

Waist-hip ratio as a predictor of myocardial infarction risk

A systematic review and meta-analysis

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Abstract

Background and aim: Several studies have identified that obesity and being overweight can increase the risk of developing myocardial infarction (MI). However, the predictive value of the central obesity index, that is, the waist-hip ratio (WHR), regarding MI risk remains unclear. This study aimed to provide a systematic review and meta-analysis of WHR as a predictor of MI incidence.

Methods: This study used relevant keywords and MeSH terms to identify studies of MI risk and WHR from PubMed, Web of Science, Embase, and Cochrane databases in November 2017.

Results: We conducted a meta-analysis of 12 case-control studies in 14 eligible trials and further explored whether the predictive value of WHR on MI risk varies according to sex. The results showed that a high WHR increased MI risk (pooled odds ratio [OR] 2.62, 95% confidence interval [CI] 2.02–3.39, $P < 0.00001$) and that elevated WHR is more strongly predictive of MI in women than in men (pooled OR 4.63, 95% CI 3.28–6.53 in women; pooled OR 2.71, 95% CI 2.15–3.41 in men).

Conclusions: MI is significantly associated with increased WHR, with a stronger association among women.

Abbreviations: BMI = body mass index, CHD = coronary heart disease, CI = Confidence Interval, HRs = hazard ratios, MI = myocardial infarction, NOS = Newcastle-Ottawa Scale, ORs = odd ratios, RRs = relative risks, WC = waist circumference, WHR = waist-hip ratio, WHtR = waist-to-height ratio.

Keywords: meta-analysis, myocardial infarction, obesity, systematic review, waist-hip ratio

1. Introduction

Overweight and obesity have been recognized as a major risk factor for coronary heart disease (CHD) with increasing prevalence.^[1–3] Experts have predicted that the current growth rate of obesity (an estimated 7% increase in men and 10% increase in women by 2020) will lead to an increase in the number of CHD events by 14% in 2035.^[4] Among the various types of CHD, myocardial infarction (MI) is associated with a high incidence rate, acute onset, and increased lethality, thereby posing a serious threat to the life of the patient.

Body mass index (BMI) can serve as a marker indicating the general obesity, and the relationship between MI and BMI has been intensively investigated, but there are still certain limitations requiring our concern.^[5,6] In relation with BMI, there seem to be closer correlations of the anthropometric measures of abdominal obesity (such as the waist circumference [WC], waist-to-height ratio [WHtR], waist-hip ratio (WHR), and the sagittal abdominal

diameter) with the metabolic risk factors, MI events, and death events.^[7] Moreover, excessive fat mass in the body, rather than excessive body weight, accounts for the leading cause of the increased risk of MI among the obese population.^[8] Consequently, some studies indicate that central obesity index, WC, WHtR, and WHR are the risk factors for predicting MI, which can also overcome the limitations of BMI.^[9,10]

Among them, WHR may serve as a preferred risk factor for predicting MI, which can be attributed to its inclusion of measuring the hip circumference. Typically, WHR is negatively correlated with the cardiometabolic risk and MI.^[11] Increase in hip circumference will lead to increases in subcutaneous fat mass in hip, gluteal muscle, and total muscle mass in leg. Specifically, the muscle mass in leg, which can serve as an indirect measurement of physical activity, is negatively correlated with the cardiometabolic risk. Besides, it is also suggested in the INTERHEART study^[12] that, among the extensively applied anthropometric measures, WHR is the most closely correlated with the risk of MI globally.

Therefore, the current meta-analysis was conducted to systemically review all related literature enrolling MI patients with available WHR measurements, so as to examine the correlation of WHR with MI and to explore whether the association intensity varied between different sexes.

2. Materials and methods

2.1. Study design

This review and meta-analysis was conducted according to the general guidelines recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.^[13]

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The author(s) report no conflicts of interest.

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2.2. Information sources

In November 2017, we systematically searched the PubMed, EMBASE, Cochrane, and Web of Science databases for articles that reported the association between WHR and MI risk.

