

INPLASY PROTOCOL

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Corresponding author:

Liao Guangzhi

soleil0726@163.com

Author Affiliation:

Sichuan university

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None declared.

Total Arterial Revascularization in Diabetic Patients Undergoing Coronary Artery Bypass Graft Surgery: A Systematic Review and Meta-analysis

Liao, GZ¹; Liu, T²; Li, YM³; Bai, L⁴; Ye, YY⁵; Chen, XF⁶; Peng Y⁷.

Review question / Objective: P: diabetic patients undergoing coronary artery bypass graft surgery; I: total arterial revascularization; C: conventional surgery with saphenous veins; O: long-term all-cause death and cardiovascular death (≥ 1 year); early mortality (≤ 30 days); S: observational studies or randomized controlled trials. **Eligibility criteria:** The studies included must meet the following criteria: 1) diabetic patients (were primarily diagnosed according to the International Classification of Diseases, 10th Revision, with insulin or oral treatment before operation) receiving isolated CABG. 2) reported on any one of the following comparisons: outcomes of TAR and CVR in diabetic patients, outcomes in diabetic and non-diabetic patients following TAR grafting, outcomes of BIMA/RA and right gastroepiploic artery (RGA) in DM; 3) provided either in-hospital or 30-day postoperative mortality, any sternal wound infection rate (superficial and deep infections, SWIs) after the operation, and Kaplan Meier survival curves of all-cause death and cardiovascular death or hazard ratio (HR) for the two outcomes; 4) published randomized controlled trials and non-randomized controlled trials, with English as the language limitation.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 December 2022 and was last updated on 01 December 2022 (registration number INPLASY2022120003).

INTRODUCTION

Review question / Objective: P: diabetic patients undergoing coronary artery bypass graft surgery; I: total arterial revascularization; C: conventional surgery with saphenous veins; O: long-term all-cause death and cardiovascular death (≥ 1 year); early mortality (≤ 30 days); S: observational studies or randomized controlled trials.

Rationale: Literature Search We searched PubMed, Embase, and Cochrane from

inception to July 2022 for studies that studied the effect of arterial revascularization in diabetic patients undergoing isolated CABG. The search strategies and related terms were provided in the supplemental file. Two reviewers (LG and LT) screened each study by title and abstract for inclusion, reviewed the full texts of studies that qualified, and then extracted the data independently. All disagreements were resolved by discussion. The references of selected articles and conference proceedings were also screened.

Eligible study and endpoints of interest

The studies included must meet the following criteria: 1) diabetic patients (were primarily diagnosed according to the International Classification of Diseases, 10th Revision, with insulin or oral treatment before operation) receiving isolated CABG. 2) reported on any one of the following comparisons: outcomes of TAR and CVR in diabetic patients, outcomes in diabetic and non-diabetic patients following TAR grafting, outcomes of BIMA/RA and right gastroepiploic artery (RGA) in DM; 3) provided either in-hospital or 30-day postoperative mortality, any sternal wound infection rate (superficial and deep infections, SWIs) after the operation, and Kaplan Meier survival curves of all-cause death and cardiovascular death or hazard ratio (HR) for the two outcomes; 4) published randomized controlled trials and non-randomized controlled trials, with English as the language limitation. We defined the long-term (≥ 12 months) all-cause death as the primary endpoint of interest. The secondary efficacy endpoints were long-term (≥ 12 months) cardiovascular death and early SWI and death. To investigate the influence of DM on the effect of arterial revascularization, we conducted a comparison between the effect of TAR in DM and that in non-DM. To avoid minor study effects, studies with a sample size of <100 patients were excluded.

Data Extraction and Quality Assessment

Two researchers (LG and LT) independently extracted the following information from each work: the first author, publication

year, type of study, and participant characteristics. Reviewers extracted the following outcomes of interest: early death, any SWI, any Kaplan–Meier curve for long-term overall survival, or cardiac mortality-free survival. For studies that reported the results of propensity-score-matched (PSM) analysis, we abstracted and pooled the PSM data. The Cochrane risk of bias tool was used to examine randomized control trials (RCTs), and the Newcastle-Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf) was used to investigate observational studies. Publication bias was evaluated by visual inspection of funnel plots.

Statistical Analysis

Risk ratios (RRs), hazard ratios (HRs), and their corresponding 95% confidence intervals (CIs) were calculated to describe short-term results and long-term survival results. The I² statistics were performed to test for heterogeneity between the included studies, and a fixed-effects model was used to obtain the combined RRs and HRs when the I² statistic was lower than 50%. Otherwise, the random-effects model would be alternatively adopted. Forest plots were then created for graphic presentation of clinical outcomes with the Review Manager and adjusted by package Forest plot of R software (version 4.1.3) successively. Funnel Plot were created for the comparisons with 10 or more studies included. In each included study, Kaplan–Meier curves for overall and cardiac mortality-free survival were first digitalized in Engauge Digitizer software (version 10.4; maintained by Mark Mitchell). HR calculations spreadsheet provided by Jayne F Tierney [8] [<http://www.biomedcentral.com/content/supplementary/1745-6215-8-16-S1.xls>] was second applied to facilitate the estimation of HRs from the data extracted from Kaplan–Meier curves. Finally, package Meta and Forest plot of R software (version 4.1.3) were used to pool HRs and generate the forest plots. Additionally, Kaplan–Meier (KM) survival curves for long-term death-free survival and digitalized KM curve data were aggregated to construct combined survival curves in package MetaSurv of R software (version 3.4.3).

