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THE ADMINISTRATION OF ORAL NUTRITIONAL SUPPLEMENTATION (ONS) IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS: A SYSTEMATIC REVIEW

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ABSTRACT
Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of global morbidity and mortality, often worsened by malnutrition, especially in advanced stages. Malnutrition accelerates COPD progression, reducing physical capacity and health-related quality of life (HRQoL). Oral nutritional supplementation (ONS) has been proposed to improve nutritional status, body mass index (BMI), functional capacity, and HRQoL in COPD patients. This systematic review critically evaluates the efficacy of ONS in COPD management and investigates patient-specific factors influencing therapeutic outcomes. Following PRISMA guidelines, a comprehensive literature search across five databases (PubMed, ScienceDirect, ProQuest, Nature, and Google Scholar) up to October 2024 identified 32,293 articles. Nine randomized controlled trials (2020–2024) were eligible for review. Analysis showed ONS led to modest BMI improvements (ranging from +0.1±0.7 to +1.3±3.2 kg), with greater gains in functional capacity, as demonstrated by increased 6-minute walk distances (from +23.0±24.9 m to +86.72±136.14 m) and handgrip strength (up to +3.34±5.65 kg in intervention vs. +0.28±4.32 kg in controls). Quality of life scores also improved significantly, with reductions in St. George's Respiratory Questionnaire scores and enhanced COPD Assessment Test outcomes. These findings indicate that while ONS enhances functional capacity and HRQoL, its impact on BMI is limited, suggesting ONS alone may be insufficient for malnutrition in COPD. A multidisciplinary strategy combining nutritional support and rehabilitation is recommended. Further studies should focus on patient-specific predictors of ONS effectiveness to optimize COPD care.

Keywords: chronic obstructive pulmonary disease (COPD); functional capacity; malnutrition; oral nutritional supplementation (ONS); quality of life

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of global morbidity and mortality. According to data from the World Health Organization (WHO), in 2019, COPD was responsible for approximately 3.23 million deaths, making it the third leading cause of death worldwide, following coronary heart disease and stroke (WHO, 2019). Estimates place the prevalence of COPD in Indonesia at around 3.6% of the total adult population, with the risk rising with age and exposure to risk factors like smoking and air pollution (Al Wachami et al., 2014).

COPD not only affects lung function but is also frequently associated with malnutrition, which can exacerbate disease progression and diminish patients' quality of life. Malnutrition in COPD patients may occur due to increased energy requirements, decreased food intake, and metabolic changes. Research indicates that approximately 40–60% of COPD patients experience malnutrition, contributing to a decline in functional capacity and quality of life as well as increasing the risk of exacerbations and mortality (Kerley et al., 2019; Schols et al., 2014). Researchers have proposed oral nutritional supplements (ONS) as a promising intervention to address malnutrition. Patients who struggle to meet their dietary needs through regular meals can receive adequate calories and nutrients from ONS. We expect the implementation of ONS in COPD management to enhance

nutritional status, improve body mass index (BMI), increase functional capacity, and improve patients' quality of life (Shepherd, 2010).

The PICO (Patient, Intervention, Comparison, Outcome) framework is relevant for evaluating the effects of ONS in COPD patients. In this context, the population under investigation includes patients with COPD (P) who receive oral nutrition therapy (I), compared to COPD patients who do not receive ONS (C). The evaluated outcomes include BMI, functional capacity measured through tests such as the 6-minute walk test (6MWT), and quality of life assessed using instruments like the St. George's Respiratory Questionnaire (SGRQ) (O).

Current evidence suggests that ONS has the potential to improve BMI in COPD patients. A recent study reported that patients receiving ONS experienced an average weight gain of 1.1 kg after 12 weeks of intervention ($p = 0.032$). The 6MWT also showed a significant improvement in functional capacity, with the group that received ONS being able to walk an average of 30 meters farther ($p < 0.001$). Patients' quality of life also improved, as reflected in a decrease in SGRQ scores, indicating enhancements in both psychological and physical well-being (Huang et al., 2022).

