

Original Article

Short-term Mortality and Postoperative Complications of Abdominal Aortic Aneurysm Repair in Obese versus Non-obese Patients

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Background: Obesity is a risk factor not only for abdominal aortic aneurysm (AAA) but also for complications after vascular surgery. This study was to determine the effect of obesity on short-term mortality and post-intervention complications after AAA repair.

Methods: A systematic review and meta-analysis were performed. A systematic search was performed in PubMed; the articles describing the differences in post-intervention complications after open or endovascular repair of an AAA between obese and non-obese patients were selected. The primary outcome was short-term mortality defined as in-hospital mortality or mortality within 30 days after AAA repair. The secondary outcomes were cardiac complications, pulmonary failure, renal failure, and wound infections. The meta-analysis was performed using OpenMeta.

Results: Four articles were included in the meta-analysis; these articles included 35,989 patients of which 10,917 (30.3%) were obese. The meta-analysis showed no significant differences for short-term mortality (odds ratio [OR], 0.85; 95% confidence interval [CI], 0.69–1.04). Also, no significant difference was found in pulmonary failure (OR, 1.09; 95% CI, 0.85–1.42). However, obese patients were less likely to suffer from cardiac complications (OR, 0.73; 95% CI, 0.55–0.96). Nevertheless, there was a significantly higher risk of renal failure (OR, 1.16; 95% CI, 1.05–1.30) and wound infections (OR, 1.92; 95% CI, 1.55–2.38) in obese patients.

Conclusion: Obesity is not a risk factor for short-term mortality after AAA repair compared to non-obesity. Moreover, obese patients suffer less from cardiac complications than non-obese patients.

Key words: Obesity, Abdominal aortic aneurysm, Postoperative complications, Mortality

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INTRODUCTION

Obesity is a worldwide epidemic. The prevalence of obesity nearly tripled to 650 million individuals between 1975 and 2016.¹ Obesity is defined as a body mass index ≥ 30 kg/m² by the World Health Organization and is a major risk factor for chronic diseases such as diabetes mellitus (DM), hypertension, cardiovascular diseases, and several cancers.¹⁻³ Moreover, obesity is associated with a higher risk of abdominal aortic aneurysm (AAA).^{4,5} Obesity is a risk factor for

complications, e.g., wound infections, after surgery in general⁶ and, more specifically, after vascular surgery.⁷

The postoperative outcomes after AAA repair in obese patients undergoing open aneurysm repair (OAR) versus endovascular aneurysm repair (EVAR) have been previously described,⁸ but the effect of obesity on the outcomes after AAA repair is unknown. Because obesity is a risk factor for morbidity after vascular surgery,⁷ obesity may also be related to negative outcomes after AAA repair. If so, health care providers should be aware of the complications that

are more likely to occur in these patients. Complications can then be diagnosed earlier, and treatment can be started earlier.

However, an obesity paradox has been described in which patients with obesity have a better prognosis than non-obese patients when diagnosed with various cardiovascular diseases⁹ or when undergoing invasive procedures such as percutaneous coronary interventions.¹⁰ Therefore, the objective of this study was to determine the effect of obesity on short-term mortality and post-intervention complications after AAA repair.

METHODS

We conducted a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹¹

Data sources and searches

A systematic search was performed employing PubMed on December 11, 2019 using the following search query: (“Body mass index”[Mesh] OR “Overweight”[Mesh]) AND “Aortic aneurysm” [Mesh] AND (“Clinical Trial”[ptyp] OR “Epidemiologic Studies” [Mesh]). To ensure that new articles not yet indexed with Mesh-term were included, a search for new articles published in 2019 was performed later. The data range was customized from January 1, 2019, to December 11, 2019, and the following query was used: (“Body mass index”[All Fields] OR “Overweight”[All Fields] OR “Obesity” [All Fields]) AND “Aortic aneurysm”[All Fields].

