News and Views

Nutritional Status and Clinical Outcomes in Elderly COPD Patients

A new study published in the journal *Aging Clinical and Experimental Research* says that malnutrition is widespread among elderly patients with chronic obstructive pulmonary disease (COPD) and is a significant risk factor for hospital readmissions within 6 months, alongside other clinical variables such as the severity of airway obstruction and the presence of multiple comorbidities[1].

This cross-sectional study from China focused on the nutritional status of 319 first-time hospitalized patients, aged 65 years or older, with COPD using the Global Leadership Initiative on Malnutrition (GLIM) criteria between March 2021 and September 2022. Two-thirds of the study group was male; the median age was 76 years. The EMRs were used to assess the primary outcome variables of malnutrition, length of hospital stay, hospitalization costs, and re-hospitalization at 180 days. As per the GLIM criteria, malnutrition is diagnosed if one of the three phenotypes (non-volitional weight loss, low body mass index, and reduced muscle mass) and one of the two etiological types (reduced food intake or assimilation, and inflammation or disease burden) are met with[2]. "COPD, an inflammatory condition, fulfills one of the etiological criteria", note the authors.

Nearly half (49.5%) of the COPD inpatients had malnutrition. The 180-day readmission rate was lower among patients without malnutrition (10.56%) vs those with malnutrition (30.38%).

Logistic regression analysis showed that malnourished patients and those with very severe airway obstruction were over three times more likely to be hospitalized again within 180 days compared to well-nourished patients with odds ratio (OR) of 3.18 and 3.73, respectively. Patients who had three or more comorbid conditions were nearly six times more likely to be readmitted (OR 5.75). Patients without malnutrition had a median hospital stay of 11 days, whereas those with malnutrition had a median hospital stay of 13 days. Malnourished patients also have higher total treatment costs. These findings indeed highlight the significant role of malnutrition in influencing outcomes for elderly hospitalized COPD patients. Malnutrition is an important risk factor for prolonged hospital stay, increased healthcare costs, and higher readmission rates.

Besides evaluation of the disease, routine assessment of the nutritional status of these patients and active management of malnutrition, if present, is therefore essential to improve clinical outcomes and should be incorporated in the treatment protocol. Additionally, evaluation of elderly COPD patients for severity of airway obstruction and the number of comorbid conditions may identify at-risk patients.

This study reiterates the crucial link between nutrition and disease. The Nikshay Poshan Yojana, which provides financial aid every month to all notified TB patients for nutritional support, is an important initiative of the Government. Patients with chronic diseases like COPD could also greatly benefit from a similar scheme.

References

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Factors Contributing to Malnutrition in Patients with Diabetes

One in three patients with diabetes suffer from malnutrition and almost half of the diabetic population is at risk for malnutrition, suggests a systematic review and meta-analysis published in the October 2024 issue of the *Journal of Diabetes*[1].

The objective of the study was to estimate the prevalence of malnutrition in patients with diabetes and identify the factors that influence malnutrition in this population. Eight databases, including Embase, PubMed, Web of Science, The Cochrane Library, China Knowledge Resource Integrated Database (CNKI), Wanfang Database, Chinese Biomedical Database (CBM), and VIP, were searched from their inception until May 4, 2023 to select studies that had reported the prevalence of malnutrition in adult patients diagnosed with diabetes. These studies were carried out in several countries, including China, Japan, Belgium, Turkey, Spain, Brazil, Pakistan and Korea. Forty-six studies involving 18,062 patients, aged 18 to 95 years, were included in the final review. Analysis revealed that the

overall prevalence of malnutrition was 33% compared to the at-risk prevalence of 44%. Sixteen factors were identified that were potentially associated with malnutrition in these patients. These included: BMI, albumin, hemoglobin, triglycerides, HDL-C, HbA1c, CRP >10 mg/L, age, duration of diabetes, Wagner grades 3-5 (for diabetic foot ulcer), presence of CVD, using insulin, smoking, female gender, with diabetic foot infection and lower education level. The evidence was however inadequate to establish an association for smoking, gender, diabetic foot infection, and lower education level, with malnutrition in diabetic patients.

