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The effect of obesity on outcomes in trauma patients: A meta-analysis

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ABSTRACT

Objective: This study aims to assess the effect of obesity on injury severity score (ISS), mortality and course of hospital stay among trauma patients.
Method: A systematic review of the literature was conducted by Internet search. Data were extracted from included studies and analysed using a random-effects model to compare outcomes in the obese (body mass index (BMI) $\geq$ 30 kg m^{-2}) with the non-obese (BMI < 30 kg m^{-2}) group.
Result: Eventually, 18 studies met our inclusion criteria with 7751 obese patients representing 17% of the pooled study population. The data revealed that obesity was associated with increased risk of mortality, longer stay in the intensive care unit and higher rates of complication. Additionally, obese patients seemed to have longer duration of mechanical ventilation and hospital length of stay but it did not reach statistical significance. No difference was observed in ISS between the two groups.
Conclusion: Evidence strongly supports the correlation of obesity with worse prognosis in trauma patients and further studies should target this kind of population for therapy and prevention.

Obesity is widely acknowledged to be a public health threat for its definite association with multiple chronic conditions such as diabetes, dyslipidaemia, hypertension, osteoarthritis, heart disease and some types of cancer.[1] Due to an increased awareness of influence of obesity in acute conditions, numerous studies were conducted to assess the relationship between obesity and prognosis after trauma. However, their results were not consistent. It was reported that obesity could be an independent risk factor of poor outcomes after adjusting for age, gender, injury severity score (ISS), injury type and other confounded factors in some studies.[2–9] Nevertheless, several well-designed trials were unable to demonstrate such an association.[10–17] Given the rising prevalence of obesity and the specific challenges these patients would face after trauma, we made a combined analysis of previous studies in an effort to answer the question: does obesity affect ISS, hospital course, complications and mortality in trauma patients?

Patients and methods

Search strategy

This study was conducted according to the guideline from the meta-analysis of observational studies in epidemiology (MOOSE) group.[18] English-language articles published in Web of Science, PubMed and Cochrane Library up to June 2012 were searched using the following strategy: ('obesity' or 'obese' or 'body mass index') and ('trauma' or 'injury'). References cited by chosen articles were checked manually for any other potential studies.

Study selection and data extraction

Studies chosen for the analysis fulfilled the following inclusion criteria: (1) population: patients older than 13 years with either blunt or penetrating, single or multiple injuries. (2) Intervention or exposure: different body weight levels based on body mass index (BMI) categorised according to the World Health Organization (WHO) guideline[19] (BMI $\geq$ 30 kg m^{-2} as obese and BMI < 30 kg m^{-2} as non-obese, 18.5–24.9 kg m^{-2} as normal, 25–29.9 kg m^{-2} as overweight, 30–39.9 kg m^{-2} as obese and $\geq$40.0 kg m^{-2} as morbidly obese). (3) Outcomes: the primary outcome was mortality. ISS, length of stay in hospital (HLOS) and ICU (ILOS), mechanical ventilation days (MVD) and complication rate were measured as secondary outcomes. (4) Study design: randomised controlled trial (RCT), prospective observational or retrospective cohort study, case–control study.

Descriptive studies without comparative data such as reviews and case reports were excluded. As to studies with overlapping patient population, only the studies with the longest time of observation and most number of patients were included.

Two investigators independently reviewed the title and abstract of all potential articles and selected articles fulfilling our inclusion criteria for full text analysis. Data extracted from these articles included first author's name, publication year, study design, inclusion and exclusion criteria, patients number of each

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BMI strata and first and secondary outcomes. Disagreements were resolved by either consensus or a third-party decision.

Study quality assessment

Because it was not viable to carry out the RCT to evaluate the effect of obesity on trauma, all studies included in the meta-analysis were observational studies combined by a cohort study and a case–control study. To assess the quality of these studies we used a previously designed criteria adapted by Taggart et al.,[20] which examined five factors: participant selection, comparability groups, outcomes, size and cohort design. Descriptions for each component of the quality assessment are outlined in Table 1. Studies without score in any category were excluded.

Statistical analysis

All statistical analysis was performed utilising Stata/SE 11.0 (Stata Corporation, College Station, TX, USA). As to studies that did not stratified outcomes based on BMI categories of $\geq$30 kg m^{-2} and $<$30 kg m^{-2}, we would make a statistical analysis using the original data from these studies to rebuild the obese and non-obese group. The random-effect model with DerSimonian–Laird method[24] was used to pool the data from individual studies to assess both within- and between-study variations. The pooled effect for mortality and complication rate were calculated as odds ratio (OR) with 95% confidence intervals (CIs), whereas ISS, HLOS, ILOS and MVD were expressed as mean differences with 95%CI. Moreover, we performed an OR estimate of mortality for subgroup analysis based on likely sources of between-study heterogeneity, such as BMI strata, ISS and mechanism of trauma. The statistical heterogeneity for all variables was quantitatively assessed by the χ^2-based Q test and the I^2 score. The funnel plot was carried out by Begg's rank correlation test to assess publication bias.[25] By convention, $p < 0.05$ was considered statistically significant.

