A Meta-Analytic Structural Equation Modeling (meta-SEM) for the Changes in Body Mass Index (BMI), Apnea-Hypopnea Index (AHI), and Oxygen Saturation (SPO2) after Bariatric Surgery

Eghbali F. MD[*], *Ahmadi S. A. Y. MD*[**], *Jahanshahi F. MD*[***], *Madankan A. MD*[****] *Jaliliyan A. MD*[*****], *Mosavari H. MD*[***], *Bighdeli A. H. MD*[******]

Abstract:

Introduction & Objective: In spite of the existence of evidence regarding the role of bariatric surgery on body mass index (BMI) reduction, improving apnea-hypopnea index (AHI) and enhancement of oxygen saturation (SPO2), there was no evidence regarding a causal network of these variables. The present study was aimed to investigate the associations using structural equation modeling (SEM).

Materials & Methods: A secondary study was conducted using SEM on the aggregate data of the literature. A directed acyclic graph (DAG) was designed and SEM was performed for verification of the hypothesized DAG at $P < 0.1$. This graph included BMI as an independent variable, percentage of oxygen saturation as a dependent variable, and AHI as a mediating variable.

Results: A total of 684 cases were studied. On the average, 12.1 kg/m2 reduction was observed for BMI, 20.0 unit reductions was observed for AHI and 2.1% increase was observed for Mean of SPO2. According to SEM, the effect of reducing the BMI on the reduction of the AHI was positive (effect coefficient = 0.28; that is, a decrease of one unit in the BMI led to a decrease of 0.28 units in the AHI) and the effect of decreasing the AHI was also positive on improving the average percentage of oxygen saturation (effect coefficient = 0.13; i.e., a decrease of one unit in the AHI led to an improvement of 0.13 units in the average percentage of oxygen saturation). Thus, the product of these two paths showed that in the indirect path, each unit reduction in body mass index leads to a 0.04% improvement in the average percentage of oxygen saturation. The coefficient of the direct path was 0.07, which means that the contribution of the mediating path to the total effect is 0.335 (about one third).

Conclusions: AHI changes were associated with BMI changes, but the association of SPO2 changes with BMI and AHI changes were not tangible. It seems that the variation of SPO2 changes may be explained by some other variables.

Key Words: Obesity, Obstructive Sleep Apnea, Metabolic Surgery, Meta-Analysis, Statistical Modeling

[*] Associate Professor of General Surgery, Iran University of Medical Sciences, Rasoul Akram Hospital
[**] Research Assistant & General Practitioner, Iran University of Medical Sciences, Preventive Medicine and Public Health Research Center, Psychosocial Health Research Institute
[***] General Practitioner, Iran University of Medical Sciences, Rasoul Akram Hospital
[****] Assistant Professor of General Surgery, Iran University of Medical Sciences, Rasoul Akram Hospital
[*****] Research Assistant & General Practitioner, Iran University of Medical Sciences, Rasoul Akram Hospital
[******] Resident of General Surgery, Iran University of Medical Sciences, Rasoul Akram Hospital
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Corresponding author: Dr. Amirhossein Bighdeli
Tel: 88580662

E-mail: Ah.bigdeli8766@gmail.com

Background and Objective

Obstructive Sleep Apnea (OSA) is a medical condition characterized by recurrent episodes of partial or complete airway obstruction during sleep.[1] The resultant hypercapnia and hypoxia, combined with the frequent sleep-wake cycles associated with OSA, can lead to significant complications across cognitive, metabolic, and cardiovascular domains.[2,3] Recognized as a major public health concern, OSA affects approximately 5% to 15% of the population.[4] Numerous studies have demonstrated that untreated OSA can precipitate both fatal and non-fatal cardiovascular events, heighten the risk of sudden death during sleep, and elevate overall mortality rates.[5,6]

