Bariatric Surgery and the Risk of Cerebrovascular Events: a Meta-analysis of 17 Studies Including 3,124,063 Subjects

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Abstract

Purpose To perform a meta-analysis of the literature to evaluate the prevalence of cerebrovascular comorbidities between patients undergoing bariatric surgery and those not undergoing bariatric surgery.

Materials and Methods Studies about the risk of cerebrovascular disease both before and after bariatric surgery were systematically explored in multiple electronic databases, including PubMed, Web of Science, Cochrane Library, and Embase, from the time of database construction to May 2022.

Results Seventeen studies with 3,124,063 patients were finally included in the meta-analysis. There was a statistically significant reduction in cerebrovascular event risk following bariatric surgery (OR 0.68; 95% CI 0.58 to 0.78; I² = 87.9%). The results of our meta-analysis showed that bariatric surgery was associated with decreased cerebrovascular event risk in the USA, Sweden, the UK, and Germany but not in China or Finland. There was no significant difference in the incidence of cerebrovascular events among bariatric surgery patients compared to non-surgical patients for greater than or equal to 5 years, but the incidence of cerebrovascular events less than 5 years after bariatric surgery was significantly lower in the surgical patients compared to non-surgical patients in the USA population.

Conclusion Our meta-analysis suggested that bariatric surgery for severe obesity was associated with a reduced risk of cerebrovascular events in the USA, Sweden, the UK, and Germany. Bariatric surgery significantly reduced the risk of cerebrovascular events within 5 years, but there was no significant difference in the risk of cerebrovascular events for 5 or more years after bariatric surgery in the USA.

Keywords Bariatric surgery · Cerebrovascular · Meta-analysis

Introduction

There has been an exponential rise in the global prevalence of obesity in recent decades. Obesity has a negative impact on life expectancy by increasing the risk of chronic health conditions, including cardiovascular disease, insulin resistance, sleep apnea, and other medical conditions [1]. There has been an exponential rise in bariatric surgery worldwide, with a significantly increasing rate every year. The NIH guidelines from 1991 advocated for bariatric surgery based on BMI and medical comorbidities. Patients suffering from obesity with a body mass index (BMI) > 40 kg/m² or a BMI > 35 kg/m² are recommended for bariatric surgery [2]. In recent years, the relationship between bariatric surgery and cerebrovascular events has received widespread attention. However, studies comparing bariatric surgery and cerebrovascular outcomes remain unclear. Thus, the aim of the current study was to conduct a meta-analysis to reveal the effects of bariatric surgery on cerebrovascular outcomes.
If bariatric surgery reduces the risk of cerebrovascular events, perhaps guidelines could be considered that recommend that overweight patients undergo bariatric operation to effectuate weight loss. Based on the above considerations, we performed a pooled analysis by integrating the results of previous works to obtain more robust and accurate estimates regarding the effect of bariatric surgery on cerebrovascular outcomes, which are vital to guide clinical management and counsel patients.

Methods

Search Strategy

The study was designed according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) checklist [3]. A systematic search was carried out on published studies for updates until May 2022 without language restriction in the PubMed, Web of Science, Cochrane Library, and Embase databases. We used the search terms “bariatric surgery” and “cerebrovascular disease.” Relevant articles were independently reviewed by two individuals.

Study Selection

We included studies according to the following inclusion criteria: (1) articles reporting the relationship between bariatric surgery and cerebrovascular outcomes; (2) studies that included patients undergoing bariatric surgery; and (3) studies in which odds ratios (ORs) and their 95% confidence intervals (CIs) were collected or could be calculated from the information given. We excluded (1) reviews, editorials, correspondence, and meta-analyses; (2) studies with insufficient data; and (3) articles in non-English languages.

Data Abstraction and Quality Assessment

We recorded the data from the selected studies using standard electronic sheets. The following information was extracted: the first author, the publication year, the study design, the source of the population, the proportion of men and women, the sample size, the postoperative period, the diagnostic criteria of the cerebrovascular comorbidities, and ORs with their 95% CIs.

The included studies were evaluated by two independent reviewers (ZC and QZ) using the quality assessment method, and disagreements were resolved via discussion. The Newcastle–Ottawa Scale (NOS) was used to assess the quality of the literature. Studies with NOS scores ≥ 7 were defined as high quality.

Results

Study Selection

A total of 758 articles were retrieved via a primary search of the literature databases. After the removal of duplicates, 362 articles remained (Fig. 1). After screening both abstracts and titles, 49 studies were retrieved for full-text screening. Fourteen articles were excluded for review, and no relevant data about outcomes were identified in 18 articles. Ultimately, a total of 3,124,063 patients from 17 articles met the inclusion criteria and were included in the final meta-analysis [6–22]. The flowchart of the study selection process for the meta-analysis is presented in Fig. 1.

