Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Impact of prior bariatric surgery on risk and severity of COVID-19 infection: A meta-analysis of observational studies

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ABSTRACT

Background: The association of prior bariatric surgery (BS) with infection rate and prognosis of coronavirus disease 2019 (COVID-19) remains unclear. We conducted a meta-analysis of observational studies to address this issue.

Methods: We searched databases including MEDLINE, Embase, and CENTRAL from inception to May, 2022. The primary outcome was risk of mortality, while secondary outcomes included risk of hospital/intensive care unit (ICU) admission, mechanical ventilation, acute kidney injury (AKI), and infection rate.

Results: Eleven studies involving 151,475 patients were analyzed. Meta-analysis showed lower risks of mortality [odd ratio (OR)= 0.42, 95% CI: 0.27–0.65, $p < 0.001$, $I^2 = 67\%$; nine studies; 151,113 patients, certainty of evidence (COE):moderate], hospital admission (OR=0.56, 95% CI: 0.36–0.85, $p = 0.007$, $I^2 = 74.6\%$; seven studies; 17,810 patients; COE:low), ICU admission (OR=0.5, 95% CI: 0.37–0.67, $p < 0.001$, $I^2 = 0\%$; six studies; 17,496 patients, COE:moderate), mechanical ventilation (OR=0.52, 95% CI: 0.37–0.72, $p < 0.001$, $I^2 = 57.1\%$; seven studies; 137,992 patients, COE:moderate) in patients with prior BS (BS group) than those with obesity without surgical treatment (non-BS group). There was no difference in risk of AKI (OR=0.74, 95% CI: 0.41–1.32, $p = 0.304$, $I^2 = 83.6\%$; four studies; 129,562 patients, COE: very low) and infection rate (OR=1.05, 95% CI: 0.89–1.22, $p = 0.572$, $I^2 = 0\%$; four studies; 12,633 patients, COE:low) between the two groups. Subgroup analysis from matched cohort studies demonstrated associations of prior BS with lower risks of mortality, ICU admission, mechanical ventilation, and AKI.

Conclusion: Our results showed a correlation between prior BS and less severe COVID-19, which warrants further investigations to verify.

1. Introduction

Obesity is considered a chronic low-grade inflammation that not only affects an individual's nutritional status and metabolic hormone secretion [1] but also adversely impacts the immune system and host defense [1,2]. Consistently, previous studies have reported that obesity could predispose to an increased susceptibility to postoperative infection [3,4] and could serve as a predictor of hospitalization from viral respiratory infections [5]. During the COVID-19 pandemic, accumulating evidence has suggested higher rates of complications and mortality together with

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the utilization of medical resources among those with obesity compared to those without [6–11]. Another study further demonstrated an association between the prevalence of obesity and that of COVID-19 as well as its related mortality by showing increases in mortality rate and prevalence by 8.3% and 6.6%, respectively, for every 1% increment in obesity prevalence [12].

Bariatric surgery (BS), a sustainable approach to achieving substantial weight loss, not only is beneficial to the cardiovascular system through the modification of cardiometabolic risk factors (e.g., diabetes) and the reduction in major adverse cardiovascular events but also can improve renal functions, alleviate obesity-related inflammation, and enhance patient survival in those with severe obesity [13–17]. In addition, patients with obesity who underwent BS were found to have a significantly lower risk of respiratory tract infections compared to those who did not receive the procedure [18]. Moreover, a recent meta-analysis of three retrospective studies that recruited a total of 9022 patients with obesity reported lower rates of COVID-related mortality and hospital admission among those with prior BS compared to those without [19]. Nevertheless, despite the relatively large sample size, the weight of pooled evidence from that meta-analysis remains limited due to the small number of studies [19]. In view of the importance of this issue, there were several recent observational studies focusing on the association between prior BS and prognostic outcomes in patients with COVID-19 [20–23]. To provide robust evidence for clinical practice, the current meta-analysis aimed at systematically addressing this issue by incorporating the updated data to investigate the correlation of prior BS with the risk of mortality as well as its relationship with other prognostic outcomes including the need for advanced hospital care and the risks of complications.

2. Methods

2.1. Protocol registration

The results of the current study (PROSPERO CRD42022332714) were reported according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. Two authors independently performed study selection and data collection as well as risk of bias assessment. A third author was involved in settling persistent disagreements between the two authors. The MOOSE checklist is shown in Supplemental Table 1.