Individuals with obesity are among the populations at greatest risk for OSA. Obesity, typically defined by a high body mass index (BMI), is associated with a range of complications, including gastroesophageal reflux disease, infertility, cardiovascular disorders, non-alcoholic fatty liver disease, and varying degrees of respiratory and upper airway dysfunction, including OSA.[7-11] Bariatric surgery is widely regarded as the most effective intervention for severe obesity and holds the potential to mitigate its associated complications.[12]

A variety of known risk factors contribute to the development of OSA, particularly in obese individuals. Factors such as abnormal craniofacial anatomy and a reduction in the pharyngeal airway's lumen size due to excess body fat significantly contribute to the risk of developing OSA.[13] There are several treatment options available for OSA, encompassing both surgical and non-surgical approaches, including Continuous Positive Airway Pressure (CPAP), Mini-Implant Assisted Rapid Maxillary Expansion (RME), and surgical procedures such as Uvulopalatopharyngoplasty.[14] Among these, obesity remains the most critical risk factor for OSA, and weight loss has been shown to improve the condition. Research indicates that bariatric surgery may alleviate symptoms associated with OSA.[15] Consequently, it is recommended that OSA screening be incorporated into bariatric surgery programs, with preoperative management of OSA being strongly advised.

In light of the existing evidence and clinical recommendations, it is imperative to investigate the effects of bariatric surgery on the amelioration of obstructive sleep apnea (OSA) by assessing its impact on the Apnea-Hypopnea Index (AHI) and arterial saturation (SpO2). A suitable methodological approach for this investigation is Structural Equation Modeling (SEM), which facilitates mediation analysis. The hypothesis posits that bariatric surgery may enhance oxygen saturation levels by mediating improvements in the Apnea-Hypopnea Index. Despite the extensive body of knowledge on this subject, there is currently a lack of documented causal networks elucidating the effects of bariatric surgery on obstructive sleep apnea and oxygen saturation.

Thus, the present study aims to explore the relationship between changes in body mass index, the Apnea-Hypopnea Index, and percentage oxygen saturation utilizing meta-analytic Structural Equation Modeling (Meta-SEM), with particular emphasis on the mediating role of the Apnea-Hypopnea Index. It is anticipated that alterations in body mass index will significantly influence percentage oxygen saturation.

Materials and Methods

Study Design

This investigation constitutes a secondary study employing meta-analysis through Structural Equation Modeling on aggregated data sourced from various scientific literature. A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 202 statement, where applicable. A meta-analytical methodology was adopted for the synthesis and modeling of the data.

The criteria for inclusion in this study were established as follows: (a) participants aged 18 years and older, (b) studies investigating surgical interventions including Roux-en-Y Gastric Bypass (RYGB), One Anastomosis Gastric Bypass (OAGB), and Laparoscopic Sleeve Gastrectomy (LSG), (c) studies that performed polysomnography assessments both preoperatively and postoperatively, and (d) studies that reported critical parameters such as mean arterial oxygen saturation, minimum oxygen saturation, and the Apnea-Hypopnea Index (AHI).

The exclusion criteria encompassed studies that (a) did not report the specified outcomes, (b) were published in languages other than English, (c) contained data that could not be reliably extracted, (d) involved non-human subjects, (e) were not published in a peer-reviewed journal of international repute, and (f) did not provide the full text of the article. Articles that met any of these exclusion criteria were excluded from the study.

Search Strategy

A comprehensive search was executed in March 2023 across the electronic databases of PubMed, Scopus, and Web of Science. A combination of keywords, including "bariatric surgery" and "sleep apnea," was employed without restrictions on publication dates. To ensure the inclusion of all relevant studies, both backward and forward citation analyses were conducted utilizing the Web of Science database. This involved the identification of studies that cited the source article as well as those that were cited by previously included studies. Additionally, a review of existing literature reviews on the subject was conducted to identify any potentially overlooked eligible studies.

