

All arterial versus non-total arterial coronary artery bypass grafting in diabetic patients: A systematic review and meta-analysis

Diyabet hastalarında total olmayanla kıyasla total arteriyel koroner arter baypas greftleme: Sistematik derleme ve meta-analiz

Erina Febriani Widiastari¹, Wirya Ayu Graha^{2,4}, Harry Raihan Alzikri¹, Nurima Ulya Dwita^{3,4}, Marolop Pardede^{3,4}

Institution where the research was done:

Harapan Kita National Cardiovascular Center Hospital, Jakarta, Indonesia

Author Affiliations:

¹Undergraduate Medical Study Program, Faculty of Medicine, YARSI University, Jakarta, Indonesia

²Division of Adult Cardiac Surgery, Harapan Kita National Cardiovascular Center Hospital, Jakarta, Indonesia

³Department of Thoracic and Cardiovascular Surgery, RSUD Dr. Chasbullah Abdulmajid Kota Bekasi, Indonesia

⁴Department of Thoracic and Cardiovascular Surgery, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

ABSTRACT

Background: In this meta-analysis, we compare total arterial revascularization versus non-total arterial revascularization coronary artery bypass grafting in diabetic patients and discuss long-term survival rate and early mortality rate, cerebrovascular accident, myocardial infarction, sternal wound infection.

Methods: We searched the Cochrane Library, PubMed, Thieme-Connect and Sage Pub databases for studies which were published from January 2003 to October 2023. Observational studies with propensity-score matched analysis comparing total arterial revascularization versus non-total arterial revascularization coronary artery bypass grafting in diabetic patients were included. The risk of bias was analyzed. Fixed-effects model and random-effects meta-analysis with leave-one-out method as sensitivity analysis were performed.

Results: Six observational studies which were published involving a total of 15,336 patients were included in the meta-analysis. There were significant differences in the long-term survival rates and early myocardial infarction. Total arterial revascularization had higher survival rate (incidence rate ratio [IRR]=0.85, 95% confidence interval [CI]: 0.74-0.98, p=0.02) and lower myocardial infarction event than non-total arterial revascularization (odds ratio [OR]=0.45, 95% CI: 0.22-0.92, p=0.03).

Conclusion: Total arterial revascularization is significantly associated with higher survival rate and lower early myocardial infarction than non-total arterial revascularization in diabetic patients undergoing coronary artery bypass grafting.

Keywords: Arterial grafting, coronary artery bypass grafting, diabetes mellitus, meta-analysis, survival rate.

ÖZ

Amaç: Bu meta-analizde, diyabet hastalarında total arteriyel revaskülarizasyon ile total olmayan arteriyel revaskülarizasyon koroner arter baypas greftleme yöntemleri karşılaştırıldı ve uzun dönem sağkalım oranı, erken mortalite oranı, serebrovasküler olay, miyokart enfarktüsü ve sternal yara enfeksiyonu olayları irdelendi.

Çalışma planı: Ocak 2003 - Ekim 2023 tarihleri arasında yayımlanmış çalışmaları belirlemek amacıyla Cochrane Library, PubMed, Thieme-Connect ve Sage Pub veri tabanlarında tarama yapıldı. Diyabet hastalarında total arteriyel revaskülarizasyon ile total olmayan arteriyel revaskülarizasyon koroner arter baypas greftleme yöntemlerini karşılaştıran ve eğilim puanı eşleştirmesi yapılan gözlemsel çalışmalar dahil edildi. Yanlılık riski analiz edildi. Sabit etkiler modeli ve duyarlılık analizi olarak çapraz doğrulama yöntemi ile rastgele etkiler meta-analizi gerçekleştirildi.

Bulgular: Toplam 15.336 hastayı içeren altı gözlemsel çalışma meta-analize dahil edildi. Uzun dönem sağkalım oranları ve erken miyokart enfarktüsü açısından anlamlı farklar bulundu. Total arteriyel revaskülarizasyon, total olmayan arteriyel revaskülarizasyona kıyasla daha yüksek sağkalım oranına (insidans oran oranı [IRR]=0.85, %95 güven aralığı [GA]: 0.74-0.98, p=0.02) ve daha düşük miyokart enfarktüsü olayına (olasılık oranı [OR]=0.45, %95 GA: 0.22-0.92, p=0.03) sahipti.

Sonuç: Koroner arter baypas greftleme uygulanan diyabet hastalarında, total arteriyel revaskülarizasyon, total olmayan arteriyel revaskülarizasyona kıyasla anlamlı düzeyde daha yüksek sağkalım oranı ve daha düşük erken dönem miyokart enfarktüsü ile ilişkilidir.

Anahtar kelimeler: Arteriyel greftleme, koroner arter baypas greftleme, diabetes mellitus, meta-analiz, sağkalım oranı.

