Research Square

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Meta-Analysis of the Association Between Body Mass Index and All-cause Mortality in Patients with Cardiogenic Shock

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Research

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Abstract

Background: the correlation between BMI and in-hospital mortality of patients with cardiogenic shock is still controversial. We hope to explore whether there is an "obesity paradox" in patients with cardiogenic shock through meta-analysis.

Methods PubMed, EMbase and Cochrane databases were searched by computer to include clinical studies related to BMI all-cause mortality of patients with cardiogenic shock. The search time was from the establishment of the database to July 2020. After screening documents, extracting data and evaluating quality according to the inclusion and exclusion criteria, two evaluators used RevMan5.3 statistical software provided by Cochrane Collaboration Network for Meta-analysis.

Results There was no significant difference in all-cause mortality (OR=0.86, 95% CI 0.71-1.06, *P*=0. 16) between the obese and the non-obese patients with cardiogenic shock. In subgroup analysis, in the American population, developed countries and retrospective studies, the all-cause mortality in the obesity group of patients with cardiogenic shock is lower than that of the non-obese group (OR=0.86, 95% CI 0.71-1.06, *P*=0. 16; OR=0.71,95%CI0.65-0.77, *P*0.00001; OR=0.71 95%CI0.66-0.76, *P*0.00001).

Conclusion For patients with cardiogenic shock, there is an "obesity paradox", there is no significant difference in all-cause mortality between obese group and non-obese group. In the subgroup analysis, it was found that the in-hospital all-cause mortality rate of patients with cardiogenic shock in obese group was lower than that in non-obese group according to the country, economic development level and research type. The exact cause of this phenomenon requires more clinical trials and meta-analysis in the future.

Introduction

Obesity is a global public health problem, which has brought huge burden to the medical system. The World Health Organization (WHO) defines obesity as abnormal or excessive fat accumulation that may lead to health damage, accompanied by weight gain. At present, body mass index (BMI) ≥ 30 kg/m^2 is defined as obesity by WHO. In 2016, WHO estimated that there were 650 million obese people and 1.9 billion overweight people in the world [1]. Obesity has been identified as a risk factor and pathogenic factor for many cardiovascular and metabolic diseases, including atherosclerosis, hypertension, heart failure, etc. [2].

Although a large number of clinical studies and statistical analysis show that obesity is related to various cardiovascular diseases, in recent years some studies have challenged the traditional concept that obesity is a protective factor for cardiovascular diseases and can reduce the mortality rate of cardiovascular diseases, namely "obesity paradox" [3–7]. In fact, the "obesity paradox" was first proposed by Gruberg et al. [3]. This study retrospectively analyzed 9633 patients with percutaneous coronary interval (PCI) and found that the one-year mortality rate of overweight and obese groups was lower than that of normal weight group. Since then, the "obesity paradox" has been confirmed in congestive heart failure, hypertension, atrial fibrillation and other diseases.

Cardiogenic shock (CS) is one of the most critical complications of acute myocardial infarction (AMI), and it is also the main cause of death of AMI patients. Even if active drug therapy is given, the mortality rate still reaches 40%-60% [8, 9]. So far, it is not clear whether there is also an "obesity paradox" in patients with cardiogenic shock. Therefore, this study uses systematic review and meta-analysis methods to comprehensively evaluate the research data of patients with cardiogenic shock, and to explore the potential correlation between BMI of patients with cardiogenic shock and all-cause mortality in hospital, so as to provide evidence-based medical evidence for the correlation between BMI of patients with cardiogenic shock and all-cause mortality in hospital.

Methods

This study followed the PRISMA statement for meta-analysis [10].

Data source and search strategy

PubMed, EMbase and Cochrane libraries were searched by computer to include clinical studies related to BMI all-cause mortality in patients with cardiogenic shock. The search time was from the establishment of the library to July 2020. In addition, the references included in the literature are traced back to supplement the acquisition of relevant literature. Search strategy: (body mass index OR BMI OR body weight OR obesity OR overweight OR underweight) AND cardiogenic shock AND (mortality OR death).