2.2. Data sources and searches

We searched the databases of Embase, Cochrane controlled trials register, and Medline to obtain a list of all published eligible records from inception to May 15, 2022 (supplemental Table 2). We used the Boolean Operators "AND" or "OR" to maximize the chances of retrieving relevant information. Subject headings were also utilized to facilitate literature search. The reference lists of relevant studies were scrutinized to identify additional articles. There were no restrictions on the date of publication, sample size, or language.

2.3. Inclusion and exclusion criteria

Studies assessing the association of prior BS with the disease severity or infection rate of COVID-19 in adult patients were considered eligible. For studies which also enrolled patients with age < 18 years, only those in which the mean or median age of the participants ≥ 30 years were recruited as the proportions of participants less than the age of 18 in those studies were deemed too low to bias our study outcomes. In addition, a study was considered eligible when fulfilling the following criteria: (a) BS group: Participants with obesity receiving previous BS regardless of the interval between surgery and study conduction or the extent of weight loss; (b) Control group: Adults with obesity without a surgical history of BS. For the current study, we defined obesity as individuals with a body mass index (BMI) ≥ 30 mg/kg^2 in both the BS and control groups [24]. Besides, a previous study has reported an association between BMI≥ 30 kg/m^2 and the need for intensive care in patients diagnosed with COVID-19 [25]; and (c) Availability of at least one prognostic outcome including the rates of COVID-19 infection, hospital admission, ICU admission, mechanical ventilation, overall mortality, and AKI. The exclusion criteria were (1) studies focused on pediatric or pregnancy population, and (2) those published as letters, case reports, conference abstracts, reviews, or other forms instead of original articles.

2.4. Data extraction, outcomes and definitions

The information extracted from each study included patient characteristics, comorbidities, author information, and outcomes. The

Table 1
Characteristics of included studies (n = 11).

Studies	Population	Match	Age (years)	Male (%)	BMI (kg/m^2)	Time interval¶	N	BS group (SG vs. LYGB)	Non-BS group	Country
Aminian 2021	Outpatients with COVID-19	1:10	46 vs. 49	21 vs. 23	37 vs. 42	46 months	363	33 (61% vs. 43%)	330	USA
Aminian 2022	Outpatients at risk for COVID-19 during pandemic	1:3	46 vs. 46	21 vs. 21	38 vs. 45	5.9 years	11,809	2958 (34% vs. 66%)	8851	USA
Blanchard 2022	Hospitalized patient with COVID-19	1:3	61 vs. 61	44 vs. 41	33 vs. 41	8.5 years	60	16 (31% vs. 38%)	44	France
Hadi 2022	Outpatient with COVID-19	1:1	48 vs. 49	18 vs. 17	NA	NA§	3880	1940 (49% vs. 46%)	1940	USA
Iannelli 2021	Hospitalized patient with COVID-19	no match	50 vs. 60	24 vs. 54	NA	5.43 years	8286	541 (NA)	7745	France
Jenkins 2021	Outpatients with COVID-19	1:4	52 vs. 52	31 vs. 31	36 vs. 41	NA	620	124 (28% vs. 36%)	496	USA
Marchesi 2021	Outpatients at risk for COVID-19 during pandemic	no match	48 vs. 47	20 vs. 27	31 vs. 44	NA	522	353 (65% vs. 32%)	169	Italy
Moradpour 2022	Outpatients at risk for COVID-19 during pandemic	no match	45 vs. 45	24 vs. 24	30 vs. 45	12–18 months	236	121 (46% vs. 54%)	115	Iran
Purdy 2022	Hospitalized patient with COVID-19	no match	NA	28 vs. 48	NA	NA	124,699	2607 (NA)	122,092	USA
Santa-Cruz 2022	Outpatients at risk for COVID-19 during pandemic	no match	35 vs. 37	21 vs. 24	41 vs. 39	3 months	66	24 (NA)	42	Brazil
Tignanelli 2021	Outpatients with COVID-19	no match	57	49	NA	NA	934	NA (NA)	NA	USA

¶Time from bariatric surgery to study recruitment; BMI: body mass index; BS: bariatric surgery; NA: not available; §inclusion of participants with a history of BS at least two weeks before the diagnosis of COVID-19; SG: sleeve gastrectomy; RYGB: Roux-en-Y Gastric Bypass

Table 2
The quality of evidence for outcome measures.

