

# The incidence of acute myocardial infarction in relation to overweight and obesity: a meta-analysis

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**Submitted:** 19 November 2013

**Accepted:** 10 February 2014

Arch Med Sci 2014; 10, 5: 855–862  
DOI: 10.5114/aoms.2014.46206  
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## Abstract

**Introduction:** Epidemiological evidence suggests that overweight and obesity have been associated with acute myocardial infarction (AMI). However, data on this issue are controversial. This study aims to use meta-analysis to determine whether overweight and obesity are related to AMI.

**Material and methods:** We searched PubMed and Embase databases up to October 23<sup>rd</sup>, 2013 for related literature. The association of overweight and obesity with AMI was assessed by odd ratio (OR) with 95% confidence interval (CI) as the effect size. Then subgroup analysis was performed according to gender, area and study type.

**Results:** Five primary studies (one cohort study and four case-control studies) were included in this meta-analysis involving 36 803 participants, 14 883 of whom had an AMI. There was a significant association between overweight and AMI (OR = 1.27, 95% CI: 1.21–1.33,  $p < 0.001$ ). Similar results revealed a relation between obesity and AMI (OR = 1.22, 95% CI: 1.07–1.40,  $p = 0.003$ ). Subgroup analysis showed that overweight and obesity were positively associated with AMI risk except for obese subjects in Europe. There was no publication bias (Begg's test  $p = 0.972$ , Egger's test  $p = 0.858$ ).

**Conclusions:** Both overweight and obesity increased the incidence of AMI, and it is necessary to control weight to prevent AMI. A large number of studies is needed to explore the mechanisms that link overweight and obesity with AMI.

**Key words:** meta-analysis, acute myocardial infarction, overweight, obesity.

## Introduction

Acute myocardial infarction (AMI) is a common disease that could lead to high mortality. In 2006, the WHO reported that 7,200,000 people died of ischemic heart disease with AMI as the major contributor [1, 2]. The AMI is fatal and often occurs in the prime of life, which brings a heavy burden for individuals and families. The risk factors of smoking, cholesterol, diabetes, obesity, left ventricular hypertrophy, and elevated triglycerides are high in AMI [3, 4]. These findings would be meaningful for preventing AMI.

In recent years, obesity and overweight have raised more and more concerns. The incidence of overweight and obesity is increasing and has been reported to be associated with type II diabetes mellitus, metabolic syndrome, cancer, hypertension and cardiovascular disease [5–8]. But the

relation of overweight and obesity with AMI is still controversial. Overweight and obesity are associated with AMI in some studies [9–11] and another study also showed an independent relationship between them [12]. Besides, evidence whether overweight and obesity are risk factors for AMI is still inconsistent. Mehta *et al.* demonstrated that the risk for mortality is lower in obese patients with AMI than patients with normal body mass index (BMI) [13]. In Dhoot's study, the mortality of patients with obesity was lower than those not obese [14]. In contrast, Yusuf *et al.* demonstrated that abdominal obesity increased the risk of AMI in both ages and sexes in all regions [15].

The present literature on the relation of overweight and obesity with AMI could not confirm obvious conclusions and there is no report about a meta-analysis on their association. In this study, a meta-analysis allowing pooling of data was used to evaluate whether overweight and obesity are risk factors of AMI. Five studies were selected for the meta-analysis. The area of the studies included Portugal, Spain, Italy, Argentina [9, 10, 12, 16, 17]. Besides, subgroup analysis was performed according to gender, geographical area and study type, and publication bias analysis was subsequently performed.

## Material and methods

### Search strategy

We searched PubMed and Embase databases for publications which were updated on October 23<sup>rd</sup>, 2013. The search strategy was ("acute myocardial infarction" or "AMI") and ("BMI" or "body mass index" or "overweight" or "obesity"). We also retrieved articles in paper version by manual searching. Reviews and reference lists of retrieved articles were also reviewed.