Results

Our search strategy identified 2073 potentially relevant publications. Twenty-six of these publications met the inclusion criteria after the abstract review and were chosen for a full-text review. Upon closer examination, another eight studies were ruled out for the following reasons: definition of obesity using a different criterion (BMI $>$ 40 kg m^{-2})[26,27]; use of overlapping data with a smaller cohort and a shorter study period[21,28]; inclusion of patients with specific injury patterns (such as head injury[29] and thoracic injury[30]) or injury mechanism[31]; and inability to extract data due to the lack of standard deviation (SD) for mean LOS and MVD.[32] Fig. 1 indicates the study selection process. Finally, eighteen articles[2–17,22,23] with five prospective cohort studies[6,8,16,17,25] and thirteen retrospective cohort studies were included in our meta analysis. Except for two of these studies that were conducted in Europe,[8,9] the remainder were all in the United States.

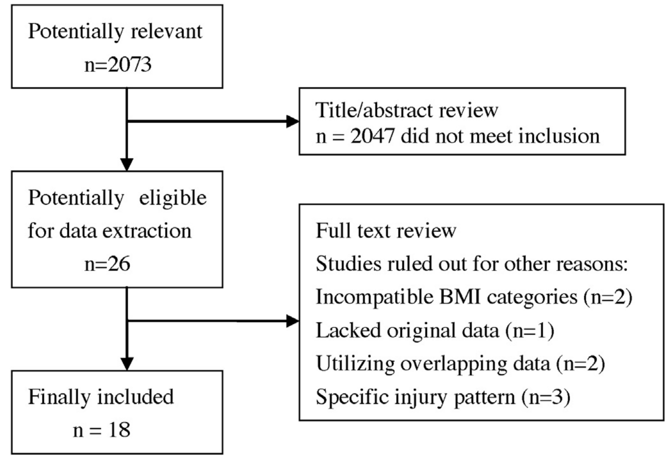

Fig. 1. Literature search and study selection process.

The results of the quality assessment are illustrated in Table 2. The overall quality of the studies selected for this meta-analysis was considered variable and the studies have some common problems. All but five of the studies used a retrospective design. Some studies used samples that could not represent the entire injured population: eight studies only included blunt trauma patients,[2,3,10,11,22,23] five studies only included patients with ISS $\geq$ 15[8,10,11,15,23] and three studies only included vehicular trauma patients.[4,5,7] Four studies had a sample size smaller than 100 in some groups.[2,4,14,15]

Table 3 provides a summary of the characteristics of all selected studies, presenting study design, BMI category, sample size (obese and total patients), inclusion and exclusion criteria, adjusted variables and whether obesity was an independent risk factor of mortality.

Table 1
Quality assessment of non-randomised studies.

Participant selection
Selected cohort was representative of the general injured population (1)
Cohort was a selected group or the selection was not described (0)
Comparability of groups
No differences between the groups explicitly reported (especially in terms of BMI, age, injury type, pre-existing disease) unless it was one of these variables that was under investigation, or such differences were adjusted for (2)
Differences between groups were not recorded (1)
Groups differed (0)
Outcomes
Referenced definition of clinical outcome including mortality, ISS, HLOS, ILOS, VD and complications (2)
Explicit definition that included trauma mechanism and patterns (1)
Outcome of trauma not defined (0)
Size
>100 participants in each group (2)
<100 participants in each group (1)
Cohort design
Prospective cohort design (2)
Retrospective design (1)

Table 2
Quality scores of included studies.

Included study	Selection	Comparability	Outcome	Size	Cohort design
Newell[10]	0	2	2	2	1
Boulanger[22]	0	1	2	2	1
Choban[2]	0	2	2	1	1
Duane[11]	0	2	2	2	1
Brown[3]	1	2	1	2	1
Belzberg[12]	1	2	2	2	1
Byrnes[23]	1	2	2	2	1
Ryb[4]	0	2	1	2	1
Mock[5]	0	1	1	2	1
Alban[13]	1	2	2	2	1
Bochicchio[6]	1	2	2	1	2
Evans[14]	1	2	2	2	1
Ciesla[15]	0	2	1	2	2
Dossett[16]	1	2	2	2	2
Arbabi[7]	0	2	1	1	1
Nelson[8]	0	2	2	1	2
Winfield[17,21]	0	2	2	2	2
Hoffmann[9]	1	2	2	2	1

Table 3
Characteristics of studies included in the meta-analysis.