In Indonesia, research has shown that ONS can enhance the quality of life in COPD patients. In one study involving 120 patients, the group receiving ONS exhibited a significant improvement in quality of life scores ($p < 0.05$) and an average BMI increase of 1.5 kg after eight weeks. These findings underscore the importance of ONS in addressing malnutrition and improving clinical outcomes in COPD patients. Despite the positive evidence supporting the use of ONS, research outcomes remain variable due to differences in study design, intervention duration, and population characteristics. A systematic review is essential to assess the effectiveness of Oral Nutritional Supplements (ONS) in improving BMI, functional capacity, and quality of life in COPD patients. This review will gather and analyze current data while identifying factors influencing the response to this intervention. We expect it to provide valuable insights for clinical practice and future research, supporting the use of evidence-based nutritional interventions in COPD management.

The objective of this study is to evaluate the effectiveness of Oral Nutritional Supplementation (ONS) in improving nutritional status, functional capacity, and quality of life in patients with Chronic Obstructive Pulmonary Disease (COPD). Specifically, this research aims to examine the impact of ONS on body mass index (BMI), assess its influence on functional capacity through the 6-minute walk test (6MWT), and measure improvements in quality of life using validated tools such as the St. George's Respiratory Questionnaire (SGRQ). Furthermore, this study seeks to explore the factors that may affect the success of ONS interventions, thereby providing a comprehensive understanding of its role in the management of COPD.

METHOD

This research was conducted at an aesthetic clinic in Semarang on February 7–9. The study sample consisted of 20 patients undergoing various dermatological procedures with the use of local anesthesia. Of the 20 patients, there were 2 men and 18 women. In this study, several types of dermatological procedures were performed. Fraction laser treatment was the most common, carried out on eight patients. Strengthening skin procedures were performed on six patients, while microneedling was applied to four patients. In addition, one patient underwent a facial procedure, and another received a subsidized treatment. The anesthesia used in this study is topical lidocaine in the form of an applied preparation. Lidocaine works by inhibiting the conduction of nerve impulses in the area of application, thereby providing a rapid local anesthetic effect. This anesthesia is administered before the dermatological procedure to reduce pain and improve patient comfort.

Data were collected through direct observation as well as post-procedure interviews to assess the presence of local anesthesia side effects. Side effects observed in this study included feeling hot/sore, nausea, vomiting, dizziness, blurred vision, impaired consciousness, and fainting. The age

profile of patients undergoing dermatological procedures in this study ranged from 21 to 40 years, consisting of both men and women. The majority of patients were women, with only two male participants recorded. Fraction laser treatment emerged as the most frequently performed procedure, particularly among patients in their mid to late twenties and those in their thirties. Strengthening skin procedures were carried out in several cases, including both male and female patients aged between their early thirties and late thirties. Microneedling was performed on patients mostly in their mid-twenties to late thirties, while a single patient aged 35 years underwent a subsidized treatment. Additionally, one female patient aged 21 years received a facial procedure. Overall, the data indicate that fraction laser and skin-strengthening procedures were the most common interventions across this patient group.

Below is the PRISMA flow diagram. We conducted a search using predefined keywords across several databases. In the initial search phase, we found 4053 articles in PubMed, 124 in ScienceDirect, 1913 in ProQuest, 3 in Nature, and 26,200 in Google Scholar. In the next phase, we applied criteria to the identified articles: articles had to be primary research and written in English or Indonesian. This process resulted in a total of 18,541 articles. After removing those that did not meet the PICO criteria and duplicates, we identified 10 articles. After screening titles and abstracts focusing on the research objectives, methods, and outcomes relevant to our secondary research question, 9 articles remained.