Description of Included Studies

The basic characteristics of the included studies and quality evaluation are shown in Table 1. Our research included studies from seven different countries. The length of follow-up ranged from 1 to 14.7 years after bariatric surgery. The results of the literature quality assessment showed that the average score for the quality of the included studies was ≥ 7, and all of them were of high quality.

Overall Analysis

A total of 17 studies with 3,124,063 patients were pooled in the meta-analysis. The heterogeneity test (I² value) revealed that the studies were heterogeneous (I² = 87.9% > 50%); therefore, a random effects model was implemented for the analysis. As a result, the meta-analysis showed that the

Statistical Analysis

ORs were used to estimate the association between bariatric surgery and cerebrovascular comorbidities. Interstudy heterogeneity was assessed using Q value and I² values. When the I² value was greater than 50%, the random effects model was selected; otherwise, the fixed-effects model was used. For the qualitative interpretation of heterogeneity, I² < 50% was considered to represent moderate heterogeneity, while I² > 75% indicated extreme heterogeneity [4]. The potential for publication bias was evaluated graphically using both funnel plot inspection and Egger’s regression method for funnel plot asymmetry in the adjusted analyses of outcomes [5]. Sensitivity analysis was also performed to explore the stability of the results. Statistical analysis was conducted using Stata Statistical Software (version 12.0; STATA Corp., College Station, TX).
surgery group had a lower risk of cerebrovascular events than the no-surgery group (OR = 0.68; 95% CI 0.58–0.78) (Fig. 2). To explore the sources of heterogeneity, subgroup analyses were conducted based on country. The results of our meta-analysis show that bariatric surgery was associated with decreased cerebrovascular event risk in the USA (OR 0.63; 95% CI 0.49 to 0.81; $I^2 = 91.5\%$), Sweden (OR 0.75; 95% CI 0.62 to 0.91; $I^2 = 8.1\%$), the UK (OR 0.38; 95% CI 0.23 to 0.63; $I^2 = 0\%$), and Germany (OR 0.16; 95% CI 0.07 to 0.36) but not in China (OR 0.90; 95% CI 0.54 to 1.52; $I^2 = 86.4\%$) or Finland (OR 0.98; 95% CI 0.84 to 1.14; $I^2 = 9.6\%$) (Fig. 3). There was no significant difference in the incidence of cerebrovascular events compared with those without bariatric surgery after bariatric surgery for more than or equal to 5 years (OR 0.86; 95% CI 0.62 to 1.19; $I^2 = 61.3\%$), but the incidence of cerebrovascular events within 5 years after bariatric surgery was significantly lower than that of non-surgery patients in the USA population (OR 0.59; 95% CI 0.41 to 0.84; $I^2 = 94.6\%$) (Fig. 4). The sensitivity and publication bias analyses are displayed in Fig. 5. The results of the sensitivity analyses indicated that the meta-analysis had low sensitivity and that the overall results were robust and stable. The funnel plot displayed a symmetrical and funneled shape and Begg’s regression test ($p > 0.05$) suggested the absence of publication bias. In addition, the pooled results of bariatric surgery and cerebrovascular events were reliable after applying the trim and fill approach (Fig. 6).

