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Cardiovascular Risk Assessment in Chronic Obstructive Pulmonary Disease Patients

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SOUHRN

Prevence nežádoucích kardiovaskulárních (KV) příhod je náročnou součástí léčby pacientů s chronickou obstrukční plicní nemocí (CHOPN). Společné patofyziologické mechanismy jsou předpokladem pro vzájemnou zátěž komorbidní patologie, CHOPN a kardiovaskulární onemocnění (KVO). Kontroverze v hodnocení tradičních KV rizikových faktorů, včasný záchyt existujících KVO, heterogenita průběhu CHOPN a vliv medikace CHOPN na KV riziko – to vše naznačuje potřebu dalších upřesnění ohledně hodnocení KV rizika u pacientů s CHOPN. Tento přehledový článek shrnuje nedávné studie o hodnocení KV rizika u pacientů s CHOPN a navrhuje přístupy ke zlepšení predikce nežádoucích KV příhod u těchto pacientů.

Keywords:
Cardiovascular risk
Chronic obstructive pulmonary disease
Major adverse cardiovascular events
Risk factors

ABSTRACT

Prevention of adverse cardiovascular (CV) events is a challenging part of managing patients with chronic obstructive pulmonary disease (COPD). Common pathophysiological mechanisms are a prerequisite for the mutual burden of comorbid pathology, COPD, and cardiovascular diseases (CVD). Controversies in the assessment of traditional CV risk factors, untimely detection of existing CVD, heterogeneity of the course of COPD, and the influence of COPD medications on CV risk – all these indicate the need for additional clarifications regarding the assessment of CV risk in patients with COPD. This review summarizes recent studies on CV risk assessment in patients with COPD and suggests approaches to improve the prediction of adverse CV events in these patients.

Introduction

Chronic obstructive pulmonary disease (COPD) remains a major healthcare burden due to significant socioeconomic and health consequences.[1] About 392 million people globally have COPD. There are an estimated 36 millions people living with COPD in Europe.[2] Currently, COPD is considered as the most common chronic respiratory disease, both in men and women. In addition, its prevalence is expected to increase in the coming years due to population aging among other causes.[3] COPD is one of the most common reasons for hospital admissions. A Canadian study found that the cost of treating COPD exacerbations leading to hospitalization accounted for 57% of the total costs of COPD care.[4]

Danish scientists, based on the results of a nationwide study, found that the risk of major adverse cardiovascular events (MACE), such as acute myocardial infarction (MI), stroke and death from cardiovascular diseases (CVD), increases significantly after the onset of COPD exacerbation. This association emphasizes the necessity of preventive measures regarding possible cardiovascular (CV) events among this category of patients.[5]

According to the World Health Organization in 2019, COPD is the third leading cause of death, accounting for 6% of all deaths worldwide, after coronary artery disease

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(CAD) and stroke, which account for 16% and 11% of the total number of deaths respectively.[6] The results of a population-based cohort Canadian study of more than 150,000 patients showed that people with COPD without a history of atherosclerotic CVD were 25% more likely to have a MACE. These data are comparable to the CV risk of patients with diabetes, which suggests the need for requiring more intensive primary CV prevention in COPD patients.[7]

The aim of the review was to highlight the latest data on approaches to the assessment of CV risk in patients with COPD. A search for publications in databases PubMed, Google Scholar and ProQuest over the last 10 years was conducted.

Modern approaches to CV risk assessment

Quantitative risk prediction is the basis of primary CVD prevention. Risk assessment is based on algorithms of multifactorial risk prediction, among which the Systematic Coronary Risk Evaluation (SCORE) is the most widely used in Europe. It is based on the assessment of "traditional" CV risk factors such as age, sex, blood pressure, serum lipid profile and smoking status. Updated risk assessment models, SCORE2 (for people aged 40–69 years) and SCORE2-OP (for old persons, over 70 years old), which determine the absolute probability (in %) of occurrence during the next 10 years of any fatal or non-fatal CV event, were included in the 2021 European Society of Cardiology prevention guidelines.[8] These models are calibrated for four subgroups of countries distinguished by low, moderate, high, and very high age-standardized CV mortality. According to the guidelines, among the diseases that reliably increase CV risk are atherosclerotic CVD, diabetes mellitus, familial hypercholesterolemia, and chronic kidney disease. The role of COPD as a proven CV risk factor has not been established yet.[8] Despite this, patients with COPD have a 2–3 times higher risk of CVD compared to healthy people of the same age, adjusted for smoking.[9–11] It is known that the most frequent causes of hospitalization and mortality of patients with moderate COPD are CV (MI, heart failure [HF] or stroke), and not respiratory failure.[12,13]