Study eligibility

Inclusion criteria

(1) Research type: observational research. (2) Subjects: Patients with cardiogenic shock. (3) Outcome index: all-cause mortality rate. (4) The study reported the number of participants and deaths in BMI categories, or reported sufficient information to calculate these numbers. (5) The study reported all-cause mortality adjusted risk ratio (HR) and corresponding 95% confidence interval (CI) for each category of BMI.

Exclusion criteria

(1) Comments, conference summaries, letters, editorials and animal studies. (2) Repeated published documents. (3) The original research data cannot be extracted and cannot be obtained after contacting the author. (4) Non-English documents.

Literature Screening and Data Extraction

Two researchers(Meng and Guo) will independently screen the literature and extract the data, and cross-check them. In case of differences, they will discuss and resolve them or submit them to the third researcher for adjudication. The lack of data will be supplemented by contacting the original author as far as possible. When screening documents, first read the text topic and abstract, and after excluding obviously irrelevant documents, further read the full text to determine whether it is finally included. The contents of the data extraction mainly include: (1) the general information included in the research, including the first author, the number of years of publication, the research time, etc.; (2) the key elements of bias risk assessment; (3) Outcome indicators and outcome measurement data of concern.

Literature Quality Evaluation

The Newcastle-Ottawa Scale (NoS) standard [11] was used to evaluate the quality of the included studies, with a full score of 9 points. The scores were scored from the following three aspects: (1) the selection of research objects in the exposed group and the non-exposed group; (2) Comparability between exposed group and non-exposed group; (3) Determination of exposure (results). The maximum score for each study is 9 points. Studies with a score of ≥ 6 are considered to be of high quality.

Statistical analysis

Meta-analysis was performed with RevMan 5.3 software. The relative risk was used as the effect index in the counting data, and the point estimation value and 95% CI of each effect quantity were given. The analysis of heterogeneity among the included research results uses the $\chi 2$ test (The inspection level is set to $\alpha = 0.1$), and quantitatively judges the heterogeneity in combination with I^2. If there is no statistical heterogeneity among the research results, Meta-analysis is carried out by using a fixed effect model. If there is statistical heterogeneity among the research results, after excluding the influence of obvious clinical heterogeneity, meta-analysis is carried out by using random effect model. For obvious clinical heterogeneity, subgroup analysis or sensitivity analysis are used to deal with it, or only descriptive analysis is used. The test level of Meta-analysis is $\alpha = 0.05$.

Results

Literature search

The process and results of literature screening are shown in Fig. 1. The initial search identified 163 documents from PubMed, Embase and Cochrane databases. After deleting 3 duplicate documents, the titles and abstracts of the remaining 160 documents were screened and 138 documents were deleted. Then through reading the full text, four documents were screened out. Finally, four documents met the exclusion criteria [12–15] and were included in this meta-analysis.

Inclusion of Research Features

Table 1 lists the detailed characteristics of the included studies. All four studies, with a total of 346,181 participants, were published between 2015 and 2019. The largest study included 290,894 participants and the smallest one included 351 patients. All NOS scores were higher than 7, indicating that the included studies were of high quality.

Table 1
Characteristics of Studies Included in the Meta-Analysis

Author	Years	Country	Enrolment	Number of patients	Age(years)	Male(%)	Smoking(%)	Dyslipidemia(%)	Diabetes mellitus(%)	Hypertension(%)
Akin et al[12]	2015	German	2001–2003 and 2005–2007	890	63.1	76.9	41.1	46.5	24.3	61.5
Chatterjee et al[13]	2017	USA	2004–2013	290894	68.8	61.9	24.9	35.7	7.6	52.2
Hashmi et al[14]	2018	Afghanistan	2014–2017	351	65.4	70.1	IN	IN	40.7	65.8
Shah et al[15]	2019	USA	2005–2014	54046	68.1	62.7	27.5	38.2	32.9	53.7

