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REVIEW

Improvement in Pulmonary Hypertension Following Metabolic and Bariatric Surgery: a Brief Review and Meta-analysis

Fidele Kakule Kitaghenda[1] · Sakarie Mustafe Hidig[2]

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Abstract

We reviewed the available evidence on the outcome of metabolic and bariatric surgery (MBS) in patients with pulmonary hypertension (PH). Five studies examining 174 patients were included; the mean age was 54.5 ± 9.27 years; the mean BMI before surgery and at the end of follow-up were 47.2 ± 5.95 kg/m^2 and 37.4 ± 2.51 kg/m^2, respectively. Furthermore, the results showed a significant decrease in the right ventricle systolic pressure (RVSP) after MBS with a mean difference of 10.11% (CI 95%: 3.52, 16.70, $I^2 = 85.37\%$, $p = < 0.001$), at 16.5 ± 3.8 month follow-up with a morbidity rate of 26% and 0 mortality. Thirty-day postoperative complications included respiratory failure, pulmonary embolism, pulmonary edema, and anastomotic leak. There appears to be a significant improvement in PH with a decrease in medication requirements after MBS.

Keywords Pulmonary hypertension · Pulmonary high blood pressure · Pulmonary systolic pressure · Bariatric surgery · Obesity surgery · Metabolic surgery · Roux-en-Y gastric bypass · One anastomosis gastric bypass · Sleeve gastrectomy · Adjustable gastric band · Biliopancreatic diversion with duodenal switch

Introduction

Pulmonary hypertension (PH) is characterized by an increase in the mean pulmonary arterial pressure of more than 20 mmHg at a resting state using the right heart catheterization (RHC). The causes of PH are diverse and have been clinically classified into five groups based on the etiology: group 1, PH from idiopathic and hereditary causes or pulmonary arterial hypertension (PAH); group 2, PH related to left-sided heart disease; group 3, PH associated with lung disease; group 4 comprises PH related to thromboembolic disorders; and group 5 includes heterogeneous conditions. The pathogenesis of this disease is multifactorial involving distinctive pathways; namely, obstructive sleep apnea (OSA), insulin resistance, metabolic syndrome, and obesity. Moreover, PH is known to be a major risk factor associated with high mortality and morbidity after cardiac and non-cardiac operations [1–5].

The current management of PH focuses on the undelaying causes and advanced therapies that arrest the disease progression with limited impact on survival. Furthermore, the morbidity and mortality rates of PH patients undergoing any kind of operation are quite high; the estimated morbidity and mortality rates among PH patients undergoing non-cardiac surgery ranges from 14 to 42% and 1 to 18%, respectively. However, the outcome of PH patients with obesity undergoing metabolic and bariatric surgery (MBS) has not been explored extensively, yet these patients could be one of the higher-risk population groups predisposed to PH [6–11].

A link between PH and obesity has been demonstrated with a minimal understanding; one of the mechanisms behind the association between PH and obesity is mediated by dysfunctional adiposity through excessive production of adipocytokines causing a state of systemic low-grade inflammation which

Key points

1. PH is a complex disease that may be associated with obesity.
2. MBS significantly reduces the RVSP in PH patients with obesity and medication requirements.
3. MBS was associated with a fairly acceptable postoperative morbidity and mortality in PH patients. A multidisciplinary team approach is necessary for better outcomes in PH patients after MBS.

✉ Fidele Kakule Kitaghenda
kfidelenever@icloud.com

[1] Department of Gastrointestinal Surgery, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, Jiangsu 221002, People's Republic of China

[2] Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, The Fourth Affiliated Hospital, Zhejiang University School of Medicine, Yiwu, Zhejiang Province 322000, People's Republic of China

may induce structural and functional changes in the pulmonary perivascular adipose tissue (PVAT). These alterations in the PVAT contribute to increased secretion of vasoconstrictors and proinflammatory factors leading to PH [12–14]. Data on the association between PH and obesity is limited; therefore, the prevalence of this condition within the obese population has not been quantified; based on a previous single-center study report, the incidence of PH was 38% in patients with obesity. Similarly, a recent study examining the association between obesity and PH found that higher BMI (obesity classes 1, 2, and 3) was associated with all forms of PH based on the hemodynamic definitions (including pre-capillary PH, post-capillary, and combined pre-and post-capillary PH) [15, 16].