### Inclusion and exclusion criteria

The prospective studies in our meta-analysis should meet these inclusion criteria: (1) subjects were adults ( $\geq 18$  years) without AMI; (2) risk factors were overweight or obese; (3) BMI was a predictor of overweight and obesity; (4) outcome of subjects was AMI or death; (5) providing adjusted RR/OR (relative risk/odd risk) and 95% CI (confidence intervals) of AMI or they could be calculated according to given data.

Case-control studies had to meet criteria as follows: (1) patients were adults ( $\geq 18$  years) with AMI for the first time; (2) participants in the control group were adults without AMI; (3) providing adjusted RR/OR and 95% CI of AMI or they could be calculated according to given data.

Exclusion criteria were (1) non-English literature; (2) reviews, letters and comments; (3) repeat

publications or multiple publications that reported the same or overlapping population information (studies with the longest follow-up and/or sufficient information were selected).

### Data extraction and quality assessment

Two investigators independently performed the literature screening according to above criteria and then extracted the information according to standardized form. The extract information should include: name of first author and publication year; geographical area; methods; age and gender of patients; number of cases and follow-up (cohort study); sample numbers in disease group and control group; adjusted RR/OR and 95% CI; adjustment factors. Then they exchanged the standardized form and solved the differences with discussion.

The Newcastle-Ottawa Scale [18], which includes strict criteria for the case-control group and cohort study, was used in our study to assess the quality of studies. The highest score is 9 and the score of a study with high quality was not less than 7.

### Statistical analysis

Stata 11.0 (Stata Corporation, College Station, Texas) was used for the meta-analysis. Pooled estimates were calculated by averaging the RR/OR and 95% CI based on a random or fixed effects model depending on heterogeneity.

We used Cochran Q and  $I^2$  for the heterogeneity test [19]. There was heterogeneity among studies when  $p < 0.05$  and/or  $I^2 \geq 50\%$  and the random effects model was used for pooling estimates. If there was no heterogeneity among studies ( $p \geq 0.05$  and/or  $I^2 < 50\%$ ), the fixed effects model was used for pooling estimates.

Subgroup analysis was performed according to gender, geographical area, study type and so on. Begg [20] and Egger [21] tests were used for publication bias assessment.

## Results

### Literature search

Figure 1 presents the details of the literature search in a flow diagram. We identified 2008 and 900 studies from Embase and PubMed databases respectively based on the search strategy. Then we excluded 2512 duplicated articles and 2489 articles based on titles and abstracts. Then 19 articles were excluded after a full-text review: 4 reviews, 3 non-English articles, 6 studies which lacked a control group; 2 meeting abstracts and 4 articles which are not about the relation between BMI and AMI. We did not find proper articles by manual searching. Finally, 5 studies including 1

cohort study and 4 case-control studies were selected for further meta-analysis [9, 10, 12, 16, 17].

### Study characteristics

We selected 5 studies in the meta-analysis including 36 803 subjects, 14 883 of whom had AMI (3 studies in Europe; 1 study included data from 52 countries; 1 study in Argentina). In the four case-control studies, control groups in 3 studies were from hospital and 1 study consisted of normal persons. In 2 studies, BMI levels were self-reported. In all 5 studies, subjects had been diagnosed with AMI. In 4 studies, BMI > 25 kg/m<sup>2</sup> was defined as overweight and BMI > 30 kg/m<sup>2</sup> was defined as obesity. All of the studies were of high quality. Table I shows the details of study baseline characteristics.

### Overall analysis

Figure 2 shows the risk of AMI in the overweight group compared with normal persons. There was no heterogeneity among overweight studies ( $I^2 = 32.2\%$ ,  $p = 0.151$ ), so the fixed effect model was applied and the results showed that overweight was significantly positively related to AMI (OR = 1.27, 95% CI: 1.21–1.33,  $p < 0.001$ ). There was heterogeneity among obesity studies ( $I^2 = 51.7\%$ ,  $p = 0.043$ ), so the random effects model was adopted and the results showed that obesity was significantly positively related to AMI (OR = 1.22, 95% CI: 1.07–1.40,  $p = 0.003$ , Figure 3).