Spain had the highest prevalence of malnutrition at 50% followed by China (31%) and Turkey (18%). Again, the prevalence of at-risk for malnutrition was highest in Spain (60%), followed by China (49%), Japan (26%), and Turkey (20%). Diabetic patients with chronic complications exhibited a 22% higher prevalence of malnutrition than those without complications.

While diabetes patients with malnutrition had elevated levels of HbA1c, they showed significantly lower levels of BMI, albumin, hemoglobin, triglycerides, and HDL-C compared to participants with normal nutrition. They were also older in age. This meta-analysis highlights the prevalence of malnutrition and various risk factors associated with malnutrition in patients with diabetes. It also showed variation in the prevalence across different countries. Routine nutritional screening for at-risk individuals is essential for early identification and prompt intervention, which can significantly enhance their quality of life.

Reference

1. Zhang T, et al. Prevalence and influencing factors of malnutrition in diabetic patients: A systematic review and meta-analysis. J Diabetes. 2024 Oct;16(10):e13610. doi: 10.1111/1753-0407.13610.

Subclinical Hypothyroidism in Early Pregnancy Linked to Risk of Postpartum Hypothyroidism

A study published in the journal *Thyroid* found that women diagnosed with subclinical hypothyroidism during the first half of pregnancy have greater likelihood of developing overt hypothyroidism within 5 years after delivery compared to women with hypothyroxinemia[1].

Researchers from the United States carried out a secondary analysis of two multicenter treatment trials conducted for subclinical hypothyroidism or hypothyroxinemia diagnosed between 8- and 20-weeks of gestation. The present analysis focused only on participants in the placebo groups in the two studies. A TSH level ≥4.0 mU/L and normal free T4 (fT4) ranging from 0.86-1.9 ng/dL was considered as subclinical hypothyroidism. Normal TSH (0.08-3.99 mU/L) but fT4 <0.86 ng/dL was diagnosed as hypothyroxinemia. After initial testing, serum samples were stored to test for thyroid peroxidase (TPO) antibodies later, but these results were not used for clinical management. The participants were followed up at 1 year and 5 years after delivery to determine if they had been diagnosed with or treated for a thyroid condition. Overt hypothyroidism was defined as TSH ≥4.0 mU/L with fT4 <0.86 ng/dL. Follow-up data at 1 year and 5 years postpartum was available for 307 of the 338 participants with subclinical hypothyroidism and 229 of the 261 participants with hypothyroxinemia.

At year 1, 13.4% of participants with subclinical hypothyroidism developed hypothyroidism, compared to only 3.1% of those with hypothyroxinemia. At year 5, 15.6% of participants with subclinical hypothyroidism developed hypothyroidism, while only 2.6% of those with hypothyroxinemia did. Elevated TSH values >10 mIU/mL is a strong predictor of progression to overt hypothyroidism. A strong association was observed between baseline TPO antibody levels >50 IU/mL and progression to hypothyroidism in participants with subclinical hypothyroidism. The rate of hypothyroidism significantly higher at 1 year in participants with TPO >50 IU/mL (26.7%) compared to those with TPO levels ≤50 IU/mL (6.5%) with odds ratio (OR) of 5.3. In year 5, the rate of hypothyroidism in the TPO >50 IU/mL group increased to 30.5%, while it remained lower at 7.5% for those with TPO levels ≤50 IU/mL. The OR remained high at 5.4.

At year 1, there was no significant difference in the rate of overt hypothyroidism between those with TPO levels >50 IU/mL (10%) and those with TPO ≤50 IU/mL (2.8%) with OR 3.9. At year 5, however, more participants with TPO >50 IU/mL developed overt hypothyroidism (20%) compared to those with TPO ≤50 IU/mL (1.8%). The OR was significantly higher at 13.4. This study suggests that subclinical hypothyroidism is associated with a greater chances of progressing to overt hypothyroidism postpartum, particularly in those with higher baseline TSH levels (>10 mIU/mL) and elevated TPO antibodies (>50 IU/mL), especially when it is diagnosed in the first half of pregnancy. Although HT was also linked to a risk of hypothyroidism, the overall progression rate within the same period was lower. Hence, thyroid function should be closely monitored in women diagnosed with subclinical hypothyroidism during pregnancy. Thyroid testing should be a part of postpartum guidelines.