Outcomes	Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
Risk of mortality	**RR 0.42**	151,113(9 studies)	⨁⨁⨁◯ Moderate	a
Hospital admission	**RR 0.56**(0.36–0.85)	17,810(7 studies)	⨁⨁◯◯Low	a, b
Intensive care unit admission	**RR 0.5**(0.37–0.67)	17,496(6 studies)	⨁⨁⨁◯Moderate	a
Mechanical ventilation	**RR 0.52**(0.37–0.72)	137,992(7 studies)	⨁⨁⨁◯Moderate	a
Acute kidney injury	**RR 0.74(0.41–1.32)**	129,562(4 studies)	⨁◯◯◯Very low	b, c
Infection rate of COVID-19	**RR 1.05**(0.89–1.22)	12,633(4 studies)	⨁⨁◯◯Low	–

Comments:
[a] upgraded due to an observed large pooled estimated effect
[b] The I square is more than 50%.
[c] wide 95% CI
GRADE Working Group grades of evidence: High certainty: We are very confident that the true effect lies close to that of the estimate of the effect **Moderate certainty**: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different **Low certainty**: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect **Very low certainty**: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

primary outcome was the association of prior BS with the risk of mortality, while the secondary outcomes included its relationship with other prognostic outcomes including the risk of hospital/ICU admission, mechanical ventilation, AKI, and infection rate. The definition of outcomes was based on that in each study. In addition, we considered the requirement for hemodialysis to be an indicator of AKI. The infection rate of COVID was calculated according to the number of cases with laboratory confirmation rather than that only based on clinical presentations. If the same outcome (e.g., mortality rate) was available at different time points, only the one with the longest follow-up period was selected for analysis. To reduce the impact of confounding factors, we conducted subgroup analyses on the study design (i.e., matched cohort) and BMI to evaluate the associations of prior BS with different clinical outcomes of COVID-19.

To minimize potential impacts of heterogeneity on our study outcomes, we analyzed our studies using three approaches, including (1) analysis of all studies with comparison between individuals with and those without receiving BS regardless of the reduction in body weight (Approach I); (2) subgroup analysis focusing on studies with a match-cohort design that attempted to match age, sex, and comorbidities between those receiving and those without undergoing BS (Approach II); and (3) studies that provided information about the BMI of their participants with and without receiving BS (Approach III).

2.5. Assessment of risks of bias and certainty assessment

The Newcastle-Ottawa Scale (NOS) was used for the assessment of the risks of bias of our included observational studies as previously described [26]. Studies assigned with more than seven stars were regarded as having a low risk of bias. Two reviewers independently evaluated the certainty of evidence about the primary and secondary outcomes by categorizing a study into one of four grades (i.e., high, moderate, low, and very low) Disagreements regarding certainty ratings were settled through discussion.

2.6. Statistical analysis

Adopting a random effects model [27,28], we used the Mantel-Haenszel (MH) method to pool dichotomous data for the computation of pooled odds ratios (ORs) and corresponding 95% confidence intervals (CIs). We presented the selected effect size as mean difference (MD) for continuous outcomes. The I^2 statistics was used to assess heterogeneity across the included studies, which was classified into low (0–50%), moderate (51–75%), and high (76–100%). The potential effect of a single trial on the overall outcomes was evaluated with sensitivity analyses that involved the removal of one study at a time from the meta-analysis. We used Egger's test for assessing the potentials of reporting and publication bias regarding the primary and secondary outcomes. All statistical analyses were conducted with the comprehensive Meta-Analysis (CMA) V3 software (Biostat, Englewood, NJ, USA). Statistical significance was set at a probability value of less than 0.05 for all analyses.

3. Results

3.1. Study selection

Fig. 1 summarizes the reasons for study exclusion in a Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram. Of a total of 1365 eligible studies retrieved from the database search, 231 were removed because of duplication. We then excluded 1111 records after the initial review of the titles and abstracts. Finally, a total of 11 studies with 151,475 patients were included in the current meta-analysis (Fig. 1).