Selection of Articles

Initially, two independent researchers screened the titles and abstracts of studies identified through the electronic search, discarding those that did not meet our criteria. One of the authors also performed both backward and forward citation searches, in conjunction with reviewing prior literature reviews for pertinent studies.

Subsequently, two independent researchers undertook a comprehensive full-text review of all selected studies based on the aforementioned eligibility criteria. Any discrepancies between the reviewers were resolved through discussion, or by consulting a third reviewer to reach a consensus.

The results of the search were systematically recorded using EndNote reference management software, version 9 (published in 2013, Clarivate, Philadelphia, Pennsylvania, USA). The "Find Duplicates" feature in EndNote was employed to identify and eliminate duplicate entries, with any remaining duplicates removed manually.

Data Extraction

Data extraction from the included studies was conducted by two independent reviewers utilizing a pre-designed Excel spreadsheet. The extracted data encompassed: (a) year of publication, (b) country of origin for the study, (c) sample size, (d) duration of follow-up, (e) type of surgical procedure, (f) characteristics of participants, and (g) measured outcomes (e.g., body mass index, Apnea-Hypopnea Index, and oxygen saturation levels) both preoperatively and post-bariatric surgery.

Quality Assessment

Full-text articles underwent a meticulous evaluation by a member of the project team specializing in quality assessment, utilizing the scoring tool from the Centre for Evidence-Based Medicine (CEBM) tailored for prognostic studies. This assessment tool is designed to evaluate the methodological quality and potential bias in studies predicting future outcomes.

Table 1- Characteristics of included studies

Author	Year	Country	Sample size	Follow-up period	Surgery type	Quality score	Weight
Fritscher	2007	Canada	12	24	Classic Bypass	3.5	13.4
Lettieri	2008	United States	24	12	Single Anastomosis Bypass	3	23
Krieger	2012	United States	20	12	Single Anastomosis Bypass	3.5	22.4
Fredheim	2013	Norway	71	12	Classic Bypass	3.5	79.5
Aguiar	2014	Brazil	16	3	Single Anastomosis Bypass	2.5	12.8
Bae E.K.	2014	South Korea	10	13.9	Classic Bypass	3.5	11.2
Ravesloot	2014	Netherlands	110	7.7	Classic Bypass, Single Anastomosis Bypass, Sleeve Gastrectomy	3	105.6
Jianyin Zou	2015	China	44	6	Classic Bypass	3.5	49.3
Xiao Jiao	2016	China	39	9	Classic Bypass	3	37.4
Shaarawy	2016	Egypt	22	12	Sleeve Gastrectomy	3	21.1
Suliman	2016	Egypt	20	8.25	Sleeve Gastrectomy	3.5	22.4
Peromaa	2017	Finland	132	12	Classic Bypass	3	126.7
Mashaqi	2018	United States	9	18	Classic Bypass, Sleeve Gastrectomy	2.5	7.2
Chen	2021	China	67	9.7	Sleeve Gastrectomy	3	64.31
Kaar	2020	United States	23	12	Classic Bypass	3.5	25.75
Kalra	2005	United States	34	5.1	Classic Bypass, Sleeve Gastrectomy	2.5	27.19
Kara	2020	Türkiye	31	12	Sleeve Gastrectomy	3.5	34.71
Average (weighted)				10.3			
Total			684				684