Reference

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SURMOUNTing the Obesity-Related OSA

In patients with obesity and moderate-to-severe obstructive sleep apnea (OSA), treatment with tirzepatide significantly reduced the apnea-hypopnea index (AHI) compared to placebo, regardless of whether patients were also using positive airway pressure (PAP) therapy. These findings from the SURMOUNT-OSA phase 3 trials were published in the New England Journal of Medicine[1].

Tirzepatide is a dual agonist of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. Two phase 3, double-blind, randomized-controlled trials were conducted to evaluate treatments in adults with obesity and moderate-to-severe OSA. Trial 1 included 234 patients who were not receiving PAP therapy at baseline, while Trial 2 included 235 patients who were not receiving PAP therapy at baseline. The mean age of the subjects was 50 years and 30% of them were female. The participants were randomized 1:1 to receive once-weekly subcutaneous tirzepatide injection (10 mg or 15 mg) (trial 1: n = 114, trial 2: n = 120) or placebo (trial 1: n = 120, trial 2: n = 115) for 52 weeks. Tirzepatide was started at 2.5 mg weekly and gradually up-titrated every 4 weeks until week 20, when the baseline AHI was measured. Throughout the study, all participants also received regular dietary and lifestyle counseling.

In trial 1, the mean AHI was 51.5 events/hour and mean BMI was 39.1 kg/m^2 at baseline. In trial 2, the mean AHI was 49.5 events/hour and mean BMI was 38.7 kg/m^2 at baseline. The mean change in AHI from baseline to the end of the study, which was the primary endpoint, in trial 1 was -25.3 events per hour with tirzepatide and -5.3 events per hour with placebo. The estimated treatment difference was -20.0 events per hour. In trial 2, the mean change in AHI at week 52 was -29.3 events per hour with tirzepatide and -5.5 events per hour with placebo, with an estimated treatment difference of -23.8 events per hour.

The secondary endpoints included the percent change in AHI and body weight, changes in hypoxic burden, patient-reported sleep impairment and disturbance, systolic BP and high-sensitivity C-reactive protein (hsCRP). Tirzepatide demonstrated significant improvements across all these parameters when compared with placebo. The most frequently reported adverse events associated with tirzepatide were related to the gastrointestinal tract (diarrhea, nausea, vomiting, and constipation), and were generally mild to moderate in severity.

Obesity is a known risk factor for OSA. Tirzepatide is FDA approved for the treatment of adults with type 2 diabetes. Last year, it was also approved for chronic weight management in adults with obesity (BMI ≥30 kg/m^2) or overweight (BMI ≥27 kg/m^2) with at least one weight-related condition along with increased physical activity and a reduced calorie diet. In both trials, by reducing body weight, tirzepatide led to a significantly greater reduction in the AHI at one year compared to placebo. It also reduced the hypoxic burden, hsCRP levels, and systolic BP and improved sleep-related patient-reported outcomes. By demonstrating a significant improvement in AHI, this study points to a potential role of tirzepatide in treatment of obesity-related OSA regardless of the use of PAP therapy.

Reference

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Impact of High-Intensity versus Low-Intensity NPPV on Intubation in Patients with Acute COPD Exacerbations

Use of high-intensity noninvasive positive pressure ventilation (NPPV) may help reduce the need for endotracheal intubation in patients experiencing persistent hypercapnia during acute exacerbations of chronic obstructive pulmonary disease (COPD), according to results of the HAPPEN trial published Sept. 16, 2024 in JAMA[1].

This randomized clinical trial conducted in China aimed to evaluate the effectiveness of high-intensity NPPV vs low-intensity NPPV in reducing the need for endotracheal intubation among patients experiencing acute exacerbations of COPD with hypercapnia in 30 general respiratory non-intensive care unit wards. The study was from January 2019 to April 2022. The study focused on patients with a partial pressure of carbon dioxide (PaCO2) level exceeding 45 mmHg after 6 hours of low-intensity NPPV.