Study (Ref.)	Study design	BMI category (kg/m^2)	Number of obese/ total patients (%)	Inclusion and exclusion criteria	Adjusted variables Obesity associated with mortality (Y/N)
Newell[10]	Retrospective cohort	18.5–24.9; 25–29.9; 30–39.9; ≥40	463/1543 (30)	Inclusion: ISS ≥ 16, blunt trauma	Age, ISS N
Boulanger[22]	Retrospective cohort	<30; ≥30	743/5625 (12)	Inclusion: blunt trauma; exclusion: survival < 24 h	No mortality mentioned
Choban[2]	Retrospective cohort	<27; 27–31; >31	19/184 (10)	Inclusion: blunt trauma	Age, gender, ISS Y
Duane[11]	Retrospective cohort	<30; >30	115/453 (25)	Inclusion: blunt trauma	Univariate analysis N
Brown[3]	Retrospective cohort	<30; ≥30	283/1153 (25)	Inclusion: blunt trauma; admitted to the ICU	ISS, GCS, age, admission hypotension Y
Belzberg[12]	Retrospective cohort	<30; ≥30	131/625 (21)	Inclusion: trauma; exclusion: severe head injury with GCS<8 or brain dead	Univariate analysis N
Byrnes[23]	Retrospective cohort	<25; ≥25 to <30; ≥30 to <35; ≥35 to <40 ≥40	290/1179 (25)	Inclusion: trauma exclusion: age < 18 years	The greatest rise in mortality was seen among patients with BMI > 35
Ryb[4]	Retrospective cohort	18.5–24.9; 25–29.9; ≥30	435/1615 (27)	Inclusion: vehicular trauma; in frontal and lateral crash Exclusion: age < 16 years	Patient and crash factors Y
Mock[5]	Retrospective cohort	<20;20–24; 25–29;30–34; 35–39; ≥40	3974/26,727 (15)	Inclusion: motor vehicular trauma Exclusion: age < 15 years	Age, gender, seatbelt use, occupant seat position, vehicle curb weight Y
Alban[13]	Retrospective cohort	<30; ≥30	135/918 (15)	Inclusion: trauma patients admitted to SICU Exclusion: age < 18 years	Age, ISS, APACHE II, mechanism of injury N
Bochicchio[6]	Prospective cohort	<30; ≥30	62/1167 (5)	Inclusion: trauma	Diabetes, age, COPD, gender, ISS Y
Evans[14]	Retrospective cohort	<18.5; 18.5–24.9; 25.0–29.9; ≥30	154/461 (33)	Inclusion: trauma; older than 45 years	Age, ISS, comorbidity-polypharmacy score (CPS) N
Ciesla[15]	Prospective cohort	<30; ≥30	152/716 (21)	Inclusion: ISS > 15; ICU admission within 24 h of injury; survival > 48 h Exclusion: age < 15 years; isolated head injuries	Age, ISS, MOF, transfusion of blood N
Dossett[16]	Prospective cohort	<18.5; 18.5–24.9; 25.0–29.9; 30–39.9; ≥40	367/1219 (30)	Inclusion: trauma patients admitted to SICU; survival >48 h Exclusion: age < 18 years	Age, gender, ISS, AIS head score Obese (N) Severe obese (Y)
Arbabi[7]	Retrospective cohort	≤25; 25–30; >30	45/189 (24)	Inclusion: motor vehicular trauma; at least one AIS score >2; in frontal and lateral crash Exclusion: age < 13 years	Age, type of impact Y
Nelson[8]	Prospective cohort	<18.5; 18.5–24.9; 25.0–29.9; ≥30	90/1084 (8)	Inclusion: ISS ≥ 16; exclusion: age < 16 years; burn injuries; delayed referrals > 12 h after trauma	Admission lactate, traumatic brain injury, NISS > 50 Y
Winfield[17,21]	Prospective cohort	18.5–24.9; 25–29.9; 30–39.9; >40	277/877 (32)	Inclusion: severe blunt trauma; need for blood transfusion with base deficit > 6 or systolic blood pressure > 90 mmHg Exclusion: isolated head injury or cervical spine injury with paralysis	Univariate analysis N
Hoffmann[9]	Retrospective cohort	<20.0; 20.0–24.9; 25.0–29.9; ≥30	760/5766 (13)	Inclusion: poly-trauma Exclusion: age < 16 years, ISS < 9	RISC score Y