3.2. Characteristics and quality of included studies

The study characteristics are described in Table 1. Seven studies enrolled hospitalized or non-hospitalized patients with COVID-19 infection [21,22,29–33], while four studies investigated the infection rate of COVID-19 in the outpatient setting during the pandemic [20,23,34,35]. To reduce potential bias, five studies were conducted with the matched-cohort design in which patients in the BS group were matched with those who did not have surgical intervention for their obesity (control group) [20–22,29,31]. The other six studies included patients with obesity as the control group without matching their baseline characteristics (e.g., age, comorbidities) [23,30,32–35]. For the seven studies that provided BMI in both groups, the range of BMI was 31–41 and 39–45 kg/m^2 in the BS and control groups, respectively [20,21,23,29,31,34,35].

Analysis of the six studies with available information about the interval between previous BS and patient recruitment revealed a wide variation ranging from 3 months to 8.5 years [20,21,23,29,30,35]. The interval was more than one year in five studies [20,21,29,30,35], while one enrolled patients undergoing BS 3 months ago as the study group and those with obesity waiting for surgical intervention as the controls [23]. Although one study reported that participants who received BS at least two weeks before the diagnosis of COVID-19 were eligible for inclusion, the actual interval was not provided [22]. The patient's age ranged from 35 to 61 years with a male proportion of 17–54%. Nine studies enrolled participants with age more than 18 years, while the other two recruited individuals with age more than 15 [30] and 16 [22]

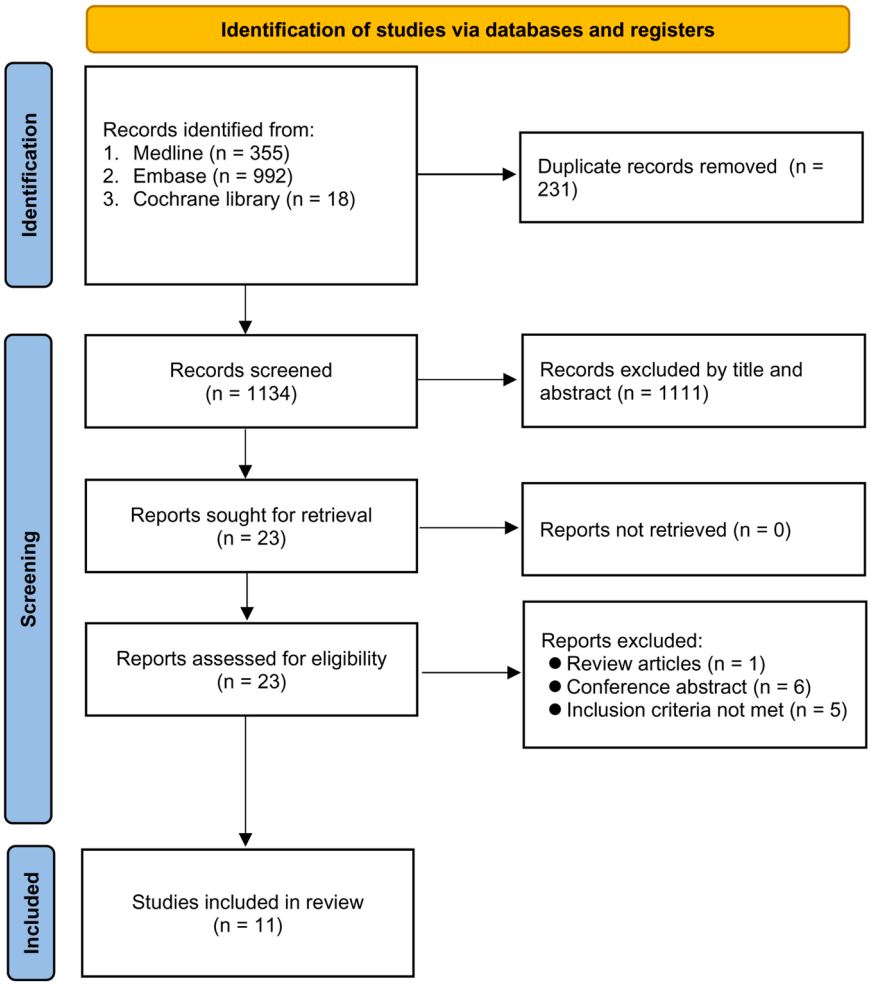

Fig. 1. Flow diagram of study selection for the current meta-analysis.

years. The eleven studies were conducted in five countries, including USA (six studies)[20,22,29,31–33], France (two studies) [21,30], Italy (one study) [34], Iran (one study) [35], and Brazil (one study) [23]. Based on NOS, 90.9% (10/11) of the comparative cohort studies exhibited an overall low risk of bias (i.e., total score ≥ 7) (Supplemental Table 3). The most common bias was the lack of confounding factor control in the comparability domain [22,23,30,32–35].