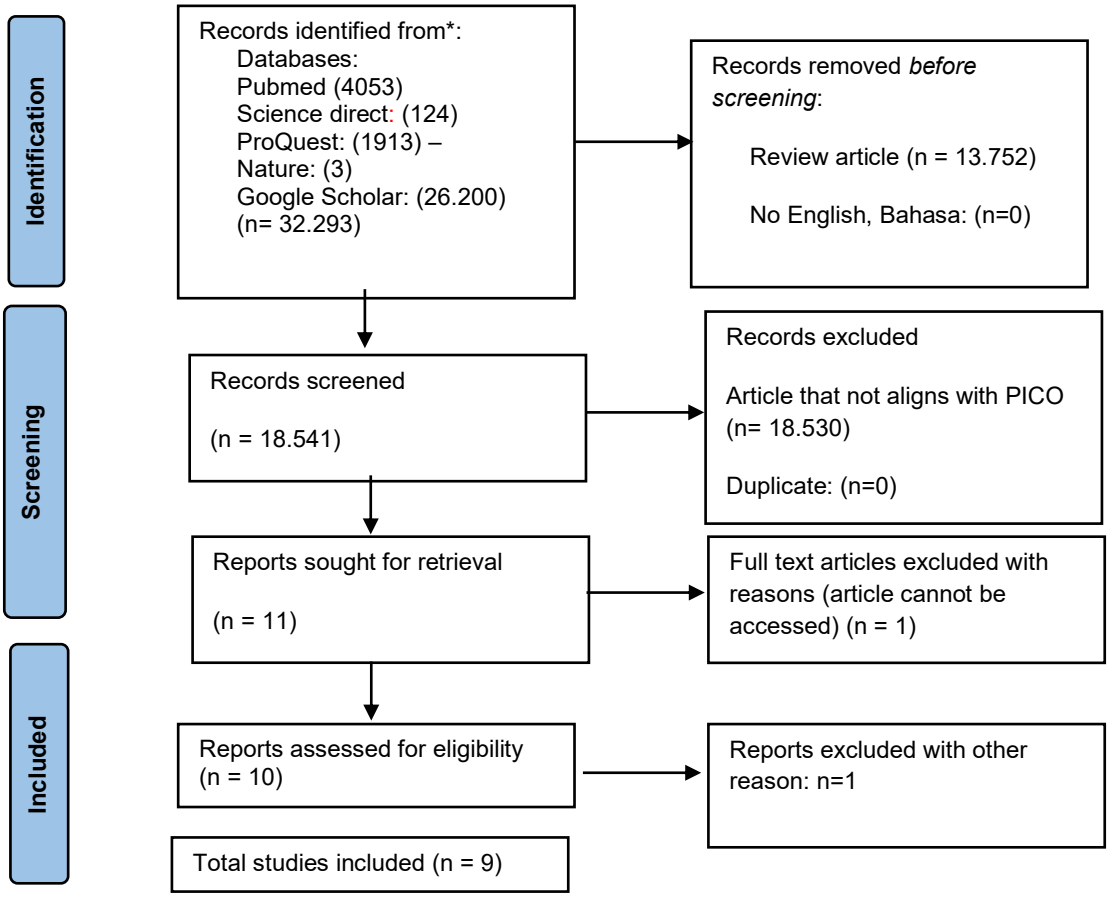

Figure 1. Flowchart PRISMA

RESULT

Nine randomized controlled trials conducted between 2020 and 2024 have provided extensive data on nutritional interventions for Chronic Obstructive Pulmonary Disease (COPD) patients. These studies explored various nutritional approaches, including leucine-enriched supplements, branched-chain amino acids (BCAA), fortified whey beverages, magnesium supplementation, and nitrate supplementation through beetroot juice. The impact of these interventions was measured across

three main domains: body mass index (BMI), functional capacity, and quality of life. In terms of BMI and body weight changes, most studies reported modest variations.