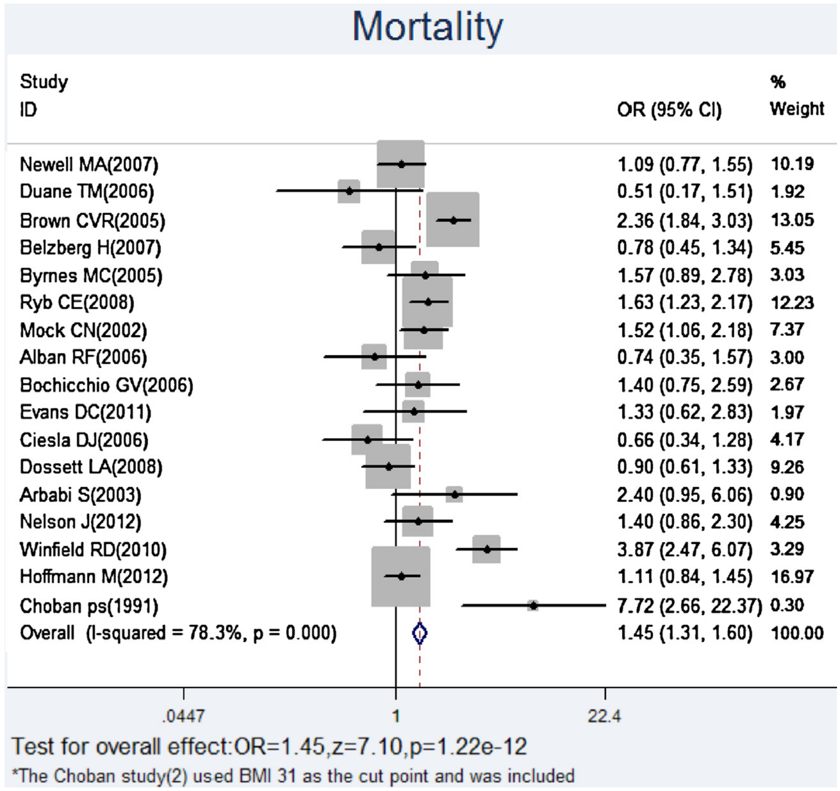

Fig. 2. Forest plot of comparison of obese versus nonobese for mortality.

Mortality

Only one of the eighteen included studies did not examine the risk of mortality in relation to BMI.[22] The overall mortality of the obese and the non-obese groups was 7.7% and 4.7%, respectively. Pooled analysis of data from selected studies generated an OR of 1.45 that indicated a significant increase in the risk of death among obese occupants compared to non-obese ones (Fig. 2). In order to eliminate the significant heterogeneity, we conducted a subgroup pooled analysis that took normal weight (BMI = 18.5–24.9 kg m^{-2})

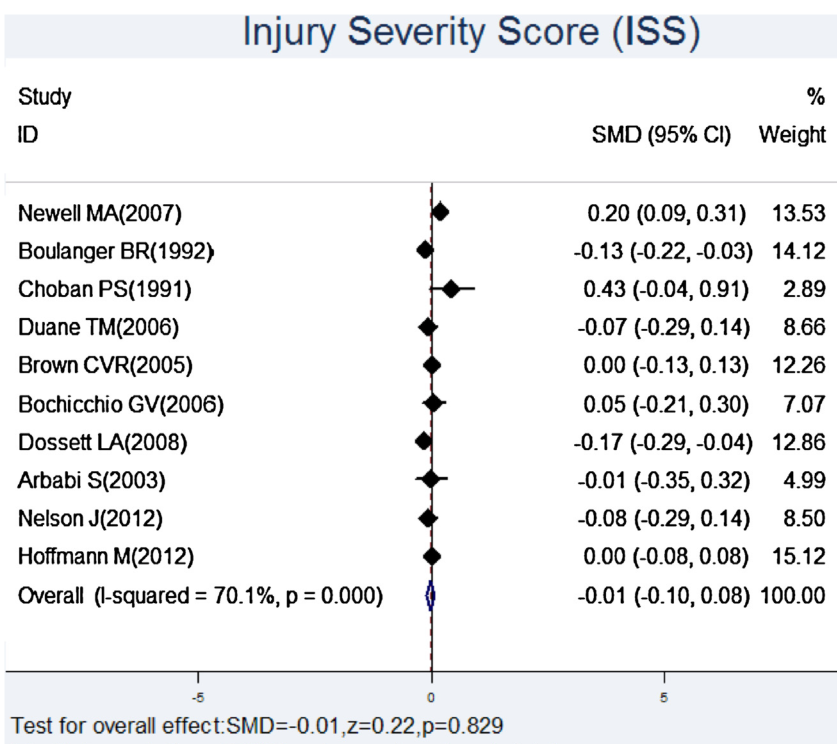

Fig. 3. Forest plot of comparison of obese versus nonobese for the outcome: injury severity score (ISS).