MBS has proven to be effective in the treatment of obesity and has been shown to have improvement in cardiovascular disease, hypertension, insulin resistance, and OSA [17–27]. Given the efficacy of MBS in the resolution and improvement of risk factors associated with PH, the effect and safety of MBS in PH patients with obesity were of much interest in investigating. To the best of our knowledge, no study has evaluated available evidence on the outcome of PH patients with obesity after MBS.

We aimed to investigate the English language literature on the outcome of PH patients with obesity following MBS in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.

Material and Methods

This systematic review was conducted in accordance with the guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol (PRISMA) 2015 statement [28]. All stages of literature search, study selection, data extraction, and quality assessment were performed independently. Any disagreement was resolved by discussion and consensus with a second reviewer (HA). This systematic review and meta-analysis was registered in the Prospective Register of Systematic Reviews (PROSPERO), with registration ID: CRD42024509571 (available at https://www.crd.york.ac.uk/PROSPERO/#recordDetails).

Literature Search

A systematic search was performed using an electronic search in the PubMed database, Google Scholar, and the Cochrane Library. The appropriate key terms and free text field search were performed for "Pulmonary hypertension," "blood pressure in pulmonary arteries," "pulmonary systolic pressure," "pulmonary blood pressure," "Bariatric surgery," "Metabolic surgery," "Sleeve gastrectomy," "Roux-en-Y gastric bypass," "gastric band," gastric plication," and "Biliopancreatic diversion." The search included all study designs, with further studies not captured by the search identified via bibliographic cross-referencing. Titles and abstracts were screened independently.

Inclusion Criteria

Included studies were limited to adults (≥ 18 years) who met the international criteria for bariatric surgery [19]; and who underwent a primary Roux-en-Y gastric bypass (RYGB), one anastomosis gastric bypass (OAGB), sleeve gastrectomy (SG), biliopancreatic diversion with duodenal switch (BPD-DS), the adjustable gastric band (AGB) and other MBS. Prospective and retrospective observational studies, randomized clinical trials, and non-comparative clinical studies were included. The date ranges from any time and the last search was performed in February, 2024.

Exclusion Criteria

Only studies published in English were included in the systematic review. Abstracts, conference articles, opinion pieces, editorial letters, single case studies, reviews, and meta-analyses were excluded from the final review. Nonhuman studies were not included. Moreover, studies without appropriate data published related to this study's primary and secondary outcomes were also excluded.

Data Extraction

Data from the included studies were author's name, year of publication, the mean age of patients, mean preoperative and postoperative body mass index, total population number and those diagnosed with pulmonary hypertension preoperatively, follow-up time, type of surgery, and the results of each study was recorded. To ensure accuracy, the data extraction process was performed independently and reviewed by an appointed second party.

Statistical Analysis

The data were retrieved as mean and standard deviation. In studies where the medians and interquartile range were given for the RVSP, the formula suggested by Hozo et al., Luo et al., and Wan et al. [29–31] was used to convert these variables to mean and standard deviation. The main measure of effect was the mean difference between preoperative and postoperative RVSP with a 95% confidence interval. The I^2 statistic was used to calculate the heterogeneity, and given an I^2 of greater than 50% of the included studies in this review, a random effect analysis was employed. Small study publication bias effects were assessed using the funnel plot and Egger's regression test. The averages of quantitative variables were reported according to studies. The threshold for statistical significance was $p = < 0.05$. Data analysis was performed using the Stata/SE 18.0 version (StataCorp LLC).

Results

A total of 230 studies were retrieved from the initial search from the database. After screening the study's title and abstracts, 31 qualified for further analysis. 23 studies were duplicates, and 2 lacked enough data and, therefore, were excluded; finally, 5 studies met the final inclusion criteria. The PRISMA flowchart of the current study is presented in Fig. 1.