Condition being studied: Coronary artery bypass grafting (CABG) has been identified as the preferred revascularization strategy in patients with multivessel disease and diabetes. As an important factor influencing the clinical outcomes of those receiving surgery, graft selection gradually attracted investigators' attention in recent years. Compared with conventional surgery with saphenous venous grafts (SVGs), using the left internal mammary artery (LIMA) to bypass a stenotic left anterior descending artery (LAD) improves outcomes and is thus considered the standard of care. However, with SVGs failure rating of up to 10% to 20% after 1 year and an additional 5% failure rate for each subsequent year, debates began to surround the application of additional arterial grafts. The association between total arterial revascularization (TAR) and the improvement of long-term survival in the general population had been established in a mounting number of studies. Still, there is a long way off before TAR can be applied widely in practice due to the elevated surgery difficulty and risk caused by some specific comorbidity, such as diabetes.

Patients with diabetes mellitus (DM) are frequently characterized by complex and three-vessel coronary artery lesions. Consequently, surgeons usually have to consider the selection of graft as the adjunct to LIMA. Despite the prolonged operation time and improved difficulty, the primary reasons hindering the application of MAR/TAR are the increased risk of sternal wound infection and potential higher perioperative mortality. Therefore, whether DM patients can get consistent long-term benefits from arterial grafts, which may outweigh the short-term risk, is a critical issue that requires investigation. Meanwhile, the clinical outcomes of arterial revascularization applying different arteries are also not clear. To provide the latest information about the effect and safety of arterial revascularization in DM, we conducted this systematic review and meta-analysis.

METHODS

Search strategy: We searched PubMed, Embase, and Cochrane from inception to July 2022 for studies that studied the effect of arterial revascularization in diabetic patients undergoing isolated CABG. The search strategies and related terms were provided in the supplemental file. Two reviewers (LG and LT) screened each study by title and abstract for inclusion, reviewed the full texts of studies that qualified, and then extracted the data independently. All disagreements were resolved by discussion. The references of selected articles and conference proceedings were also screened.

Participant or population: Diabetic patients undergoing isolated CABG.

Intervention: Total arterial revascularization with arterial deployments.

Comparator: Conventional surgery with at least one saphenous vein.

Study designs to be included: Observational trials or randomized controlled trials.

Eligibility criteria: The studies included must meet the following criteria: 1) diabetic patients (were primarily diagnosed according to the International Classification of Diseases, 10th Revision, with insulin or oral treatment before operation) receiving isolated CABG. 2) reported on any one of the following comparisons: outcomes of TAR and CVR in diabetic patients, outcomes in diabetic and non-diabetic patients following TAR grafting, outcomes of BIMA/RA and right gastroepiploic artery (RGA) in DM; 3) provided either in-hospital or 30-day postoperative mortality, any sternal wound infection rate (superficial and deep infections, SWIs) after the operation, and Kaplan Meier survival curves of all-cause death and cardiovascular death or hazard ratio (HR) for the two outcomes; 4) published randomized controlled trials and non-randomized controlled trials, with English as the language limitation.

Information sources: Electronic databases, contact with authors, trial registers.

Main outcome(s): We defined the long-term (≥ 12 months) all-cause death as the primary endpoint of interest.

Additional outcome(s): The secondary efficacy endpoints were long-term (≥ 12 months) cardiovascular death and early sternal wound infection and death.

Data management: Endnote was used to manage the studies and excel was applied to manage the data we extracted from the studies.

Quality assessment / Risk of bias analysis: The Cochrane risk of bias tool was used to examine randomized control trials (RCTs), and the Newcastle-Ottawa Scale (http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf) was used to investigate observational studies.

Strategy of data synthesis: Risk ratios (RRs), hazard ratios (HRs), and their corresponding 95% confidence intervals (CIs) were calculated to describe short-term results and long-term survival results. The I² statistics were performed to test for heterogeneity between the included studies, and a fixed-effects model was used to obtain the combined RRs and HRs when the I² statistic was lower than 50%. Otherwise, the random-effects model would be alternatively adopted. Forest plots were then created for graphic presentation of clinical outcomes with the Review Manager and adjusted by package Forest plot of R software (version 4.1.3) successively. Funnel Plot were created for the comparisons with 10 or more studies included. In each included study, Kaplan-Meier curves for overall and cardiac mortality-free survival were first digitalized in Engauge Digitizer software (version 10.4; maintained by Mark Mitchell). HR calculations spreadsheet provided by Jayne F Tierney [8] [<http://www.biomedcentral.com/content/supplementary/1745-6215-8-16-S1.xls>] was second applied to facilitate the estimation

of HRs from the data extracted from Kaplan-Meier curves. Finally, package Meta and Forest plot of R software (version 4.1.3) were used to pool HRs and generate the forest plots. Additionally, Kaplan-Meier (KM) survival curves for long-term death-free survival and digitalized KM curve data were aggregated to construct combined survival curves in package MetaSurv of R software (version 3.4.3).

Subgroup analysis: Comparisons between the effects of arterial revascularization using different arterial conduits and conventional surgery with saphenous venous grafts.

Sensitivity analysis: NA.

Language restriction: English.

Country(ies) involved: China.

Keywords: systematic review, meta-analysis, total arterial revascularization, diabetes, survival analysis.

Contributions of each author:

Author 1 - Guang-zhi Liao.

Email: soleil0726@163.com

Author 2 - Ting Liu.

Email: liutingmed@163.com

Author 3 - Yi-ming Li.

Email: 573299924@qq.com

Author 4 - Lin Bai.

Author 5 - Yu-yang Ye.

Author 6 - Xue-feng Chen.

Author 7 - Yong Peng.

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