

Risk factors and potential outcomes of COVID-2019 — a narrative review with focus on cardiovascular health

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Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2), spreads rapidly and has been announced a pandemic by the World Health Organization (WHO). COVID-19 especially affects cardiovascular system, mostly by leading to the dysfunction of endothelium and its consequences. On the other hand, patients with a history of chronic disease are believed to have a more severe course of COVID-19. Furthermore, apart from an undoubted influence on morbidity and mortality, COVID-19 results in changes in many aspects of human life. It is worth noting that pandemic will also affect people who did not suffer from disease. Nevertheless, due to constantly elevated stress level, COVID-19 may have influence on mental health. Paradoxically, in dealing with stress and COVID-related problems, faith and religiosity can play a leading role. In this review, attention was paid not only to possible cardiac complications of infection but also to the impact of the pandemic on psychological and spiritual effects of the pandemic.

Key words: cardiovascular risk; SARS-CoV-2 infection; religiosity; health

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Introduction

Coronavirus disease 2019 (COVID-19), announced by the World Health Organization (WHO) as a pandemic, undoubtedly will influence worldwide medicine and health care system. Severe acute respiratory syndrome coronavirus (SARS-CoV-2) causing COVID-19, may manifest in multiple ways: from asymptomatic, through mild fever, dry cough to severe pneumonia requiring a hospitalization in an intensive care unit (ICU) and necessity of intuba-

tion. Such a variety of symptoms certainly does not make the diagnosis simple, and may even delay appropriate diagnosis, leading to treatment delay and complications.

By the beginning of November, almost 46 million people worldwide were tested positive for SARS-CoV-2, of whom up to 13% have died [1]. Originating in the Chinese town of Wuhan single-stranded ribonucleic acid (RNA) virus may affect both short- and long-term outcomes, including cardiovascular ones [2]. The present analysis reveals a potential

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relationship between SARS-CoV-2 infection and chronic diseases.

Origins of COVID-19 complications

SARS-CoV-2 is a pathogen with high affinity to lungs endothelial cells. An essential part of entering virus into the human host cells is angiotensin-converting enzyme 2 (ACE2) receptor and transmembrane protease serin receptor 2 (TMPRSS2) [2]. Immune system stimulation results in a cytokine storm with interleukin secretion, macrophage activation and finally, endothelial cells dysfunction. The endothelium is essential in appropriate hemostasis. However, activated endothelial cells play a negative role in thrombogenesis.

The endothelium is the most affected in SARS-CoV-2 infection. The study conducted by Ackermann et al. on a small group of post-mortem lungs examination of seven patients deceased due to COVID-19 revealed significant lesions in endothelium [3]. Similar observations were provided by numerous studies from a dozen countries [4]. Based on these observations, SARS-CoV-2 was announced vascular disease. Therefore, it is worth noting that most long-term COVID-19 complications result from chronic inflammation leading to the dysfunction of the endothelium. Furthermore, these mechanisms are responsible for molecular mimicry, activation of autoimmune processes, ultimately manifesting in left ventricle impairment.

Possible complications of COVID-19 infection

Although it has not been long since the first diagnosed case, reports of possible cardiovascular outcomes are available. Based on data available from the previous SARS epidemic in 2003, it can be assumed that hypotension and arrhythmias, including sudden cardiac death, are mostly described in patients suffering from SARS infections without the previous cardiovascular disease [5]. Taking into consideration pro-coagulation conditions during infection, the risk of pulmonary embolism (PE) increases significantly. A study conducted in a group of 689 patients hospitalized in an intensive care unit at the beginning of pandemic revealed that 7.5% developed PE, despite almost two-thirds of them were receiving anticoagulation treatment [6]. In Dutch hospitals, this percentage was even higher, and PE complicated 31% cases of severe COVID-19 [7]. Another observa-

tional study showed that new-onset atrial fibrillation (AF) worsened outcome in COVID-19, especially by leading to the combined endpoint of thrombosis and death [8].