Table 2- Results of target variables in included studies

Author	Body Mass Index Before Surgery	Body Mass Index After Surgery	Apnea-hypopnea index before surgery	Apnea-hypopnea index after surgery	Mean arterial oxygen saturation before surgery	Mean arterial oxygen saturation after surgery
Fritscher	55.5	34.1	46.5	16	85.7	94.5
Lettieri	51	32.1	47.9	24.5	*91.84	*94.55
Krieger	47.18	35.62	34.2	19	95.15	95.39
Fredheim	47.5	33.5	29.3	7.7	92.80	95.10
Aguiar	48.15	36.91	15.65	6.26	93.30	94.3
Bae E.K.	39.9	26.9	51	9.3	93.5	95.8
Ravesloot	45.4	36.3	39.5	15.6	92.20	94.40
Jianyin Zou	31.1	24.4	22.4	7.1	93.40	95.50
Xiao Jiao	3.037	24.24	13	3	*94.05	*95.08
Shaarawy	48.2	35.9	55.8	12.8	*88.10	*95.45
Suliman	60.51	41.49	18	10	*92.86	95
Peromaa	43.9	33	27.6	9.9	92	93.30
Mashaqi	49	30.3	40.6	6.9	90.40	94.2
Chen	42.6	31.9	31.9	13.3	*92.84	*94.84
Kaar	50.6	*35.1	24.7	2.6	92.6	92.80
Kalra	60.8	41.6	9.1	0.65	94.5	95.50
Kara	49.8	33.2	36.1	10.3	91.5	94
Average (weighted)	45.3	33.2	30.6	10.5	92.4	94.5

* Missing data were imputed using linear regression.

Table 3- Structural equation modeling results

Variables	*Path coefficient* *95% confidence interval (lower limit - upper limit)*	*Probability value*	*Standardized path coefficient (standard error)*
Apnea-hypopnea index reduction	*Endogenous*		
• *Body mass index reduction*	*028(0.14-0.42)*	*<0.001*	*0.15(0.037)*
• *Baseline width*	*16.68*	*<0.001*	
Increase in oxygen saturation	*Endogenous*		
• *Apnea-hypopnea index reduction*	*0.13(0.12-0.14)*	*<0.001*	*0.65(0.022)*
• *Body mass index reduction*	*0.07(0.05-0.09)*	*<0.001*	*0.19(0.027)*
• *Baseline width*	*-1.47*	*<0.001*	
Error variance			
• *Apnea-hypopnea index reduction*	*53.05*		
• *Body mass index reduction*	*1.18*		
Goodness of fit			
• *Model vs. saturation*	*Chi-square: 0.000*	*1.000*	
• *Baseline vs. saturation*	*Chi-square: 470.7*	*<0.001*	

The units of body mass index and oxygen saturation percentage are kilograms per square meter and percentage, respectively.

The following criteria were assessed for each study:

1. “Was a representative sample of patients collected at a common point (typically at the onset of the disease)?”
2. “Was the follow-up duration sufficiently long and complete?”
3. “Were outcome criteria objective or assessed in a blinded manner?”
4. “If subgroups with varying conditions were identified, were adjustments made for significant prognostic factors?”

Custom questions specific to the focus of this study included:

1. “Were representative cases of obese patients eligible for bariatric surgery included, and were preoperative body mass index, Apnea-Hypopnea Index, and oxygen saturation levels evaluated appropriately?”

2. “Was the follow-up period adequate to assess body mass index, Apnea-Hypopnea Index, and oxygen saturation levels for a minimum of six months post-surgery?”
3. “Were outcomes such as the Apnea-Hypopnea Index and oxygen saturation levels assessed objectively and in a blinded manner?”
4. “Was a specific subgroup analysis conducted based on the type of surgical procedure, or were results reported according to each surgical subgroup?”

Each criterion was rated based on expert opinion as either “Yes” (one point, or half a point for partial compliance), “No” (zero points), or “Unclear” (half a point).

Data Synthesis

This secondary study utilized structural equation modeling to conduct a meta-analysis involving aggregated data sourced from a diverse array of scientific literature. The primary effect sizes analyzed encompassed mean body mass index (BMI), Apnea-Hypopnea Index (AHI), and percentage of oxygen saturation both pre- and post-surgery. These means facilitated descriptive comparisons as well as the meta-analytical process. The data were subsequently organized into tables, and missing values were estimated and imputed. The estimation process employed linear regression when the absence of data did not significantly compromise the quality assessment scores of the included articles; alternatively, cases with significant missing data were excluded from the analysis.