3.3. Outcomes

3.3.1. Impact of previous bariatric surgery on risk of mortality

A comparison of patient characteristics and comorbidities between the BS and non-BS groups for studies with available information is shown in supplemental Table 4, which demonstrated no difference in age and male distribution. Regarding comorbidities, the proportion of patients with diabetes mellitus was lower in the BS group than that in the non-BS group (OR: 0.71 95% CI: 0.52–0.98), while the proportion of other comorbidities such as hypertension and lung disease was comparable between the two groups (supplemental Table 4). A total of 151,113 patients were available for mortality analysis, which showed a lower risk of mortality in the BS group compared to the non-BS group (OR=0.42, 95%CI: 0.27–0.65, $p < 0.001$; I^2 =67%) (Fig. 1)[20–22,29–35]. Sensitivity analysis demonstrated no significant impact on outcome by omitting certain studies. An investigation into the risk of publication bias with Egger's test showed negligible risk ($p = 0.131$).

3.3.2. Impact of previous bariatric surgery on disease severity of COVID-19

A forest plot demonstrated a lower risk of hospital admission (OR=0.56, 95%CI: 0.36–0.85, $p = 0.007$; I^2 =74.6%) (Fig. 2a)[20,22,23,29,33–35], ICU admission (OR=0.5, 95%CI: 0.37–0.67, $p < 0.001$; I^2 =0%) (Fig. 2b) [20,22,23,29,31,35], mechanical ventilation (OR=0.52, 95%CI: 0.37–0.72, $p < 0.001$; I^2 =57.1%) (Fig. 2c)[21–23,29–32] in the BS group compared with those in the non-BS group, while there was no significant difference in the risk of AKI between the two groups (OR=0.74, 95%CI: 0.41–1.32, $p = 0.304$; I^2 =83.6%) (Fig. 2d)[22,29,31,32].

Sensitivity analysis showed no significant impact on three outcomes (i.e., hospital admission, ICU admission, mechanical ventilation), while there was a lower risk of AKI in the BS group compared to non-BS group when one study [32] was removed (OR=0.52, 95%CI: 0.39–0.7, $p < 0.001$; I^2 =0%). Publication bias assessed with Egger's test indicated no bias in these four outcomes (all p value>0.05).

3.3.3. Impact of previous bariatric surgery on infection rate of COVID-19

Four studies involving 12,633 patients investigated the infection rate of COVID-19 in those with or without previous BS [20,23,34,35]. Three studies that provided raw data for calculation of the difference in BMI, which revealed a lower BMI in participants in the BS group compared to those in the non-BS group (mean difference: −11.49 kg/m^2, 95%CI: −16.22 to −6.76, $p < 0.0001$, I^2 =96%) (figure not shown) [23,34,35]. One study reported BMI values of 38.3 kg/m^2 and 46.3 kg/m^2 for the BS and non-BS groups, respectively, giving a mean difference of 7.9 kg/m^2 (95%CI: 6.4–9.5; $p < 0.001$) [20]. The current meta-analyses showed no