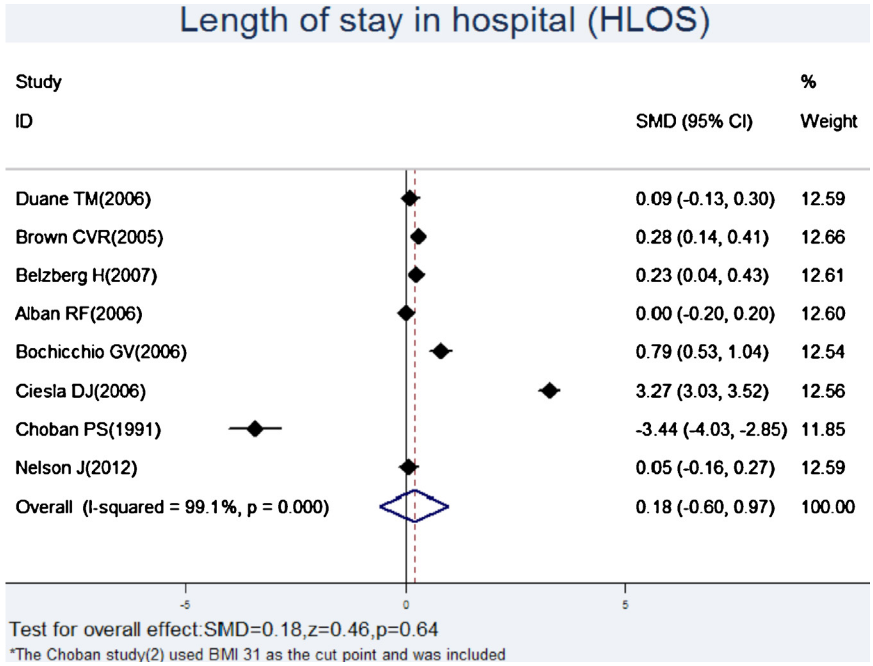

Fig. 4. Forest plot of comparison of obese versus nonobese for the hospital course: length of stay in hospital (HLOS).

as the reference category instead of the non-obese group and drew the same conclusion (OR = 1.42; 95%CI, 1.22–1.64; $p < 0.001$; $I^2 = 49.5\%$). Obesity was also a risk factor of fatality for blunt trauma patients (OR, 2.02; 95%CI, 1.69–2.40; $p < 0.001$; $I^2 = 88.1\%$) but not for severe trauma individuals with ISS ≥ 15 (OR, 1.01; 95%CI, 0.79–1.27; $p = 0.25$; $I^2 = 26.3\%$). Heterogeneity was reduced sharply in some of these subgroups.

Injury severity score

Fifteen studies used ISS to evaluate the severity of injury in the obese and the non-obese groups. However, pooled analysis revealed no difference between the two groups (Fig. 3).

Hospital course

Eight studies[2,3,6,8,11–13,15] reported the HLOS for the BMI categories while six of them[3,6,8,11,13,15] included the period living in ICU (ILOS) and five of them[2,3,6,8,11] contributed to the analysis of MVD. The combined mean difference in HLOS comparing the obese group (BMI $\geq$ kg m^{-2}) to the non-obese group (BMI < 30 kg m^{-2}) was 0.18 (Fig. 4), whereas for MVD it was 0.17 (Fig. 5). Obese patients appeared to have longer HLOS and MVD, but the estimates did not reach statistical significance. The pooled average ILOS was lower by 1.97 days in the non-obese group compared with the obese one (Fig. 6). There was also obvious heterogeneity across studies in these variables.

