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Research advancements on the correlation between sarcopenia and gastroesophageal reflux disease

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Abstract. With the advancement of population aging, it is increasingly vital to focus on the health conditions of the elderly. Sarcopenia is a condition characterized by gradual and systemic loss of skeletal muscle that may result in various outcomes, such as vulnerability, injuries and metabolic disorders, its impact on the lives of the elderly can't be ignored. Non-erosive reflux disease (NERD) is the most prevalent phenotype of gastroesophageal reflux disease (GERD), a major clinical gastrointestinal illness. Therefore, this article provides an overview of the definition, diagnosis, epidemiology, pathophysiology, and treatment of GERD and sarcopenia, with the intention of offering fresh viewpoints to improve the elderly's quality of life.

Keywords: gastroesophageal reflux disease, sarcopenia, relationship

1. Introduction

Sarcopenia, as a chronic disease that leads to muscle loss and decreased strength [1, 2], is associated with mobility limitations, reducing the quality of life [3], and complications such as metabolic syndrome [4]; prevalence of GERD increases over time in the elderly [5]. With the aging of society and growth of population, it will increase the public health burden [6]. Therefore, this article provides an overview of the definition, diagnosis, epidemiology, pathophysiology, and treatment of GERD and sarcopenia, with the intention of offering fresh viewpoints to improve the elderly's quality of life.

2. The definition and diagnosis of GERD

The lower esophageal sphincter temporarily relaxes in GERD patients, leading to weakening of the anti-reflux barrier and its main clinical manifestations are heartburn and reflux [7]. Research has demonstrated a correlation between GERD incidence and age [8]. Thus, public health burden increases as society aging and the population grows [6]. The diagnosis of GERD lacks an absolute standard. Therefore, symptoms like reflux and heartburn are used to make the diagnosis. Esophageal mucosal endoscopy, dynamic reflux monitoring can be used to evaluate esophageal acid exposure and high-resolution manometry can be used to assess motility disorders associated with GERD [9]. The Lyon Consensus 2.0 [10] enhances diagnostic specificity and offers a contemporary diagnosis for GERD: for undiagnosed GERD patients, esophagogastroduodenoscopy and/or outpatient reflux monitoring can provide conclusive evidence; ancillary examinations like endoscopy, pH impedance monitoring, and manometry may impact the conclusion when the evidence is inconclusive; the only approach for

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determining whether a patient with GERD is experiencing refractory reflux is through pH impedance monitoring.

3. The definition and diagnosis of sarcopenia

Sarcopenia is characterized by a progressive loss of both skeletal muscle quality and strength. in skeletal muscle quality and strength [11], primarily due to long-term accumulation of adverse changes in the muscles. A meta-analysis by Petermann and colleagues [12] indicates that the incidence of sarcopenia under the diagnostic standard of the European Working Group on Sarcopenia in Older People 2(EWGSOP2) is 10% (95% CI: 0.02-0.17). Sarcopenia has several diagnostic criteria. Currently the most commonly used diagnostic standard of sarcopenia has been revised by EWGSOP2 for the algorithms used in identifying and diagnosing of sarcopenia [13]: (1) The amount of muscle mass in the limbs, for males should be less than 20 kilograms, and for females less than 15 kilograms; (2) Low muscular strength is defined as grip force below the normal range, with less than 27 kilograms for males and less than 16 kilograms for females; (3) a step rate of ≤ 0.8 m/s, a score of ≤ 8 on the Simple Physical Assessment Scale (SPAS), and a chair stand test of 5 repetitions >15s. Reduction of muscular mass, combined with a decline in muscle strength or low fitness, can be used to diagnose sarcopenia.

4. The epidemiology of GERD and sarcopenia

4.1. Researches on the risk of developing sarcopenia among patients with GERD

A cross-sectional study by Kim and his colleagues [14] which included 8,218 patients (3,414 in the GERD category and 4,804 in the non-GERD category) found that 16.8% of GERD patients suffered from sarcopenia and sarcopenia is an independent predictor of GERD. Besides sarcopenia incidence was significantly more in the GERD category compared to the non-GERD category. Imagama and colleagues [15] conducted a prospective longitudinally cohort investigation with a 5-year follow-up and discovered that sarcopenia and reduced back muscle strength were important risk factors for the onset of GERD.

4.2. Researches on the relationship between GERD and sarcopenia

There is a current study [14] indicating that GERD is connected to sarcopenia. Sarcopenia may cause metabolic syndrome [4] which affects the mechanical barrier's function of the esophagus and stomach, so this triggers gastroesophageal reflux. Meanwhile cytokine signaling may play a role between sarcopenia and GERD [16-18]. A Mendelian study by Hu and colleagues [19] also discovered that features associated with sarcopenia such as decreased grip strength, decreased walking speed, and decreased appendicular lean mass were causally related to GERD. There is a deficit of sufficient evidence to substantiate a direct link between GERD and sarcopenia, so further analysis of the pathophysiological mechanisms of GERD and sarcopenia is needed.