Inclusion and exclusion criteria

Two reviewers (BZ and DV) independently screened all identified studies for eligibility. Articles were required to be written in English and to describe the differences in post-intervention complications after OAR or EVAR between obese and non-obese patients. Articles were included or excluded based on the titles and abstracts. Last, full articles were reviewed and included if at least one of the following complications was discussed: short-term mortality, cardiac complications, pulmonary complications, renal complications, or wound infections. Articles were excluded if the data did not include the exact number of patients who experienced complications.

Quality assessment

The quality of the included studies was determined using the Newcastle-Ottawa scale (NOS) for cohort studies. Five or less points on the NOS were considered as poor quality. Articles were not excluded due to poor quality, but quality results were used to interpret the results of the meta-analysis.

Outcomes

The primary outcome was short-term mortality. Short-term mortality was defined as in-hospital mortality or mortality within 30 days after AAA repair. The secondary outcomes were cardiac complications (myocardial infarction, cardiac arrest, heart failure, or arrhythmias), pulmonary failure (unplanned reintubation, need for ventilation > 48 hours after surgery, or in hospital pneumonia), renal failure (increased levels of plasma creatinine or dialysis use), and wound infections.

Data extraction

For each study the following data were collected: first author, year of publication, country, study type, number of included patients, gender of patients, number of obese and non-obese patients, definition of obesity, number of obese and non-obese patients undergoing different surgery type(s), number of ruptured AAAs, and number of obese and non-obese patients with DM. Moreover, the following outcome data were collected for both obese and non-obese patients: short-term mortality, pulmonary failure, cardiac complications, renal failure, and wound infections. Absolute numbers were calculated by both authors when the collected data were given in percentages.

Statistical analysis

Proportions of patients diagnosed with postoperative complications in the obese and non-obese groups were calculated. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each individual study using OpenMeta. Results were considered statistically significant if $P < 0.05$ (two-sided). The meta-analysis was also performed using OpenMeta, and ORs were used as metric. The value of Cochran's Q was used to evaluate heterogeneity between the included studies. Heterogeneity was defined as $P < 0.1$ for the Cochran's Q statistic. If heterogeneity was present, a ran-

dom-effects model was applied; otherwise, a fixed-effects model was applied.

RESULTS

Study selection

A total of 124 articles were found; 82 articles were identified by the first search query, 45 by the second, and three in both. By screening the titles and the abstracts of the 124 articles, 115 articles were

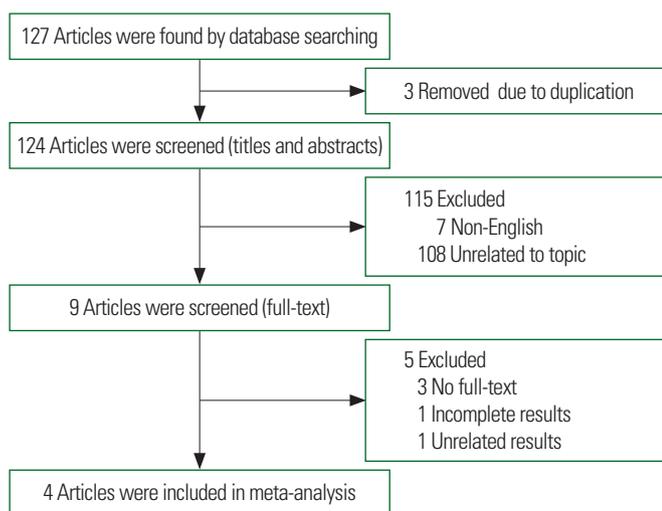


Figure 1. Flow diagram of identification and study selection.