2.3. Search

Keywords and medical subject headings (MeSH) were used for specific searches. In each database, the MeSH terms “myocardial infarction” or “percutaneous coronary intervention” or “coronary artery bypass surgery” were combined with the MeSH term “waist-hip ratio.” The keyword terms corresponding to each of these MeSH terms were also mapped in a similar manner. To obtain relatively complete data, the search strategy had no language, study type, or publication date restrictions. In addition, the reference sections of relevant reviews or systematic reviews were also searched.

2.4. Study eligibility criteria

The study inclusion and exclusion criteria are presented in Table 1. Only studies that met the eligibility criteria were included in the analysis.

2.5. Study selection

Independent dual-selection of the eligible articles was conducted by the first 2 investigators (C.Q.Q. and Y.S.). Any discrepancies between reviewers in the determination of study eligibility were resolved by consensus and consultation with the third author if necessary.

2.6. Data abstraction

Data extraction for the included studies was independently performed by the first 2 authors, and a third researcher was consulted for input in the event of uncertainties. All sources of data were derived from the original literature, and data on the basic characteristics of the eligible articles were collected as follows: first author, year of publication, location, study design, age population, case matched control, subgroup (age/sex), MI type, MI cases (total subjects), WHR sources, WHR cutoff values, adjusted odd ratios (ORs), relative risks (RRs), or hazard ratios (HRs) (95% confidence interval [CI]), adjustments, and Newcastle-Ottawa Scale (NOS) scores.

2.7. Study appraisal

The modified NOS was used to appraise the quality of the included studies.^[14] Study quality was evaluated independently by 2 researchers. Any disagreements were resolved by discussion with the third researcher.

2.8. Statistical analysis

2.8.1. Synthesis of results. The meta-analysis was assessed using Review Manager 5.3 software from the Cochrane Collaboration (London, United Kingdom). Random-effects models with the generic inverse variance method were used to calculate pooled odds risks (ORs). All analyses were calculated at the 95% CI level. Statistical heterogeneity was assessed using Cochran Q statistics and quantified using I^2 statistics. The I^2 statistic denotes the percentage of total variation attributable to between-study heterogeneity rather than chance. The presence of publication bias was determined by examining the funnel plot symmetry and whether the included studies fell within the boundaries. Sensitivity analysis was performed by deleting individual studies while observing any changes in the I^2 statistic.

2.8.2. Summary measures. Summary effect measures were reported as ORs and 95% CIs in this study. The RR for 1 included case-control study^[15] was also reported as the OR. As 2 cohort studies^[16,17] used survival analysis as opposed to logistic regression to determine the effects of the HR, they were not included in the final meta-analysis.

The information presented in this study was collected from the previous research, so there was no need for approval by an ethical review board or informed consent.

3. Results

3.1. Literature search

A total of 1723 potentially relevant articles (325 articles from PubMed, 304 articles from EMBASE, 37 articles from Cochrane, and 1057 articles from Web of Science) were obtained after the published data search. First, using EndNote X6, we deleted 377 duplicate records, filtered out 1004 unrelated studies, and deleted 214 other duplicate records by reading the title and abstract. After browsing the remaining 128 studies, 61 were deleted. Then, 67 review articles/commentaries were screened, of which 45 studies identified as eligible for further full-text (or abstracts as necessary) review. Finally, after reading the literature, reviews, and references, a total of 14 studies,^[12,15–27] including 12 case-

Table 1

PICOS criteria for inclusion and exclusion of studies into quantitative (meta-analysis) analyses.

Parameter	Inclusion criteria	Exclusion criteria
Patients	Adults with myocardial infarction (STEMI and/or NSTEMI), regardless of treatment (fibrinolysis, PCI, CABG) General population—studies with subgroups (i.e., age or sex) were included only if there was possibility to compile subgroups into one cohort	Population limited to a subgroup (i.e., age 65 years' old or men only included)
Intervention	Groups of WHR	Studies without WHR groups
Comparator	Normal WHR group	
Outcomes	WHR and MI related to the incidence OR or RR or HR value can be used	Incomplete data
Study design	Cross-sectional study	Case reports
	Case-control study	Editorials &
	Cohort studies	Opinion pieces

CABG = coronary artery bypass grafting, HR = hazard ratio, MI = myocardial infarction, NSTEMI = non-ST-segment elevation myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention, RR = risk ratio, STEMI = ST-elevation myocardial infarction, WHR = waist-hip ratio.