Discussion

Association Between Bariatric Surgery and Cerebrovascular Events

This study evaluated 17 studies involving 3,124,063 individuals from a broad range of populations. Overall, the results from our study indicated that people with bariatric surgery had decreased odds of cerebrovascular comorbidities compared to non-bariatric surgery controls. Bariatric surgery significantly reduced the risk of cerebrovascular events within 5 years, but there was no significant difference in the risk of cerebrovascular events for 5 or more years after bariatric surgery in the USA. Weight loss after bariatric surgery is difficult to predict. Weight gain after bariatric surgery demonstrates the chronic and progressive nature of obesity. Therefore, follow-up after bariatric surgery is critical and requires a team approach for long-term benefits after bariatric surgery. This finding was consistent across most countries.
| Number | Author          | Year | Country | Design            | Number   | Age       | Male percent | Diagnostic criteria of cerebrovascular time | Follow-up   | NOS | OR  | Ci 1 | Ci 2 |
|--------|-----------------|------|---------|-------------------|----------|-----------|--------------|--------------------------------------------|-------------|-----|-----|-----|-----|
| 1      | Jiewen Jin      | 2020 | China   | Retrospective     | 1,526,820 | 57.06 (0.08) | 35.8% Male   | Death                                      | NA          | 9   | 0.71 | 0.62 | 0.81 |
| 2      | Ali Aminian     | 2019 | USA     | Retrospective cohort | 48,300    | 60.84 (10.59) | 27.8% Male   | Ischemic cerebrovascular accident           | 4 years     | 9   | 0.54 | 0.37 | 0.79 |
| 3      | David P. Fisher | 2018 | USA     | Cohort            | 20,235    | 49.5 (10.0)  | 24.1% Male   | Ischemic stroke, hemorrhagic stroke, carotid stenting, or carotid endarterectomy | 1 year      | 7   | 0.39 | 0.21 | 0.71 |
| 3      | David P. Fisher | 2018 | USA     |                   |          |           |              |                                            |             |     |      |      |      |
| 3      | David P. Fisher | 2018 | USA     |                   |          |           |              |                                            |             |     |      |      |      |
| 3      | David P. Fisher | 2018 | USA     |                   |          |           |              |                                            |             |     |      |      |      |
| 4      | Michael D       | 2021 | USA     | Retrospective cohort | 1,390,804 | 45 ± 9     | 20.8% Male   | Ischemic stroke                                | 1 year      | 8   | 0.54 | 0.47 | 0.61 |
| 4      | Michael D       | 2021 | USA     |                   |          |           |              |                                            |             |     |      |      |      |
| 4      | Michael D       | 2021 | USA     |                   |          |           |              |                                            |             |     |      |      |      |
| 5      | Ali Aminian     | 2020 | USA     | Retrospective observational | 7201     | 53.1 (44, 60.8) | 32.2% Male | Cerebrovascular events (ischemic stroke, hemorrhagic stroke, or carotid intervention/surgery) | 4.9 years   | 7   | 0.73 | 0.49 | 1.08 |
| 6      | Erik Stenberg   | 2020 | Sweden  | Cohort            | 11,863    | 52.1 ± 7.46 | 34.2% Male   | Subarachnoid hemorrhage, intracerebral hemorrhage, ischemic stroke, or acute cerebral event not specified as hemorrhage or ischemia registered in the NPR for in-hospital or outpatient care | 4 years     | 8   | 0.81 | 0.63 | 1.01 |
| 7      | Henry Buchwald  | 1998 | USA     | Retrospective     | 838       | 51         | 90.7% Male   | Cerebrovascular events (cerebrovascular accidents and transient ischemic attacks)       | 5 years     | 7   | 1.3  | 0.91 | 1.85 |
| Number | Author               | Year | Country | Design     | Number | Age     | Male percent | Diagnostic criteria of cerebrovascular time                                                                 | Follow-up | NOS | OR   | Ci 1  | Ci 2  |
|--------|----------------------|------|---------|------------|--------|---------|--------------|-----------------------------------------------------------------------------------------------------------|-----------|-----|------|------|------|
| 8      | Osama Moussa        | 2021 | UK      | Cohort     | 8424   | 50      | 20.1% Male   | Cerebrovascular events: composite of acute ischemic stroke, transient ischemic event, non-traumatic subarachnoid hemorrhage, and non-traumatic intracranial hemorrhage | 11.4 years | 8   | 0.352 | 0.195 | 0.637 |
| 9      | Osama Moussa        | 2020 | UK      | Cohort     | 3701   | 36 (29–44) | 20.2% Male   | Ischemic stroke                                                                                           | 11.2 years | 7   | 0.536 | 0.164 | 1.748 |
| 10     | Thomas R            | 2017 | USA     | Retrospective | 45,462 | 44.6 (11.3) | 23.8% Male   | Cerebrovascular accident/transient ischemic attack                                                                 | NA        | 8   | 0.03  | 0.01  | 0.25  |
| 11     | Shao-Lun Hung       | 2020 | Germany | Retrospective | 6265   | 32.39(8.63) | 39.55% Male | Intracranial hemorrhage, epidural hemorrhage, ischemic stroke, and transient ischemic attack                  | 3 years   | 7   | 0.162 | 0.073 | 0.36  |
| 12     | Hedong Han          | 2019 | China   | Retrospective | 24,534 | 60.94 (0.10) | 38.6% Male   | Acute ischemic stroke                                                                                       | NA        | 8   | 1.21  | 0.84  | 1.73  |
| 13     | Maddalena Ardissino | 2020 | UK      | Cohort     | 1186   | 49.63   | 34.91% Male  | Ischemic stroke or transient ischemic attack or established cerebrovascular atherosclerosis                   | 42.7 months | 7   | 0.0227 | 0.0000946 | 5.451 |
| 14     | STEFANO ROMEO       | 2012 | Finland | Prospective | 607    | 49 (6)  | 41% Male     | Stroke                                                                                                | 13.3 years | 7   | 0.73  | 0.41  | 1.3   |
| 15     | Lars Sjostrom       | 2012 | Sweden  | Prospective | 2037   |         | 29.4% Male   | Stroke                                                                                                | 14.7 years | 7   | 0.66  | 0.49  | 0.9   |
| 16     | Christian Herder    | 2013 | Finland | Prospective | 3299   | 47.2(6) | 30.9% Male   | Stroke                                                                                                | 10–13 years | 7   | 0.998 | 0.921 | 1.083 |
| 17     | Wenjing Tao         | 2014 | UK      | Cohort     | 22,487 | NA      | 25% Male     | Cerebrovascular disease (cerebral infarction or bleeding)                                                | 1 years    | 9   | 0.48  | 0.07  | 3.47  |
Underlying Mechanisms of Bariatric Surgery Effects on Cerebrovascular Events

