Transient Ischemic Dilatation Ratio in Stress Myocardial Perfusion SPECT in Diabetic Patients-A Systematic Review and Meta-Analysis

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Abstract

Objective: Abnormal values of the transient ischemic dilation (TID) ratio are associated with severe and extensive coronary artery disease (CAD). TID can be used as a diagnostic and prognostic marker of CAD in diabetic patients. The aim of current study was to determine the pooled estimate of TID ratio in single myocardial perfusion scan in diabetic patients by a systematic review and meta-analysis.

Materials and Methods: The electronic databases of PubMed/MEDLINE, Scopus (EMBASE), Web of Science, and Cochrane Library up to December 30, 2013 were searched. The reference lists of all included studies were searched for further studies. The search strategy was according to PICO characteristics. The heterogeneity between the studies was accounted with $P<0.1$. The random/fixed effect model was used according to the heterogeneity. Point estimates were pooled estimate of TID ratio with 95% confidence interval (CI) by pooling available data. Egger's test was used to assess publication bias.

Results: The primary search contained 423 studies. Totally, 17 studies met the inclusion criteria and the critical appraisal scores. The TID ratio in four single pharmacological stress studies with angiographic evidence of low risk or normal coronary artery disease was 1.079 (95% CI: 1.07-1.089).

Conclusion: Our findings were achieved according to the purpose of the study and the pooled estimate of TID±SD was calculated. The pooled estimate of TID was so smaller than the TID calculated in individual studies and so precise.

Keywords: Transient ischemic dilatation, Single myocardial perfusion scan, Diabetes, Systematic review, Meta-analysis

Introduction

The coronary artery disease (CAD) is still the major cause of mortality and morbidity in diabetic patients (1). Stress gated myocardial perfusion single-photon emission computed tomography (SPECT) is widely used for the diagnosis of CAD and patients' risk stratification (2-4). Transient ischemic dilation (TID) is a method to discover balanced coronary artery disease in patients with actually normal myocardial

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perfusion scintigraphy (5). The silent ischemia in diabetic patients requires an accurate diagnostic method. TID is the mean left ventricular size after stress divided by the mean left ventricular size at rest. While elevated to around 1.2 or greater, it increases the risk of advanced cardiovascular disease. The TID ratio is strongly correlated with the extent and severity of stress-induced perfusion abnormality; thus higher TID ratios propose a greater ischemic burden (3,6). The maximum value of an abnormal TID ratio may be different according to stress type, type of isotope, and imaging protocols (7). TID has been shown to correlate with the presence of multi-vessel disease and indicates adverse outcomes, even in the absence of significant perfusion defects (8,9). Although TID of the left ventricle during stress MPS has been demonstrated in different individual studies, rare information is present about the real value of TID to assess CAD and the values to be used for better risk stratification of the patients with extensive CAD.

With this systematic review we aim to point out the normal threshold of TID ratio in diabetic patients undergoing separate-acquisition single-isotope 99m Tc-sestamibi or 201Tl Myocardial Perfusion Scintigraphy (MPS) with pharmacological or physical exercise stress as established in published studies.

Materials and Methods

Data sources

We performed a systematic search of all studies that evaluated TID of the left ventricle in patients undergoing separate-acquisition single-isotope 99m Tc-sestamibi or 201Tl MPS. The electronic databases of PubMed/MEDLINE, Scopus (EMBASE), Web of Science, and Cochrane Library up to December 30, 2013 were searched. The reference lists of all included studies were searched for further studies.

Search strategy

The search strategy was according to PICO characteristics. The search strategy was a combination of the key words of medical subject headings and Emtree terms (EMBASE and Cochrane Library). The search terms were “transient ischemic dilatation”, “myocardial scintigraphy” and “coronary angiography”. The complementary table contains the key words of medical subject headings for our search and the PubMed search strategy example.

Eligible studies

We included all interventional studies if they reported Transient ischemic dilation (TID) of the left ventricle with standard deviation. There was no language restriction. Studies had to been published as full text article. We excluded studies if they were reviews, letters, case reports, case series, cross sectional studies and the studies that did not report obviously the population sources or the available data to calculate TID of the left ventricle with standard deviation. In addition, the included studies should contain the coronary angiography result as the gold standard method for comparison. Figure 1 depicts the selection process for the studies included in the systematic review-Meta analysis.