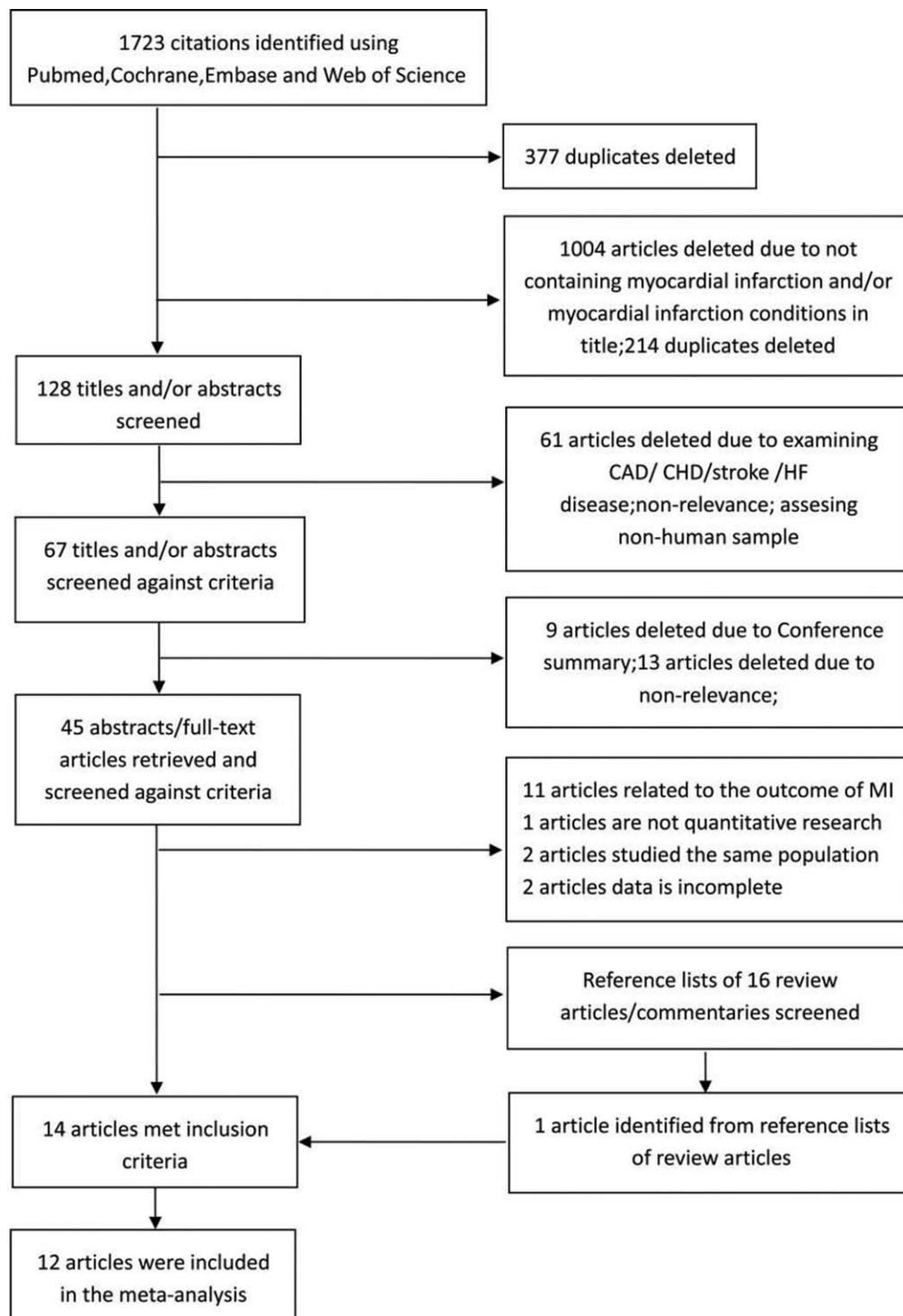


Figure 1. Flow diagram of the study (according to PRISMA statement). CAD=coronary artery disease, CHD= coronary heart disease, HF= heart failure.

control studies,^[12,15,18–27] met the inclusion criteria and were included in the meta-analysis. Specific details as to the screening and article deletion processes are shown in Figure 1.

