REVIEW ARTICLE

COVID-19 AND PRIMARY CARE: POSSIBILITIES FOR INCREASING POSITIVE OUTCOMES

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ABSTRACT

The aim: Determine the most common non-communicable diseases which are associated with an increased rate of moderate and severe COVID-19 infection. Identify the best tools for diagnosing COVID-19 and predicting the deterioration of the disease.

Materials and methods: Publications were processed and analyzed according to the keywords of the topic of work "COVID-19", "non-communicable disease", "obesity", "hypertension", "Comorbidities", "frailty", "diabetes", "chronic obstructive pulmonary disease", "cardio-vascular diseases", "liver diseases", "diagnostic tools", "outcomes" in the databases of PubMed, MEDLINE, Web of Science.

Conclusions: As a result of the analysis, we found that patients with concomitant obesity, diabetes mellitus, COPD, CVD and liver diseases have an increased the risk of severe forms and death from COVID-19.

KEY WORDS: COVID-19, non-communicable disease, diagnostic tools, outcomes, primary care

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INTRODUCTION

In 2020, the world was hit by a global pandemic of the SARS-CoV-2 virus, which causes COVID-19. Currently, there is no reliable data on any specific treatment of this disease, and the only method of prevention is vaccination. Despite the fact that the campaign began at the end of 2020, several types and brands of vaccines are available and vaccination is promoted widely, the number of people in the world who have undergone a full vaccination course as of August 2021 is about 1 billion, which is insufficient to create collective immunity [1–3]. Combined with the rise of vaccine hesitancy, the emergence of new strains and the threat of a new spike in the number of infected people, this may mean that the pandemic will continue further and will not be gone soon [4]the illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2.

In most countries of the world and in Ukraine in particular, patients seek medical help from family doctors. Therefore, to minimize the spread of the virus and to prevent and timely detect a severe case of the disease, it is important that physicians of first contact have data on vulnerable populations and diagnostic algorithms. Special attention should be paid to the criteria for timely early detection of risk groups requiring hospitalization in order to prevent severe form of the disease.

THE AIM

Determine the most common non-communicable diseases which are associated with an increased rate of moderate and severe COVID-19 infection. Identify the best tools for diagnosing COVID-19 and predicting the deterioration of the disease.

MATERIALS AND METHODS

Publications were processed and analyzed according to the keywords of the topic of work "COVID-19", "non-communicable disease", "obesity", "hypertension", "comorbidities", "frailty", "diabetes", "chronic obstructive pulmonary disease", "cardio-vascular diseases", "liver diseases", "diagnostic tools", "outcomes" in the databases of PubMed, MEDLINE, Web of Science.

REVIEW AND DISCUSSION

Non-communicable diseases and COVID-19 infection have similar risk factors and although infectious and non-communicable diseases differ in the way they spread and how they effect the body, it should not be assumed that they cannot complement and worsen each other's course [5]. As the number of COVID-19 cases increases, a link has been established between comorbid conditions and the severity of COVID-19 infection [6]. One review article published in July 2020 showed that, the most common concomitant diseases observed in patients with COVID-19 ending in death were: obesity (observed in 48% of patients and in 68% of cases ended in death), liver disease (43 and 29%, respectively), chronic obstructive pulmonary disease (COPD, 52 and 20%, respectively), cardiovascular diseases (CVD, 17 and 15%, respectively), diabetes mellitus (58% and

8%, respectively), hypertension (23 and 6%, respectively) [6] mild, or severe pneumonia-like symptoms. COVID-19 patients with diabetes, chronic obstructive pulmonary disease (COPD. In addition, it is noted that patients over 50 years of age are significantly more likely to get infected [7].

Obesity was often observed in patients with COVID-19, which may be due to the fact that the obesity pandemic is currently ongoing. A review study that analyzed and compiled data regarding any links between COVID-19 and an increased BMI and obesity found that obese patients were 46% more likely to have a positive COVID-19 test result, were hospitalized and ended up in the intensive care unit (ICU) 2.13 and 1.74 times more often, and mortality increased by 48% compared to persons without obesity [8].

An analysis of data from 7,606 patients of the American Heart Association's COVID-19 Cardiovascular Disease Registry showed that with an increase in body mass index (BMI), the risk of hospitalization also increased, with patients with third stage obesity having a 26% higher risk of in-hospital death [9]. Obese patients of I, II and III stages were more likely to die in hospital or receive mechanical ventilation of the lungs (by 28, 57 and 80%, respectively) [9]. Currently, it is known that adipocytes produce hormones – adipokines, which have regulatory function and affect energy metabolism. At the same time, their effect on systemic inflammatory diseases is also worth noting, the manifestations of which are enhanced with excessive amounts of adipose tissue in the body. Studies suggest that leptin and adiponectin play a role in inflammatory lung diseases [10]. By intensifying the overall inflammatory reaction of the body, obesity can lead to a more severe course of acute COVID-19. Given that the obesity pandemic is currently underway and the implementation of conditions that adversely affect the physical activity and mental state of the population, which in turn leads to chronic stress, we can assume that the number of obese people will increase. This in turn will increase the frequency of other comorbid conditions, such as hypertension and CVD, creating a vicious circle of deteriorated health [11].