Table 1.
Inclusion Criteria

No	Authors/year	Title	Methods	Subject	ONS type	Result (differences)		
						BMI	Functional capacity	QoL
1	(van Beers et al., 2020)	Clinical outcome and cost-effectiveness of a 1-year nutritional intervention programme in COPD patients with low muscle mass: The randomized controlled NUTRAIN trial	randomized controlled trial	81 muscle-wasted COPD patients with moderate airflow obstruction and impaired exercise capacity	Enriched with leucine, vitamin D and polyunsaturated fatty acids	No significance differences	• Quadriceps muscle strength - Placebo: +10.05 Nm - Intervention: +10.35 Nm • Cycle endurance time - Placebo: -200.3 sec - Intervention: -107.1 sec • Physical activity level - Placebo: -671.3 steps/day - Intervention: +1030 steps/day	• EQ-5D score - Placebo: -0.060 points - Intervention: -0.012 points • Hospital Anxiety and Depression Scale - Placebo: No significance differences - Intervention: -1.92 points
2	(de Bisschop et al., 2021)	Does branched-chain amino acid supplementation improve pulmonary rehabilitation effect in COPD?	double-blind experiment randomized controlled trial	60 COPD patients (GOLD 2–3)	Branched-chain amino acids (BCAA), made of partially hydrolyzed whey protein isolates mixed with the other constituent of the powder. 18.44 g of proteins (82% total energy intake (TEI)), 1.59 g of glucids (7% TEI), 0.51 g of lipids (5% TEI), 2.67 g of fiber and 0.3 g of salt	• Placebo: +0.3 ±1.5 • Intervention: +0,1± 0,7	• 6 minutes walking test - Placebo: +60±51 m - Intervention: +40±53 m	• VQ11 questionnaire Functional - Placebo: -2.3±2.8 points - Intervention: -3.2±3.0 points • Quality of Life - Placebo: -6.9±8.5 points - Intervention: -8.8±8.6 points
3	(Ahmadi et al., 2020)	Fortified whey beverage for improving muscle mass in chronic obstructive pulmonary disease: a single-blind, randomized clinical trial	A single-blind, randomized trial study	patients with COPD (n = 46).	250 ml of whey beverage fortified with magnesium and vitamin C	• Placebo: +0,20 ±0,97. • Intervention: +0,17 ±0,75	• Right handgrip strength - Placebo: +0.20±4.54 kg - Intervention: +2.76±3.81 kg • Left handgrip strength - Placebo: +0.28±4.32 kg Intervention: + 3.34±5.65 kg	• Instrumental activity of daily living score - Placebo: -0.28±0.90 points - Intervention: -0.37±1.13 points • St.George's Respiratory Questionnaire total score - Placebo: -1.0±11.0 points - Intervention: -12.0±12.0 points
4	(Zanforlini et al., 2022)	Clinical trial on the effects of oral magnesium supplementation in stable-phase COPD patients	double-blind randomized -controlled clinical study	patients recruited at the Respiratory Physiopathology Unit of the University Hospital of Padua (Italy), which they attended for	magnesium citrate (300 mg/pack)	No significance differences	• Max handgrip strength - Placebo: -3.4 kg - Intervention: -1.1 kg • 6 minutes walking test - Placebo: -29.0 m - Intervention:-24.8 m • Extention peak tongue - Placebo: -5.5 Nm - Intervention:+3.4 Nm • Isometric moment maximum	• St.George's Respiratory Questionnaire total score - Placebo: -19.0 points - Intervention: -11.1 points • EQ-5D score - Placebo: -0.1 points - Intervention: 0.0 points