### Subgroup analysis and publication bias

Subgroup analysis showed that the results were consistent with previous results except those for obese persons in Europe, which showed a negative correlation with AMI (OR = 1.09, 95% CI: 0.80–1.47) (Table II). The results of publication bias were: overweight vs normal, Begg test ( $p = 0.972$ ), Egger ( $p = 0.858$ ); obesity vs. normal, Begg test ( $p = 0.978$ ), Egger test ( $p = 1.00$ ). The results showed that there was no significant publication bias among studies (data not shown).

### Discussion

Overweight and obesity are increasing problems in many countries and contribute to chronic disease [22], nonalcoholic fatty liver disease [23], inflammatory bowel disease [24], cardiovascular disease [25], heart disease [26] and hypertension [27]. In this study, we evaluated whether overweight and obesity were related to AMI by meta-analysis for the first time. Based on data from 5 studies from prospective cohort and case-control studies, overweight and obesity increased the risk of AMI compared with normal individuals. Besides, there was no significant publication bias

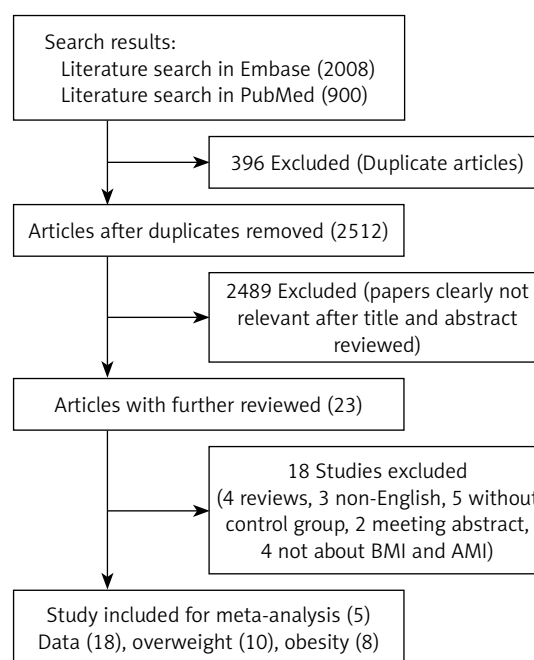


Figure 1. Flow diagram of study selection process

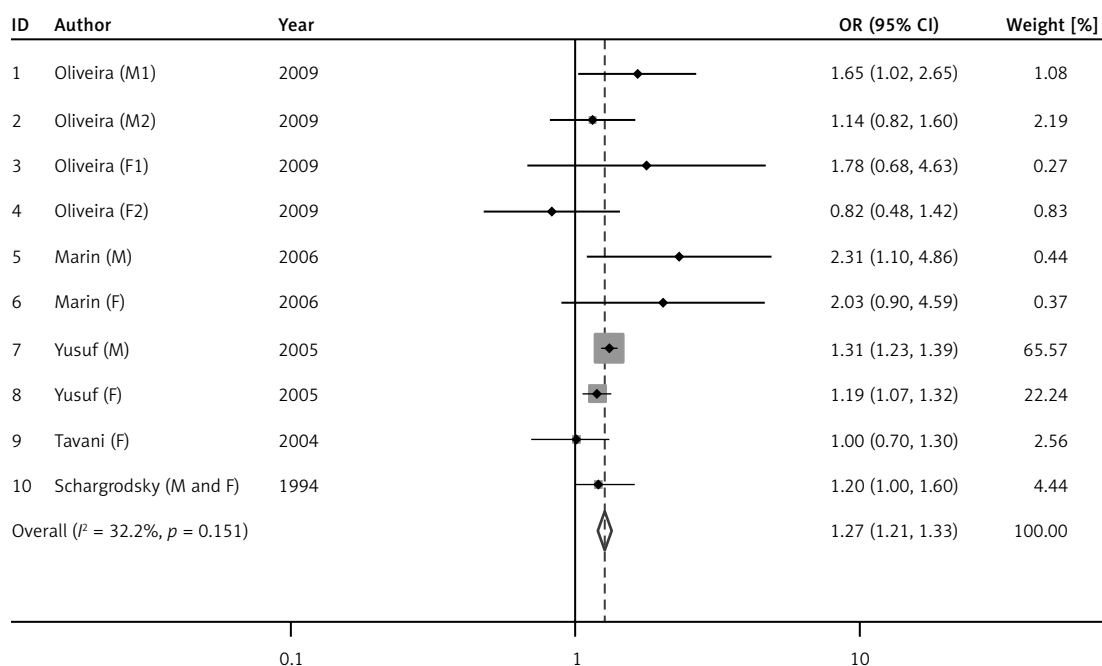
among these studies. Confounders such as smoking, hypertension, diabetes and alcohol account for most of the risk of MI worldwide [15]. So they were adjusted to reduce the interference.

