Original Article

Measures of Abdominal Adiposity and Risk of Stroke: A Dose-Response Meta-analysis of Prospective Studies*

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Abstract

Objective Waist circumference, waist-to-hip ratio and waist-to-height ratio, which are the indicators or measures of abdominal adiposity, have long been hypothesized to increase the risk of stroke; yet evidence accumulated till date is not conclusive. Here, we conducted a dose-response meta-analysis to summarize evidences of the association between these measures of abdominal adiposity and the risk of stroke.

Methods PubMed and Web of Science databases were searched from inception to May 2015. Two investigators independently conducted the study selection and data extraction. Dose-response relationships were assessed by the generalized least squares trend estimation, while the summary effect estimates were evaluated by the use of fixed- or random-effect models. Subgroup and sensitivity analyses were performed to assess the potential sources of heterogeneity and the robustness of the pooled estimation. Publication bias of the literature was evaluated using Begg's and Egger's test.

Results Altogether 15 prospective cohort studies were identified in this study. The summary of relative risks (95% confidence intervals) of stroke for the highest versus the lowest categories was 1.28 (1.18-1.40) for waist circumference, 1.32 (1.21-1.44) for waist-to-hip ratio, and 1.49 (1.24-1.78) for waist-to-height ratio. For a 10-cm increase in waist circumference, the relative risk of stroke increased by 10%; for a 0.1-unit increase in waist-to-hip ratio, the relative risk increased by 16%; and for a 0.05-unit increase in waist-to-height ratio, the relative risk increased by 13%. There was evidence of a nonlinear association between waist-to-hip ratio and stroke risk, $P_{nonlinearity}$=0.028.

Conclusion Findings from our meta-analysis indicated that waist circumference, waist-to-hip ratio, and waist-to-height ratio were positively associated with the risk of stroke, particularly ischemic stroke.

Key words: Abdominal adiposity; Waist circumference; Waist-to-hip ratio; Waist-to-height ratio; Stroke; Cohort studies; Meta-analysis

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INTRODUCTION

Stroke is the second most common cause of death worldwide and the leading cause of long-term neurological disability in adults, with more than half the survivors depending on others for everyday activities[1-2]. Obesity is a major public health concern worldwide and is associated with increased risk of atherosclerotic vascular disease, including myocardial infarction and stroke[3-4].

Abdominal obesity is more closely related to metabolic dysfunctions connected with cardiovascular disease (CVD), than general obesity[4]. Moreover, visceral adipose tissue secretes higher amounts of inflammatory cytokines and is associated with a greater atherosclerotic risk profile than subcutaneous fat, when present in excess[5-7]. Waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) are proxy measures of visceral adipose tissue[8]. A previous pooling analysis of 15 prospective studies showed that WC and WHR were strongly associated with the risk of cardiovascular disease incidence[9]. Waist-to-height ratio is less commonly used than WC and WHR, while the cut-off point for CVD is subject to less ethnic variation[10], and several studies have shown that WHtR correlates better to cardiovascular risk factors than BMI[11]. During the past decades, a number of prospective studies have evaluated the association between the measures of abdominal obesity and the risk of stroke[12-29]. However, these results were inconsistent mainly owing to differences in sample size, sex, study population, study quality, or residual confounding among these studies. Some reports have demonstrated a significant correlation of measures of abdominal adiposity with stroke, while others have not. Furthermore, the exact shapes of the dose-response curves for WC, WHR, or WHtR and stroke risk have not been clearly defined.

Thus, we conducted a dose-response meta-analysis to clarify and quantitatively assess the relationship of WC, WHR, and WHtR with stroke risk.

METHODS

Data Sources and Search Strategy

This review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement, 2009[30]. Any prospective study that examined the relationship between measures of abdominal adiposity and stroke was eligible for inclusion in our study. We searched PubMed and Web of Science databases for articles published until May 2015, and used the keywords 'WC', 'WHR', 'WHtR', 'waist', 'waist circumference', 'waist-to-hip ratio', 'waist-to-height ratio', or 'abdominal obesity'; 'stroke', 'cerebral infarction', 'brain infarction', 'cerebrovascular disease', 'cerebral hemorrhage', 'intracranial hemorrhage', or 'cerebrovascular disorder'; and 'nested case-control', 'follow-up study', 'prospective study', or 'cohort study'. We also conducted manual searches of the reference lists of all the retrieved papers and recent reviews to identify additional eligible studies.

Study Selection

The eligible studies met the following inclusion criteria: 1) the study had a prospective design (prospective cohort or prospective nested case-control study); 2) the study investigated the association between measures of abdominal adiposity (WC, WHR, or WHtR) and the risk of nonfatal and/or fatal stroke; 3) the authors reported effect estimates [risk ratio (RR), hazard ratio (HR), or odds ratio (OR)], and 95% confidence intervals (CIs) for at least 3 quantitative categories of abdominal adiposity indices. We excluded all case-control studies because various confounding factors could bias the results. If multiple articles were published from the same cohort, we selected the article for which the primary focus was the association between measures of abdominal adiposity and stroke risk[20,28]. Study selection was conducted independently by two authors (CKZ and XYZ) by using a standardized approach. Any disagreements were resolved by discussion.

Data Collection and Quality Assessment

Data extraction and quality assessment were independently performed by two investigators (CKZ and XYZ), and independently checked for accuracy by a third investigator (YHZ). The following data elements were extracted from each study: first author's or study group's name, publication year, country, study design, sample size, assessment of exposure, number of events, age at baseline, percentage of male, follow-up duration, and covariates in the fully adjusted model. In addition, we extracted the number of cases, person-years or number of non-cases, effects of the different exposure categories, and the 95% CIs. For the studies that reported several multivariable-adjusted