Quality evaluation of articles and data extraction

Two independent investigators (NN and SKR) conducted data extraction using pre-specified inclusion and exclusion criteria. The disagreements in data extraction were discussed and if required, a third investigator (VD) qualified the studies. The consolidated standard of reporting trials (CONSORT-2010) was used as the quality assessment scales for clinical trial studies.

All of included studies (100%) fulfilled the key questions. Complementary figures contain the study appraisal tools that were used to avoid the risk of bias of individual study. The data were extracted from each eligible study.

The extracted data included: first author name, the country of origin, date of study, date of publication, sampled population, sample size, study design, angiographic variables (type of

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vessel, degree of CAD), SPECT variables (type of scan, type of stress), effect size (TID, SD). The crude TID of the left ventricle with standard deviation was extracted as the principal summary measure of different groups. The sensitivity and specificity were extracted or calculated. The high-risk group included patients with multivessel CAD or single left main obstruction>50%. The low-risk group included normal coronary artery or single vessel obstruction<50%, discrepancies were resolved by discussion between reviewers and reaching to consensus.

Statistical analysis and synthesis of results

The heterogeneity between the studies was defined as $P<0.1$ or I^2 Index>50%. I^2 Index was calculated as 100 × (Cochrane Q - df)/Cochrane Q; if there were heterogeneity between the studies, the random-effect method meta-analysis was used. Egger's test was used to indicate the publication bias ($P<0.05$). STATA version 10 software (Statacrop, Texas, US) was used for statistical analysis.

This study was approved by research and ethical committees of Yazd Shahid Sadoughi University of Medical Sciences.

Results

Search results

After removing 54 duplicated records, 369 studies were screened according to their titles and abstracts of which 261 were excluded, 108 were critically appraised, and 17 were selected (5,9-23). Four (11,13,21,23) studies included in the analysis of the TID ratio in diabetic patients undergoing separate-acquisition single-isotope 99m Tc-sestamibi or 201Tl MPS (Figure 1). Table 1 demonstrates each study characteristics and results.

Bias across studies

There was no evidence of publication bias. The funnel plot results for publication bias are shown in Figure 2, which indicates no significant publication bias.

Synthesis result

The single pharmacological stress

The TID ratio in four studies with angiographic evidence of low risk or normal CAD was 1.079 (95%CI: 1.07-1.089). The pooled sensitivity and specificity were 23% and 81.6%, respectively (Figure 3).

Discussion

TID as a prognostic and diagnostic marker of CAD is documented in previous studies (15,17,24,25). Our findings were achieved according to the purpose of study and the pooled estimate of TID±SD was calculated. The pooled estimate of TID was so smaller than the TID which was calculated in individual studies and so precise. This can be the consequence of notable number of individual studies excluded due to not performing the angiography as the gold standard of CAD diagnosis. In addition, the included studies were accurate and obtained high quality score of critical appraisal.

The sensitivity of pooled estimate of TID was not high, but the specificity was acceptable. This result is completely concordant with the individual studies' findings.

As the other considerable point of our findings, TID was reported after the use of attenuation correction in some studies (26); but for the protection of our study's homogeneity, none-attenuation correction of TID was included to the final calculation of pooled TID estimation. These remarkable points may not be limitations of this systematic review but must be considered before using the results.

Table 1. Individual studies characteristics

First author	Publication year	Sample size	Comorbidity	Type of radionuclide	Type of scan
D vijay A	1990	180	diabetes	technetium-99m	single
Adamikova A	2006	38	diabetes	technetium-99m	single
Fallahi B	2010	86	diabetes	technetium-99m	Single
Petretta M	2013	672	diabetes	technetium-99m	single