In this analysis, although the number of studies is only 5, the sample size is large (36 803 participants; 14 883 incident cases of AMI) and included studies were all of high quality. We included both cohort studies and case-control studies to assess whether overweight and obesity are related to AMI to minimize the potential bias. Moreover, we did not only score the included studies but also inclusion and exclusion criteria were established to ensure the minimum quality. We assessed the study through representativeness, ascertainment of exposure, outcomes, follow-up time and other criteria (see Supplementary Table I). The meta-analysis results showed that both overweight and obesity increased the risk of AMI. Several reports were consistent with our results. Schargrodsy *et al.* demonstrated that overweight is an independent risk factor for MI [12]. The metabolic syndrome including abdominal obesity increased 2-fold in cardiovascular outcomes and 1.5-fold in all-cause mortality [28]. Overweight and obesity independently increased the risk of cardiovascular disease in patients with type 2 diabetes [29]. Yatsuya *et al.* found that both overweight and obesity increased the risk of cerebral infarction and hemorrhage in men and women [30]. In Strazzullo's study, overweight/obesity was associated with increased risk of ischemic stroke [31]. However, other studies led to the opposite conclusions. Park *et al.* found that low BMI was associated with increased risks of major cardiovascular events and

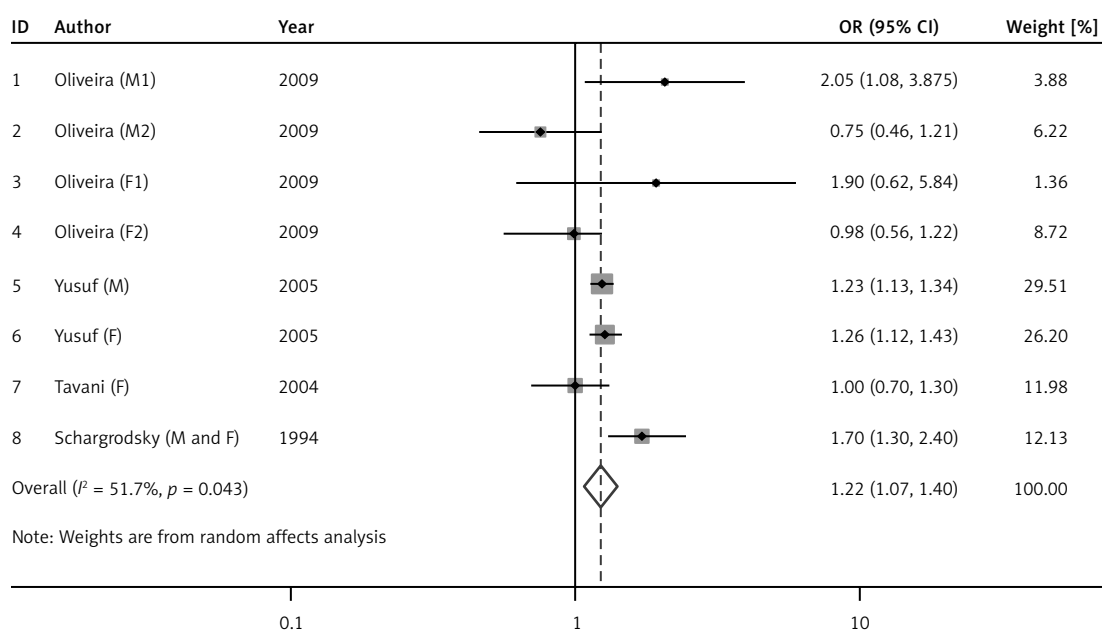
Table 1. Characteristics of 5 studies about the relation between BMI (body mass index) and AMI (acute myocardial infarction)