In this study, 300 patients with acute exacerbations of COPD and hypercapnia were randomized in a 1:1 ratio to two different NPPV strategies. The 147 patients in

the High-intensity NPPV Group received NPPV with inspiratory positive airway pressure (IPAP) adjusted to achieve a tidal volume between 10 mL/kg and 15 mL/kg of predicted body weight. The Low-intensity NPPV Group, comprising 153 patients, continued with lower IPAP settings aimed at achieving a tidal volume between 6 mL/kg and 10 mL/kg of predicted body weight. Patients in the low-intensity NPPV group were allowed to switch to high-intensity NPPV as a crossover intervention, if they met specific criteria indicating a need for endotracheal intubation.

The 300 patients who completed the trial had a mean age of 73 years, with 68% being men. Enrollment required an acute exacerbation of COPD, an arterial pH level of less than 7.35, and a PaCO2 level greater than 45 mm Hg after 6 hours on low-intensity NPPV. Thus, the results can't be extrapolated to apply to patients with more severe respiratory distress, "particularly those who are likely to develop dynamic hyperinflation," the editorialists cautioned.

There was a significant difference between the two groups in the primary outcome of the study, which was the need for endotracheal intubation during hospitalization as per prespecified criteria. In the High-intensity NPPV Group, 4.8% (7/147) met the criteria for intubation compared to 13.7% in the Low-intensity NPPV Group. The absolute difference between the two groups was -9.0%. Although fewer patients met the criteria for intubation in the high-intensity NPPV group, the actual rates of endotracheal intubation was comparable between the two groups; 3.4% (5/147) in the high-intensity NPPV group and 3.9% (6/153) in Low-Intensity NPPV Group. The absolute difference was -0.5%. The incidence of abdominal distension was higher in the high-intensity NPPV group (37.4%) compared to the low-intensity group (25.5%). Notably, high-intensity NPPV resulted in more abdominal distention (37.4% vs 25.5%) and more intolerance of NPPV due to abdominal distention (3.4% vs 0.7%).

Severe alkalosis (pH >7.55) was "mildly higher" in the high-intensity NPPV group as well (4.1% vs 0%), but other severe adverse events "were rare and similar between groups," the researchers noted.

The study therefore concluded that patients with COPD and persistent hypercapnia who received high-intensity NPPV were less likely to reach the criteria requiring endotracheal intubation compared to those treated with low-intensity NPPV. But, because patients in the low-intensity group had the option to switch to high-intensity NPPV if necessary, the overall rate of endotracheal intubation did not differ significantly between the two groups.

A limitation of the study, as per the authors, was that the trial was terminated early by the data and safety monitoring board and the trial steering committee following an interim analysis involving the first 300 patients, "which revealed a substantial and statistically significant difference in the primary outcome between the study groups". They further that these findings "may not be generalizable to patients with evident emphysematous bullae and presence of restrictive ventilatory dysfunction (e.g., pulmonary consolidation) because these patients were excluded from this trial".

Reference

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The Lasting Legacy of Severe Childhood Asthma

Among adults aged 65 years and older, who had severe asthma in childhood, only one in ten achieved asthma remission, while one in three experienced persistent airflow limitation, according to a 60-year follow-up study of adults with a history of severe childhood asthma published in the journal Chest[1].

A 60-year follow-up study was conducted with individuals with a documented history of severe childhood asthma to evaluate their disease characteristics in adulthood. The study included Danish adults who had a history of severe asthma during childhood and had undergone a 4-month stay at an asthma care facility in Kongsberg, Norway, between 1950 and 1979. After an average follow-up of 60 years, the patients were assessed via questionnaires and laboratory tests, spirometry, fractional exhaled nitric oxide (FeNO), bronchodilator reversibility, bronchial provocation with mannitol, and measurements of static lung volumes. Written informed consent was obtained from all participants. Patients in remission had not used any asthma medication and had been asymptomatic within the past one year. The others were categorized as having current asthma.

A total of 1394 individuals were eligible for the study; of these, 232 completed the follow-up. Their mean age was 66.1 years. Among these, 89.7% had current asthma and 10.3% were classified as having asthma remission. Twenty-six percent reported experiencing exacerbations

within the previous year. 21.6% had been treated with antibiotics for lower airway infection. Only 15.7% of all the participants were managed in secondary care.