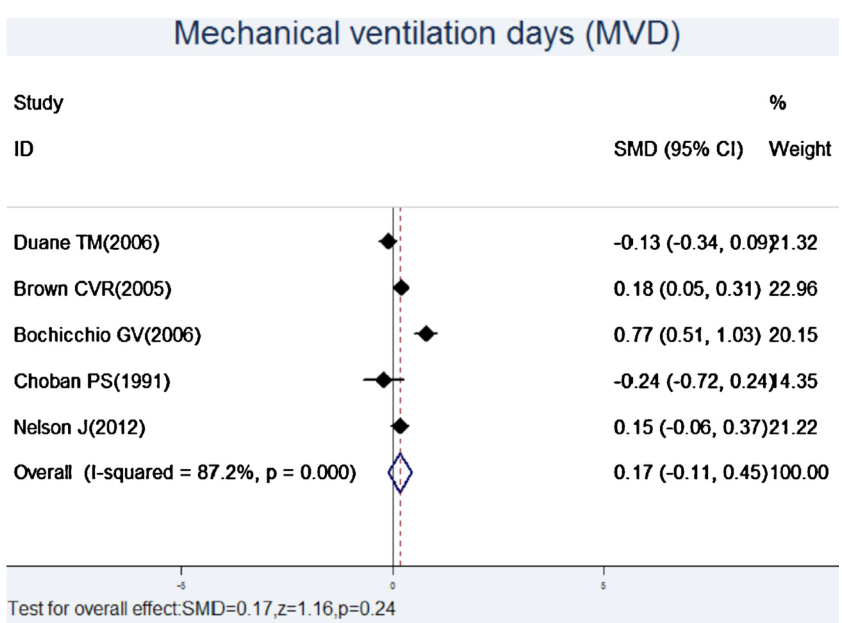

Fig. 5. Forest plot of comparison of obese versus nonobese for the hospital course: mechanical ventilation days (MVD).

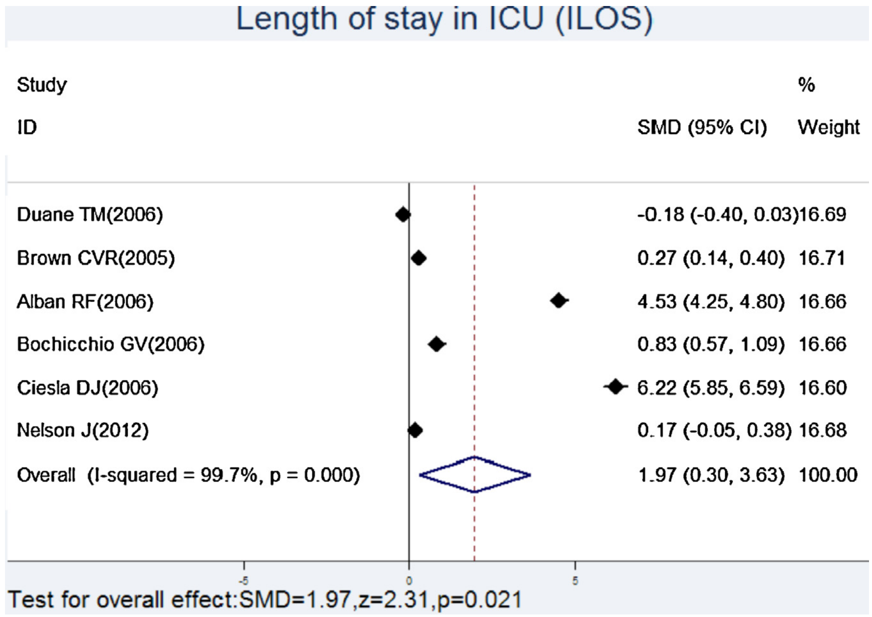

Fig. 6. Forest plot of comparison of obese versus nonobese for the hospital course: length of stay in ICU (ILOS).

Complications

Acute respiratory distress syndrome (ARDS),[3,12,14–17] acute renal failure (ARF)[3,12,14,15,17] and multiple organ failure (MOF)[3,9,15,17] were major complications after trauma. By pooling the studies, we found a significantly increased risk of all these three complications in obese patients compared to the non-obese ones (Figs. 7–9).

Publication bias

Publication bias was not detected by constructing statistical test – Begg's rank correlation ($p = 0.58$).

Discussion

There were two meta-analyses in past 5 years investigating the outcomes in obese patients in the critical care setting.[33,34] To our knowledge, despite strong heterogeneity among studies about the influence of obesity in trauma patients, there has been no meta-analysis in this field. The reason for the discrepancy in prior published studies had not been fully elucidated. A common shortcoming of these studies was that a substantial number of patients had to be excluded because of the lack of data regarding height and/or weight. These individuals had the similar characteristics with included patients. In addition, in some studies authors used their own criteria to define obesity when reporting the effect