Another frequent condition is diabetes mellitus (DM). A cohort study of the population of Scotland in the first wave of the COVID-19 pandemic showed that out of 2,724 patients with acute COVID-19 and concomitant DM, 1,082 people were hospitalized in ICU, of which 963 died [12]. Compared to the population without concomitant DM, the risk of being transferred to ICU for patients with DM was higher by 39.5% [12].

In addition, in a case-control study of patients with DM and COVID-19, it was found that old age (>60 years), higher levels of alkaline phosphatase (>270 U/L) and urine nitrogen (>=20 mg/dL) were predictors of impaired course and death in these patients [13].

DM is a serious risk factor for many diseases and often leads to a deterioration in the quality of life and a more severe course of disease. DM, especially in the stage of decompensation, causes a chronic inflammatory reaction, increases the risk of infectious diseases and blood thickness [14,15]. Patients with DM had a severe course of COVID-19, and inflammation mediators in combination with viral load caused damage to the pulmonary tissue [16].

It is well known that patients with COPD have an increased risk of respiratory tract infections, which is especially relevant for community acquired pneumonia and influenza. When assessing the impact of COPD on the course of COVID-19, it was found that it also worsens the course of infection. For example, a meta-analisis of data regarding the impact of COPD on COVID-19 up until July 2020 showed that in patients with pre-diagnosed COPD, the risk of death from COVID-19 was 3 times higher compared to patients without COPD [17]. A similar paper, in which the impact of COPD on the frequency of hospitalization, transfer to ICU and death as a result of COVID-19 was analyzed, showed that the presence of COPD in patients significantly increased the risk of their hospitalization, transfer to ICU and mortality from COVID-19 (by 39, 34 and 28%, respectively) [18].

A certain link was also found between liver diseases, liver lesions and COVID-19. Thus, according to a meta-analysis that assessed the link between manifestations of the gastrointestinal tract , liver disease and COVID-19 infection, the most significant symptoms are diarrhea and anorexia, especially in ICU patients. In such patients alanine aminotransferase (ALT) and aspartate aminotransferase (AST) was elevated (higher than 40 and 64 U/L) [19]. Another study assessed the effect of nonalcoholic fatty liver disease (NAFLD) on the course of coronavirus infection and found that the presence of NAFLD in patients history was associated with a worsened course of COVID-19 [20]. In regards to the link between abnormal liver function tests and the course of infection, it was found that in addition to the significant elevation of AST and ALT levels in patients with acute COVID-19, other liver indicators were also increased, namely, total bilirubin (> 22 μmol/L), gamma-glutamyl transferase (>30 IU/L), alkaline phosphatase (>116 U/L) [21]. Higher levels of AST were observed in patients with severe COVID-19, compared to patients with a mild or medium course [21].

Currently, the main factors that cause liver damage in severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) are direct damage to cholangiocytes, cytokine storm and drug-induced liver damage. It is assumed that drug-induced liver damage plays the most important role. During hospitalization, most patients with acute COVID-19 had a deterioration in liver performance. This was especially true for elderly patients [22]there have been more than one hundred million confirmed cases of coronavirus disease 2019 (COVID-19.

CVD rank first among causes of death worldwide. Obviously, this group of diseases will affect the course of infectious diseases, including acute COVID-19. In the course of a meta-analysis that examined CVD burden among COVID-19 patients showed that among this group of diseases, acute myocardial infarction, heart failure and coronary artery disease were associated with a greater risk of death with COVID-19 (in 13.29, 6.72 and 3.78 times higher respectively) [23]. In addition, patients with concomitant CVD, namely arrhythmia, acute myocardial infarction, coronary artery disease and hypertension, had a higher risk of getting requiring treatment in ICU compared to patients without concomitant pathologies (in 7.03, 15.58, 2.61 and 1.95 times, respectively) [23].

Special attention should be paid to older people and with frailty. COVID-OLD study in the Netherlands showed that mortality of COVID-19 patients over 70 years of age was 38%.

At the same time, frailty was an independent predictor of a severe course of COVID-19, despite the fact that such patients had previously experienced less pronounced symptoms [24]. In addition, a meta-analysis of the relationship between the clinical frailty score (CFS) and COVID-19 assessment showed that an increase of 1 point on the CFS scale increased the risk of death by 12% [25].