Table 1. Characteristics of the included studies

Author	Country	Study type	Population	Sex			Weight class		NOS
				Male	Female	Unknown	Obese	Non-obese	
Locham et al. ¹²	USA	Retrospective cohort study	33,082	26,450 (80.0)	6,630 (20.0)	2 (0.0)	10,139 (30.6)	22,943 (69.4)	7
Johnson et al. ¹³	USA	Retrospective cohort study	2,201	2,187 (99.4)	14 (0.6)		595 (27.0)	1,606 (73.0)	8
Jonker et al. ¹⁴	USA	Retrospective cohort study	80	77 (96.0)	3 (4.0)		26 (32.5)	54 (67.5)	5
Park et al. ¹⁵	USA	Retrospective cohort study	626	502 (80.2)	124 (19.8)		157 (25.1)	469 (74.9)	4

Values are presented as number (%).
NOS, Newcastle-Ottawa scale.

Table 2. Prevalence of obesity in the included studies

Author	Definition of obesity	Obesity OAR (%)	Obesity EVAR (%)	Non-obesity OAR (%)	Non-obesity EVAR (%)	Ruptured AAA (%)	DM in obese patients	DM in non-obese patients
Locham et al. ¹²	BMI ≥ 30 kg/m ²	17.3	82.7	20.1	79.9	0.0	2,864 (28.2)	3,665 (16.0)
Johnson et al. ¹³	BMI ≥ 30 kg/m ²	49.6	50.4	55.5	45.5	3.1	155 (26.1)	252 (15.7)
Jonker et al. ¹⁴	BMI ≥ 30 kg/m ²	0.0	100.0	0.0	100.0	0.0	12 (46.2)	12 (22.2)
Park et al. ¹⁵	BMI ≥ 30 kg/m ²	65.0	35.0	64.2	35.8	0.0	33 (21.0)	72 (15.4)

Values are presented as number (%) unless otherwise indicated.
OAR, open aneurysm repair; EVAR, endovascular aneurysm repair; AAA, abdominal aortic aneurysm; DM, diabetes mellitus; BMI, body mass index.

excluded. Another five articles were excluded after screening the full texts. Four articles met the selection criteria and were included in the meta-analysis (Fig. 1).

Study characteristics

All four studies were retrospective cohort studies and included 35,989 patients of which 10,917 (30.3%) were obese. 28.1% of the obese patients versus 16.0% of the non-obese patients suffered from DM. Characteristics of the studies are shown in Tables 1 and 2, and all studies discussed short-term mortality.¹²⁻¹⁵ Three articles discussed pulmonary failure and cardiac complications,¹³⁻¹⁵ and renal failure and wound infections were discussed in all four articles.

Short-term mortality

Short-term mortality occurred in 453 out of 35,989 patients (Ta-

Table 3. Percentages and ORs of short-term mortality in obese and non-obese patients undergoing AAA repair

Author	Obese (n = 10,917)	Non-obese (n = 25,072)	OR (95% CI)
Locham et al. ¹²	96 (0.9)	253 (1.1)	0.86 (0.69–1.08)
Johnson et al. ¹³	19 (3.2)	70 (4.4)	0.74 (0.46–1.19)
Jonker et al. ¹⁴	1 (3.8)	0	6.88 (0.35–133.79)
Park et al. ¹⁵	3 (1.9)	11 (2.3)	0.82 (0.24–2.78)

Values are presented as number (%) unless otherwise indicated.
OR, odds ratio; AAA, abdominal aortic aneurysm; CI, confidence interval.