BMI and all-cause mortality

There was statistical heterogeneity in the four included studies (I^2 = 94%, P< 0.00001) [12–15], therefore, the random effects model is used for analysis. The results showed that there was no significant difference in all-cause mortality between the obese and the non-obese cardiogenic shock patients (OR = 0.86, 95% CI 0.71–1.06,P= 0. 16), as shown in Fig. 2. In subgroup analysis, according to national grouping, in the American population [13, 15], the in-hospital all-cause mortality rate of patients with cardiogenic shock in the obese group is lower than that in the non-obese group, the difference was statistically significant(OR = 0.71,95% CI 0.65–0.77, P< 0.00001); In German and Pakistani populations [12, 14], there was no significant difference in all-cause mortality between the obese and the non-obese patients with cardiogenic shock (OR = 1.47, 95% CI 0.31–6.84, P= 0.63). According to study design, in the prospective study [12, 14], there was no significant difference in all-cause mortality between the obese group and the non-obese group (OR = 1.47, 95% CI 0.31–6.84, P= 0.63); In the retrospective study [13, 15], the in-hospital all-cause mortality rate of patients with cardiogenic shock in obese group was lower than that in non-obese group, with statistically significant difference (OR = 0.71,95% CI 0.65–0.77,P< 0.00001). According to whether it is a developed country, the in-hospital all-cause mortality rate of patients with cardiogenic shock in developed countries [12, 13, 15] and obese groups is lower than that in non-obese groups, and the difference is statistically significant (OR = 0.71, 95% CI 0.66–0.76, P< 0.00001) (Table 2).

Table 2
Subgroup analysis according to country, national development and study design

Group	OR/RR 95%CI	P	I^2	Pheterogeneity
Country				
USA	0.71(0.65–0.77)	<0.00001	82%	0.02
German	0.64(0.26–0.54)	0.32		
Pakistan	3.06(1.96–4.78)	<0.00001		
National development				
Developed country	0.71(0.66–0.76)	<0.00001	65%	0.06
Developing country	3.06(1.96–4.78)	<0.00001		
Design				
Prospective	1.17(0.42–3.26)	0.76	82%	0.02
Retrospective	0.71(0.65–0.77)	<0.00001	82%	0.02

Sensitivity analysis excluding one study at a time showed that when Hashmi et al [14] was excluded, the in-hospital all-cause mortality rate of patients with cardiogenic shock in obese group was lower than that in non-obese group, with statistically significant difference (OR = 0.71,95% CI 0.65–0.77, P< 0.00001). The exclusion of other studies cannot change the overall risk assessment. Due to the small number of documents included, there may be publication bias.

Discussion

The global epidemic of obesity is becoming more and more serious. It is not only a risk factor for chronic diseases such as type 2 diabetes, cardiovascular diseases, hypertension and stroke, but also considered as an independent disease [16]. Obesity can be accompanied by diabetes, hypertension and heart failure, which can increase the morbidity and mortality of cardiovascular diseases. However, the existing clinical evidence suggests that in patients with cardiovascular diseases, the long-term death risk and the incidence of major cardiovascular events are both high with low body mass and normal body mass. This phenomenon is called "obesity paradox" in patients with myocardial infarction, coronary heart disease, heart failure, hypertension, etc. Cardiogenic shock is a common clinical critical and severe disease, a serious complication of cardiovascular diseases, with high mortality [8, 9]. So far, it is not clear whether there is also an "obesity paradox" in patients with cardiogenic shock. Swaminathan et al. [17] first studied 61 patients with cardiogenic shock, showing that the mortality rate of obese patients with cardiogenic shock is higher than that of non-obese patients. Since then, a multi-center German network registration study [12], a study of 890 patients with ST-segment elevation myocardial infarction complicated with cardiogenic shock, found that there was no evidence that the in-hospital all-cause mortality rate of obese cardiogenic shock patients was higher than that of non-obese patients. Chatterjee et al. [13] For 290,894 patients with cardiogenic shock, after adjusting for demography, hospital characteristics, complications and clinical manifestations, the study found that the in-hospital mortality rate of obese patients with cardiogenic shock was slightly lower than that of non-obese patients (OR = 0.89, 95% CI 0.86–0.92, $p < 0.001$). Shah et al. [15] evaluated the clinical outcomes of non-obese, obese (BMI 30.0-39.9 kg/m^2) and extremely obese (BMI ≥ 40 kg/m^2) cardiogenic shock patients based on Chatterjee et al. [13]. The study found that compared with non-obesity, obesity predicted lower in-hospital mortality (OR = 0.82,95% CI 0.76–0.90), while extreme obesity predicted higher in-hospital mortality (OR = 1.17. 95% CI 1.05–1.32). We conducted a meta-analysis of the included studies and found that there was no significant difference in all-cause mortality between obese and non-obese cardiogenic shock patients in the two groups. In the subgroup analysis, it was found that the in-hospital all-cause mortality rate of patients with cardiogenic shock in obese group was lower than that in non-obese group according to the country, economic development level and research type.