To date, the effect of bariatric surgery on cerebrovascular events is still unclear. The significantly lower risk of cerebrovascular events in the bariatric surgery group was related to the following: dyslipidemia, hypertension, and diabetes [23, 24].

Bariatric surgery has been reported to reduce the thickness of the media wall and pulse wave velocity of patients with dyslipidemia and hypertension [25]. Bariatric surgery has also been reported to attenuate inflammatory responses in patients with atherosclerosis [26, 27]. With weight reduction being an important measure to improve hypertension, bariatric surgery may also reduce the need for antihypertensive medications, reducing the risk for the development of organ damage [28].

Glycemic control is associated with the microvascular and macrovascular complications of diabetes, and it is reasonable to hypothesize that the improvement in glycemic control may translate to improved cerebrovascular events in these patients. Several studies have validated the benefits of bariatric surgery in long-term weight management, with peak weight loss 2 years post-surgery and stable good glycemic control for up to 20 years [29].

Laparoscopic sleeve gastrectomy, gastric bypass, and duodenal switch can alter hormone levels, such as those of ghrelin or GLP-1 [30]. Moreover, GLP-1 has been reported to influence blood glucose levels by decreasing hepatic gluconeogenesis [31]. Ghrelin promoted the synthesis of liver glycogen [32], increased blood glucose, and inhibited insulin release [33], all of which underscore the important effect of ghrelin in modulating glucose metabolism.

Strengths and Limitations

The present study has a number of strengths in terms of the following aspects. First, this is the first study to report a meta-analysis comparing bariatric surgery and cerebrovascular events, including the largest highly representative population in the relevant area. Second, we searched and collected articles from four comprehensive electronic databases (PubMed, Embase, Web of Science, and the Cochrane library) without any restriction date; therefore, we were able to retrieve as many relevant articles as possible from all over the world and avoid the impact of publication bias. Third, several approaches, including subgroup analysis, sensitivity analysis, and publication bias analysis, were applied to establish whether the results of the present meta-analysis are reliable. Our results remained constant among these analyses.

There are several shortcomings in this meta-analysis that warrant mentioning. First, although we performed a subgroup analysis, we did not find the source of heterogeneity. Some confounding factors did not have enough studies to conduct...
Fig. 3  The odds of cerebrovascular risk between bariatric surgery and nonbariatric surgery patients stratified by country

Overall (I-squared = 87.9%, p = 0.000)