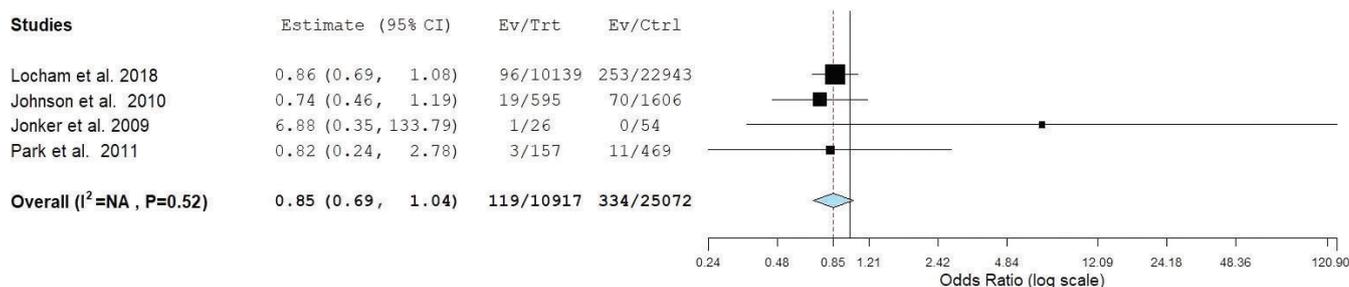


Figure 2. Forest plot of short-term mortality in obesity patients versus non-obese patients. CI, confidence interval; Ev, events; Trt, treatment group; Ctrl, control group; NA, not available.

ble 3). A total of 119 obese patients (1.1%) and 334 non-obese patients (1.3%) died. Three out of the four studies showed that obese patients had a tendency towards a lower short-term mortality. However, none of these findings were statistically significant. No significant heterogeneity was found among the studies; therefore, a fixed-effects model was used for the meta-analysis ($P=0.52$). Fig. 2 shows that the OR for the total population was 0.85 (95% CI, 0.69–1.04; $P=0.10$).

Pulmonary failure

Pulmonary failure was discussed in three out of the four articles (Table 4) and was reported in 333 patients. A total of 94 obese patients (12.1%) and 239 non-obese patients (11.2%) were diagnosed with pulmonary failure after AAA repair. None of the articles showed a significant difference between groups. There was no significant heterogeneity among the studies; therefore, a fixed-effects model was used for the meta-analysis ($P=0.27$). Fig. 3A shows the meta-analysis with an OR of 1.09 (95% CI, 0.85–1.42; $P=0.50$).

Cardiac complications

Three of the four articles discussed cardiac complications (Table 4). These were reported in 298 patients of which 62 (8.0%) were obese and 236 (11.1%) were non-obese. All articles found a tendency towards fewer cardiac complications in obese patients compared to non-obese patients, but none of the results were statistically significant. Again, the fixed-effect model was applied for the meta-analysis because there was no heterogeneity among the studies ($P=0.94$). The meta-analysis showed a significant difference in cardiac complications between obese and non-obese patients. These were significantly more frequent in the non-obese group. Fig. 3B shows

Table 4. Percentages and ORs of diagnoses with post-intervention complications in obese and non-obese patients undergoing AAA repair

Author	Obese	Non-obese	OR (95% CI)
Pulmonary failure			
Johnson et al. ¹³	65 (10.9)	181 (11.3)	0.97 (0.72–1.30)
Jonker et al. ¹⁴	3 (11.5)	4 (7.4)	1.67 (0.32–8.64)
Park et al. ¹⁵	26 (16.6)	54 (11.5)	1.57 (0.92–2.70)
Cardiac complication			
Johnson et al. ¹³	33 (5.5)	117 (7.3)	0.76 (0.52–1.11)
Jonker et al. ¹⁴	0	1 (1.9)	0.70 (0.04–13.52)
Park et al. ¹⁵	29 (18.5)	118 (25.2)	0.69 (0.45–1.06)
Renal failure			
Locham et al. ¹²	504 (5.0)	998 (4.3)	1.15 (1.03–1.29)
Johnson et al. ¹³	32 (5.4)	63 (3.9)	1.42 (0.90–2.26)
Jonker et al. ¹⁴	1 (3.8)	1 (1.9)	2.43 (0.11–44.07)
Park et al. ¹⁵	10 (6.4)	31 (6.6)	0.96 (0.46–1.20)
Wound infection			
Locham et al. ¹²	123 (1.2)	166 (0.7)	1.76 (1.37–2.26)
Johnson et al. ¹³	50 (8.4)	67 (4.2)	2.32 (1.52–3.52)
Jonker et al. ¹⁴	0	1 (1.9)	0.70 (0.04–13.52)
Park et al. ¹⁵	3 (1.9)	1 (0.2)	14.43 (1.50–139.18)

Values are presented as number (%) unless otherwise indicated. OR, odds ratio; AAA, abdominal aortic aneurysm; CI, confidence interval.

that the OR was 0.73 (95% CI, 0.55–0.96; $P=0.03$).