At present, the exact mechanism of obesity paradox in patients with cardiogenic shock is still unclear, but it can be inferred from the results of current research: firstly, confounding factors can lead to obesity paradox, such as muscle quantity, drug therapy, exercise, age, etc. in patients with cardiogenic shock [18]. Secondly, it is bias. Obese patients are more likely to diagnose cardiovascular diseases, which leads to misclassification bias, or obese patients'

symptoms may appear earlier, which leads to lead time bias [19]. The existence of these two biases may lead to the observation that the survival time of obese patients with cardiovascular diseases is longer than that of non-obese patients with cardiovascular diseases [20]. Third, the marker defining obesity is not ideal. BMI is not as good as body fat, fat distribution, thin body mass and body fluid composition, which can properly reflect the important components of the body [21].

Our meta-analysis still has some limitations. First of all, the main limitation is the lack of randomized controlled studies. Secondly, most of the included studies are retrospective studies. There is obvious selective bias in observational research. Although we do subgroup analysis as much as possible, the potential bias still exists. Third, BMI classification was not further refined, and only the in-hospital mortality of patients with cardiogenic shock in obese and non-obese groups was compared, which may affect the accuracy of the results. Fourth, for cardiogenic shock, there is no further comparison of etiology, revascularization or conservative drug treatment. Fifth, BMI is commonly used in epidemiological investigation and population prevention to measure overall obesity, but a single indicator cannot fully and correctly reflect the relationship between obesity and diseases. Sixth, there are many prognostic indicators. We only evaluate all-cause mortality in hospital. The relationship between other prognostic indicators and BMI needs further study. Seventh, there was no long-term follow-up outside the hospital.

Conclusion

To sum up, for patients with cardiogenic shock, there is an "obesity paradox", that is, for patients with cardiogenic shock in obese group and non-obese group, there is no obvious abnormality in the hospital all-cause mortality rate of the two groups. In the subgroup analysis, it was found that the in-hospital all-cause mortality rate of patients with cardiogenic shock in obese group was lower than that in non-obese group according to the country, economic development level and research type. The exact cause of this phenomenon requires more clinical trials and meta-analysis in the future.

Abbreviations

WHO: World Health Organization; BMI: body mass index; CS: Cardiogenic shock; AMI: acute myocardial infarction; NOS: New Castle Ottawa Scale; OR: Odds Ratio; CI: Confidence Interval

Declarations

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Authors' contributions

Fan-hua Meng and Fei-yan Guo contributed equally to this work. Fanhua Meng and Fei-yan Guo were responsible for the statistical analysis and wrote this paper. Burebiguli Abulimiti provided the database. Ying Dong were responsible for collecting clinical data. Zhen-yan Fu and Yi-Tong Ma revised the paper critically for important intellectual content. Zhen-yan Fu is accountable for all aspects of the work and funding. All authors reviewed the results and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

All the authors have consented for the publication of this study.

Competing interests

The authors declare that they have no competing interests.