Descriptive Characteristics

Among the 5659 patients who underwent MBS, 174 patients had PH, therefore, were included in this systematic review and meta-analysis. The mean age of the patients was 54.5 ± 9.27 years; the mean BMI before surgery and at the end of the follow-up were 47.2 kg±5.95/m^2 and 37.4 ± 2.51 kg/m^2, respectively. The included studies were retrospective/prospective cohorts, case series, and matched cohort studies. The basal characteristics of the patients included in this review are shown in Table 1.

Comorbidities and Treatment

The included patient preoperative comorbidities were diabetes mellitus (1.8%), hypertension (86.7%), dyslipidemia (43%), obstructive sleep apnea (46.1%), reflux disease (1.21%), chronic obstructive pulmonary disease (36.9%), non-alcoholic fatty liver (3.7%), renal impairment (43.3%), coronary artery disease (3.5%), heart failure (0.6%), and hypothyroidism (3.7%). Obesity and related comorbidities were treated with

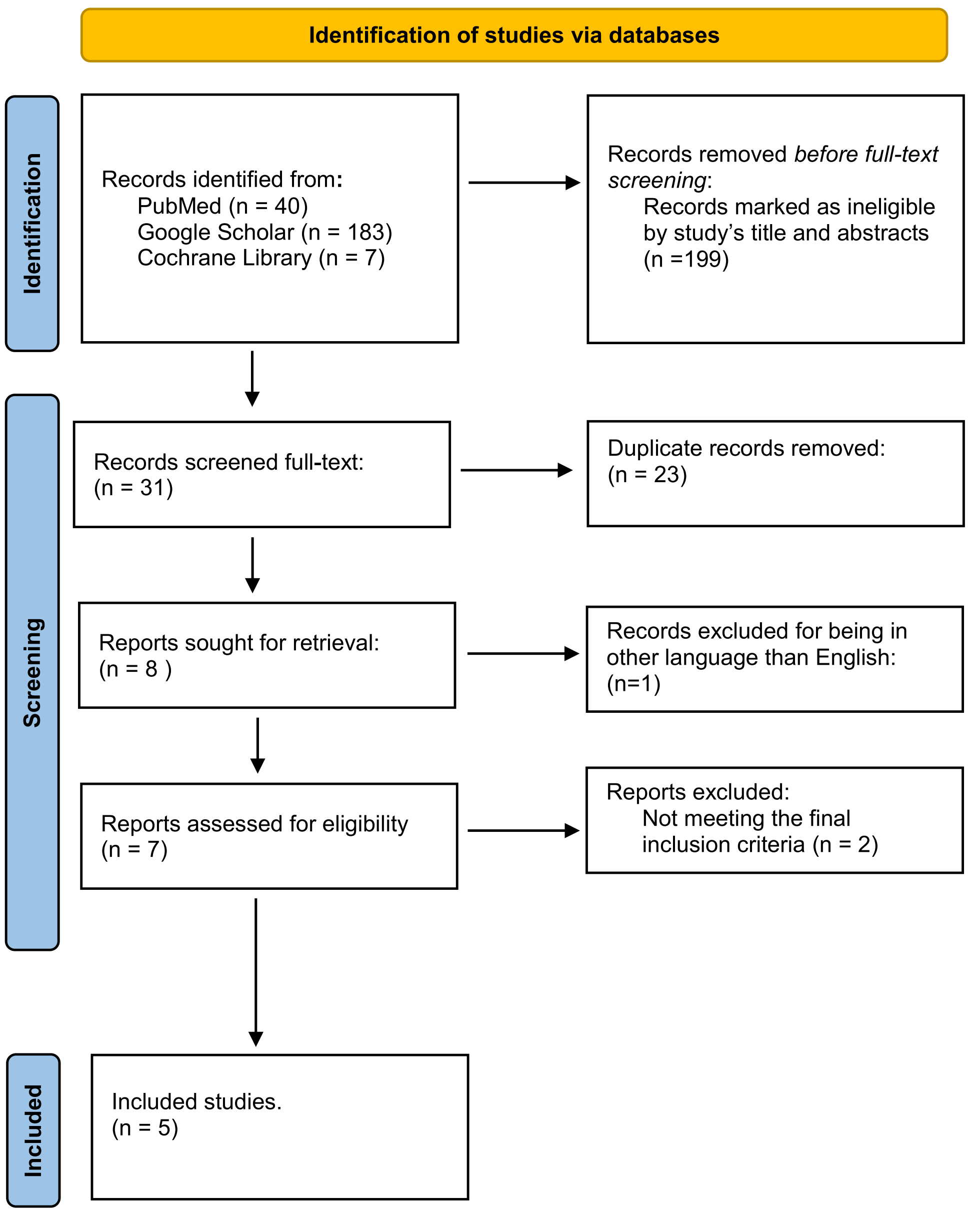

Fig. 1 PRISMA flowchart of literature search and data extraction and selection (*n* represents the number of articles included)

Table 1 Basal characteristics of included studies in this review

Author	Age	Overall (*n*)	Study design	Pre-op BMI (kg/m^2)	Post-op BMI (kg/m^2)	Imaging technique	Surgery
Valencia et al. (2004) [29]	37.9	65	Case serries	56.5	39.2	Echo	VBG, RYGB, distal-RYGB
Sheu et al. (2015) [28]	55.8	20	Retrospective chart review	43.7	-	Echo, RHC, pulmonary function test, chest CT, 6-min walk test	SG, RYGB
Hanipah et al. (2018) [36]	58	5298	Retrospective chart review	49	38	Echo, RHC	RYGB, SG, AGB, BGP
Salman et al. (2020) [31]	49.5	256	Prospective study	45.9	33.8	Echo	SG
Valera et al. (2020) [30]	61.5	20	Retrospective cohort study	41.01	38.99	Echo	-