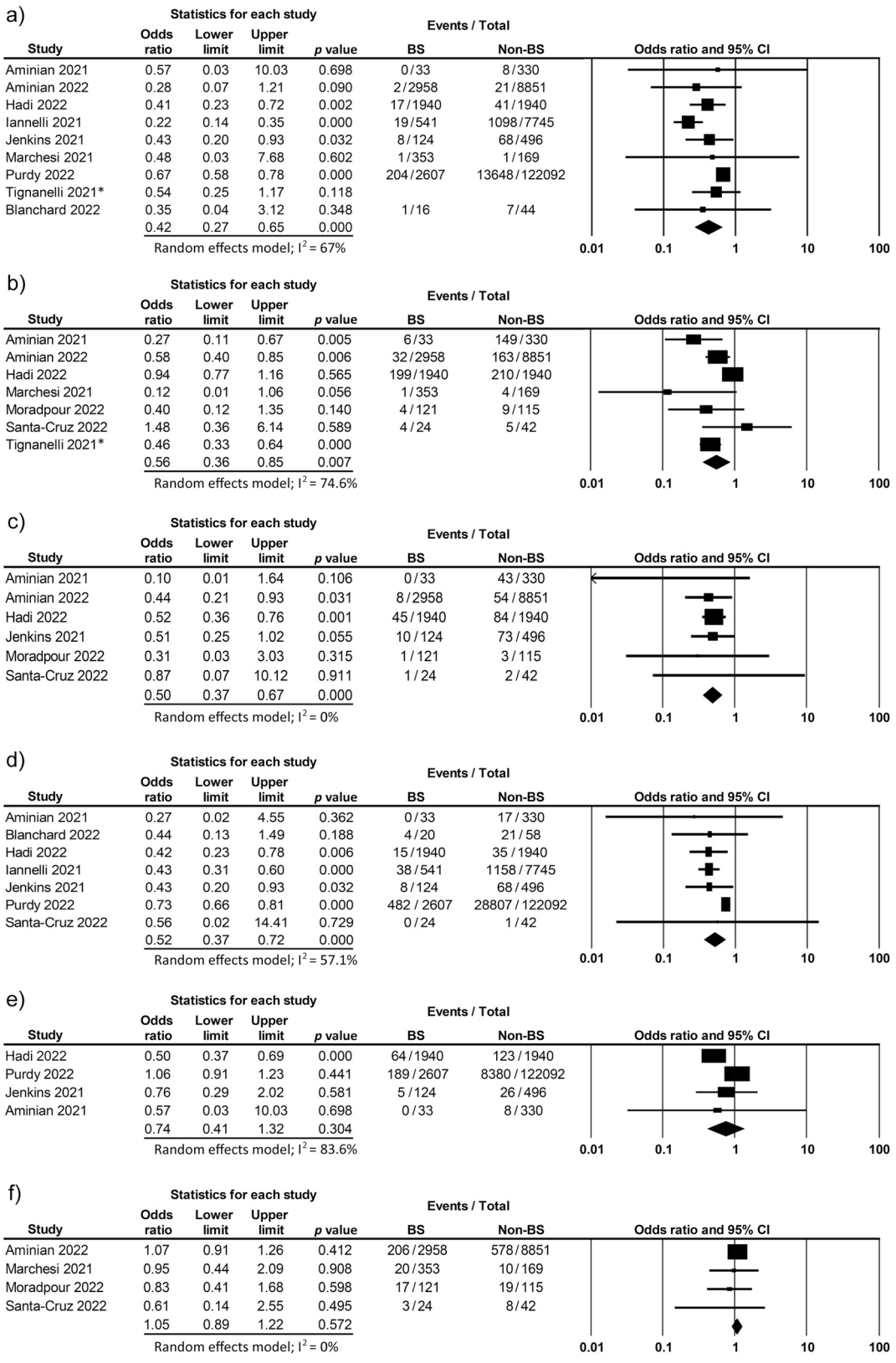

Fig. 2. Forest plots comparing risks of (a) mortality (odds ratio = 0.42, 95% CI: 0.27–0.65, $p < 0.001$; $I^2 = 67\%$), (b) hospital admission (odds ratio = 0.56, 95% CI: 0.36–0.85, $p = 0.007$; $I^2 = 74.6\%$), (c) intensive care unit admission (odds ratio = 0.50, 95% CI: 0.37–0.67, $p < 0.001$; $I^2 = 0\%$), (d) mechanical ventilation (odds ratio = 0.52, 95% CI: 0.37–0.72, $p < 0.001$; $I^2 = 57.1\%$), (e) acute kidney injury (odds ratio = 0.74, 95% CI: 0.41–1.32, $p = 0.304$; $I^2 = 83.6\%$), and (f) infection (odds ratio = 1.05, 95% CI: 0.89–1.22, $p = 0.572$; $I^2 = 0\%$) between previous bariatric surgery (BS) and non-BS groups. CI, confidence interval. *Only odds ratio available for risk calculation.

difference in the infection rate of COVID-19 between the both groups (OR=1.05, 95%CI: 0.89–1.22, $p = 0.572$; I^2 =0%) (Figure 3). There was no significant impact on the outcome on sensitivity analysis. Besides, Egger's test showed no publication bias in the outcomes ($p = 0.057$).