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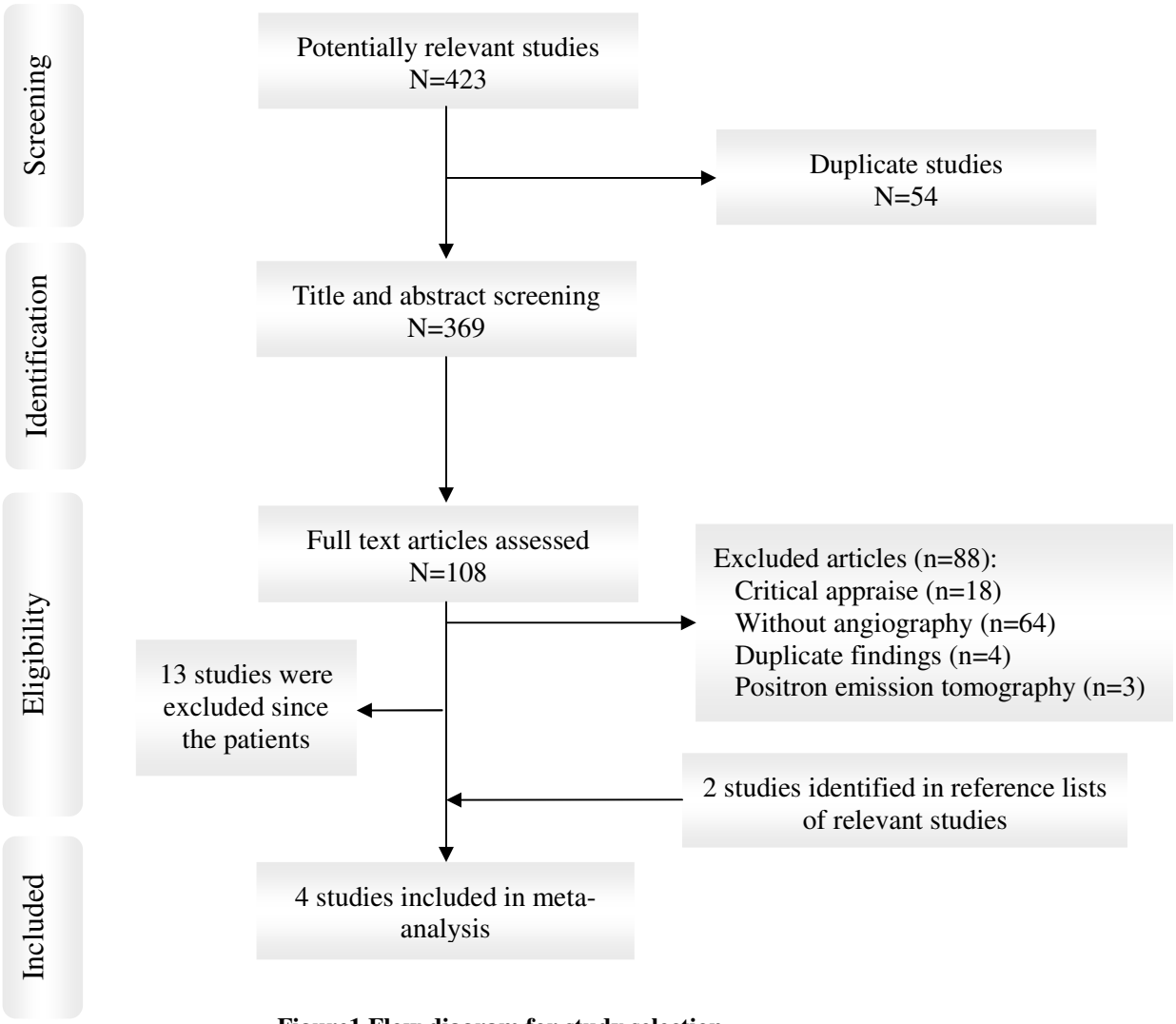