Renal failure

All four articles discussed renal failure after surgery (Table 4); renal failure was reported in 1,640 patients of which 547 (5.0%) were obese and 1,093 (4.4%) were non-obese. Three of the four articles showed that renal failure occurred more often in obese patients than in non-obese patients. However, only one of these studies demonstrated a significant difference. A fixed-effects model was used for the meta-analysis ($P=0.76$), and the meta-analysis (Fig. 3C) showed a significant difference in occurrence of renal failure between obese

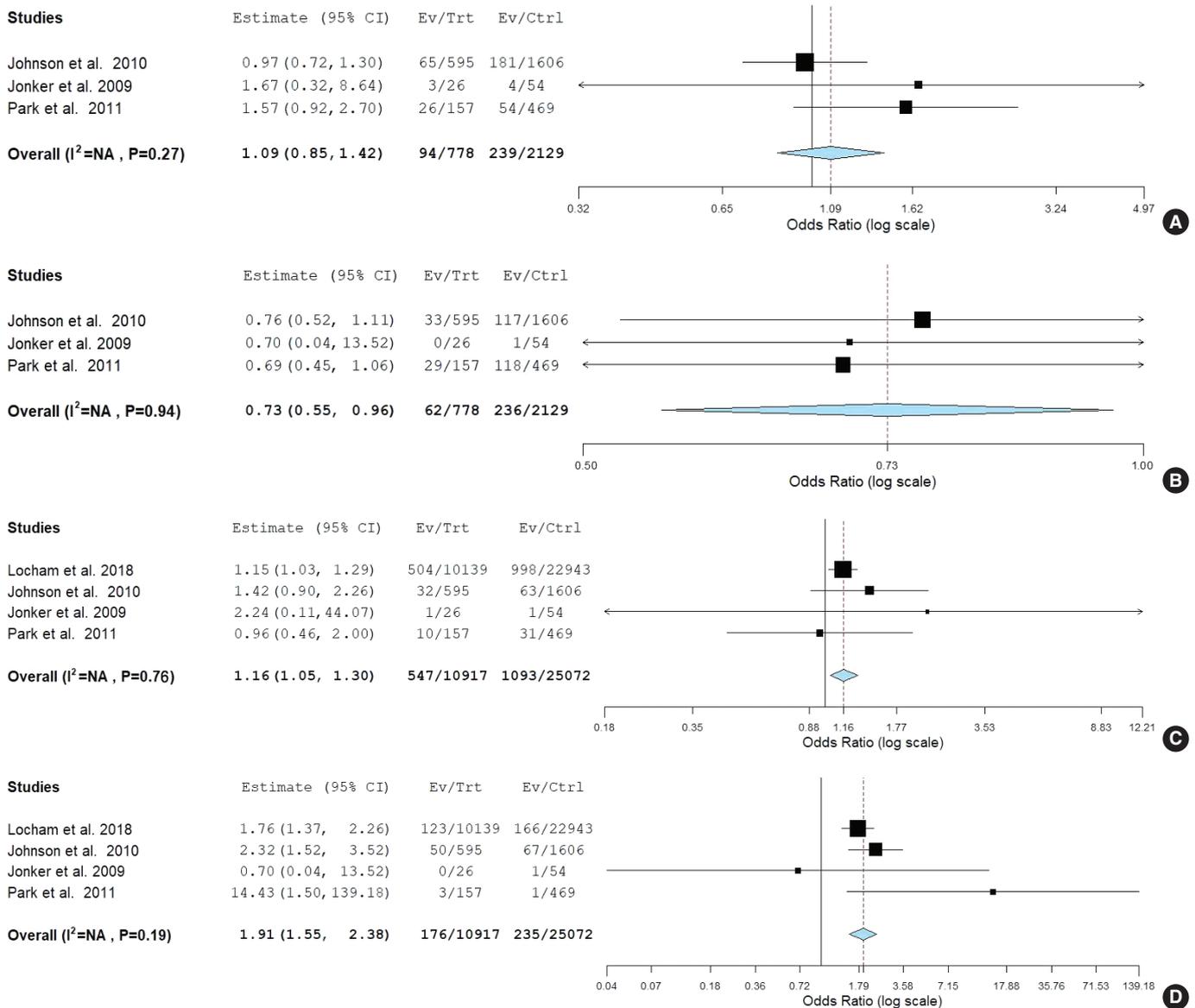


Figure 3. (A) Forest plot of diagnoses with pulmonary failure in obesity patients versus non-obese patients. (B) Forest plot of diagnoses with cardiac complications in obesity patients versus non-obese patients. (C) Forest plot of diagnoses with renal failure in obesity patients versus non-obese patients. (D) Forest plot of diagnoses with wound infections in obesity patients versus non-obese patients. CI, confidence interval; Ev, events; Trt, treatment group; Ctrl, control group; NA, not available.

and non-obese patients. The OR was 1.16 (95% CI, 1.05–1.30; $P=0.01$).

Wound infections

All four articles discussed wound infections (Table 4). These occurred in 411 patients: 176 obese patients (1.6%) and in 235 non-obese patients (0.9%). Three of the four studies showed that obese patients had significantly more wound infections than non-obese patients. The fixed-effect model was again used ($P=0.14$). In the

meta-analysis, a significant difference in wound infections was found between the groups. Fig. 3D shows that the OR was 1.92 (95% CI, 1.55–2.38; $P<0.001$).

DISCUSSION

A meta-analysis on short-term mortality and post-intervention complications after AAA repair in obese patients compared to non-obese patients was performed. The major finding of the study is

that obesity does not appear to be a risk factor for short-term mortality after AAA repair compared to non-obesity. Obesity is also not a risk factor for postoperative pulmonary failure. Moreover, obese patients suffer less from cardiac complications than non-obese patients. However, obesity does appear to be a risk factor for both postoperative renal failure and wound infections.