3.2. Study characteristics and quality

For the included studies, 12 studies^[12,15,18–27] were case-controls and 2^[16,17] were cohort studies. These articles enrolled 23,163

patients with MI between 1996 and 2016. The majority of included studies were conducted in Europe and Africa,^[15–20,24,26,27] whereas 2 studies were conducted in South America,^[22,23] 1 study was conducted in Latin America,^[21] 1 study was conducted in South Asia,^[25] and a large sample study was carried out in 52 countries.^[12]

For the quality assessment using the Newcastle-Ottawa Scale criteria, all of the included studies scored ≥ 7 of 9, and

10 studies^[12,15–19,23–26] were high-quality with scores of 8 or 9. Of the 12 case-control studies^[12,15,18–27] that were included, there were 5 control group studies^[12,20–23] with population biases, as they included hospitalizations or lacked descriptions. The exposure factor for this meta-analysis was high WHR. Among the total studies, WHR was measured in 10,^[12,16,17,19,21,23–27] 1 study^[18] used recorded WHR data and WHR was not specifically described in the other 3.^[15,20,22] The characteristics and quality assessment information for all included studies are provided in Table 2.

Among the 12 case-control studies,^[12,15,18–27] 3^[19,21,26] investigated whether there were sex differences in the prediction of MI by WHR measurement. Based on the OR values yielded by these findings, we performed a meta-analysis to evaluate the association between sex and the predictive value of WHR on MI. Three studies^[22,23,26] used tertiles for the cutoff values of WHR rather than categorizing the WHR as normal or abnormal; therefore, to ensure the consistency of the research, we adopted the second tertile versus the first tertile as a reference. Finally, we conducted a meta-analysis of 10 articles^[12,15,18,20–25,27] with a general population along with a meta-analysis of three articles^[19,21,26] that provided separate OR values for men and women.

3.3. Association between WHR and MI

3.3.1. General population. Our findings from the meta-analyses support previous systematic and narrative reviews.^[28,29] The pooled OR for WHR as a predictor of MI was 2.62 (95% CI 2.02–3.39, $P < .00001$) with high and significant heterogeneity ($I^2 = 95\%$) (Fig. 2). Of the 10 studies included in the meta-analysis, 7 of the studies reported ORs that adjusted for age and sex. This further increases the credibility of the results of this analysis.

To minimize between-study heterogeneity, we conducted a sensitivity analysis. In the influence study, correlations were statistically affected with significance when 1 study was excluded at a time, and we found that Yusuf et al's study^[12] had a higher heterogeneity. After both Yusuf et al's^[12] and Piegas et al's studies^[23] were eliminated, the heterogeneity between studies was significantly reduced (pooled OR, 2.95, 95% CI 2.49–3.49, $I^2 = 51\%$) (Fig. 3).

Additionally, our funnel plots for the meta-analysis were symmetrical above the average value, suggesting no publication bias.

3.3.2. Men and women. As previously mentioned, 3 case-control studies^[19,21,26] provided data stratified by sex. The ORs for both sexes were computed, and the results showed that high WHR increased the MI risk in each sex (pooled OR 4.63, 95% CI 3.28–6.53 in women; pooled OR 2.71, 95% CI 2.15–3.41 in men) (Fig. 4). However, as seen in Figure 4, there was no heterogeneity in the female group, but high heterogeneity in the male group. Owing to the small number of included studies, we did not conduct further sensitivity analyses.

4. Discussion

This systematic review and meta-analysis appraises and summarizes the currently available evidence over the past 20 years concerning the predictive value of WHR on MI. The present study is the first to investigate WHR and MI using a meta-analysis, and the current data add to the available evidence that WHR is a promising factor in the prediction of MI risk, with a

strong predictive ability. This result is similar to the findings in patients with other cardiovascular diseases,^[30] suggesting that the consideration of WHR may be critical in identifying at-risk individuals and for population projections of the burden of disease for young to middle-aged adults.

