

Obesity and Pulmonary Hypertension

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INTRODUCTION

Obesity is a global public health problem that exacerbates the burden of many health issues including cardiovascular disease, stroke, diabetes, liver disease, and many cancers.¹ From 2017 to 2018 the prevalence of obesity in adults living in the United States was 42.4%.² Obesity is characterized by excessive adipose tissue resulting in increased body weight defined in terms of body mass index (BMI; kg/m²). The World Health Organization defines class I obesity as a BMI of 30 to 34.9 kg/m², class II obesity as a BMI of 35 to 39.9 kg/m², class III obesity as BMI \geq 40 kg/m², class IV obesity as BMI \geq 50 kg/m², and class V obesity as BMI \geq 60 kg/m². Epidemiological data support that there is a link between obesity and pulmonary arterial hypertension (PAH), as 30% to 40% of PAH patients are reported as obese.¹⁻³ One study showed obesity and BMI had no significance to overall mortality rate in patients with PAH) however, there is an age-obesity interaction. PAH patients < 65 years of age with morbid obesity had increased mortality rates.⁴

Adipose tissue is now understood to be an endocrine organ. Excessive amounts of adipose tissue leads to derangement of adipose function and creates the pathological conditions of systemic low-grade inflammation, insulin resistance, and

oxidative stress that may contribute to the progression of vascular remodeling associated with PAH.⁴ Obesity exacerbates cardiac and pulmonary pathologies that precipitate pulmonary hypertension (PH) secondary to left heart disease and PH secondary to hypoxemia as seen in obstructive sleep apnea and obesity hypoventilation syndrome. Hemodynamic, neurohormonal, and metabolic abnormalities associated with obesity can lead to morphological alterations of the cardiac system, predisposing individuals to right and left ventricular dysfunction.⁵ Caring for a PH patient with obesity requires a collaborative approach that involves the patient, family, and multidisciplinary team for improved outcomes, quality of life (QoL), and resilience.^{1,6,7}

NUTRITION

While there is limited research on the impact of nutrition and lifestyle interventions for PH patients, there are well-established nutrition and lifestyle modification recommendations for patients with heart failure and evidence that these interventions improve prognosis.^{4,6,8} Although the pathophysiology of PH and heart failure are different, both diseases often result in malnutrition and muscle wasting, which are linked to exercise intolerance, fatigue, and muscle

weakness.^{6,8,9} There are no established dietary recommendations or nutrient supplementation for PH patients; however, it is recommended that patients with heart disease follow a diet rich in grains, fruits, vegetables, and lean protein; low in sodium; and with restricted fluids and alcohol.^{6,8,10} Consultation with a registered dietician or nutritionist may be warranted to further optimize weight and prevent nutritional deficiencies.^{4,6,7,11}

NUTRITIONAL DEFICIENCIES

There is evidence that PH patients may be likely to suffer from nutritional deficiencies due to a variety of factors including right ventricular (RV) dysfunction, inflammation, and comorbidities such as connective tissue disease which may ultimately contribute to gastrointestinal edema and subsequent malabsorption of nutrients.^{6,8}

Vitamin D and iron deficiencies are more prevalent among PH patients and may lead to disease progression.¹⁰ Vitamin D deficiency is also related to infection, cancer, and respiratory and cardiovascular diseases.^{6,10,11} In one study, PH patients received vitamin D (cholecalciferol) supplementation at a dose of 50 000 IU weekly for 3 months. Results showed significant improvements in 6-minute walk distance and RV size.¹²

Finally, some PH medications, such as prostacyclins, may contribute to nutrition deficiencies in PH patients due to side effects including anorexia, nausea, and diarrhea.⁶ Diuretics are associated

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with thiamine deficiency, impacting energy and carbohydrate regulation, as well as electrolyte imbalances.¹⁰

EXERCISE

General exercise recommendations for adults include at least 150 minutes of moderate physical activity or at least 75 min of high-intensity physical activity every week.¹³ A formal exercise program not only aids in weight-loss efforts, but can improve functional status, slow chronic disease progression, and increase QoL.¹⁴ In PH patients, benefits from exercise programs have been demonstrated by increases in exercise capacity measured by maximal oxygen consumption; increases in 6-minute walk distance; decreases in RV systolic pressure, mean pulmonary arterial pressure, and pulmonary vascular resistance; and improved QoL scores.¹⁵

Previously, the overall consensus for patients with PH was that exercise should be avoided. This stemmed from the belief that it was unsafe for patients with PH to exercise, primarily due to fear of dangerous decreases in cardiac output or even sudden death.^{9,14,16} However, recent guidelines set forth by the European Respiratory Society,¹⁷ as well as recommendations from the 6th World Symposium on PH, emphasize the safety and stress the importance of a regimented exercise program for patients' overall health and well-being.¹⁸

Despite these new recommendations, many studies have demonstrated that patients with PH do not meet the daily physical activity requirements, leading to physical deconditioning. For those patients with a history of obesity, this further exacerbates their sedentary lifestyle.^{9,13,16} Therefore, it is important for providers to encourage and promote exercise training into the patient treatment plan, particularly for those that are overweight.⁹