Figure1.Flow diagram for study selection

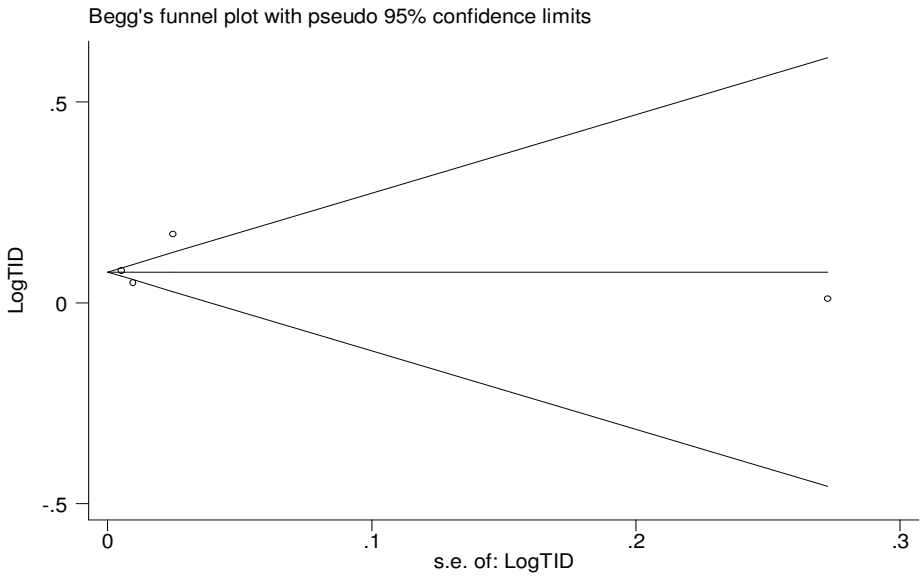
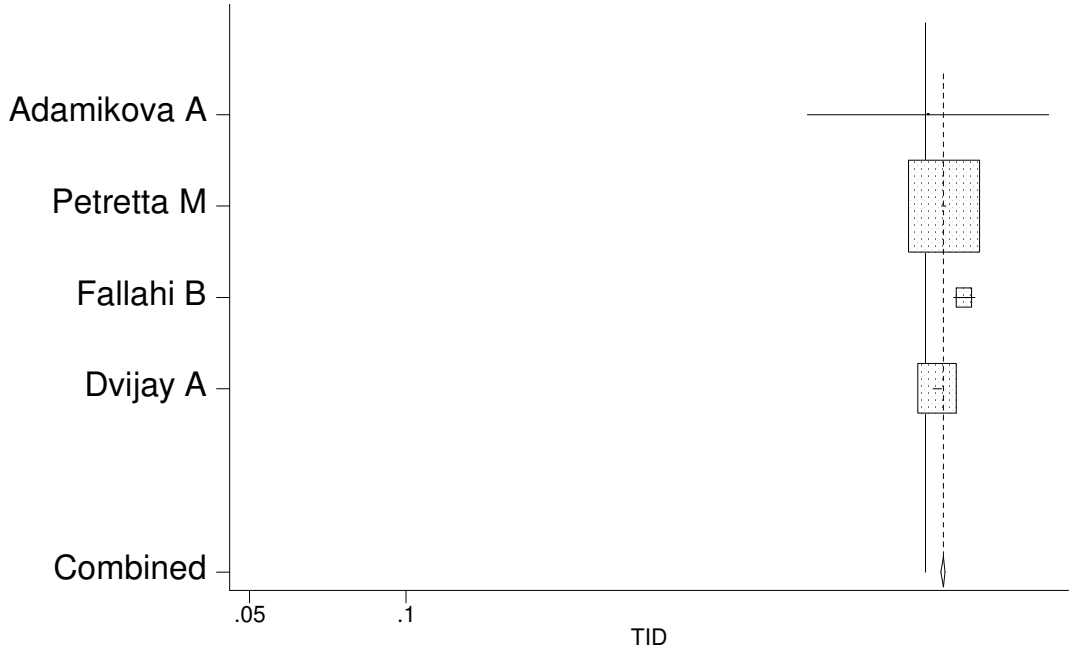


Figure 2. The funnel plots of TID in single pharmacological stress test

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Cochrane Q: 22.184
Degree of freedom: 4
***P*<0.001**
Figure 3. Forest plots of TID in single pharmacological stress test

The risk factors of CAD as the pre-test probability were not considered in this systematic review. Risk stratification of CAD by underlying disease, age, sex and other factors was not considered that is one of the most important limitations of this study. In addition, the prognosis and diagnosis usage of TID was not stratified. The source of these limitations was lack of high quality individual studies. The authors suggest consideration of these limitations in future studies. As a conclusion, while the study is restricted by some limitations, the findings are reliable.

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