To explore whether MI risk differed between men and women, we stratified our analyses by sex. We found a sex difference in the moderately adjusted subgroup analysis, according to which elevated WHR is a stronger predictor of MI in women than in men. This is consistent with Wiklund et al's^[31] study in which WHR and WC were found to be predictors of CVD according to sex differences. This may be related to the reduced psychological health and lower levels of physical activity among women compared to men.

Two larger cohort studies that were not included in the meta-analysis concluded that an increased WHR was a predictor of MI. To verify the rationality of deleting the 2 studies, we included 2 studies in the meta-analysis and found that the heterogeneity of the study increased significantly. Egeland et al^[16] observed 140,790 subjects for 9 years and found that WHR was a significant predictor of MI among men and women without an enlarged WC (<102 cm for men and <88 cm for women) in adjusted analyses. The study also indicated that WHR far more accurately identifies individuals at risk for MI compared to conventional risk factors, BMI, or an enlarged WC in middle-aged adults. During an average of 15.7 years of follow-up of 6379 subjects, Horvei et al^[17] found that WHR and WHtR, in comparison to WC and hip circumference, yielded the highest risk estimates for MI. The results have implications for improving the identification of high-risk individuals and for the prediction of the burden of obesity in populations.

Central obesity, which refers to a high WHR, likely contributes to MI via multiple pathways involving oxidative stress and inflammation, steroid hormones, free fatty acids, and altered production and function of adipocyte-derived hormones.^[32,33] Recent cardiac metabolism imaging studies conducted in large cohort studies (the Framingham Heart Study^[34] and Jackson Heart Study^[35]) have shown that visceral fat hyperplasia can exceed its storage capacity and become oversaturated, leading to a spillover of lipids that are then stored in normally lean tissues such as the heart, liver, and intrathoracic fat, contributing significantly to cardiac and metabolic abnormalities. In addition, adipose tissue fat cells are involved in the promotion of atherosclerotic regulation processes, and excessive visceral fat is associated with insulin resistance, hypertriglyceridemia, highly atherogenic small LDL particles, and low HDL levels, all proatherogenic factors.^[36] Subsequently, endothelial vasomotor dysfunction, a hypercoagulable state, and dyslipidemia are triggered, eventually leading to MI.^[37]

In light of these results, first, the ability of WHR to predict MI risk is evident, and healthcare professionals should consider the pivotal role of WHR in identifying populations at higher risk of MI, especially in women. Second, further work is needed to discern the best practice guidelines for capturing the various dimensions of WHR that contribute to MI risk. Third, the potential risk of high WHR should be included in the health education of patients so that patients understand that a normal body weight does not preclude the presence of abdominal obesity. Fourth, this study presents a new challenge to medical rehabilitation professionals involved in monitoring the physical activity of obese patients in that they should pay more attention to the patient's WHR and not just the BMI. Finally, as a central obesity index, WHR is more clinically relevant than BMI and

Table 2

Characteristics of the included Studies.