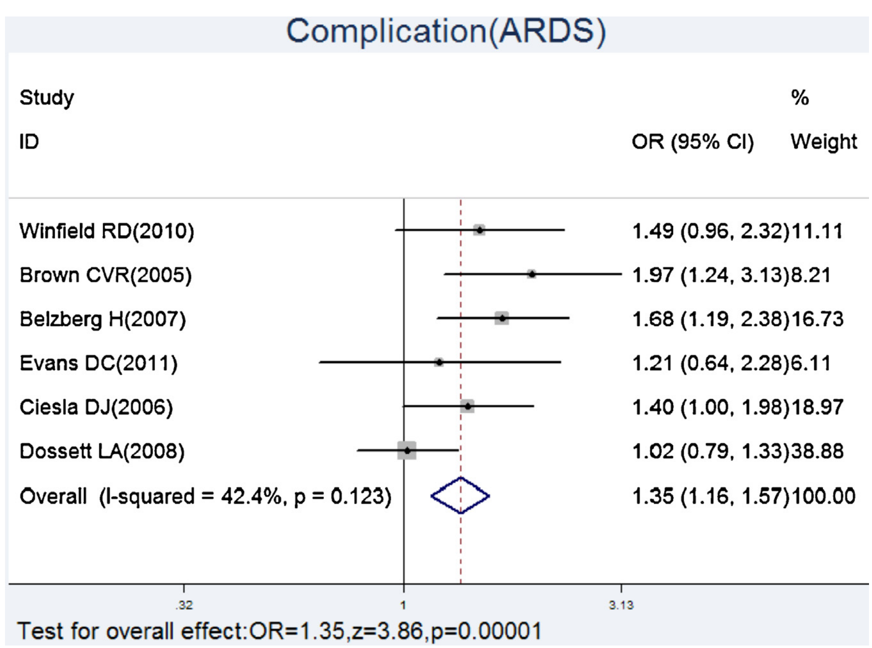

Fig. 7. Forest plot of comparison of obese versus nonobese for the complication: acute respiratory distress syndrome (ARDS).

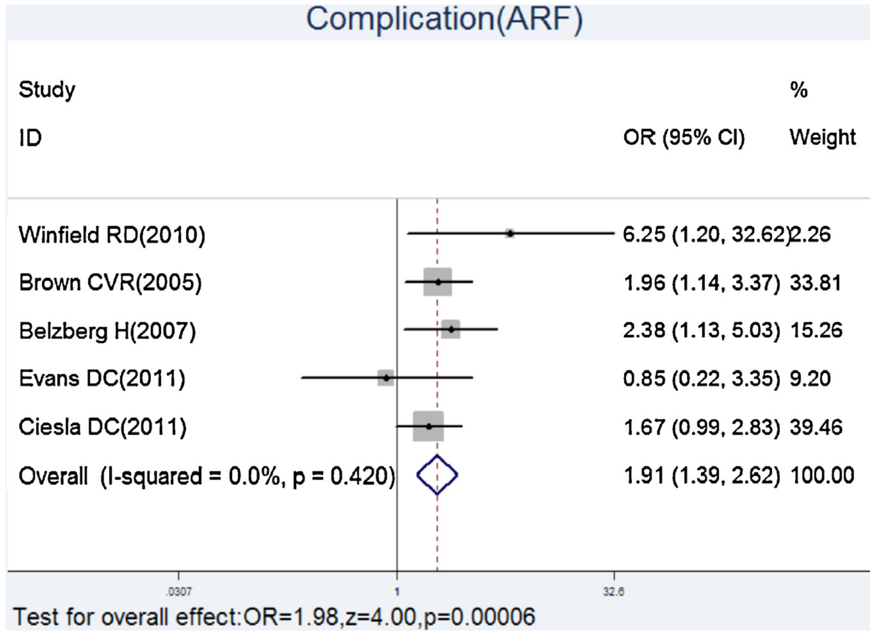

Fig. 8. Forest plot of comparison of obese versus nonobese for the complication: acute renal failure (ARF).

of obesity on trauma rather than the standard one set by WHO.[3,13,16,23] These authors suggested that a cut-off BMI of >30 kg m^{-2} may have been validated in the chronic setting but not in trauma patients. Furthermore, the differences in trial design and quality, inclusion criteria and pre-existing medical co-morbidities also contributed to the controversy. This controversy was the source of significant degrees of heterogeneity among the selected studies and it was certified by the I^2 test.