The principal methodology for data synthesis was meta-analysis employing structural equation modeling (SEM). A Directed Acyclic Graph (DAG) was developed based on consensus among senior researchers, depicting BMI as the independent variable, the percentage of oxygen saturation as the dependent variable, and AHI as the mediating variable. This graph was grounded in biological and temporal rationale, suggesting that BMI precedes AHI, which subsequently influences the percentage of oxygen saturation. This sequence constituted the basis of the graph’s hypothesis. Importantly, no latent variables were incorporated in this meta-analysis, and factor analysis was deemed inapplicable; thus, the modeling was confined to path analysis. Following the establishment of the DAG, structural equation modeling was conducted to validate its assumptions. Studies were weighted according to adjusted sample sizes and quality scores derived from a quality assessment tool. A multi-level latent variable, categorized by country and type of surgery, was employed to segregate random effects from estimates of path coefficients, thereby addressing heterogeneity among study outcomes.

Model estimation was performed using the maximum likelihood method. Paths with P-values exceeding .1 were systematically removed through a backward stepwise approach, prioritizing the elimination of the largest P-values. A 95% confidence interval (95% CI) was utilized to evaluate the reliability and error range of the estimates. The goodness of fit for the model was assessed utilizing the chi-squared test. All statistical analyses were conducted employing Stata 14 software (Stata Corp, Texas, USA).

Findings

Study Selection and Quality Assessment

A thorough search across multiple databases yielded a total of 2,537 articles (PubMed: 1,094; Web of Science: 1,553; Scopus: 1,766). After the removal of duplicates and subsequent screening of titles and abstracts, we proceeded to review the full texts of 59 studies. Ultimately, 24 studies were selected for inclusion, encompassing a total of 684 participants who met the pre-established criteria.

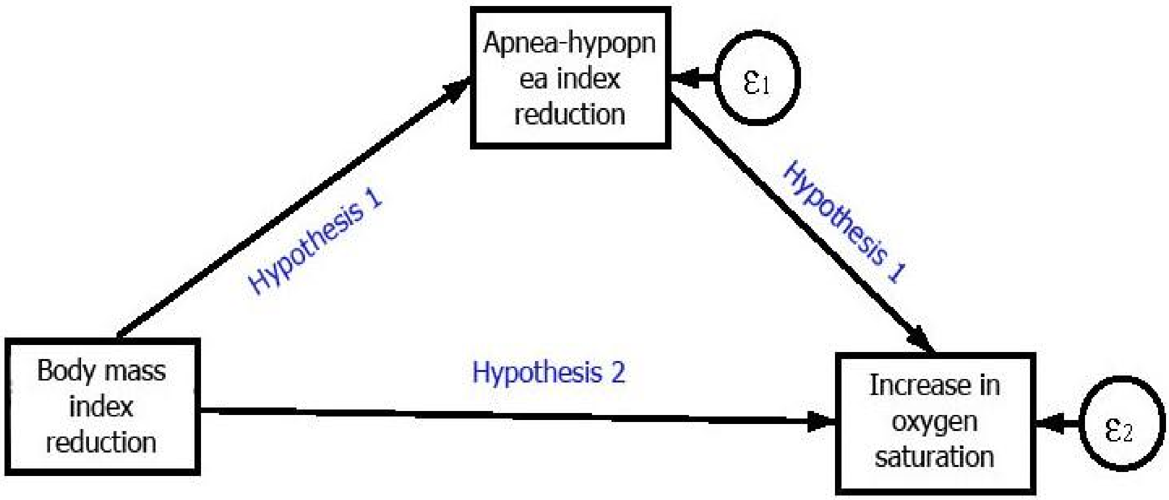

Figure 1- Structural equation modeling hypothesis graph; Hypothesis 1: Reducing body mass index increases oxygen saturation percentage by reducing apnea-hypopnea index; Hypothesis 2: Reducing body mass index directly increases oxygen saturation percentage.