Studies	Location	Ascertainment of AMI	Type of study	Ascertainment of BMI	Cases	Cohort/control	Age [years] gender	BMI range [kg/m <sup>2</sup> ]	Adjusted OR (95% CI)	Adjustment for covariates	Quality score
Oliveira 2009 [10]	Portugal	Hospital diagnosis	Population-based case-control	Measured	732	1914	≤ 45	25.0–29.9	1.65 (1.02, 2.65)	Age, education, smoking and family history of AMI	8
							M	≥ 30.0	2.05 (1.08, 3.87)		
							F	25.0–29.9	1.78 (0.68, 4.63)		
							≥ 30.0	1.90 (0.62, 5.84)			
Marin 2006 [16]	Spain	Hospital diagnosis	Prospective cohort	Measured	74	1381	≥ 25 M	≥ 25	2.31 (1.10, 4.86)	Age, gender, smoking, and LDL/HDL	7
							≥ 25 F	≥ 25	2.03 (0.90, 4.59)		
							M	25	1.31 (1.23, 1.39)		
							F	> 30	1.23 (1.13, 1.34)		
Yusuf 2005 [9]	52 countries	Hospital diagnosis	Hospital-based case-control	Physical examinations	12461	14637	M	25	1.31 (1.23, 1.39)	Curved	8
							F	> 25	1.19 (1.07, 1.32)		
Tavani 2004 [17]	Italy	Hospital diagnosis	Hospital-based case-control studies	Self-reported	558	1044	18–79 F	24–27	1.0 (0.7, 1.3)	Age, education, smoking, hypertension, diabetes, alcohol, hyperlipidemia, family history of AMI	7
							> 27	> 27	1.0 (0.7, 1.3)		
Schargrofsky 1994 [12]	Argentina	Hospital diagnosis	Hospital-based case-control study	Self-reported	1000	1000	35–65 M and F	25–30 > 30	1.2 (1.0, 1.6) 1.7 (1.3, 2.4)	Age, smoking, diabetes, sex, hypertension, family history of coronary heart disease	7

M – male, F – female, LDL – low-density lipoprotein, HDL – high-density lipoprotein, OR – odds ratio, CI – confidence interval



**Figure 2.** Odds ratio (OR) for the association between overweight and acute myocardial infarction (AMI). Squares represent study-specific relative risk estimates (size of the square reflects the study-specific statistical weight); horizontal lines represent 95% CI (confidence interval); diamonds represent summary relative risk estimates with corresponding 95% CI



**Figure 3.** Odds ratio (OR) for the association between obesity and acute myocardial infarction (AMI). Squares represent study-specific relative risk estimates (size of the square reflects the study-specific statistical weight); horizontal lines represent 95% CI (confidence interval); diamonds represent summary relative risk estimates with corresponding 95% CI

death among patients who underwent percutaneous coronary intervention [32]. Among overweight and obese older patients after non-ST-segment-elevation myocardial infarction, all-cause long-term mortality was lower than among those with normal weight [33]. There are some explanations for the paradoxical results. First, waist-to-hip ratio not BMI showed a more significant association with

MI risk [9]. Maybe some unmeasured factors influence the low BMI. Second, the patients who had higher BMI tended to have higher rates of medication use at 12 months after percutaneous coronary intervention [34]. Third, overweight seems to be protective in older populations, but the association is reversed in younger cohorts, indicating that the relation is likely age dependent [35, 36].