The obesity paradox is that obese patients with several diseases, such as cardiovascular disease and cancer, have a better prognosis than non-obese patients.^{9,16} The mechanism through which this paradox functions is most likely multifactorial.¹⁷ For example, obese patients have a higher lean mass, including total body water, and skeletal muscle. When patients are diagnosed with a cardiovascular disease, increased lean mass causes higher cardiorespiratory fitness because of higher muscle diffusion capacity and mitochondrial respiration capacity at the skeletal muscle level. Higher cardiorespiratory fitness may be the reason for a better prognosis in these patients.^{9,18} Although the obesity paradox has been extensively described in a broad range of conditions¹⁹⁻²¹ and interventions,^{22,23} its applicability to AAA repair was unknown.

Three out of the four articles we have selected reported a (non-significant) trend towards a lower short-term mortality in obese patients. In the other study, only one person died; this patient was in the obesity group.¹⁴ Consistent with our results, Mariscalco et al.²² showed that overweight and obese patients undergoing cardiac surgery had lower in-hospital mortality compared to non-obese patients. The authors hypothesized that the survival benefit of obese patients may reflect worse outcomes of patients with either other severe diseases or underweight patients. These patients have decreased survival for reasons such as chronic diseases and cachexia.²⁴ This may also be the most logical explanation for our finding of obesity not being a risk-factor for short-term mortality after AAA repair. We did find a lower chance of cardiac complications in obese patients; this is consistent with the obesity paradox. An explanation of this finding might be the higher cardiorespiratory fitness in obese patients with cardiovascular disease, as already described.