Corresponding author: Wirya Ayu Graha.

E-mail: wirya.btkv@gmail.com

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Coronary artery bypass grafting (CABG) is widely acknowledged as a preferred method for revascularization, particularly in patients with diabetes and multiple vessel disease.^[1-3] Globally, surgeons more commonly use traditional approaches to revascularization rather than total arterial revascularization (TAR), with TAR being selected in fewer than 5% of CABG cases in the United States throughout 2019.^[4] Total arterial revascularization typically involves bilateral internal mammary arteries (BIMAs), radial artery (RA), or combination of arterial grafts, while non-TAR typically combine arterial conduit with saphenous vein grafts.^[4,5] Recent studies have suggested that TAR may offer better outcomes in both the early and long-term compared to the conventional use of a single internal mammary artery (SIMA).^[5] Research by Dominici et al.^[6] reported that TAR was associated with certain advantages over conventional revascularization approaches in both the short and long term within the overall population. For individuals with diabetes undergoing CABG, who typically face poorer clinical outcomes, TAR may offer more favorable long-term benefits.^[7-9] Despite its merits, TAR presents increased surgical complexity and a higher likelihood of sternal wound infections (SWIs), which may concern surgeons. Given the growing body of research highlighting the benefits of TAR, it becomes essential to investigate whether diabetic patients consistently benefit from TAR despite these risks. In this systematic review and meta-analysis, we discuss the most recent findings on this subject.

MATERIALS AND METHODS

We performed a systematic review and meta-analysis according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statements. This study was registered at PROSPERO CRD42023475871.

Eligibility criteria

Inclusion criteria were as follows: (i) Study design: Observational studies with propensity-score matched analysis; (ii) Participants: Adult diabetic patients (≥ 18 years old) undergoing emergency, urgency or scheduled, isolated or non-isolated, on-pump or off-pump, whether first-time or redo CABG; (iii) Intervention: CABG using TAR; (iv) Comparison: CABG using non-TAR; and (v) Outcomes: report survival rate. The inclusion of only observational studies with propensity score-matched analysis and exclusion of randomized-controlled trials is to minimize confounding and selection bias. Review

articles, unpublished studies, abstracts, case reports, editorials, study protocols, commentaries, letters, studies not written in English language, as well as studies which did not fulfill the inclusion criteria, were excluded from the analysis.

Search strategy

We searched PubMed, Cochrane, Thieme-Connect, and Sage Pub from January 2003 to October 2023 for studies comparing TAR and Non-TAR in diabetic patients undergoing CABG. We carried out the search with the following terms: ("diabetes" OR "diabetes mellitus") AND ("arterial graft" OR "arterial conduit" OR "arterial revascularization") AND ("coronary artery bypass" OR "coronary artery bypass grafting" OR "CABG").

Study selection

After retrieving the initial results, duplicate papers were removed. Titles and abstracts were reviewed independently by three reviewers to determine whether the retrieved studies met the inclusion criteria. Studies were selected based on the inclusion and exclusion criteria outlined above. The full paper was obtained for studies which appeared to meet the inclusion criteria or where a decision could not be made from the title and/or abstract alone. The full text was independently assessed for eligibility by two reviewers. Discrepancies were resolved through an initial discussion with a third reviewer. A PRISMA flowchart was created to demonstrate the search strategy (Figure 1).

Data extractions, quality assessment, and variable definition

Data extraction was completed by three independent reviewers using Microsoft Office, Excel software (Microsoft Corp., NM, USA). A third reviewer confirmed all the extracted data. The following data were extracted from each study: author, publication year, study type, country, study period, number of patients, type of graft with its harvesting technique and type of CABG used in diabetic patients, outcome of interest reported, mean follow-up, and patient baseline characteristics. This meta-analysis identified several potential sources of heterogeneity, including variations in patient characteristics, outcome definitions, and the type of CABG procedure used. To address heterogeneity, we applied both fixed-effect and random-effects models depending on the level of heterogeneity indicated by the I^2 statistic. Additionally, to assess the robustness of our findings, we performed