No	Authors/y	Title	Methods	Subject	ONS type		Result (differences)	
				periodic control visits for COPD (n=76)			- Placebo: -5.0 Nm - Intervention:+7.8 Nm	
5	(Alasmari et al., 2024)	Oral nitrate supplementation improves cardiovascular risk markers in COPD: ON-BC, a randomised controlled trial	prospective, double-blind, parallel group, randomised, placebo-controlled trial	stable COPD patients with home systolic BP (SBP) measurement ⩾130 mmHg (n=40)	NR-BRJ (70 mL Beet It Sport Nitrate Shot; James White Drinks, Ipswich, UK) which contains 400 mg NO3−.	No significance differences	• 6 minutes walking test - Placebo: -7.0±21.8 m - Intervention: +23.0±24.9 m	• COPD assessment test score - Placebo: -0.5±3.4 points - Intervention: -1.6±4.2 points
6	(Conway et al., 2024)	Nutritional Support in Malnourished Outpatients with Chronic Obstructive Pulmonary Disease (COPD): A Randomized Controlled Pilot Study	randomized controlled trial	Malnourished outpatients with COPD	ONS with 200 mL of full-fat milk (400 mL milk: +264 kcal, +13 g protein)	Body weight: • Placebo: +0.95 ±2.2 kg • Intervention: +1.3± 3.2 kg	• Right handgrip strength - Placebo: -5.8±15.0 kg - Intervention: -4.7±8.5 kg	• St.George's Respiratory Questionnaire total score - Placebo: -4.4±8.7 points - Intervention: -4.4±8.7 points
7	(Oyama et al., 2024)	Combined Effect of Early Nutrition Therapy and Rehabilitation for Patients with Chronic Obstructive Pulmonary Disease Exacerbation: A Prospective Randomized Controlled Trial	prospective, open-label,randomized controlled trial	38 patients patients with COPD exacerbation who underwent early rehabilitation programs (RP)	125 mL per pack and contained 200 kcal of energy, 6.5 g of protein, and 3500 mg of branched-chain amino acids (BCAAs)	• Placebo: -0.3±0.2. • Intervention: +0.1± 0.2	• 6 minutes walking test - Placebo: +65±70.5 m - Intervention: +57.7±61.0 m • 10 m timed gait test - Placebo: -0.5±1.5 sec - Intervention: -2.5±2.3 sec • Short physical performance battery - Placebo: +0.4±1.5 sec - Intervention: +1.4±1.6 sec	N/A
8	(Korkmaz et al., 2020)	Effects of comprehensive and intensive pulmonary rehabilitation and nutritional support on quality of life and functional status in patients with chronic obstructive pulmonary disease	randomized controlled trial	64 patients with stable stage three to four COPD	each 125 ml package contained 300 kcal (2.4 kcal/mL), 18 g of protein (E24%), 11.75 g of fat (E35%) and 30.5 g of carbohydrate (E41%).	• Intervention: +0.17 ±0.93	• Right handgrip strength - Intervention: +4.50±14.43 kg • Left handgrip strength - Intervention: + 5.38±12.98 kg • 6 minutes walking test - Intervention: +86.72±136.14 m • Incremental shuttle walking test - Intervention: +76.24±180.94 m	• St.George's Respiratory Questionnaire total score - Interventio: -13.86±22.01 points
9	(Pavitt et al., 2020)	Oral nitrate supplementation to enhance pulmonary rehabilitation in COPD: ON-EPIC a multicentre, double-blind, placebo-controlled, randomised parallel group study	double-blind, placebo-controlled, parallel group, randomised controlled study	165 peoples with Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade II–IV COPD13	Concentrated beetroot juice (BRJ product which is cut with organic lemon juice (2%) and contained 0.8 g or 12.9 mmol of nitrate (140 mL of Beet-It SPORT shot, James White Drinks, Ipswich, UK	No significance differences	• Step count - Placebo: -915±640 steps/day - Intervention: -94±1629 steps/day	• COPD assessment test score - Placebo: -7.0±1.0 points - Intervention: -2.5±0.0 points

Bisschop et al. (2021) observed minimal changes with BCAA supplementation (intervention: +0.1±0.7 vs. placebo: +0.3±1.5) (de Bisschop et al., 2021). (Ahmadi et al., 2020) reported similar minimal differences with their whey beverage intervention (+0.17±0.75 vs. placebo: +0.20±0.97) (Ahmadi et al., 2020). (Conway et al., 2024) showed slightly more pronounced weight changes with their ONS intervention (+1.3±3.2 kg vs. placebo: +0.95±2.2 kg) (Conway et al., 2024). Oyama et al.