Echo Echocardiogram; *RHC* Right heart catheterization; *CT* Computerized tomography; *BMI* Body mass index; *RYGB* Roux-en-Y gastric bypass; *SG* Sleeve gastrectomy; *AGB* Adjustable gastric band; *VBG* Vertical banded gastroplasty; *BGP* Banded gastric plication

Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), adjustable gastric band (AGB), vertical banded gastroplasty (VBG), and banded gastric plication (BGP). The etiology of PH in patients included in this review was reported in two studies, one study reported patients diagnosed with PH from all etiology (PH groups 1 to 5) [32], and in the other study with PH groups 1, 2, 3, and 5) [33]. The assessment of the RVSP was performed using the right heart catheterization (RHC) and echocardiogram (ECHO) (Table 1).

Outcomes

The random pooled analysis of 5 studies examining 174 patients demonstrated that RVSP decreased significantly after BS in patients with preoperative PH with a mean difference of 10.11% (CI 95%: 3.52, 16.70, $I^2=85.37\%$, $p=<0.001$) (Fig. 2). The improvement of pulmonary hypertension was observed at 16.5 ± 3.8-month (range 13–22 months) follow-up period on average. Furthermore, During the 30-day postoperative period, the morbidity rate was 26% and the mortality 0 during follow-up time in all studies. Major complications assessed in a few patients were respiratory failure, pulmonary embolism, pulmonary edema, and anastomotic leak (Table 2); furthermore, pneumonia, pleural effusion liver abscess from cholecystitis, and upper gastrointestinal bleeding from a gastrojejunal ulcer at 1-year follow-up [28].

Publication Bias

To assess the potential impact of publication bias, we initially performed the funnel plot for studies symmetry, which was not easy to interpret since there were few studies (Fig. 3). Moreover, the results of Egger's regression test revealed no statistically significant evidence of publication bias ($t=0.17$, $p=0.88$).