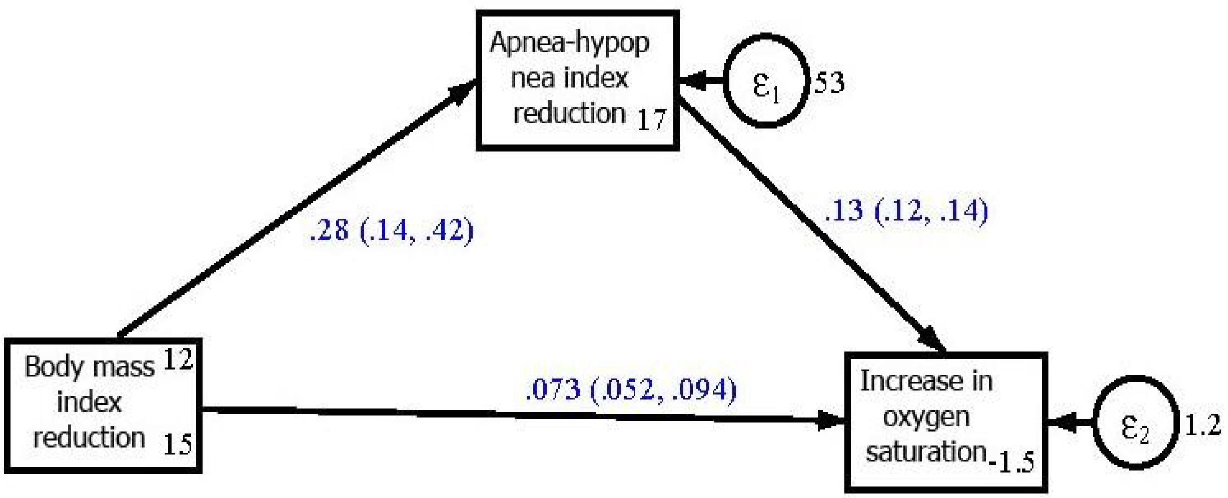

Figure 2 - Structural equation modeling graph with unstandardized path coefficient and 95% confidence interval. The numbers in the right corner of the boxes are the width from the origin. Mediator path contribution: 0.335 (about one-third).

Characteristics of the Studies

The characteristics of the studies included in this analysis, which collectively involved 684 patients, are summarized in Tables 1 and 2. Following obesity surgery, a mean reduction of 1.12 kg/m² in body mass index (BMI), a decrease of 1.20 units in the Apnea-Hypopnea Index (AHI), and a 1.2% increase in the average percentage of oxygen saturation were observed over a follow-up period of approximately 10.3 months.

The mean BMI prior to surgery was 45.3 kg/m² (ranging from 30.73 to 60.8), which decreased to 32.2 kg/m² post-surgery (ranging from 24.24 to 41.6). With respect to the AHI, the mean score before surgery was 30.6 (range: 9.1 to 55.8), which reduced to 10.5 (range: .65 to 24.5) following the procedure. The mean oxygen saturation level prior to surgery was 92.4% (range: 85.7 to 95.15), which subsequently increased to 94.5% (range: 92.8 to 95.8) following the surgical procedure.

Quality Assessment

The findings of the quality risk assessment are presented in Table 1. The quality assessment scores for the studies ranged from 2 to 3.5 on a four-point scale. Studies that (a) lacked data on measured outcomes—specifically body mass index (BMI), Apnea-Hypopnea Index (AHI), and percentage of oxygen saturation; (b) had a follow-up period shorter than six months; and (c) failed to provide subgroup results based on the type of surgery, were assigned scores below 2.5. A total of 17 studies, representing 70%, were selected for qualitative analysis. This selection comprised 14 studies with quality assessment scores of 3 or higher, in addition to three studies that received a score of 2.5, having missing data for only one measured outcome. These quality scores were employed to adjust the weighting of the studies in the subsequent analysis.