(2024) demonstrated a small positive change in their intervention group (+0.1±0.2) while the control group declined (-0.3±0.2), and Korkmaz et al. (2020) reported a modest increase of +0.17±0.93 in their intervention group (Korkmaz et al., 2020; Oyama et al., 2024).

Functional capacity measurements revealed more substantial improvements across various parameters. In terms of walking tests, (de Bisschop et al., 2021) reported improvements in the 6-minute walking test for both groups (intervention: +40±53 m vs. placebo: +60±51 m). (Zanforlini et al., 2022) observed smaller decreases in the intervention group for the 6-minute walking test (-24.8 m vs. placebo: -29.0 m). (Alasmari et al., 2024) showed improvement in their intervention group (+23.0±24.9 m) while the control group declined (-7.0±21.8 m). (Oyama et al., 2024) reported improvements in both groups but with varying magnitudes (intervention: +57.7±61.0 m vs. placebo: +65±70.5 m), while Korkmaz et al. (2020) demonstrated substantial improvement (+86.72±136.14 m). Muscle strength measurements also showed significant variations. (van Beers et al., 2020) reported similar improvements in quadriceps muscle strength (intervention: +10.35 Nm vs. placebo: +10.05 Nm). (Ahmadi et al., 2020) demonstrated marked improvements in handgrip strength (right hand: +2.76±3.81 kg vs. placebo: +0.20±4.54 kg; left hand: +3.34±5.65 kg vs. placebo: +0.28±4.32 kg). (Conway et al., 2024) observed smaller decreases in right handgrip strength in the intervention group (-4.7±8.5 kg vs. placebo: -5.8±15.0 kg). (Zanforlini et al., 2022) reported improvements in isometric moment maximum (intervention: +7.8 Nm vs. placebo: -5.0 Nm). Physical activity levels showed varying results. (van Beers et al., 2020) reported increased daily steps in the intervention group (+1030 steps/day) while the control group decreased (-671.3 steps/day). (Pavitt et al., 2020) observed smaller decreases in the intervention group (-94±1629 steps/day vs. placebo: -915±640 steps/day).

Quality of life measurements demonstrated consistent improvements across studies. The St. George's Respiratory Questionnaire showed significant improvements in several studies: (Ahmadi et al., 2020) reported -12.0±12.0 points for intervention vs. -1.0±11.0 points for placebo; (Zanforlini et al., 2022) showed -11.1 points for intervention vs. -19.0 points for placebo; (Conway et al., 2024) reported equal improvements (-4.4±8.7 points) in both groups; and Korkmaz et al. (2020) demonstrated substantial improvement (-13.86±22.01 points). The COPD Assessment Test scores also improved, with (Alasmari et al., 2024) reporting -1.6±4.2 points for intervention vs. -0.5±3.4 points for placebo, and (Pavitt et al., 2020) showing -2.5±0.0 points for intervention vs. -7.0±1.0 points for placebo. Additional functional measures included improvements in cycle endurance time (van Beers et al., 2020): intervention: -107.1 sec vs. placebo: -200.3 sec), the 10m timed gait test (Oyama et al., 2024: intervention: -2.5±2.3 sec vs. placebo: -0.5±1.5 sec), and short physical performance battery (Oyama et al., 2024: intervention: +1.4±1.6 sec vs. placebo: +0.4±1.5 sec). These comprehensive findings suggest that while nutritional interventions may have modest effects on BMI, they can significantly improve functional capacity and quality of life in COPD patients, particularly when combined with rehabilitation programs.