**Table II.** Subgroup analysis of relation between overweight/obesity and AMI (acute myocardial infarction)

Group	No. of studies	OR (95% CI)	Heterogeneity test		Significance test (p)
			p	I <sup>2</sup> (%)	
Overweight:					
All studies	10	1.27 (1.21, 1.33)	0.151	32.2	< 0.001
Area:					
Europe	7	1.21 (1.01, 1.44)	0.114	41.5	0.039
52 countries	2	1.28 (1.21, 1.35)	0.121	58.4	< 0.001
Argentina	1	1.20 (1.00, 1.60)	–	–	0.128
Type of research:					
Cohort	2	2.18 (1.26, 3.77)	0.818	0.0	0.005
Case-control	8	1.26 (1.20, 1.33)	0.221	26.1	< 0.001
Gender:					
M	4	1.31 (1.24, 1.39)	0.285	20.9	0.959
F	5	1.17 (1.06, 1.29)	0.264	23.5	0.001
M and F	1	1.20 (1.00, 1.60)	–	–	0.621
Obesity:					
All studies	8	1.22 (1.07, 1.40)	0.043	51.7	0.003
Area:					
Europe	5	1.09 (0.80, 1.47)	0.118	45.7	0.593
52 countries	2	1.24 (1.16, 1.33)	0.751	0.0	< 0.001
Argentina	1	1.70 (1.30, 2.40)	–	–	0.001
Gender:					
M	3	1.19 (0.79, 1.80)	0.040	69.0	0.398
F	4	1.17 (1.01, 1.36)	0.305	17.2	0.041
M and F	1	1.70 (1.30, 2.40)	–	–	0.001

Considering that the results may be due to different gender, geographical area and study type, we further conducted a subgroup analysis, and the results showed that the different regions could influence the results of this meta-analysis and was one of the sources of heterogeneity in this study.

There were several limitations to this meta-analysis study. First, we only searched PubMed and Embase datasets. Other datasets such as Medline and Cochrane Library databases could also be included. Second, heterogeneity was significant due to diversity in gender and regions in studies. But this was not surprising due to unavoidable variation in populations among studies. Although confounders such as age, education and smoking [17, 37] have been adjusted, the relation of obesity and AMI was still affected by other factors. Thus, it is necessary to adjust for more factors which may affect the study analysis. Third, BMI of participants in some studies was calculated according to self-reported height and weight. So bias might have occurred in these studies. It has been reported that there were large differences between measured and self-reported data [38, 39]. Thus, the self-reported

data inevitably led to bias in the meta-analysis. Fourth, most of the studies were carried out with non-comprehensive coverage of areas, which were only Europe and South America, and it is necessary to investigate the relation in other populations. Finally, we only included published studies in our meta-analysis. Therefore, although no publication bias was indicated from either Begg's test or Egger's test, publication bias may have occurred.

In conclusion, this meta-analysis of previous studies suggested that overweight and obesity are associated with higher risk of AMI. Overweight and obesity may affect health, and it is necessary to control one's BMI to prevent AMI. However, large primary studies are needed to confirm our results, and mechanisms of the relation need to be explored.

### Acknowledgments

Co-first author: Jun Zhu and Xiaohua Su

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Supplement Table 1. Methodological quality of cohort/case-control studies included in the meta-analysis<sup>1</sup>

Cohort	First author	Representativeness of the exposed cohort	Selection of the unexposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Control for important factor or additional factor <sup>2</sup>	Outcome assessment	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total quality scores
(1)	Marin	☆	☆	☆	☆	☆	☆	☆	-	7
Case-control	First author	Representativeness of the cases	Case definition adequate	Ascertainment of exposure	Same method of ascertainment for cases and controls	Comparability of cases and controls <sup>2</sup>	Selection of controls	Definition of controls	Non-response rate	Total quality scores
(1)	Oliveira	☆	☆	☆	☆	☆	☆	☆	☆	8
(2)	Yusuf	☆	☆	☆	☆	☆☆	-	☆	☆	8
(3)	Tavani	☆	☆	-	☆	☆☆	-	☆	☆	7
(4)	Schargrodsky	☆	☆	-	☆	☆☆	-	☆	☆	7

<sup>1</sup>A study could be awarded a maximum of one star for each item except for the item Control for important factor or additional factor. <sup>2</sup>A maximum of 2 stars could be awarded for this item.

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