Results of Structural Equation Modeling Meta-Analysis

The structural equation modeling (SEM) meta-analysis was conducted using the calculated weights applied to a hypothetical graph (Figure 1), which was based on causal criteria that take into account temporal precedence and biological plausibility. In this model, the reduction of BMI leads to an improvement in the percentage of oxygen saturation, mediated by a decrease in AHI (Hypothesis 1: indirect pathway), as well as through direct effects or other unspecified pathways (Hypothesis 2: direct pathway). Initially, a multilevel random intercept model was introduced, consisting of individual patients (level 1), types of surgical studies (level 2) nested within the countries of the studies (level 3). However, due to the lower variance of the random effect compared to the error variance, this multilevel variable was ultimately excluded from the model. Upon executing the model, all path coefficients were found to be statistically significant, with P-values less than .001 (as illustrated in Table 3 and Figure 2), thus corroborating the hypothesized model.

Given that this SEM meta-analysis encompassed both direct and indirect pathways, a mediation analysis was performed to compute the coefficients for these pathways. In summary, the effect of reducing BMI on decreasing AHI was positive (effect coefficient = 0.28), indicating that a one-unit reduction in BMI corresponds to a decrease of .28 units in AHI. Similarly, the effect of reducing AHI on improving the mean percentage of oxygen saturation was also positive (effect coefficient = 0.13), suggesting that a one-unit reduction in AHI results in an increase of 0.13 units in the mean percentage of oxygen saturation.

The findings from this analysis indicate that the interaction between the two pathways suggests that in the indirect pathway (Hypothesis 1), each unit decrease in body mass index (BMI) corresponds to a 0.04% improvement in mean oxygen saturation. The direct path coefficient (Hypothesis 2) was determined to be 0.07, with the mediating pathway contributing approximately one-third (0.335) to the overall effect (Table 4).

Table 4 - Path analysis of total, direct and indirect effects on outcomes

Effect (path)	*Path coefficient* *95% confidence interval (lower limit - upper limit)*	*Probability value*	*Standardized path coefficient*
Direct	*0.07(0.05-0.09)*	*<0.001*	*0.19*
Indirect	*0.04(0.02-0.06)*	*<0.001*	*0.09*
Total	*0.11(0.08-0.14)*	*<0.001*	*0.28*
Intermediary Share	*0.335*		

We calculated the total effect of reducing BMI on increasing mean oxygen saturation and conducted a sensitivity analysis to explore various scenarios of BMI reduction.

Table 5- The effect of reducing body mass index on reducing apnea-hypopnea index and the average increase in oxygen saturation percentage

Amount of decrease in body mass index	*Apnoea-hypopnea index decrease*	*Total amount of increase in oxygen saturation percentage*
1 unit	*0.28*	*0.11*
5 units	*1.39*	*0.55*
10 units	*2.77*	*1.1*
15 units	*4.16*	*1.65*

Notably, in a scenario involving a 15-unit decrease in BMI, the Apnea-Hypopnea Index (AHI) decreased by 4.16, while mean oxygen saturation improved by 1.65% (Table 5). However, the contribution of the indirect pathway to the enhancement of mean oxygen saturation was found to be clinically negligible within this context.

Discussion

This study aimed to investigate whether bariatric surgery, in addition to its established role in reducing BMI, could also lead to improvements in the Apnea-Hypopnea Index and overall oxygen saturation levels. A comprehensive review of existing literature and studies was conducted, resulting in the identification of 17 articles deemed most pertinent for analysis following a rigorous screening process. To enhance the accuracy and reliability of the findings, these articles were evaluated using a quality scoring system with a maximum score of four. Articles exhibiting higher quality and more relevant data in relation to the research objectives were assigned greater weight in the meta-analyses.