| Study ID | ES (95% CI) | Weight |
|----------|-------------|---------|
| China    | 0.71 (0.62, 0.81) | 10571   |
| Hedong Han 2019 | 1.21 (0.84, 1.73) |         |
| Subtotal (I-squared = 86.4%, p = 0.007) | 0.90 (0.54, 1.52) |         |
| USA      | 0.53 (0.37, 0.79) |         |
| David P. Fisher 2018 | 0.39 (0.21, 0.71) |         |
| David P. Fisher 2018 | 0.49 (0.22, 0.88) |         |
| David P. Fisher 2018 | 0.69 (0.38, 1.29) |         |
| David P. Fisher 2018 | 0.58 (0.25, 1.36) |         |
| Michael D 2021 | 0.54 (0.47, 0.61) |         |
| Michael D 2021 | 0.58 (0.47, 0.61) |         |
| Michael D 2021 | 0.78 (0.65, 0.90) |         |
| Ali Aminian 2020 | 0.73 (0.49, 1.08) |         |
| Thomas R 2017 | 1.30 (0.91, 1.85) |         |
| Subtotal (I-squared = 91.5%, p = 0.000) | 0.03 (0.01, 0.25) |         |
| Sweden   | 0.63 (0.49, 0.81) |         |
| Erik Stenberg 2020 | 0.81 (0.63, 1.01) |         |
| Lars Sjostrom 2012 | 0.66 (0.49, 0.90) |         |
| Subtotal (I-squared = 8.1%, p = 0.297) | 0.75 (0.62, 0.91) |         |
| UK       | 0.35 (0.19, 0.64) |         |
| Osama Moussa 2021 | 0.54 (0.16, 1.75) |         |
| Maddalena Ardissino | 0.02 (0.00, 0.55) |         |
| Wenjing Tao 2014 | 0.48 (0.07, 3.47) |         |
| Subtotal (I-squared = 0.0%, p = 0.692) | 0.38 (0.23, 0.63) |         |
| Germany  | 0.16 (0.07, 0.36) |         |
| Shao-Lun Hung 2020 | 0.16 (0.07, 0.36) |         |
| Subtotal (I-squared = .%, p = .) | 0.16 (0.07, 0.36) |         |
| Finland  | 0.73 (0.41, 1.31) |         |
| STEFANO ROMEO 2012 | 0.70 (0.92, 1.05) |         |
| Christian Herder 2013 | 0.58 (0.41, 0.84) |         |
| Subtotal (I-squared = 9.6%, p = 0.293) | 0.59 (0.41, 0.84) |         |
| Overall (I-squared = 87.9%, p = 0.000) | 0.68 (0.58, 0.79) | 100.00   |

NOTE: Weights are from random effects analysis

Fig. 4  The odds of cerebrovascular risk between bariatric surgery and nonbariatric surgery patients stratified by follow-up time (<5 years or ≥5 years)

Overall (I-squared = 61.3%, p = 0.051)

| Study ID | ES (95% CI) | Weight |
|----------|-------------|---------|
| < 5 years | 0.54 (0.37, 0.79) | 10.40   |
| All Aminian 2019 | 0.54 (0.37, 0.79) | 10.40   |
| David P. Fisher 2018 | 0.39 (0.21, 0.71) | 7.36    |
| David P. Fisher 2018 | 0.39 (0.22, 0.68) | 7.36    |
| Michael D 2021 | 0.54 (0.47, 0.61) | 13.52   |
| Michael D 2021 | 0.54 (0.47, 0.61) | 13.52   |
| Ali Aminian 2020 | 0.73 (0.49, 1.08) | 10.18   |
| Subtotal (I-squared = 94.6%, p = 0.000) | 0.59 (0.41, 0.84) | 63.40   |
| ≥ 5 years | 0.69 (0.38, 1.25) | 7.52    |
| David P. Fisher 2018 | 0.69 (0.38, 1.25) | 7.52    |
| David P. Fisher 2018 | 0.58 (0.25, 1.36) | 5.09    |
| Michael D 2021 | 0.76 (0.65, 0.90) | 13.23   |
| Henry Buchwald 1998 | 1.30 (0.91, 1.85) | 10.76   |
| Subtotal (I-squared = 61.3%, p = 0.051) | 0.86 (0.62, 1.19) | 36.60   |
| Overall (I-squared = 91.1%, p = 0.000) | 0.68 (0.53, 0.86) | 100.00  |

NOTE: Weights are from random effects analysis

| Study ID | ES (95% CI) | Weight |
|----------|-------------|---------|
| < 5 years |             |         |
| ≥ 5 years |             |         |
subgroup analysis. Second, most of the included studies were cross-sectional studies and the causal relationship between bariatric surgery and cerebrovascular events could not be identified; therefore, further prospective longitudinal cohort studies are needed. Finally, variability in the diagnostic criteria of cerebrovascular events may have contributed to the high heterogeneity.

**Conclusion**

Our study demonstrates the benefit of bariatric surgery on the risk of cerebrovascular disease. Based on our meta-analysis, bariatric surgery was associated with a lower rate of cerebrovascular disease. The risk of cerebrovascular disease was significantly reduced in the USA, Sweden, the UK, and Germany and was not significant in China or Finland. It is advisable to monitor patients closely after bariatric surgery, especially those at a high risk of cerebrovascular disease after bariatric surgery.

**Author Contribution** JZ coordinated the study. ZC conceived the study, and QZ, YJ, WL, and JZ contributed to the study design, literature search, figures, statistical analysis, and data synthesis of the outcomes and drafted and edited the final paper. All authors critically revised the report. All members have confirmed and agreed to the submission of the manuscript.

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Data Availability All data generated or analyzed during the present study are included in this published article.

Declarations

Ethics Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Consent to Participate Informed consent does not apply.

Conflict of Interest The authors declare no competing interests.

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