According to the results of a post hoc cohort analysis from the SUMMIT (Study to Understand Mortality and Morbidity in COPD) randomized clinical trial conducted by Kunisaki, Dransfield, Anderson, et al., it was established that the risk of an adverse CV event increases 10 times with an exacerbation of COPD requiring hospitalization. After an exacerbation, the 4-fold risk persists for at least a month.[14] British scientists (Rothnie, Connell, Müllerová et al.) also emphasize the association of exacerbation of COPD with MI and ischemic stroke (IS). After the onset of exacerbation of COPD, the maximum risk of MI was observed in the first 3 days, and IS from 4 to 7 days. The risk was significantly reduced after 28 days. For IS, it remained elevated longer compared to MI. Although, the risk remained elevated up to 91 days after the onset of exacerbation. Moreover, a direct dependence of the risk with the severity of the exacerbation was observed. The risk of MI remained 2.5 times higher than in stable COPD after a severe exacerbation (requiring hospitalization) and 1.6 times higher after a moderate exacerbation; the risk of IS exceeded the stable period after a severe exacerbation by 1.7 times and by 1.4 times after a moderate exacerbation.[15] Decreased forced expiratory volume in the first second (FEV_1) is a significant predictor of mortality and CVD, including MI, stroke, congestive HF, and cardiac death, even after adjusting for "traditional" risk factors. Based on the results of the international, community-based cohort study conducted by Duong, Islam, Rangarajan et al., it was found that the population attributable risk of mortality from a decrease in FEV_1 was greater than the risks associated with smoking, hypertension, and a history of CVD. In addition, reduced FEV_1 was only the second to hypertension in terms of its contribution to incident CV events, suggesting that FEV_1 impairment is an important and under-recognized risk factor that contributes significantly to the global CVD burden.[16]

The majority of COPD patients do not even suspect that they have concomitant CVD and metabolic diseases. Four out of five patients with COPD with post-infarction changes on the electrocardiogram are unaware of a MI. Only one out of seven patients knows about the presence of dyslipidemia when it is objectively detected. Similarly, only one in four patients with COPD knows about diabetes.[17] Furthermore, in COPD patients with shortness of breath, HF often remains undiagnosed, although it is known that concomitant HF is associated with an increased risk of hospitalization in COPD patients, regardless of the degree of airflow limitation.[18,19]

Thus, it is extremely important to regularly screen patients with COPD for the presence of D and CV risk factors. Although it is obvious that currently available CV risk assessment tools are not able to reflect the risk in patients with COPD sufficiently, which indicates the need to search for prognostically significant factors that can explain the increased CV risk in COPD.

COPD categories requiring attention

The significant heterogeneity of the course of COPD, the difficulty of predicting future adverse events, and exacerbations indicate the need for a personalized approach to the diagnosis and management of patients with COPD. The first step towards optimizing the diagnosis, treatment, and prevention of exacerbations and complications, as well as reducing the burden of comorbidities and adverse CV events, is the division of patients with COPD into subgroups, phenotypes and endotypes, which will help to understand the pathophysiological features of the course of COPD and develop a rational approach to patient management. The airflow limitation degree is not a determining criterion for the severity and prognosis of COPD. Much more important criteria are the frequency of exacerbations and their severity, symptoms and the degree of their impact on the daily life of a COPD patient, the rate of progression of airflow limitation, the presence and severity of comorbid diseases.

The frequency of exacerbations, as a criterion that determines the severity of COPD, was first included in the Global Initiative on Obstructive Lung Disease (GOLD)