Almost all the participants with current asthma were receiving inhaled controller therapy (83%). And two-thirds of those with current asthma used short-acting β2-agonists as reliever, while others used long-acting β2-agonists, inhaled corticosteroids (ICS), or long-acting muscarinic antagonists.

Sixty percent of those having current asthma had allergic rhinitis; 21% had hypertension, 16% had eczema and 8% had cataract. Participants with persistent asthma had significantly higher total IgE levels, lower FEV1 % predicted, and a reduced FEV1/FVC ratio compared to those in remission. They also showed numerically higher levels of FeNO (26.7 ppb vs 20.1 ppb) and blood eosinophil count (0.19 vs 0.17 109/L). The definition of asthma remission used in this study emphasizes symptom management and medication use in the previous 12 months, recognizing asthma management from the patient's perspective. It considers how individuals perceive their symptoms and acknowledges that the treatment they report through questionnaires may differ from the prescribed treatment. This study offers valuable insights into the long-term prognosis of severe childhood asthma. It showed that nearly 90% of patients with a history of severe childhood asthma continued to have asthma during adulthood at a mean age of 66 years. Those with persistent asthma exhibited impaired lung function and elevated levels of type 2 inflammatory biomarkers compared to the 10% in remission. Hence, severe childhood asthma is a risk factor for potentially debilitating lung disease later in life.

Reference

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Screening for Exercise-induced Desaturation in Normoxemic ILD

The 1-minute sit-to-stand test (1minSTS) is a viable alternative to the 6-minute walk test (6MWT) for measuring exercise-induced desaturation in normoxemic patients with interstitial lung disease (ILD), suggests a study published in the journal *Respiratory Medicine*[1]. A nadir SpO2 (nSpO2) threshold of 94% during the 1minSTS was found reliably detect prognostically significant desaturation during the 6MWT.

This study compared the utility of the 1minSTS vis-à-vis the 6MWT for detecting exercise-induced desaturation in patients with ILD. Patients attending a tertiary referral clinic were enrolled for the study. These patients had undergone both tests on the same day. The study also evaluated the predictive ability of nSpO2 measured during the 1minSTS for identifying participants who would experience significant desaturation (SpO2 ≤88%) during the 6MWT. This was done using the area under the receiver operating characteristic curve (AUC).

The study included 24 patients (48%) with idiopathic pulmonary fibrosis, 20 patients (40%) with connective tissue disease-associated ILD, while 6 had other types of ILD (12%).

The mean forced vital capacity percentage predicted (FVC%pred) was 73%. The mean diffusing capacity of the lungs for carbon monoxide percentage predicted (DLCO%pred) was 57% At rest, the mean SpO2 was high, with an average of 99%. Analysis of exercise-induced desaturation indicated that the 1minSTS resulted in less exercise-induced desaturation compared to the 6MWT with a median IQR nSpO2 (nadir oxygen saturation) of 95% and 93%, respectively. The mean difference between the two was 3.2%.

The study found that the 1minSTS was highly effective in identifying participants who experienced significant oxygen desaturation (nSpO2 ≤88%) during the 6MWT. Oxygen desaturation ≤94 % during the 1minSTS test demonstrated 100% sensitivity and 87% specificity for oxygen desaturation ≤88% at 6MWT.

The study has demonstrated a significant correlation between exercise-induced oxygen desaturation during the 1minSTS and the 6MWT suggesting that the 1minSTS can effectively show the desaturation patterns observed during more extensive exercise testing. The 100% sensitivity indicates that the 1minSTS test could correctly identify all participants who experienced desaturation (SpO_2 ≤88%) during the 6MWT. The 87% specificity means that it could identify 87% of participants who did not experience desaturation to ≤88% on the 6MWT; only 13% were false-positives. Given these findings, the 1minSTS therefore may serve as a practical and accessible alternative screening tool for detecting exercise-induced oxygen desaturation in patients with ILD in office practice "who would benefit from further exercise testing".

Reference

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