Discussion

The management of PH is quite difficult, and the best approach has been through the treatment of the etiology of PH, diuretic therapy, oxygen supplementation, and advanced

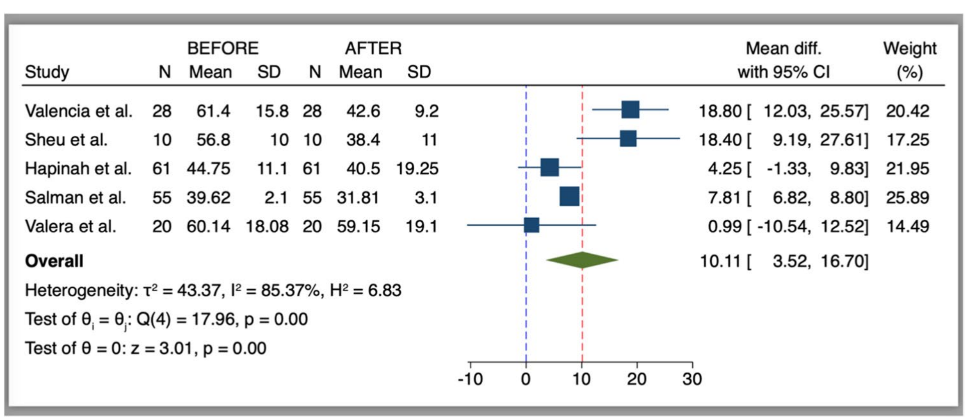

Fig. 2 Effect of bariatric surgery on RVSP in PH patients with obesity

Table 2 RHC, Echo parameters, and postoperative outcomes of PH patients

Author	PH (*n*)	Pre-op RVSP (mmHg)	Post-op RVSP (mmHg)	*P*-value	Follow-up time (months)	Morbidity	Mortality	30-day postop complications
Valencia et al. (2004) [29]	28	61.4	42.6	< 0.02	13.7	-	0	-
Sheu et al. (2015) [28]	10	56.8	38.4	0.02	21	4 (40%)	0	Direct ICU readmission, anastomotic leak
Hanipah et al. (2018) [36]	61	44.75	40.5	0.03	22	10 (16%)	0	Respiratory failure, pulmonary embolism, anastomotic leak
Salman et al. (2020) [31]	55	39.62	31.81	< 0.001	15	18 (32%)	0	Respiratory failure, pulmonary embolism, pulmonary edema, pneumonia
Valera et al. (2020) [30]	20	60.14	59.15	0.87	-	-	-	-

PH Pulmonary hypertension; *mmHg* Millimeters of mercury; *RVSP* Right ventricle systolic pressure