guidelines in 2011. Since then, views on the assessment of exacerbations have changed significantly due to their prognostic impact on the course of COPD. Current recommendations emphasize identifying the risk of exacerbation and, if it occurs, providing care and assessing the severity of the exacerbation. The main limitation of the current approach to assessing the severity of exacerbations of COPD is that the severity of an exacerbation is determined ex post facto based on the use of health care resources (use of systemic corticosteroids and antibiotics, need for hospitalization, presence of acute respiratory failure).[20] The use of "The Rome Proposa" suggested by Celli, Fabbri, Aaron et al. can help determine the severity of exacerbations at initial presentation based on the severity of symptoms using visual analog scales, pulse oximetry, laboratory assessment, C-reactive protein, arterial blood gases, and exclusion of other possible causes.[21] The NOVELTY (NOVEL observational longiTudinal studY) study found that frequent productive cough is an indicator of the risk of exacerbations over the next 12 months. At the same time, the number of patients with frequent productive cough increased with increasing severity of COPD. In addition, it was found that patients with frequent productive cough were more likely to have CVD more often compared to patients without frequent productive cough. Thus, frequent productive cough was associated with a significant burden of COPD and was an important predictor of risk for adverse clinical outcomes.[22] The WISDOM (Withdrawal of Inhaled Steroids During Optimized bronchodilator Management) study showed that a decrease in mean daily FEV_1 was observed approximately two weeks before the onset of an exacerbation. This can contribute to improving the timely diagnosis and treatment of exacerbations. After an exacerbation, lung function improves, but unfortunately does not return to pre-exacerbation levels.[23] Results from the SUMMIT study, which included patients with COPD and comorbid CVD or the presence of several CV risk factors, showed that the greatest increase in the risk of MACE was observed within the first 30 days after the onset of an COPD exacerbation, followed by the maintenance of the risk at an increased level throughout the entire year of observation.[14] Duration of increased CV risk may be facilitated by elevated levels of proinflammatory biomarkers, which may slowly return to baseline after an exacerbation of COPD. The results of the international initiative EXACOS-CV (EXAcerbations of COPD and their OutcomeS in CardioVascular disease) recently obtained in the USA showed that the risk of both general and CV mortality increases after exacerbations of COPD. Moreover, there was a gradual increase in the risk of mortality after each subsequent exacerbation. Risks increased immediately after exacerbation and remained elevated at 1 year for acute CV events and at 2 years for all-cause mortality. Within 30 days of the first COPD exacerbation, regardless of whether CV events occurred on the date of diagnosis of COPD, there was the highest risk for acute HF, atrial fibrillation and flutter, pulmonary embolism or deep vein thrombosis and CV death. These results show that patients with newly diagnosed COPD are at a risk of MACE and CV mortality even after the first exacerbation of COPD.[24] The association of exacerbation with MI was stronger for patients with severe (GOLD 3–4) compared with mild and moderate (GOLD 1–2) airflow limitation. The association of exacerbation with IS was independent of the severity of airflow limitation.[15] The risk of MACE was significantly higher for severe, requiring hospitalization, compared with moderate COPD exacerbation, and the association of exacerbation with MACE risk was stronger among infrequent exacerbators compared with frequent exacerbators. According to Rothnie, Connell, Müllerová et al., infrequent exacerbators had a 69% higher incidence of MI within 91 days after the onset of an exacerbation compared with their stable periods compared with 42% increase for frequent exacerbators; and infrequent exacerbators had a 68% higher incidence of IS after an exacerbation compared with a 30% increase for frequent exacerbators.[15] The modern approach to assessing the severity of COPD exacerbations and predicting the risk of MI and IS is presented in **Table 1**.[15,20,21] In addition to the high frequency of atherothrombotic arterial vascular events in COPD exacerbations, there is some evidence of excess venous thromboembolism due to clotting system activation.[25,26]

The term "PRISm" (Preserved Ratio Impaired Spirometry) first appeared in 2014 and was included in the GOLD guidelines in 2023.[20,27] It describes individuals with an FEV_1 less than 80% of the predicted value after bronchodilation, but preserved the ratio of FEV_1 to forced vital capacity (FVC) $\geq$0.7 after bronchodilation. A decrease in FVC, reflecting restrictive changes, results in an increase in the FEV_1/FVC ratio, which may mask existing obstruction.[28] PRISm is associated with female gender, abnormal body mass index (underweight, overweight, and obesity), multimorbidity (hypertension, type 2 diabetes mellitus, CAD, HF, stroke and chronic kidney disease).[29,30] According to Wan, Balte, Schwartz et al., PRISm, compared with normal spirometry, was associated with an increased risk of mortality (all-cause, CHD-related and respiratory-related mortality) and adverse CV and respiratory outcomes. Although, PRISm, compared with obstructive spirometry, was associated with a significantly higher risk of all-cause mortality, CHD-related mortality and CHD-related events, but with a significantly lower risk of respiratory-related mortality and respiratory-related events.[29]