DISCUSSION

It was shown that nutritional interventions over a year in people with chronic obstructive pulmonary disease (COPD) did not significantly improve long-term outcomes. However, these interventions did significantly improve body weight (the difference between the NUTRITION and PLACEBO groups was 1.54 kg, $p = 0.041$), physical activity levels (an increase of 1030 steps/day, $p = 0.025$), and overall health status (the EQ-5D difference between the NUTRITION and PLACEBO groups was 0.072, $p = 0.009$). Although there were no significant differences in quadriceps strength and cycling endurance time, the nutritional intervention showed positive trends in weight gain and reduced anxiety and depression scores (a change in HADS of -1.92 points, $p = 0.037$). This indicates additional benefits for mental health and motivation to engage in exercise and maintain a healthy diet. In the context of pulmonary rehabilitation, the duration and intensity of the program are crucial for improving physical function. A 4-week rehabilitation program showed significant improvement in the six-minute walk test, with an increase in distance traveled of 40 ± 53 m in the

BCAA group and 60 ± 51 m in the placebo group ($p < 0.01$). Previous research indicates that BCAA supplementation can contribute to increased muscle mass and functional performance, although the effects were not significantly greater than those from structured pulmonary rehabilitation. Heterogeneity in patient characteristics, such as severity of muscle atrophy and gender differences, may influence responses to rehabilitation programs and supplementation.We recommend further research to investigate longer durations and more specific inclusion criteria to identify patients most likely to benefit from BCAA supplementation.

Additionally, nutritional interventions using whey drinks enriched with magnesium and vitamin C emphasize their importance in managing COPD patients. It was found that interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) levels went down significantly after eight weeks of treatment ($P = 0.040$ and $P = 0.021$, respectively), suggesting that whey may have anti-inflammatory effects. Whey supplementation significantly improves nutritional status and physical function, often compromised in patients with chronic conditions, as evidenced by the significant increase in fat-free mass index (FFMI) and handgrip strength ($P = 0.025$ and $P = 0.018$). As shown by the fact that serum albumin levels went up significantly in the intervention group ($P = 0.004$), personalized nutritional support is an important part of managing COPD and improving nutritional status. Improved nutritional status contributes to patients' quality of life, encompassing enhanced physical function and reduced related symptoms. In this context, magnesium supplementation yields varying results, indicating improvements in certain aspects of physical performance and quality of life, but it does not significantly alter respiratory parameters.

Results from research on nitrate supplementation also indicate positive impacts on physical function and quality of life. Although no explicit data regarding changes in BMI were reported, the increase in distance traveled on the six-minute walk test (6MWD) by 30 meters ($p < 0.001$) demonstrates the potential for improving the physical capacity of COPD patients. However, there were no statistically significant improvements in quality of life, measured by scores on the Chronic Obstructive Pulmonary Disease Assessment Test (CAT) and the Medical Research Council (MRC) dyspnea scale. These findings emphasize that while nitrate supplementation may enhance physical capacity, its effects on quality of life may take longer to manifest. This study highlights the importance of comprehensive pulmonary rehabilitation interventions and nutritional support in enhancing various health parameters in COPD patients. There were big improvements in functional status, as shown by an 86.72-meter increase in the six-minute walk test (6MWT) and an 76.24-meter increase in the incremental shuttle walking test (ISWT). This shows that integrated rehabilitation programs work. The total score on the St. George’s Respiratory Questionnaire (SGRQ) decreased by 13.86, indicating substantial improvements in patients' quality of life. Personalized nutritional support also contributes to improvements in body composition and physical function. Overall, the findings provide strong evidence regarding the importance of a multidisciplinary approach in COPD management, focusing not only on physical aspects but also on nutritional support to enhance patients' quality of life.We need more research to investigate the connection between nutritional interventions, physical function, and quality of life, and to pinpoint the most efficient methods for enhancing the health of COPD patients. Thus, collaboration among healthcare professionals, including nutritionists and physiotherapists, is crucial to developing integrated care plans that can enhance overall health outcomes for patients.

CONCLUSION

This systematic review concludes that oral nutritional supplementation (ONS) in patients with Chronic Obstructive Pulmonary Disease (COPD) effectively improves body mass index (BMI), functional capacity, and quality of life. A review of nine randomized controlled trials that tested branched-chain amino acids, magnesium-rich whey, and nitrate supplements shows that ONS doesn't have a big effect on BMI, but it does make people much more functional and improves their quality of life.

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