3.3.4. Subgroup analysis

The results of subgroup analysis based on the matched cohort studies (Approach II) [20–22,29,31] are shown in supplemental Table 5. Meta-analysis of results demonstrated an association between previous BS and lower risks of mortality, ICU admission, mechanical ventilation, and AKI compared to the control group (all $p < 0.001$). However, the correlations of previous BS with the risk of hospitalization ($p = 0.081$) and infection rate ($p = 0.41$) were non-significant. Subgroup analysis based on the studies in which BMI was available (Approach III) [20,21,23,29,31,34,35] demonstrated no differences in the risks of AKI and COVID-19 infection between the BS and non-BS groups despite a significantly lower BMI in the former. On the other hand, the former exhibited lower risks of mortality, hospital/ICU admission, and mechanical ventilation compared to the latter (supplemental Table 6).

3.3.5. Certainty of evidence

The quality of evidence for outcome measures based on the GRADE (Grading of Recommendations Assessments, Development, and Evaluation) system is shown in Table 2. The levels of evidence were graded as very low for the risk of AKI, low for the risks of hospital admission and infection rate of COVID-19, and moderate for the risks of mortality, ICU admission, and mechanical ventilation.

4. Discussion

This meta-analysis involving 151,475 patients showed an association between BS and a lower severity of COVID-19 infection, as manifested by the notable reductions in the risks of mortality, hospital and ICU admissions as well as mechanical ventilation without a significant impact on the infection rate and the risk of AKI. With the exception of the risks of hospital admission and infection, the findings remained consistent on subgroup analysis in which matched cohort studies were included for comparison.

The risk of mortality was chosen as the primary outcome in the current meta-analysis because other severity-related outcomes (e.g., risk of hospital admission) may be influenced by the hospital policy for COVID-19 treatment. A previous meta-analysis of three studies recruiting 9022 patients reported an association between previous BS and a reduced risk of mortality [19]. In addition to being consistent with their findings, our results provided more robust evidence as the number of participants in the current meta-analysis was 17-fold higher than that in the previous study [19]. Furthermore, taking into account the potential influences of uncontrolled confounders (e.g., age) of retrospective or observational studies on their study outcomes, the current study demonstrated a lower incidence of diabetes mellitus and BMI in the BS group without significant differences in other patient characteristics and comorbidities between the two groups based on the studies with data available for analyses (supplemental Table 4). The lower incidence of diabetes mellitus may be attributable to the remission of diabetes mellitus after surgically induced weight loss [36]. Furthermore, subgroup analysis based on matched cohort studies to minimize selection bias also supported the beneficial effects of previous BS on the reduction of the risks of ICU admission, mechanical ventilation, and mortality. Our results were consistent with the previous finding that obesity is a recognized risk factor for the need of intensive care [6,7,25], highlighting the potential benefits of weight reduction in the critical care setting.

A previous large-scale retrospective study has reported that prior BS may decrease the risk of hospitalization due to influenza infection [5]. Consistently, our analysis of all studies comparing individuals diagnosed with COVID-19 who received BS and those without undergoing BS (Approach I) as well as studies with available information about BMI of their participants (Approach III) showed a decreased risk of hospitalization in those with prior BS. On the other hand, the reduction in risk was non-significant when focusing on studies adopting a cohort design (Approach II). One possible explanation may be the strong influence on this outcome from non-medical factors, such as bed availability and variations in admission criteria [29].

The incidence of AKI has been shown to increase during the COVID-19 pandemic, leading to an increased mortality [37–39]. Possible reasons may be the direct impacts of inflammation, complement activation, and coagulopathy on the kidneys in COVID-19 patients with AKI [40]. In addition, current evidence suggests that obesity further increases the risk for AKI and dialysis in COVID-19 patients [41,42]. Despite sporadic reports of a short-term impairment of renal function after BS [39,40], pooled evidence still supported the association between BS and a long-term improvement in renal function [43,44]. Nevertheless, the current meta-analysis was unable to show the protective effect of prior BS on the risk of AKI in patients with COVID-19 possibly attributable to the presence of confounding factors and the limited number of included studies. For example, among the four studies [22,29,31,32] that provided detail for AKI risk analysis, two did not mention the interval between BS and study participation [31,32] and one reported eligibility of participants who underwent BS within two weeks [22] so that the potential impact of recovery from BS on renal function could not be assessed. The importance of confounding effect was further underscored by the demonstration of a significantly lower risk of AKI in the BS group than in the non-BS group after including only matched cohort studies in our subgroup analysis. Further studies with less heterogeneity are warranted to elucidate this issue.