Bronchiectasis can be an independent CV risk factor. Patients with bronchiectasis have a greater number of comorbid CVD and cerebrovascular diseases compared to the general population, adjusted for age, gender, smoking, and other CV risk factors.[31] According to Navaratnam, Millett, Hurst et al., one in five patients with bronchiectasis has a CVD or cerebrovascular disease. These patients have a much higher risk of future MACE and premature death. A 5-year follow-up of a cohort of 100 patients with bronchiectasis showed three CV events and five cerebrovascular events, compared with one in patients without bronchiectasis.[32] Higher exacerbation rates and lower FEV_1 were associated with increased aortic pulse wave velocity, arterial stiffness indicator and an independent predictor of CV risk. An increase in pulse wave velocity of 1.3 $m \cdot s^{-1}$ in patients who have three or more exacerbations per year compared with infrequent exacerbations corresponds to an increase in CV risk by 12–18%.[33] A population-based cohort study in Taiwan found that bronchiectasis to be an independent risk factor of IS, with

Table 1 – Assessment of the severity of COPD exacerbations and prediction of the risk of MI and IS

COPD exacerbation severity	Assessment criteria	The scope of medical care	The 3-month risk compared to stable periods	
			of MI[15]	of IS[15]
Mild	VAS < 5, RR < 24, HR < 95; $SaO_2 \geq 92$ (decline ≤ 3), CRP < 10	SABDs only	Unknown	Unknown
Moderate	VAS ≥ 5, RR ≥ 24, HR ≥ 95; $SaO_2 < 92$ (decline > 3), CRP ≥ 10, ABG may show hypoxemia ($PaO_2 \leq 60$) and/or hypercapnia ($PaCO_2 > 45$) but no acidosis	SABDs, corticosteroids, antibiotics	More than 1.6 times	More than 1.4 times
Severe	VAS ≥ 5, RR ≥ 24, HR ≥ 95; $SaO_2 < 92$ (decline > 3), CRP ≥ 10, ABG shows new onset/worsening hypercapnia and acidosis ($PaCO_2 > 45$ and pH < 7.35).	Patient requires hospitalization, supplemental oxygen	More than 2.5 times	More than 1.7 times

ABG – arterial blood gases; CRP – C-reactive protein, mg/L; HR – heart rate, beats/min; PaO_2 – partial pressure of oxygen, mmHg; $PaCO_2$ – partial pressure of carbon dioxide, mmHg; RR – respiratory rate, breaths/min; SABDs – short-acting bronchodilators; SaO_2 – oxygen saturation, %; VAS – visual analog dyspnea scale, points.

an incidence rate of 11.20 vs 8.53 per 1000 person-years in bronchiectasis patients with COPD compared to non-bronchiectasis patients with COPD. A 1.74-fold increase in the risk of IS was found in patients with bronchiectasis after controlling for age, gender, and comorbidities.[34] Multimorbidity (coexistence of two or more chronic diseases), which is common in COPD patients with bronchiectasis, has a negative impact on the prognosis of these patients.[35]

The physical and emotional frailty phenotype is noteworthy because of its significant impact on the prognosis of COPD patients. Frailty in COPD affects almost half of patients, especially the elderly.[36] It is closely associated with extrapulmonary (systemic) effects, including weight loss, malnutrition, and sarcopenia.[20] In addition, frailty is associated with a significant airflow limitation, emphysema, osteoporosis, severe dyspnea, and reduced exercise tolerance.[37] Symptoms of anxiety and depression also carry a high risk of adverse health outcomes.[36] Frailty is a risk factor for high CV morbidity and mortality, and also a potential modifier of global CV disease risk.[8] However, there is evidence to suggest a beneficial effect of non-pharmacological interventions (balanced diet, micronutrient supplementation, exercise training, social activation) aimed at preventing, attenuating or reversing frailty. Patients with frailty should be identified early and enrolled in comprehensive pulmonary rehabilitation programs.[8,20]

Obstructive sleep apnea (OSA) in COPD patients associated with increased adverse CV outcomes.[38] CAD, HF, and pulmonary arterial hypertension are more common in patients with OSA.[39] OSA is associated with obesity, the so-called blue bloater phenotype and accelerated pulmonary hypertension.[37] During sleep, these patients are more likely to suffer from episodes of oxygen desaturation and cardiac arrhythmias.[20] Positive pressure ventilation usage by COPD patients with OSA reduces moderate and severe exacerbations, all-cause hospitalizations and healthcare costs.[40]