Our meta-analysis did not show a significant difference in pulmonary failure events. On the contrary, Eichenberger et al.²⁵ showed that morbidly obese patients are more likely to suffer from atelectasis than non-obese patients after general anesthesia, even 24 hours after extubation. Anesthesia and paralysis can cause reduced end-

expiratory lung volumes in morbidly obese patients leading to atelectasis and a fall in arterial oxygenation.²⁶ An explanation for our results may be that we did not differentiate between obese and morbidly obese patients. Because of this, the worst outcomes of the morbidly obese patients might be nullified by the outcomes of the non-morbidly obese patients. We also did not differentiate between normal and underweight patients. The worst outcomes of obese patients might be outweighed by the worst outcomes of the underweight patients. Engel et al.²⁷ showed that underweight patients suffered more from respiratory problems, and, therefore, required longer ventilation after coronary artery bypass graft surgery than normal weight patients.

Obese patients are more likely to suffer from postoperative renal failure after AAA repair than non-obese patients. Three of the four studies¹²⁻¹⁴ used in the meta-analysis described these results. However, one study¹⁵ described obese patients as having a lower chance of postoperative renal failure, but this study scored low on the quality assessment analysis. In line with our results, Moon et al.²⁸ also showed that obesity is a risk factor for acute kidney injury (AKI) after coronary artery bypass grafting. Also, Billings et al.²⁹ showed that obese patients have a greater risk of developing renal failure after cardiac surgery in general. These researchers found that the concentration of intraoperative F2-isoprostane, a marker for oxidative stress, may predict AKI after cardiac surgery and also suggested that obesity is associated with higher intraoperative concentrations of F2-isoprostane. Reducing the formation of F2-isoprostane could potentially reduce the risk of developing AKI in obese patients.

Finally, three out of the four studies^{12,13,15} and the meta-analysis showed that obese patients were significantly more likely to suffer from wound infections than non-obese patients. DM is a risk factor for surgical site infections for surgery in general, but especially for cardiac surgery.³⁰ DM also has a strong association with obesity; obese adults are seven times more likely to suffer from type 2 diabetes than non-obese adults.³¹ Consistent with this, DM was more common in obese patients than in non-obese patients in our study (28.1% vs. 16.0%). This association may be the reason that obese patients suffer more from wound infections than non-obese patients. Also, Rahmanian et al.³² showed that obese patients are at significantly higher risk of developing wound infections after coronary bypass

grafting or valve surgery. This group also mentioned that the patients who had wound infections had a higher rate of other infections, e.g., gastrointestinal complications and renal failure, and increased mortality. Therefore, in obese patients, the prevention, diagnosis, and early treatment of wound infections require emphasis.

Limitations

This study included a large patient population and contributed to the knowledge base concerning the obesity paradox. However, a limitation of this study is that we did not distinguish between the two different types of surgery as we were only interested in the effect of obesity on AAA repair. However, Saedon et al.⁸ had previously determined that EVAR is superior to OAR in obese patients. Also, corrections were not made for differences between elective and emergent surgeries; this could have influenced the primary outcome.³³ Another limitation is the small number of articles in this meta-analysis, and some of these articles did not describe the different subgroups of obesity. Therefore, subgroup analyses could not be made. Finally, quality assessment was performed using the NOS. Two of the four studies scored five or lower on the quality assessment.^{14,15} These two studies included the lowest number of patients. However, these studies could have influenced the final conclusions on short-term mortality and other postoperative complications.

The obesity paradox appears to apply to obesity patients undergoing AAA repair. Although the underlying mechanism remains to be elucidated, this finding underlines that judgement on operability and the ability to intervene in obese patients should be based on a holistic approach considering all available patient data without overestimating potential harmful effects of obesity.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Study concept and design: BZ and DV; acquisition of data: BZ and DV; analysis and interpretation of data: BZ and DV; drafting of the manuscript: BZ and DV; critical revision of the manuscript: SMS, IK, and, BMD; statistical analysis: BZ and DV; administra-

tive, technical, or material support: SMS, IK, and, BMD; and study supervision: SMS and BMD.

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