Another important cardiac complication which may be developed is myocarditis, probably as an effect of chronic inflammation, resulting in infiltration of myocardium by cytokines [9]. Moreover, COVID-19 associated pneumonia also contributes to myocardial damage, and thus, to acute heart failure and in long-term observation, chronic heart failure with cardiomyopathy. Further diagnostics with cardiac magnetic resonance is needed in order to assess early myocardial damage. It is worth emphasizing that routine cardiac diagnostics, including ECG or echocardiography, do not reveal subclinical heart injury. Also, laboratory markers, such as elevated high-sensitivity cardiac troponin (hs-cTn) level, are unspecific in predicting side effects of COVID-19.

Moreover, patients with acute infection are at higher risk of developing cardiac complications, especially myocardial infarction and mortality [2]. Even though these observations were made for influenza, it is highly probable that similar conclusions will be taken in long-term assessment of SARS-CoV-2 pandemic. Not surprisingly, another potential cardiac complication in the course of SARS-CoV-2 infection seems to be takotsubo syndrome (TTS), resulting from emotional and physical stress or pharmacotherapy [10, 11].

Impact of chronic disease on the SARS-CoV-2 infection's course

Undoubtedly patients with typical cardiovascular risk factors, including male sex, advanced age, obesity, with concomitant diabetes and hypertension have a greater risk of mortality due to COVID-19. One of the earliest published analyses from Wuhan showed that almost one-third of 138 patients hospitalized due to SARS-CoV-2-acquired pneumonia were previously diagnosed with hypertension, and 14.5% had concomitant cardiovascular disease [12]. Another meta-analysis confirmed that patients with a severe course of SARS-CoV-2 were more frequently diagnosed with previous hypertension, chronic heart failure, as well as chronic kidney disease, diabetes, chronic lung disease and malignancy [13]. Role of co-existing cardiovascular disease and greater risk of mortality from SARS-CoV-2 was established in a meta-analysis of more than 65 thousand people [14]. Similarly, a large meta-analysis of 41 studies confirmed 3.42 times higher risk of death in co-

Table 1. Factors associated with worsened COVID-19 course

Clinical conditions with a definitive association with an increased risk of severe course of COVID-19	Clinical conditions with a probable association with an increased risk of severe course of COVID-19
Cancer	Asthma (moderate to severe)
Chronic kidney disease	Other cardiovascular diseases
Chronic obstructive pulmonary disease	Cystic fibrosis
Cardiovascular diseases, such as: chronic heart failure, chronic coronary syndrome, cardiomyopathies	Arterial hypertension
Immunodeficiency (e.g. after organ transplantation)	Neurological diseases such as dementia
Obesity	Liver diseases
Sickle cell disease	Overweight
Smoking	Pregnancy
Diabetes mellitus type 2	Pulmonary fibrosis
	Diabetes mellitus type 1
	Thalassemias

existing cardiovascular disease [15]. Retrospective American study analyzed 6,439 patients hospitalized due to COVID-19 presented that patients previously diagnosed with heart failure had poorer outcome, stayed in the hospital longer and had a higher risk of mechanical ventilation and mortality, regardless of left ventricle ejection fraction [16]. Zhang et al. confirmed that inappropriate lipid parameters described as increased triglycerides/high-density lipoprotein cholesterol (TG/HDL-C) ratio had been considered as risk factors of myocardial injury, heart failure, COVID-19 severity and fatal outcome [17].

Conditions linked to a higher risk of severe COVID-19 course are listed in Table 1.

Other aspects of SARS-CoV-2 infection

COVID-19 has an impact not only on the cardiovascular system but also on physical aspects of human's life. Zandifar et al. had researched 106 patients with mild, uncomplicated SARS-CoV-2 infection. The study aimed to establish a prevalence of depression, anxiety and stress among hospitalized patients. Finally, almost every participant had symptoms of depression, anxiety and was stressed, which was evaluated on the basis of the appropriate questionnaires [18]. It should be emphasized that stress level also increases in healthy people, who have been affected by the socio-economic consequences of the pandemic. The

prospect of losing a job, a brief period of introducing governments' restrictions and, consequently, a short time to prepare for the situation have an impact on mental health and physical well-being. Spanish study involved 21 207 respondents and presented an association between unstable situation and depressive disorders, ranging from 40.9% to 74.4% [19]. Inflammatory reaction, secretion of cytokines, including C-reactive protein (CRP), was strongly associated with an increased level of depressive disorders among COVID-19 patient [20].