First Author	Year	Location	Study design	Age population (mean), y		Case matched Control	Subgroup (age/sex)	MI type	Cases (total subjects)	WHR data sources	WHR cutoff values	Adjusted OR or HR (95% CI)	Adjustments	NOS score
				Case	Control									
Kaur et al ^[18]	2012	North India	Case-control	49.6	31.1	Geographic-, origin-, and ethnicity-matched	Age	AMI	(350) 700	Investigated	M: ≤0.8 F: <0.95	OR: 4.8 (3.2–7.3)	Confounder effects of traditional coronary risk factors	9
Oliveira et al ^[19]	2010	Portugal	Case-control	Women: 49.6 men: 31.1	Women: 49.6 men: 31.1	NR	Sex	AMI	(653) 2366	Measured	M: ≤0.9 F: <0.85	OR: women: 5.8 (3.37–10.1); men: 10.9 (6.10–19.4)	Age, education, alcohol consumption, current smoking, leisure-time physical activity, family history of infarction, and menopause and hormone replacement therapy in women	8
Carevic et al ^[20]	2010	Southern Croatia	Case-control	Wome: 58.2 men: 64.5	None	Age- and sex-matched	None	MI	(263) 527	NR	M: 0.9–0.95 F: 0.83–0.90	OR: 1.96 (1.21–3.18)	Age and sex	7
Lanas et al ^[21]	2007	Latin America	Case-control	59	1 or 2 age-matched	Age-, sex- and center-matched	Sex	AMI	(1237) 3125	Measured	M: 0.9–0.95 F: 0.83–0.90	OR: 2.49 (1.97–3.14); women: 5.8 (3.37–10.1); men: 10.9 (6.10–19.4)	Age, sex, and smoking	7
Yusuf et al ^[12]	2005	52 Countries	Case-control	Age-matched (±5 y)	Age- and sex-matched	Age- and sex-matched	Age	MI	(12,461) 27,098	Measured	M: ≤0.9 F: <0.83	OR: 1.77 (1.67–1.88)	Age, sex, region, and smoking	8
Avezum et al ^[22]	2005	São Paulo	Case-control	58	47	NR	None	STEMI	(271) 553	NR	Second tertile	OR: 3.07 (1.66–5.66)	Age and sex	7
Piegas et al ^[23]	2003	Brazil	Case-control	56	53	Age- and sex-matched	None	STEMI	(1279) 2558	Measured	Second tertile	OR: 1.52 (1.06–2.18)	Current smoking, glucose, family history of CAD, LDL-cholesterol, hypertension, diabetes mellitus, alcohol intake	8
Kumar et al ^[24]	2003	North India	Case-control	36.2	36.4	Age- and sex-matched	None	MI	(35) 80	Measured	M: <0.95 F: <0.8	OR: 5.6 (1.4–21.1)	Family history of CAD, Smoking, BMI, Hypertension, total cholesterol, Serum triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, lipids, genotypes with apo E4	9
Gerstein et al ^[25]	1999	South Asia	Case-control	47.2	46.8	Age- and sex-matched	None	AMI	(300) 600	Measured	<0.89	OR: 2.41 (1.75, 3.31)	Age and sex	8
Azevedo et al ^[26]	1999	Portugal	Case-control	≥40	≥40	NR	Sex	AMI	(338) 1000	Measured	Second tertile	OR: women: 3.0 (0.6–14.6); men: 2.5 (1.3–4.9)	Age, education, family history of acute myocardial infarction, and smoking	8
Pais et al ^[27]	1996	India	Case-control	47.3	47	Age- and sex-matched	None	AMI	(200) 400	Measured	<0.92	OR: 3.12 (1.80–5.40)	Smoking, hypertension, income, non-vegetarianism, and fasting blood glucose	7
Kumar et al ^[15]	2009	India	Case-control	60.5	61.8	Age- and sex-matched	None	AMI	(165) 330	NR	≥0.95	RR: 3.9 (2.1–6.3)	Age, sex and hospital	8
Egeland et al ^[16]	2016	Norway	Cohort	<60: 41 ≥60: 70	NR	NR	Age Sex	AMI	(4653) 140790	Measured	M: <0.91 F: <0.8	HR: men <60 y: 1.22 (1.07, 1.40); Men ≥60 years of age: 1.09 (0.97, 1.23); women <60 y: 1.76 (1.37, 2.25); women ≥60 y: 1.05 (0.90, 1.24)	Age, current daily smoking, BMI, mean systolic blood pressure, self-reported diabetes, and total cholesterol–HDL-C ratio	9
Honei et al ^[17]	2014	Norway	Cohort	61	NR	NR	Sex	MI	(925) 6379	Measured	M: <0.95 F: <0.85	HR: women: 1.09 (0.6–14.6) men: 2.5 (1.3–4.9)	Age, smoking, systolic blood pressure, total cholesterol, HDL cholesterol, triglycerides, HbA1C and self reported-diabetes mellitus	8

AMI = acute myocardial infarction, BMI = body mass index, CAD = coronary artery disease, F = female, HDL = high-density lipoprotein, HR = hazard ratio, LDL = low-density lipoprotein, M = male, MI = myocardial infarction, NOS = Newcastle-Ottawa Scale, NR = not report, OR = odds ratio, RR = risk ratio, STEMI = ST-elevation myocardial infarction, WHR = waist-hip ratio.