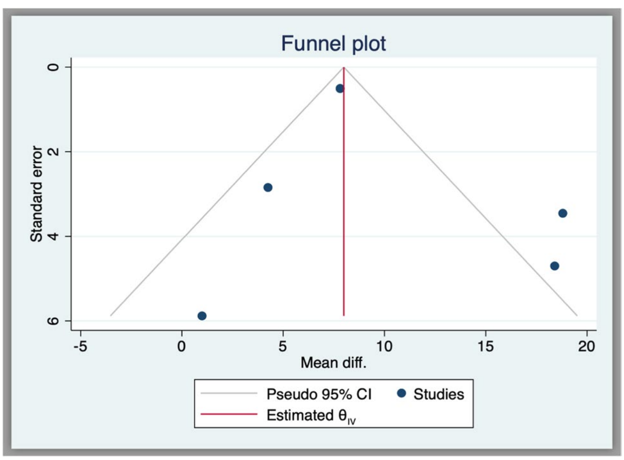

Fig. 3 Bias publication assessment in the funnel plot

therapies including prostacyclin, endothelin receptor antagonists, etc., which have been shown to arrest the progression of this disease from worsening without major improvement [33]. However, based on our findings, a significant improvement in PH was observed after MBS in the context of a decrease in the RVSP after surgery (Fig. 2, Table 2) [34, 35]. Furthermore, a decrease in PH medication requirement was observed in PH patients after surgery. A study by Sheu et al. compared the improvement of PH among patients with PH who underwent MBS ($n = 10$) versus those who received medical treatments ($n = 10$) at a follow-up of 21 months; the authors noticed a drastic reduction of the vasodilator and diuretic medication requirement in the surgical group than in the medical group (67% versus 0) and (86% versus 13%), respectively [33]. Similar findings were reported by Salman et al. where not only MBS decreased the requirement of PH medications but also a decrease in oxygen supplemental requirements in patients who underwent MBS [32], suggesting that MBS could be a more effective and better management tool in some patients with PH needing surgery. Therefore, larger randomized clinical studies with long-term follow-up are needed to demonstrate the superiority of MBS in the management of PH versus that of patients with PH taking medication only and to determine whether complete reversal of certain subgroups of PH can be possible after MBS.

PH has been associated with certain conditions, namely, coronary artery disease (CAD), systemic hypertension, and OSA, which are known risk factors for PH and have been shown to resolve or improve after MBS. A previous study comprising 113 patients found that MBS reduced the risk of CAD by about 29% [36]. A meta-analysis consisting of 2141 bariatric patients with hypertension reported 78.5% improvement or complete remission after MBS [37]. The UK National Bariatric Surgery Registry (NBSR), in their study of 4015 bariatric patients diagnosed with OSA, showed a significant resolution of 59.2% of patients after MBS [38]. This suggests that the efficacy of MBS in the remission of certain risk factors associated with PH may partially contribute to the improvement in PH after surgery. Moreover, it has been speculated that MBS may have hormonal and metabolic effects that act directly on pulmonary vessels [33, 39]. The mechanism by which MBS contributes to the improvement of PH is not understood; therefore, more studies are needed to elucidate the potential beneficial effects of MBS on PH.

PH is a complex and serious disease and has been reported with higher morbidity and mortality rates in cardiac and non-cardiac surgeries. Based on our findings, MBS was associated with a relatively lower morbidity rate (26%) and 0 mortality after surgery which were significantly lower than those from other non-cardiac surgery reports with morbidity and mortality estimation rates of up to 42% and 18%, respectively [6–11]. Furthermore, the largest National Inpatient Sample (NIS) database, consisting of 10,811 PH patients who underwent non-MBS matched with 3605 PH patients with a history of MBS, reported a higher in-hospital mortality rate of 3.4% in the non-MBS group than a moderately lower rate of 2.3% in the MBS group with a difference that amounted to statistical significance ($P = 0.001$); their study further suggested that MBS was independently associated with 34% reduced odds of in-hospital mortality in PH patients [36]. These findings showed that MBS could result in a not-so-bad outcome in this high-risk group. Although there was no mortality reported in the studies included in this review, care must be taken since mortality cases have been reported in PH patients with a history of MBS and given that these patients are still at a higher risk.

A possible reason leading to better outcomes in PH patients after MBS could be the multidisciplinary management of patients with obesity perioperatively, consisting of experienced bariatric surgeons, pulmonologists, anesthesiologists, cardiologists, and postoperative care with dietetic recommendations, nutrient supplementation, counseling, regular visits for a check-up as reported in a previous study [40]; all of which may enhance the safety and long-lasting efficacy of MBS in PH patients after surgery. Given that MBS has increasingly been performed globally in recent years, multidisciplinary management of patients with obesity is becoming a common practice in bariatric centers and has strongly been recommended [41, 42].

The causes of PH have been clinically classified into five groups based on the etiology as mentioned previously [1–5]. Among the five studies included in this review, only two studies reported the etiology of PH in their patients, who were diagnosed with PH of all etiology groups, whereas the impact of MBS on specific subgroups of PH was not examined. Given these limitations, we could not determine whether specific subgroups of PH respond better than others to MBS or which subgroups of PH resulted in the improvement of PH seen in this study. Moreover, some authors have suggested that there seems to be an additional group of PH that is driven by obesity, mediated by chronic inflammation commonly found in patients with obesity [43–49]. This speculation could not be confirmed merely from the findings of this study; more studies are needed before any confirmation can be made. Conversely, an overlap between the prevalence of obesity and PH of different etiologies has been shown, suggesting that obesity could play a role in these. A study by Frank et al. consisting of 8940 patients found that class 2 obesity was associated with a 16% increase in precapillary PH and 36% in postcapillary PH [16]. A meta-analysis of 18,000 patients with CAD revealed a significant correlation between higher BMI and increased risk of CAD which has been shown to lead to left-sided heart disease and possibly PH [25, 26, 50].