For millennia religion played a key role in dealing with threats, including global crises. Collaboration between religion, government and science has been underlined in SARS-CoV-2 pandemic. Such activities increase the sense of security and reduce the level of stress, which helps in faster recovery from the disease [21]. Spirituality also played a fundamental role in the end-stage of the disease. Spiritual support provided by chaplains during palliative care was recommended as a part of treatment by the European Respiratory Society [22]. This statement was strongly supported by American health care providers [23]. Results from cross-sectional Brazilian study revealed that people taking part in private religious activities better dealt with social isolation were less stressed and had a lower level of sadness [24]. Nevertheless, it is worth to note that many chaplains, especially in Italy in the critical period of the pandemic, sacrificed their lives, repeatedly exposed to infection by giving spiritual assistance both to patients in the end-stage of disease and their families [25].

The last aspect of the pandemic worth noticing is its impact on science and evidence based medicine. The coronavirus disease-2019 (COVID-19) pandemic has profoundly changed clinical care and research, including the conduct of clinical trials which are now hard to conduct and require additional measures. [26] On the other hand, trials of potential COVID-19 drugs and vaccines are being conducted faster than ever. Recently, on the American scientific arena a series of meetings of scientists and representatives of the industry, were convened to address the challenges caused by the COVID-19 pandemic. [26]. A series of recommendations were issued which will probably change the science as we know it.

Conclusion

COVID-19 pandemic will undoubtedly affect each of us and change many parts of our lives. However, the impact of the infection on physical condition is obvious, and we should also be aware of the long-

Table 2. Impact of COVID-19 pandemic on the rate of cardiovascular events [26]

Effects on Events	Type of Event	
	Nonfatal CV Events	Fatal CV Events
Reduction in event rates	<p>Fear of hospitalization and contracting COVID-19 in the inpatient setting (↓ CV and HF hospitalizations, ↓ myocardial infarctions)</p> <p>Hospitalization attributed to COVID-19 (↓ CV and HF hospitalizations, even with concurrent exacerbation)</p> <p>Decreased patient physical activity and provoked symptoms (↓ clinical visits and hospitalizations)</p> <p>Potential increased adherence to CV therapies (↓ CV and HF fatal and nonfatal events)</p>	<p>Fear of hospitalization, reducing adjudication (↓ CV and HF deaths)</p> <p>Sicker patients may reside in skilled nursing facilities with exposure to COVID-19 (↑ COVID-19 deaths with ↓ CV and HF deaths)</p> <p>Financial incentive to attribute death to COVID-19 in the United States (↓ CV and HF deaths)</p>
Increase in event rates	<p>COVID-19 infection and inflammation increases risk of underlying HF exacerbation (↑ CV and HF events including ↑ myocardial infarctions)</p> <p>Increased thrombosis associated with COVID-19 (↑ CV events)</p> <p>COVID-19 increases risk of renal injury (↑ renal injury)</p> <p>Concern that cardiovascular medications such as angiotensin system antagonists may increase risk for or worsen COVID-19 (↑ CV and HF events and ↑ CV and HF deaths)</p> <p>Inability to obtain therapies, including due to cost (due to loss of employment) or fear of contracting COVID-19 (↑ CV events, ↑ outpatient worsening HF events, ↑ CV and HF deaths)</p>	<p>Delayed presentations to medical care (↑ deaths)</p>
Unclear effect on event rates	<p>Overlapping biomarker or clinical profiles of HF and CV diseases with COVID-19 (↓ or ↑ CV and HF events including myocardial infarctions)</p>	
Increased missing events or events of unknown cause	<p>Increased comingled events at home without documentation or reporting</p> <p>Decline or reassignment of study personnel with decreased source documentation and data collection</p> <p>Undiagnosed COVID-19</p>	

COPD — chronic pulmonary obstructive disease; COVID-19 — coronavirus disease-2019; CV — cardiovascular; HF — heart failure

term effects of the pandemic on physical and mental health. The summary of the probable impact of COVID-19 on the cardiovascular events rate — the most frequent cause of mortality and morbidity — is shown in Table 2. Nevertheless, it seems that religiosity and spirituality may have one of the largest influences on mental well-being and help in recovery from disease. Further analysis is still needed to prove this statement.

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