function. A compromised endothelium increases the risk of blood clots and thrombotic complications in COVID-19 and coronary artery disease by losing its ability to regulate vascular tone, substance permeability, and inflammation [20, 21]. Endothelial dysfunction needs oxidative stress. Endothelial NO increases vWF interaction, preventing blood clots. NO levels drop due to active oxygen radicals, activating vWF and causing thrombosis. NO relaxes blood vessels and prevents platelet aggregation and clots, but hydrogen peroxide and superoxide lower it. Platelets clot when active vWF displaces them. NO decreases and vWF increases with oxidative stress, causing endothelial dysfunction and thrombosis [22].

COVID-19 and chronic CHD patients have severe endothelial dysfunction, including inflammation, vaso-regulatory factor imbalances, and oxidative stress. This group has higher vWF levels than CHD patients without COVID-19, indicating increased blood coagulation and thrombogenicity. Complex changes in CHD pathomorphology caused by COVID-19 may increase cardiovascular complications. Inflammatory pathways, platelet adhesion and aggregation, endothelial dysfunction, and blood coagulation system imbalances may cause this. This aspect of COVID-19 and CHD interactions needs more molecular, cellular, and organ research to understand and find the best treatments.

Research shows that COVID-19 and chronic CHD increase endothelial dysfunction, affecting CHD development and progression. This effect causes complex pathomorphological changes in CHD involving multiple biological processes and mechanisms, not just a combination of COVID-19 and CHD causal factors. More research is needed to understand this phenomenon and develop effective treatments. COVID-19-CHD interac-

tions at molecular, cellular, and systemic levels should be studied. These studies will reveal the mechanisms that worsen COVID-19 and CHD patients' conditions, leading to new treatments and prevention methods.

S.A. Saha et al. [23] say lifestyle changes detect and treat high blood pressure. Eating a balanced diet with salt restrictions, quitting smoking, exercising, and managing weight can lower blood pressure. A balanced diet low in carbohydrates and saturated fats lowers atherosclerosis risk and improves vascular function [24]. Lifestyle changes may fail, so blood pressure medications may be prescribed. ACE inhibitors, beta-blockers, calcium antagonists, and diuretics are examples. Medication, lifestyle changes, and other interventions can lower vascular resistance and improve heart function. Improving myocardial blood flow may require coronary angioplasty—stenting or bypass grafting. Understanding that high blood pressure management is patient-specific is crucial. Success and efficacy vary by case. Along with lifestyle changes and drug therapy, stress management is essential. Stress management lowers hypertension.

M. Thakur et al. report that the novel coronavirus SARS-CoV-2 causes COVID-19, which can inflame the cardiovascular system due to its direct effect on the heart or systemic inflammatory response [25]. When the virus activates the immune system, inflammation rises. Heart muscle and cardiovascular inflammation can spread. Heart muscle conduction is hampered by inflammation. It can cause tachycardia. Poor heart rhythm-regulating electrical signal conduction. Cardiovascular inflammation causes blood clots and vessel damage. A heart attack, stroke, or other complications may occur. Recent research shows COVID-19 can damage the cardiovascular system and cause cardiac issues [26]. This emphasises the importance of COVID-19 prevention, early diagnosis, and treatment, especially for cardiovascular risk patients.

COVID-19-induced cardiovascular inflammation can impair heart function and organ and tissue blood supply, according to R.I. Matos and K.K. Chung [27]. The main result is systolic dysfunction and low cardiac output. COVID-19-induced inflammation reduces heart muscle contractility and blood ejection per heartbeat. Oxygen and nutrients are denied to organs and tissues due to reduced cardiac output. COVID-19 inflames blood vessels, including the microcirculatory system. Vascular inflammation and damage increase blood flow resistance, making the heart work harder and lowering cardiac output. COVID-19-related cardiovascular inflammation lowers cardiac output and raises circulatory resistance, causing cardiac dysfunction. These changes disrupt organ and tissue blood and oxygen supply, which could be dangerous. COVID-19-related cardiovascular inflammation causes cardiac function deteri-

oration due to reduced cardiac output and increased circulatory resistance, which has serious health consequences [28].

According to O.C. Liesdek et al., the vWF protein is crucial to platelet coagulation and blood clotting [29]. Damage to the vascular endothelium activates vWF, increasing blood levels. High vWF levels activate platelets, which clot blood. Thrombin, fibrinogen, and platelets have not been shown to interact with vWF. Platelet dislodgement at vascular injury sites helps form a primary thrombus. The vWF stabilises and fixes platelets at the injury site, forming a stable thrombus.

Platelet activation causes blood clots, especially in CHD patients. Atherosclerosis causes angina and myocardial infarction by depositing fatty plaques on blood vessel walls. Vascular atherosclerosis increases clot risk. COVID-19 endothelial damage increases atherosclerotic vessel vWF activity and blood clot formation. Thrombosis results from clots blocking vessel blood flow. Atherosclerotic lesions make thrombosis especially dangerous in coronary artery disease patients. Blood clots can worsen myocardial infarction and stroke, endangering the patient's life. COVID-19 endothelial damage increases vWF, platelet activation, and blood clot formation, which is dangerous for atherosclerotic coronary artery disease patients.

CONCLUSIONS

This study confirms a significant connection between von Willebrand factor levels, an indicator of endothelial dysfunction, and intracardiac haemodynamics in patients affected by both Coronary Heart Disease and COVID-19. It's observed that most patients show increased von Willebrand factor activity, indicating progressive endothelial damage when CHD and COVID-19 coexist. Moreover, this combination is associated with marked elevations in key markers like CRP and NT-proBNP.

The positive correlations found between von Willebrand factor, CRP, and NT-proBNP levels suggest the involvement of inflammation in the development of CHD in the presence of COVID-19. It also underscores the detrimental impact of elevated CRP levels on CHD progression and heart failure, as reflected by NT-proBNP. Importantly, von Willebrand factor in blood plasma is a recognized marker of endothelial dysfunction, providing an accurate assessment of endothelial damage in CHD combined with COVID-19.

This study also suggests the potential use of ejection fraction as an additional criterion for assessing cardiovascular damage in these patients. Elevated levels of von Willebrand factor, CRP, and NT-proBNP, which stimulate the release of vasoactive substances, may exacerbate endothelial dysfunction and indicate the

involvement of inflammatory processes in the development of CHD in conjunction with COVID-19, contributing to diastolic dysfunction and left ventricular remodeling.

Given the results, the research objective was achieved. Further investigation of the mechanisms of the relationship between endothelial dysfunction, von Willebrand factor and intracardiac haemodynamics in patients with coronary artery disease with COVID-19 is recommended. It is necessary to investigate the possibility of using the von Willebrand factor as a prognostic and diagnostic marker in assessing the risk and course of CHD in patients with coronavirus disease. Another important area for further research is the development of treatment strategies aimed at reducing von Willebrand factor activity and preventing endothelial dysfunction in patients with CHD with COVID-19.

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