Furthermore, a previous study investigating the characteristics of chronic thromboembolic PH between Austrian and Japanese found that obesity was prevalent in Austrian PH patients [51]. Therefore, it could be reasonable to think that after MBS, PH from different etiology may be affected positively and enhance possible improvement. More studies are needed to determine the link between obesity and PH.

The golden standard for diagnosing PH is through the right heart catheterization (RHC) which can directly measure the pulmonary arterial pressure. However, this method is invasive, and costly, with potentially fatal complications [1–5]. In this regard, echocardiography (ECHO) has been preferred which mainly estimates the probability of PH by estimating the systolic pulmonary arterial pressure (sPAP) and combining other manifestations. Due to its noninvasive nature, convenience, and accuracy, the ECHO has widely been used as seen in a few studies included in this review, whereas the role of ECHO in the diagnosis of PH remains controversial [52–54]. A more recent umbrella review study of 13 systematic reviews and meta-analysis on the diagnostic and prognostic value of ECHO in PH suggested that the ECHO can be used clinically for the diagnosis of PH due to the sensitivity of sPAP in detecting PH [55]. Therefore, there is a need for more clarification and consensus on the role of ECHO in the diagnosis of PH.

While a significant improvement in RVSP and a decrease in medication and oxygen requirements were assessed in PH patients following MBS, a considerable postoperative morbidity rate of 26% was found in this study, suggesting that the risks of surgical intervention should not be overlooked. Pulmonary complications were commonly seen in PH patients in this study during the 30 days following MBS (Table 2), which could have been due to the susceptibility of these patients. A previous meta-analysis showed that PH is independently associated with a higher risk of pulmonary embolism (OR = 4.16) in patients undergoing non-cardiac surgery, indicating that there could be a consideration for venous thromboembolic prophylaxis in this group of patients [56], whereas the potential causes of other complications such as pulmonary edema and respiratory failure were not indicated in the studies included in this review. Moreover, in one study, major complications such as pneumonia, pleural effusion, liver abscess due to cholecystitis, upper gastrojejunal bleeding, etc., were frequently seen after RYGB at 1-year follow-up in PH patients, highlighting the fragility of these patients with a medically complex disease when undergoing surgery [28]. These findings did suggest that MBS in PH patients should be undertaken in a multidisciplinary center with more experienced surgical, cardiopulmonary, critical care, and interventional radiology, where the rate of rescue from complications is higher [57]. Given limited data from the available evidence and the results of this study, we could not determine the course of action in terms of management of these complications, namely, anticoagulation medications or the implementation of a specific enhanced recovery after bariatric surgery (ERABS) protocol in PH patients after MBS; therefore, more studies are needed.

Although this study was the first to investigate available evidence on the outcome of PH patients following MBS, it had a few limitations worth mentioning: First, a small number of included studies with small sample sizes could have impacted the between-study heterogeneity and limited our understanding of the outcome of MBS in PH patients. Second, most studies were of retrospective design without a control group to further validate the outcome of MBS in PH patients. Third, there was a quite high attrition rate during the follow-up in a few studies which could have been due to any reasons (death, cardiac event, etc.), and influenced the results.

Conclusion

The management of PH can be challenging. Based on our findings, there appears to be a significant improvement in PH following MBS, a decrease in PH medication requirements, and no mortality; nevertheless, with a not-so-low postoperative morbidity. Therefore, a multidisciplinary team approach is necessary to achieve better outcomes in this high-risk group of patients when undergoing MBS. Given the limitations of this study, the results should be interpreted with care.

Declarations

Ethics Approval For this type of study, formal consent is not required.

Conflict of Interest The authors declare no competing interests.

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