Our meta-analysis supports a BMI effect in the development of three most common and fatal complications following trauma – ARDS, ARF and MOF. At baseline, obese patients have an impaired respiratory physiology characterised by reduced lung volume and compliance that leads to a hypoxaemic state. This effect will be aggravated after trauma due to limited ability to compensate.[35] Obese patients may suffer more chest injury including rib fractures and pulmonary contusions.[22] Procedures such as tracheal intubation or tracheotomy and nursing care are huge challenges for obese patients that may increase the risk of procedures and influence the treatment effect of mechanical ventilation. All these factors can contribute to the high rate of ARDS in obese patients and longer mechanical ventilation days. Our meta-analysis is in keeping with the findings of previous studies that obesity is an independent risk factor for the incident of post-injury organ dysfunction. A generally accepted explanation for it is a systemic pro-inflammatory state response to trauma initiated by abundant adipose tissue in the obese population, which is characterised by elevated circulating levels of inflammatory mediators including tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6), leptin and many others.[36,37] In contrast, Winfield et al.[21] could not conclude that it was the early inflammatory response that resulted in the high rates of complication in obese patients by finding no difference in the measurement of leucocyte genomic expression. Moreover, prolonged metabolic acidosis[17] and inappropriate resuscitation and nutritional support neglecting specific physiology of obese patients[8,12] may also play important roles in organ failure.

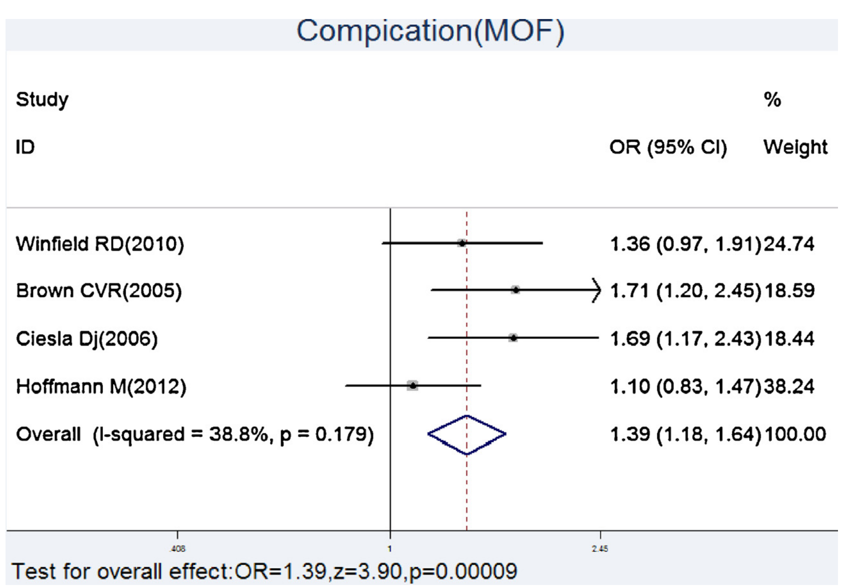

Fig. 9. Forest plot of comparison of obese versus nonobese for the complication: multiple organ failure (MOF).

A consistent finding across the majority of the combined studies is the prolonged ICU length of stay in obese patients. The increase in post-injury organ dysfunction, MVD and infections may explain it. It is reported that obese patients are more susceptible to infection because of insulin resistance and hyperglycaemia.[38] In critically ill obese patients, the persistent need for central venous access and monitoring urine output will increase the risk of catheter-associated sepsis and urinary tract infections. As to LOS, it is often confounded by some subjective factors such as bed availability and insurance status.

In our analysis ISS does not differ between the obese and the non-obese group, so the difference in survival could not explained by severity of trauma. Presumably, this increase in mortality is related to the post-injury organ dysfunction, infections, co-morbidities of obesity and emergent or postoperative care challenges. Population studies have demonstrated U-shaped curves relating BMI to mortality, suggesting increased mortality at both extremes of body weight.[39] It may explain why some studies did not find difference in mortality between obese and non-obese patients. Hence, we have tried using normal weight as the reference instead of non-obese; however, the result is the same.

There are limitations of this meta-analysis worth noting. First, the majority of included studies are retrospective by designs that have methodology shortcomings by nature. Second, the data of our study are predominantly from North American or European research. Indeed, the obesity epidemic is not restricted to the Western world and has become a global problem. Third, this study is based on *Results* section from published reports; therefore, some articles with high quality cannot enter pooled analysis for lack of primary data.

Conclusion

The evidence presented here strongly supports the association of obesity with higher mortality in trauma patients despite comparable injury severity. The post-injury course for obese trauma patients is more complicated, characterised by extended ICU length of stay and increased rate of ARDS, acute renal failure and MOF. These findings might lead to potential therapeutic targets to improve outcomes in obese trauma patients.

Conflict of interest

This studied was supported by the Ministry Of Health Industry Special Fund of China (NO. 201002014) and the National key Technology R&D Program (Grant NO. 2012BAI11B00). The study was also funded by Wuhan Planning Project of Science and Technology (NO. 201161038339-03).

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