The course of the disease in patients with COPD combined with CV pathology is complex and diverse. It is characterized by substantial differences in some demographic data, the severity of symptoms, the frequency and severity of exacerbations, the amount of treatment and the frequency of adverse CV events. Scientists from the United Kingdom have developed a model that allows predicting the type of CV phenotype of COPD with a high accuracy (92%) and is a reliable preliminary basis for predicting concomitant CVD in COPD patients. They identified three types of COPD CV phenotype – A, B, and C. Phenotype A was characterized by the highest prevalence of severe COPD, higher prevalence of emphysema and almost all patients had hypertension. Phenotype A was the most-treated – nearly all patients treated with inhaled corticosteroids (ICS) and/or a combination of ICS and long-acting β_2-agonists (LABA); more than half of the patients also received long-acting muscarinic antagonists (LAMA); some patients used mucolytics. Phenotype B was characterized by an overwhelming majority of males (while males accounted for a small majority of the other phenotypes). Phenotype B had the lowest prevalence of hypertension, but the highest prevalence of CAD, acute MI, congestive HF and diabetes. Just under half of patients with phenotype B were treated with LAMA; the next most common medications were ICS, followed by ICS with LABA. Phenotype C was characterized by the lowest prevalence of severe COPD, the highest prevalence of mild COPD and the greatest majority of patients without exacerbations in the past year and almost all patients had hypertension (similar to phenotype A). Phenotype C received less treatment, with only one third of patients treated with LAMA.[41] Therefore, these data confirm that the greatest burden of cardiometabolic comorbidities is observed mainly in patients with moderate COPD and is a risk factor for poor prognosis.[37,41]

Controversies in the assessment of traditional risk factors in patients with COPD

In COPD patients, there is evidence for an "obesity paradox", with higher survival in overweight and obese compared with normal weight. However, extreme obesity (BMI >40 kg/m^2) was not a protective factor for morta-

lity, primarily CV, among patients with moderate COPD and increased CV risk according to the SUMMIT study results.[42] One of the systemic effects of COPD is sarcopenia, a progressive loss of skeletal muscle mass and strength, which significantly affects the daily life and prognosis of patients with COPD.[20] Sarcopenic obesity, sarcopenia with increased fat mass, is associated with a higher risk of CVD compared with obese individuals with normal muscle mass. According to Leem, Kim, Chung et al., sarcopenia is an independent factor for an increased risk of atherosclerotic CVD in men with moderate to very severe COPD.[43] The use of BMI as a common tool to determine the presence and degree of obesity in patients with COPD is inadequate because changes in body composition are not taken into account.[44] Assessment of cardiorespiratory fitness, abdomen-to-hip ratio, and mid-upper arm circumference may be useful in patients with COPD.

The 2021 ESC Guidelines on CVD prevention propose a new index, non-high-density lipoprotein cholesterol (HDL), to define CV risk instead of total cholesterol, which encompasses all atherogenic (apo-B-containing) lipoproteins and is calculated as total cholesterol minus HDL cholesterol. The level of non-HDL cholesterol is identical to the measurement of apo-B plasma concentration.[8] Based on the results of a Danish population-based cohort study with a 10.2-year follow-up, it was found that a lower low-density lipoprotein cholesterol was associated with a higher risk of exacerbations, a severe phenotype of COPD, a lower FEV_1/FVC ratio and COPD mortality.[45] The researchers noted that low cholesterol may be seen as a marker of frailty in elderly patients. Freyberg, Landt, Afzal et al. emphasize that these findings should not be used as an argument against the use of statins in patients with COPD, as there is evidence from randomized controlled trials of improved lung function and reduced exacerbations in COPD patients treated with statins.[45,46] This issue remains debatable and requires further research.

Additional factors to consider in COPD patients

An increase in troponin can be observed in patients with COPD, especially during exacerbations, in the absence of obvious CV reasons.[8] According to the results of an analysis of multicentre COSYCONET (COPD and Systemic Consequences – Comorbidities Network) cohort study conducted by Waschki, Alter, Zeller et al., it was established that high-sensitivity troponin I (hsTnI) is a strong predictor of all-cause mortality in patients with stable COPD, regardless of their CV risk profile. A history of severe exacerbations is associated with higher hs-TnI levels, even during a stable COPD period. Patients with hs-TnI levels > 6 $ng \cdot L^{-1}$ had a 1.6-fold higher risk of death during the 3-year follow-up compared to patients with levels < 6 $ng \cdot L^{-1}$, even after adjusting for other risk factors. Scientists found that concentrations of hs-TnI, which are significantly lower than the threshold value used to diagnose MI, provide prognostic information in stable COPD. The authors recommend the use of hs-TnI to improve the risk stratification of COPD patients, regardless of the existing CV risk. In these patients, COPD treatment should be optimized first, including assessing the risk of exacerbations. After that, patients should be referred for additional cardiological examination for timely detection of potential threats from the CV system.[47]