Pulmonary rehabilitation (PR), is a regimented program that incorporates supervised exercise training based on a multidisciplinary approach to improve a patient's physical and cognitive health, as well as foster long-term, healthy lifestyle changes.^{14,16} The PR structure allows for patients to safely learn appropriate exercise techniques in a controlled environment, focusing on a patient's personal physical capabilities, as well as

recognizing their limitations.¹⁶ Multiple studies suggest that PR programs using a combination of aerobic exercise, resistance training, and inspiratory breathing techniques promote significant benefit in terms of exercise tolerance and functional capacity, which leads to longstanding compliance and sustainability.^{14,16} Despite the known benefits of PR, not all patients have access to such programs, whether it be due to insurance or financial limitations, geographic availability, or even lack of provider support.⁹

When PR is not an option, or after a patient completes PR, there are many innovative technologies in the current market that allow for patients to track their daily physical activity. One such technology is in the form of wearable technology (WT), which allows for daily measurement of total steps, calories, distance travelled, and exercise intensity.^{19,20} These data can be transferred and accessed by a patient's smartphone, watch, or wristband.²⁰ Studies have shown that WT is easy to use, promotes patient self-monitoring and compliance, and increases overall daily movement.^{19,21} One meta-analysis performed by Kirk et al²⁰ found that patients who used WT compared to control groups averaged more than 2500 steps per day, and spent 30 more minutes a day walking, with all WT participants reaching 10000 steps per day. Increased weekly step counts and total active minutes per week both strongly correlate with increased weight loss overall.¹⁹

Patients with PH and obesity will benefit from an exercise regimen of some form. However, it must be emphasized that all patients participating in any form of exercise training should be optimized on PH medical therapy prior to starting. This is not only for success in the benefits of training, but for safety concerns as well.^{14,16,18} Guidance and support from the patient's entire medical team, as well as patient motivation and social network encouragement, is crucial in the success of an exercise-based weight loss program.⁹

LIQUID DIETS

For some PH patients who have difficulty losing weight, a medically supervised meal replacement program that consists of a calorie-restricted liquid diet may be

appropriate. One study done in the United Kingdom showed that a liquid diet was effective in a 12-month weight maintenance program for morbidly obese patients and that patients were able to maintain a weight loss of over 15 kg throughout the study period.²² The diet followed by the participants included an 810 kcal/d liquid diet for 12 weeks followed by reintroduction of low-calorie solid foods that included 30% of energy from fats. Management by a physician specializing in clinical nutrition as well as involvement of a registered dietitian should be incorporated into the plan of care to ensure weight loss is safely achieved.

THE ROLE OF BARIATRIC SURGERY

Bariatric surgery (BS) is an effective therapy for morbidly obese patients, resulting in significant weight loss.^{23,24} This is particularly important in patients who struggle with meaningful weight loss and in select cases where candidacy for eventual lung transplantation may be denied due to morbid obesity.

PH patients may not be considered candidates for BS as they are considered medically high risk for adverse outcomes following noncardiac surgical procedures.^{24,25} However, case reports and recent studies have shown improved outcomes following BS in carefully selected patients with PH, including reducing the need for PH medications, recovery of RV function, and improvements in oxygen requirements, functional status, and insulin resistance.²⁶⁻²⁹ In a retrospective study, Sheu et al²⁸ compared patients who underwent BS to BMI-matched individuals. Primary outcomes in this cohort were significantly improved in the surgical group (those with BS) which consisted of decrease in the use of pulmonary vasodilator and diuretic medications, decreased need for home oxygen, and improvement in mean pulmonary arterial pressure. Although there were 7 significant postoperative complications cited, there were no mortalities. Similarly, Hanipah et al²⁹ reported favorable results in a retrospective review of 61 patients with PH and a mean BMI of 49 who underwent gastric bypass. All patients had a mean RV systolic pressure ≥ 35 mm Hg on Doppler echocardi-

gram. The 30-day complication rate was 16%, with 3 patients having major early pulmonary complications: respiratory failure (2 patients) and pulmonary embolism (1 patient). There was no 30-day mortality reported. One year follow-up showed a reduced mean BMI of 36 kg and a significant improvement in echocardiographic RV systolic pressure from 44 to 40 mm Hg. Employment of a multidisciplinary approach at an experienced center, including a bariatric surgeon, pulmonologist, cardiologist, cardiac anesthesiologist, dietician, and psychologist was cited as a possible factor related to the positive outcomes reported.²⁹

SUMMARY

Obesity is a global health epidemic that affects a large portion of patients with PH, negatively affecting QoL. Meaningful weight loss can be difficult to achieve for this patient population; thus, a multidisciplinary approach should be employed when designing a weight loss program for PH patients. Interventions should include strategies that incorporate both nutrition and safe exercise training. WT has proven to be effective in improving patients' awareness of their physical activity habits and overall compliance. Implementation of a medically supervised liquid diet and/or BS have proven successful in select cases of morbid obesity. Providers should incorporate weight loss strategies for the obese PH patient to include exercise and nutrition as part of a holistic approach to improve overall health outcomes.

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