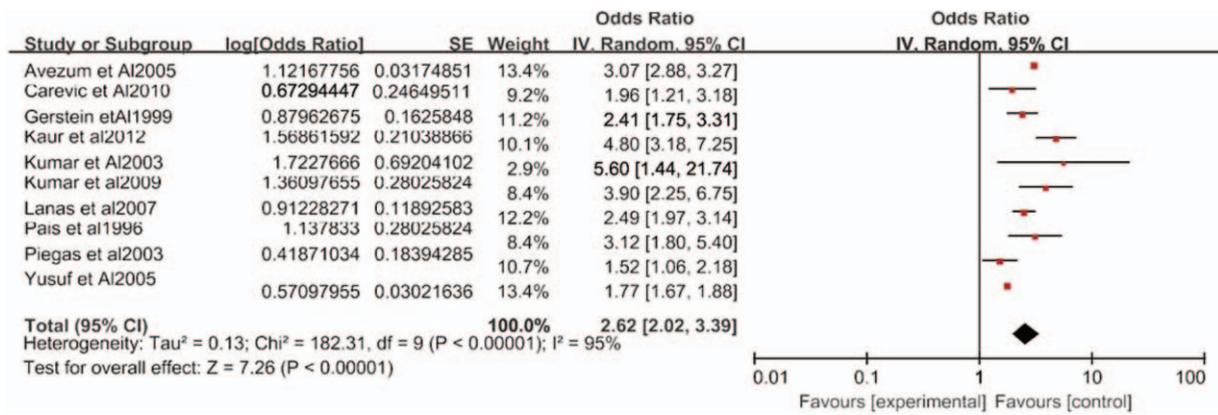


Figure 2. Forest plot of the odds ratio for waist-hip ratio as a predictor of myocardial infarction risk. CI=confidence interval, SE=standard error.

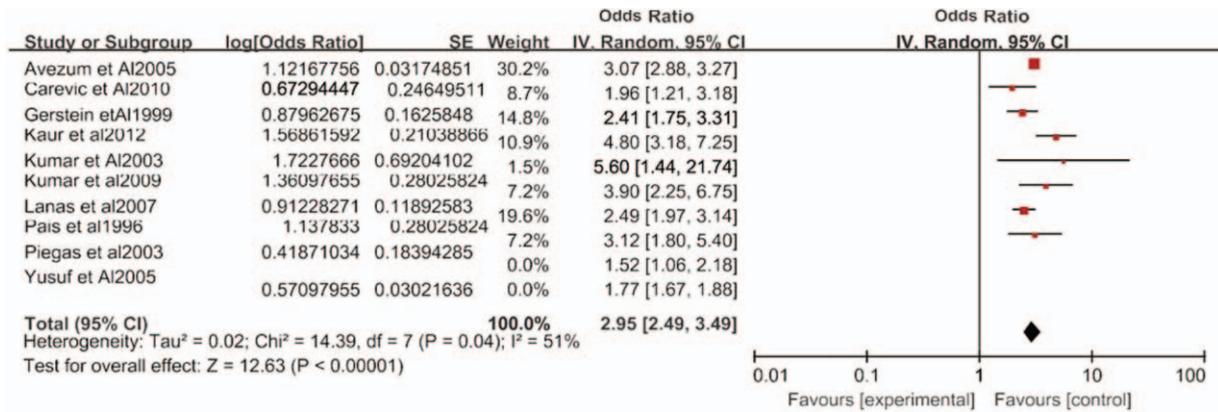


Figure 3. Sensitivity analysis of the odds ratio for waist-hip ratio as a predictor of myocardial infarction risk. CI=confidence interval, SE=standard error.