It is known that persons of the older age group (>50 years) are more likely to suffer from chronic diseases of various origins [26]. This is due to the peculiarity of low intensity systemic inflammation at this age, without clinical symptoms of inflammation [27]. In addition, the gradual depletion of T-cell immunity and a general decrease in immune function, as well as frailty, put this group at a disadvantage not only in relation to COVID-19, but also other infectious and non-communicable diseases. The combination of these factors may play a role in the worsened course of COVID-19 in this age category, the risk of death and the development of residual symptoms after the acute phase of the disease [28]. Taking into account the increasing number of elderly people in the world, accompanied by the simultaneous growth of people with frailty, the presence of a convenient clinical method for assessing the severity of this condition, which is CFS, enables physicians to manage such patients more carefully and recommend more intense healthcare options in order to prevent the deterioration of their condition [29].

Among the prognostic indicators of the adverse course of COVID-19, d-dimer is worth noting. At the beginning of the pandemic, a cohort study found that d-dimer levels above normal ranges during hospitalization were associated with a higher risk of in-hospital mortality [30]2019, Wuhan, China, has experienced an outbreak of coronavirus disease 2019 (COVID-19. A meta-analysis of the link between d-dimer levels on admission and the severity of the disease and risk of death in COVID-19 showed that d-dimer levels in non-survivors were significantly higher compared to survivors (weighted mean difference was 5.32 mg/L) [31]. In addition, levels of d-dimer above normal limits were strongly correlated with a higher risk of severe course of the disease and death (1.58 and 1.82 risk ratios respectively) [31].

An important component of COVID-19 management at the primary level is its reliable diagnosis and prognosis of a deteriorating course of the disease. One review comparing the sensitivity and specificity of polymerase chain reaction (PCR) testing and computer tomography (CT) scans showed that CT had sufficient specificity (up to 98%), but low sensitivity (up to 25%). The main diagnostic criterion for COVID-19 infection was the consolidation of the opaque area with smoothing the edges of the bronchus and blood vessels (the so-called "ground-glass opacification"). PCR showed sensitivity at 60-71%, but this test gives many false negative results [32]the most appropriate approach to control this infection is to quarantine people and isolate symptomatic people and suspected or infected cases. Although real-time reverse transcription-polymerase chain reaction (RT-PCR. A meta-analysis of data on the sensitivity and specificity of radiological diagnostic methods of COVID-19 showed that the total sensitivity and specificity of chest CT is 87.9% and 80%, respectively. For chest X-ray, these figures were 80.6 and 71.5%, respectively, and for lung ultrasound – 86.4 and 54.6%, respectively [33].

One retrospective study which analyzed most common findings in COVID-19 patients in relationship to duration of infection found that chest CT changes were more frequently seen in patients 3-5 and 6-12 days after symptoms onset, and 44% of the patients had abnormal CT-scan findings at 0-2 days after onset [34]chest CTs of 121 symptomatic patients infected with coronavirus disease-19 (COVID-19.

CONCLUSIONS

As a result of the analysis, we found that patients with concomitant obesity, diabetes mellitus, COPD, CVD and liver diseases have an increased the risk of severe forms and death from COVID-19. Therefore, primary care physicians and doctors of first contact, when treating patients with these conditions in the presence of a positive PCR test for COVID-19, regardless of the presence of clinical symptoms at the time of referral, recommended to preform the following set of examinations: chest X-ray or chest CT, d-dimer (normal range (NR) – <0.5 g/L), ALT (NR <40 U/L), AST (NR <40 U/L), total bilirubin (NR – < 22 μmol/L), alkaline phosphatase (NR – <116 U/L), urine nitrogen(NR – <=20 mg/dL). If a patient has any abnormalities detected during radiologic studies and/or any of the aforementioned laboratory signs higher than their respected upper limit, we recommend transferring these patients to inpatient treatment for further evaluation and prevention of severe and lethal outcomes.

Special attention should be paid to persons older than 60, because of higher risks of severe infection and death, especially in the presence of signs of frailty. In such patients, in addition to the above examinations, we recommend evaluating them on the CFS scale. If a patient scores 4 (vulnerable) or higher, you should be consider referring them to inpatient treatment to prevent rapid deterioration of their health status due to COVID-19.

Objectively, in Ukraine X-ray is much more affordable and available, especially in rural and mountainous regions, in addition, compared to CT, which is several times more expensive. Given this, as well as a slight difference in the sensitivity and specificity of these methods, we recommend using chest x-ray as a routine method in COVID-19 patients.

We believe that such measures lead to a reduced risk of developing severe forms, as well as mortality from COVID-19 in patients from appropriate risk groups.

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