The literature indicates that grade 2 obesity (BMI between 35 and 40 kg/m²) and grade 3 obesity (BMI over 40 kg/m²) are associated with lower AHI and compromised oxygen saturation levels.[11]

Given the heightened risk of complications and mortality among these patients, the need for effective interventions is evident. Recent studies have demonstrated that bariatric surgery can reduce the AHI by over 10 units within a timeframe of six months to one year.[16] In contrast, our study observed an average reduction of 20.1 units in AHI at a follow-up of 10.3 months.

Considering the average results for both BMI and AHI, the reductions observed were clinically significant. Post-operative oxygen saturation rates averaged 92.4% before surgery and improved to 94.5%, which is significant from a clinical perspective. The statistical power of the study was bolstered by a total of 684 patients, providing a robust foundation for the structural equation modeling in the meta-analysis.

Numerous studies evaluating the efficacy of bariatric surgery have established its effectiveness in alleviating symptoms and improving AHI scores in patients with obstructive sleep apnea syndrome.[17] Upon examining the structural equation modeling and the causal pathways in this study, it was found that a reduction of 15 kg/m^2 in BMI resulted in a significant improvement of 4.16 units in AHI.

However, this improvement translated to only a 1.65% increase in oxygen saturation, which may not be clinically significant (Table 5). This finding implies that over time, patients may adapt to their apnea conditions, resulting in minimal perceptible changes in their symptoms. Furthermore, evidence suggests that individuals experiencing hypoxia following bariatric surgery may encounter unreliable oxygen saturation measurements, accompanied by notable variability.[4]

This study encountered a significant limitation. Specifically the weighting of studies according to sample size resulted in inflated findings, yielding statistically significant outcomes for small effect sizes. In essence, while some smaller results may attain statistical significance, they may lack substantial relevance.

Nevertheless, the final results aligned with our initial hypothesis, as no paths were excluded due to a lack of significance. This indicates that even minor effect sizes can clinical importance. The strengths of this study are rooted in the comprehensive aggregation of high-quality research that examines changes in body mass index (BMI), Apnea-Hypopnea Index (AHI), and oxygen saturation, all aimed at establishing a causal network.

Conclusion

The present study demonstrated a reduction in the Apnea-Hypopnea Index and an improvement in oxygen saturation levels following bariatric surgery. Structural equation modeling of the meta-analysis revealed that changes in the Apnea-Hypopnea Index were associated with alterations in body mass index. However, the relationship between changes in oxygen saturation and changes in both body mass index and the Apnea-Hypopnea Index, while statistically significant, did not appear to possess meaningful clinical implications. It appears that variations in oxygen saturation may be influenced by factors that warrant further investigation in future studies.

Conflict of Interest

The authors declare no conflicts of interest.

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Eghbali F. MD[*], Ahmadi S. A. Y. MD[**], Jahanshahi F. MD[***], Madankan A. MD[****] Jaliliyan A. MD[*****], Mosavari H. MD[***], Bighdeli A. H. MD[******]

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Conclusions: AHI changes were associated with BMI changes, but the association of SPO2 changes with BMI and AHI changes were not tangible. It seems that the variation of SPO2 changes may be explained by some other variables.

Key Words: Obesity, Obstructive Sleep Apnea, Metabolic Surgery, Meta-Analysis, Statistical Modeling

[*]Associate Professor of General Surgery, Iran University of Medical Sciences, Rasoul Akram Hospital, Tehran, Iran
[**]Research Assistant & General Practitioner, Iran University of Medical Sciences, Preventive Medicine and Public Health Research Center, Psychosocial Health Research Institute, Tehran, Iran
[***]General Practitioner, Iran University of Medical Sciences, Rasoul Akram Hospital, Tehran, Iran
[****]Assistant Professor of General Surgery, Iran University of Medical Sciences, Rasoul Akram Hospital, Tehran, Iran
[*****]Research Assistant & General Practitioner, Iran University of Medical Sciences, Rasoul Akram Hospital, Tehran, Iran
[******]Resident of General Surgery, Iran University of Medical Sciences, Rasoul Akram Hospital, Tehran, Iran

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