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Figures

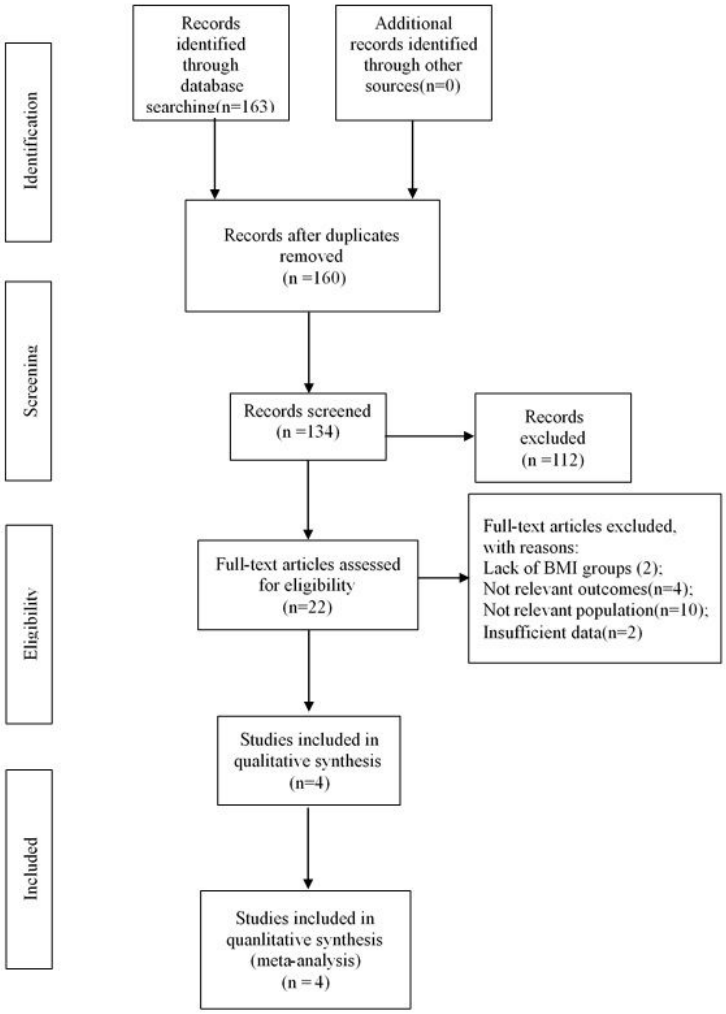


Figure 1

Flow diagram for the inclusion of identified trials.

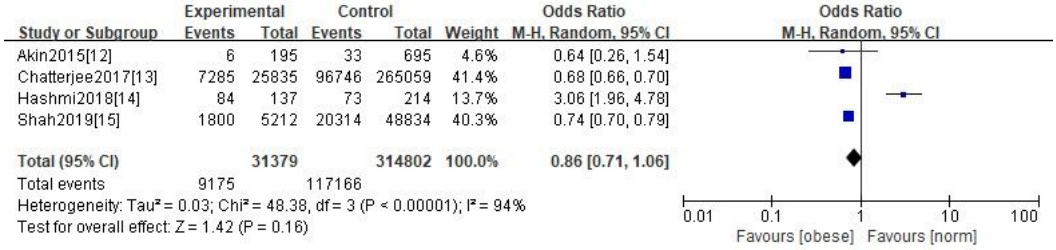


Figure 2

Forest plot showing pooled risk ratio of obese and all-cause mortality.

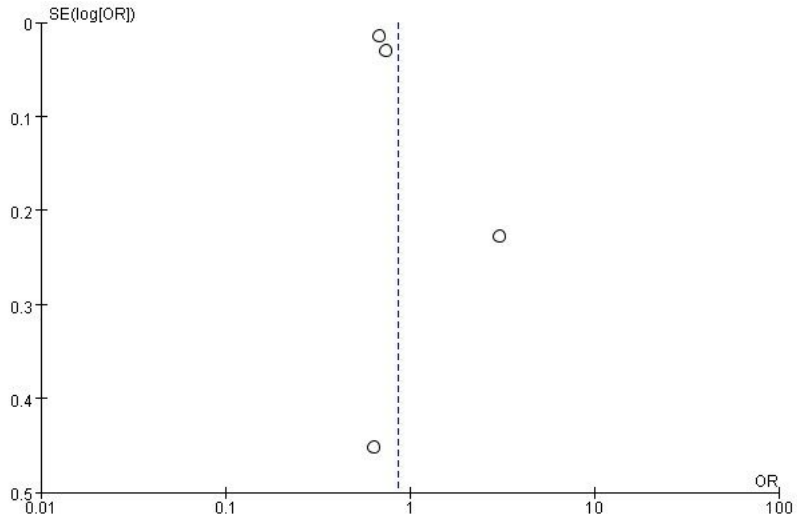


Figure 3

The publication bias analysis.

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