Our meta-analysis is the first to explore the association of prior BS with infection rate of COVID-19 through a systematic approach. Previous observational studies have revealed an increased susceptibility of individuals with obesity to COVID-19 infection and a higher probability of viral test positivity compared to those without [6,45]. Taking into consideration the fact that SARS-CoV-2 infects human lung and other tissues through binding to angiotensin-converting enzyme 2 (ACE2) receptors on the plasma membrane [46] and the increased ACE2 receptor expression in adipose tissue, individuals with obesity are believed to have an increased ACE2 receptor expression that facilitates the entry of SARS-CoV-2 into adipocytes [47]. In this way, adipose tissue not only serves as a reservoir for the virus but may also expedite its spread to surrounding organs [48,49]. Nevertheless, despite the lower BMI in the BS group compared to the non-BS group in four of our included studies available for infection rate analysis, our results did not support an association between prior BS-induced weight loss and a lower risk of COVID-19 infection.

Of the six parameters investigated, four showed significant heterogeneity, namely risk of mortality (I^2 =67%), hospital admission (I^2 =74.6%), mechanical ventilation (I^2 =57.1%), and AKI between the two groups (I^2 =83.6%). Variations in study design, population, follow-up period, type of BS, and country of origin may be potential sources of heterogeneity. To investigate the impact of research design on our study outcomes, we performed subgroup analysis focusing on matched cohort studies (Supplemental Table 5). The results demonstrated that, with the exception of the parameter of hospital admission that still showed notable heterogeneity (i.e., 81%), no heterogeneity was noted in all other outcomes (i.e., I^2 =0%). Therefore, the findings may suggest a significant impact of study design (i.e., non-matched studies) on heterogeneity across our included studies. In addition, the annihilation of heterogeneity of all the other outcome parameters supported the robustness of evidence for these outcomes.

There were several limitations in the current meta-analysis. First, inclusion of observational and retrospective studies precluded our elucidation of causality. Nevertheless, because the conduction of clinical trials is not feasible in this clinical setting, our findings represented the best available evidence regarding the correlation between weight loss intervention and COVID-19 outcomes. In addition, the limited number

of matched cohort studies available for our subgroup analyses could not rule out the influence of potential confounders on the study outcomes. Second, because our pooled result from seven studies with information on BMI (Approach III) demonstrated a reduction after BS (mean difference: −8.8 kg/m^2) without a control group showing non-significant BMI reduction for comparison (supplemental Table 4), the effect of BMI on our study outcomes could not be clarified. Third, although previous studies have identified ethnicity as an independent predictor of hospitalization after SARS-CoV-2 infection [29,50], relevant information was not available for analysis. Fourth, the possible correlations between the degree of body weight loss and our study outcomes remain unclear because of limited data available. Finally, the impact of different types of bariatric procedures (restrictive v. malabsorptive procedures) on disease progression requires further studies for elucidation.

5. Conclusion

The findings of the present meta-analysis demonstrated that prior bariatric surgery was associated with lower rates of mortality (0.42-fold decreased risk), hospital (0.56-fold decreased risk), ICU admission (0.5-fold decreased risk), and mechanical ventilation (0.52-fold decreased risk) with no impact on the risk of acute kidney injury and infection rate of COVID-19. The protective effects of bariatric surgery may be attributed to substantial weight loss, highlighting the importance of obesity as a modifiable risk factor for disease progression after contracting COVID-19. Further studies are warranted to verify our findings and to identify those who may benefit most from bariatric surgery.

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CRediT authorship contribution statement

Sheng-Fu Chiu and Cheuk-Kwan Sun contributed equally as corresponding authors to this work. Kuo-Chuan Hung and Hsiao-Tien Chen: Conceptualization; Chung-Hsi Hsing and Ying-Jen Chang: methodology; Jinn-Rung, Kuo: software; Chun-Ning Ho: validation; Yao-Tsung Lin: formal analysis and investigation; Kuo-Chuan Hung: resources and data curation; Sheng-Fu Chiu and Cheuk-Kwan Sun: writing—original draft preparation; Kuo-Chuan Hung and Cheuk-Kwan Sun: writing—review and editing; Kuo-Chuan Hung: visualization; Cheuk-Kwan Sun: supervision. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.orcp.2022.10.005.

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