B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) have prognostic significance in COPD patients without clinical signs of HF and primary CVD. Shafuddin, Fairweather, Chang et al. found that increases in NT-proBNP during COPD exacerbations were associated with higher long-term mortality and future CV hospitalizations.[48] NT-proBNP is a biomarker of cardiac stretch and is a sensitive indicator of asymptomatic HF. HF with preserved ejection fraction often remains underdiagnosed in patients with COPD due to the similarity of clinical signs – shortness of breath, limitation of physical activity. Right ventricular (RV) pressure overload caused by hypoxic pulmonary vasoconstriction stimulates BNP/NT-proBNP production. In patients with signs of RV dysfunction, pulmonary hypertension, cor pulmonale, even with stable COPD, BNP and NT-proBNP increase, but due to the smaller RV myocardial mass, the level of BNP and NT-proBNP elevation is lower than in COPD patients with left ventricular dysfunction.[49]

The level of eosinophils in the peripheral blood can be considered as a prognostic marker for future adverse CV events and COPD exacerbations. A blood eosinophil count ≥300 cells/μL indicates a high risk of further exacerbations in COPD patients and can be used to identify patients most likely to benefit from inhaled corticosteroids.[20] A reduction in MACE on ICS-containing therapy was observed in patients with higher baseline blood eosinophils.[50] At the same time, according to Prudente, Ferrari, Mesquita et al., a blood eosinophil count < 150 cells/μL may be associated with a three-fold increased risk of death (including CV) within nine years in patients with COPD.[51] The cardioprotective role of eosinophils in cardiac hypertrophy and remodeling has been reported.[51] Eosinophils promote myocardial regeneration during acute MI by maintaining an anti-inflammatory environment in the infarct zone. A blood eosinophil count < 40 cells/μL is associated with worse clinical outcomes during long-term follow-up in patients with acute MI.[53]

Medications and CV risk in patients with COPD

Maintenance therapy for COPD consists of LAMA and LABA, which can be combined with ICS.[20] Daily maintenance therapy may include one, two or three of the above medications. The ETHOS (Efficacy and Safety of Triple Therapy in Obstructive Lung Disease) and the IMPACT (Informing the Pathway of Chronic Obstructive Pulmonary Disease Treatment) trials found fewer deaths from CV causes in the triple therapy group compared to the LAMA/LABA group. The SUMMIT trial found that ICS/LABA treatment did not reduce CV events compared with placebo in patients at high CV risk.[50] According to the PRIMUS (Prompt Initiation of Maintenance Therapy in US) study, in case of two moderate or one severe exacerbation of COPD within a year, it is recommended to switch to triple therapy. Delaying triple therapy increases the likelihood

of COPD re-exacerbation by 11% every 30 days during the 12-month follow-up period. Moreover, patients who delay triple therapy for > 6 months bear an even greater burden of comorbidities, including CVD.[54]

Nevertheless, the impact of COPD therapy on CV risk is not so clear-cut. One of the challenges of treating COPD is that patients who are more in need of exacerbation prevention may be at a higher risk of developing CV side effects. Although in general the benefits of combined inhalation therapy clearly outweigh the risks, the optimal solution is to adhere to a personalized approach to the management of such patients with an individual assessment of the benefits and risks for each patient.[55]

The use of β-blockers in patients with COPD is not only safe, but also beneficial. It has been proven that β-blockers reduce mortality from CVD in these patients. Cardioselective β-blockers do not affect the effectiveness of bronchodilators and can even reduce the risk of COPD exacerbations. In addition, β-blockers reduce bronchodilator-induced heart rate acceleration, contributing to a reduction in CV risk in patients with COPD.[56]

Conclusions

Currently, there is no unified approach to the assessment of CV risk in patients with COPD. The use of standard scales in these patients often leads to an underestimation of CV risk and untimely measures to diagnose and prevent adverse CV events. Patients with mild to moderate COPD are 10 times more likely to die from CVD than from respiratory failure. Early identification of risk factors for the development of CVD, periodic screening for damage to target organs, prevention of COPD exacerbations and personalization of diagnosis and treatment of patients with COPD are the keys to successful management of such patients. Thus, clinicians should be more vigilant about CV risk in patients with COPD, especially during and after exacerbations.

Conflict of interest

The authors declare that they have no conflict of interest.

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