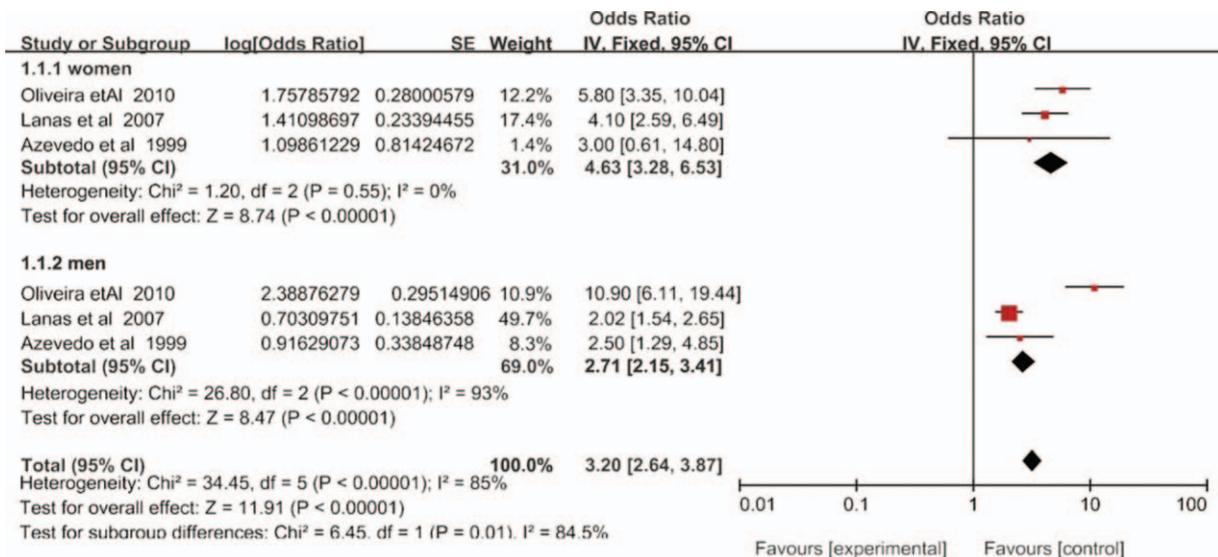


Figure 4. Forest plot of the odds ratio for waist-hip ratio as a predictor of myocardial infarction risk, stratified by sex. CI=confidence interval, SE=standard error.

merits increased attention, especially in terms of the acute onset of disease, to reduce the risk of morbidity.

The heterogeneity of the studies must be addressed because it may affect the justification for pooling the data into one analysis. In the present meta-analysis, statistical heterogeneity may have been caused by clinical heterogeneity, such as differences in the study population and different WHR cutoff points, as well as by different study quality characteristics. Among them, the high heterogeneity of Yusuf et al's research^[12] may be attributed to the fact that it was a study with a large sample size involving 52 countries. Although the major influencing factors such as age, sex, and geographical location were adjusted for, there are still some differences in methodological quality compared with the other studies. However, the statistical tests of heterogeneity were within the acceptable range for the pooling of studies.

Our study has several strengths. First, the studies included in the meta-analysis are all case-control trials to minimize the potential deviations associated with research design. Second, the number of patients evaluated in the included studies was high with some very large samples such as those of the INTERHEART^[12] and CONO^[16] studies. Finally, most of the WHR data were measured, not reported, making the findings more objective and relevant.

Potential limitations should also be noted with our review. Although the process of a systematic literature review and meta-analysis is a robust way of generating a more powerful estimate of true effect size with less random error than individual studies, it does come with limitations. For example, the articles included in this study were case-control trials, and we lacked cohort studies with high levels of evidence. Clearly, more cohort studies should be conducted in the future to enhance the level of evidence of the findings. Another limitation was the use of different cutoff values for WHR between studies, thereby preventing the identification of a single threshold for WHR that is potentially predictive of MI risk. Finally, there are discrepancies between the various studies in terms of the measurement of WHR, which should be objectively measured using standard techniques in future studies.

5. Conclusions

Based on our pooled results, WHR can be deemed an excellent predictor of MI risk, as there is a significantly increased risk of MI among patients with a high WHR. The predictive effect of WHR on the risk of MI is even more significant in women than in men. Thus, the measurement of WHR may have clinical utility in MI risk assessments, particularly for those patients with elevated WHRs.

Author contributions

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Writing – review & editing: Qinqin Cao, Feng Li.

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