5. Researches on the shared pathophysiological mechanisms of GERD and sarcopenia

5.1. Inflammations

Inflammation is one of the most crucial pathophysiologic mechanisms of gastroesophageal reflux. Gastroesophageal reflux overactivation of NF-κB increases cytokine levels such as TNF-α and IL-6 in esophageal epithelium [16]. One of the most important pathophysiologic mechanisms of sarcopenia is also inflammation. In a multicenter prospective longitudinal study by Li and colleagues [17], sarcopenia patients had significantly higher inflammatory mediator (IL-6, IL-18, TNF-α) levels in serum compared to non-sarcopenia patients. In the meantime, a study found that lower skeletal muscular strength and lower quantity of muscle were substantially correlated with greater levels of circulating inflammatory markers, with IL-6 and TNF-α being particularly linked to these outcomes [18]. Systemic inflammatory indicators typically rise with age, with TNF-α being one of the main culprits [20]. Elevated TNF-α levels (>11.15 pg/ml) have been linked to a 7.6-fold increase in the likelihood of sarcopenia [17]. By activating the ubiquitin-proteasome pathway, TNF-α causes a disorder in the production and metabolism of

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proteins in skeletal muscle, which results in atrophy and a loss in skeletal muscle mass [21], thus, both muscle mass and strength in skeletal muscles are reduced [18].

5.2. Body mass index and obesity

A cohort study showed higher BMI independently linked to GERD symptoms [22]. It has also been shown that there is a genetic link to the greater BMI susceptibility, which increases the chance of having GERD [23]. Obese subjects have an increased prevalence of esophageal dyskinesia, transient relaxation of lower esophageal sphincter tension, and esophageal hiatal herniation, thus leading to an increased incidence of GERD. Obesity also leads to increased intra-abdominal pressure, which increases the likelihood of stomach contents passing through the lower esophageal sphincter [24]. Centripetal obesity also impairs the structure and function of the esophageal epithelial barrier [25]. It has been shown that the accumulation of lipids and their byproducts inside and causes protein breakdown to worsen, dysfunction in the mitochondria to be induced, and a variety of cytokines that trigger inflammation to be produced more often, which can exacerbate muscle atrophy [26, 27]. Sarcopenia is made worse by obesity, which also enhances the chance of mortality, reduces physical functioning, and promotes the infiltration of fat into muscles. [13]. But there is a study finding that people with sarcopenia had a relatively low BMI compared to patients without sarcopenia [28].

5.3. Diabetes mellitus type 2, T2DM

The results of two Mendelian randomization (MR) analyses [23, 29]have both suggested that genetic susceptibility to T2DM increases the chance of developing GERD. Mechanisms involved in both are likely to be altered glucose and insulin metabolism in patients with T2DM, which leads to increased vascular endothelial damage and chronic inflammation [30]. Additionally, sarcopenia was more common in T2DM patients than in participants without diabetes by 18% [3]. Patients with T2DM have dramatically lower muscle power and resistance, and poor glycemic control may further lead to reduced muscle mass [31]. In addition, lack of exercise in patients with T2DM leads to muscle atrophy and mitochondrial dysfunction, due to the inhibition of the nuclear receptor's gamma coactivator-1 alpha peroxisome proliferator-activated receptor [32].

5.4. Smoke

A cohort Study Shows Smoking Independently Associated with GERD Symptoms [22]. According to a meta-analysis conducted by Larsson and colleagues [33], there is a correlation between smoking habit and a higher chance of getting reflux disease of the stomach. The outcomes of two other MR analyses [23, 34] similarly come to the conclusion that genetic predisposition to start smoking is linked to a higher chance of developing GERD. Because tobacco prolongs gastroesophageal acid clearance and decreases lower esophageal sphincter pressure [35]. MR analysis by Park et al [36] showed that there was a strong correlation found between lower appendicular lean mass index and increased genetic vulnerability to smoking and slower walking speed in the sarcopenia phenotype and was not significant for the grip strength phenotype. Smoking leads to skeletal muscular dysfunction by reducing the amount of oxygen that reaches the mitochondria, where long-term illnesses can cause sarcopenia and muscle atrophy [36]. Simultaneously exposure to cigarette smoke extracts leads to a roar in muscle growth inhibitors and a decline in the rate of myosin synthesis [37].

5.5. Psychological factor

According to a meta-analysis conducted by Zamani and colleagues [38] indicated that genetic susceptibility to anxiety and depression was related to a higher chance of developing GERD. The outcomes of MR analysis by Ruan et al [39] indicated that genetic predisposition to depression was related to a higher prevalence of GERD. Because psychological factors like sensitivity to esophageal stimulation alter esophageal dynamics and lower esophageal sphincter pressure, people who suffer from combined psychological disorders often experience pain from low-intensity esophageal stimulation [40]. Additionally, the use of medications like tricyclic antidepressants can cause a decrease in esophageal

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sphincter lower pressure [40], which in turn can increase the incidence of reflux episodes [41]. According to both meta-analyses [42, 43], depression was independently correlated with sarcopenia and was more common in sarcopenia patients than in the overall population. Sarcopenia can result from depression, which can also cause a decrease in regular social interactions. People with sarcopenia may also become disabled or become less active due to a loss of muscular mass and strength [43].

6. Conclusion

In conclusion, although GERD and sarcopenia are two completely different diseases, existing research suggests that there is a link between the two in terms of epidemiology and pathophysiology, especially in terms of inflammation, obesity, and psychiatric factors. The treatment of sarcopenia has a protective effect on GERD, and there are also Common potential treatment modalities such as lifestyle improvements like weight loss, smoking cessation, etc. Consequently, clinicians need to pay enough attention to this. It is hoped that the combination of exercise and taking vitamin D as needed with conventional treatment will enhance the patient's prognosis.

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