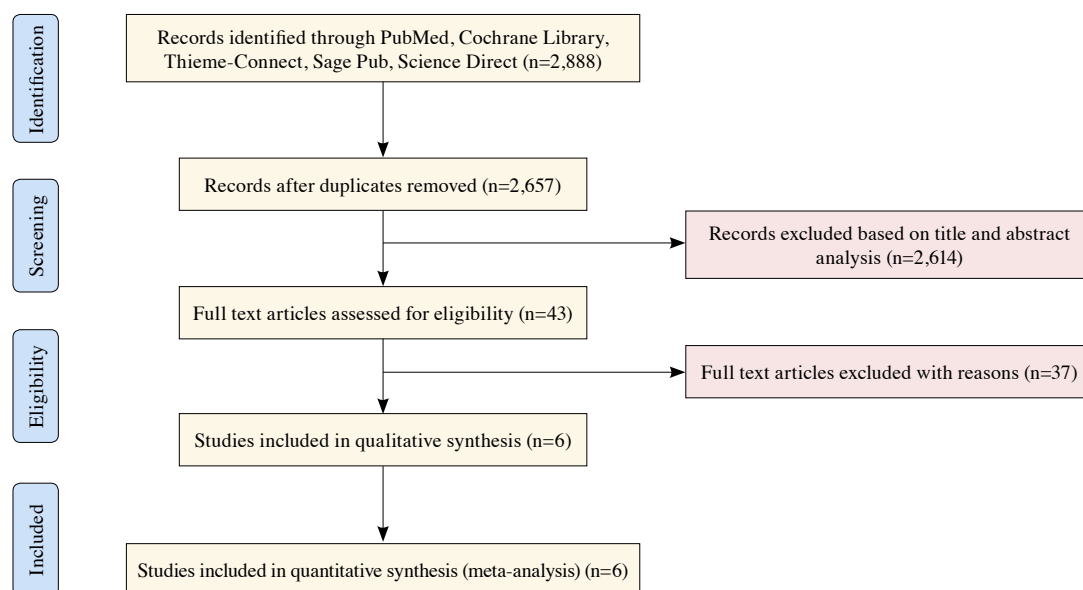


Figure 1. PRISMA flowchart.

sensitivity analyses to examine the impact of individual studies on the overall results. The Cochrane risk of bias tools will be utilized in quality assessment. The Cochrane risk of bias tool, Risk of Bias in Non-Randomized Studies-of Interventions (ROBINS-1), was used to investigate observational studies. Total arterial revascularization is defined as surgical revascularization carried out exclusively with arterial conduits. Non-TAR is defined as surgical revascularization carried out with venous and arterial conduits. The primary outcome of this review is long-term (≥ 10 years after the surgery) survival rate. The secondary outcomes are mortality rate, cerebrovascular accident (CVA), myocardial infarction (MI), and SWI including deep and superficial SWI which occurred in the early-term (the perioperative period, in-hospital and maximum 30 days after the surgery).

Statistical analysis

This meta-analysis was performed using Review Manager software version 5.4 software (The Cochrane Collaboration, Oxford, UK) and R version 4.3.1 software (R Foundation for Statistical Computing, Vienna, Austria). The pooled effect size with odds ratio (OR) and 95% confidence interval (CI) were calculated for secondary/early-term endpoints (perioperative, in-hospital, and 30-day). The incidence rate ratio (IRR) and 95% CI were calculated for long-term survival rate (≥ 10 years). Forest plots were created to represent

the main outcome and determine the effect size. The I^2 test was performed to assess the statistical heterogeneity. Heterogeneity was defined as low if I^2 ranged from 0 to 25%, moderate if I^2 ranged from 26 to 50%, or high if I^2 was greater than 50%. A fixed-effects model was selected, if the I^2 value was $< 50\%$, suggesting minimal variation between studies. This approach assumed that the effect sizes were homogeneous across studies. In cases with an I^2 value $> 50\%$, a random-effects model was used. This model accounts for variability between studies and provides a more conservative estimate of the overall effect, acknowledging that the true effect size may vary across studies. Funnel plots were also created to graphically represent publication bias, which was assessed using the Trim & Fill method. Sensitivity analysis was applied to assess the influence of a single study on the overall effect of TAR treatment on the main outcome by sequentially removing one study according to outlier detection and the leave-one-out method. A two-tailed p value of < 0.05 was considered statistically significant.

RESULTS

Study characteristics

A total of 2,888 studies were identified through the initial search. Of these, 2,657 were excluded due to duplicate titles, 2,614 were excluded based on title and abstract screening, and 37 were excluded after full-text review for various reasons. In particular,

Table 1. Study characteristics

Author	Study type	Country	Study period	Number of patients, type of grafts, harvesting technique, type of CABG			Outcome of interest reported	Mean follow-up
				TAR	Non-TAR			
Bacco et al. ^[4] (2019)	Observational retrospective	Italy	2005-2015	Number of patients; - Before propensity: 618 - After propensity: 359 Type of grafts: - LIMA-LAD - RIMA/RA-Diag/Cx/RCA (T/Y graft)/ RA (if stenosis >90%) - In situ RIMA for RCA Harvesting technique: - ITA: skeletonized - RA: pedicled - SVG: N/A Type of CABG: - Off-pump technique: TAR; 126 (35.1%), conventional; 76 (21.1%) - Standard CPB	Number of patients; - Before propensity: 382 - After propensity: 359 Type of Grafts: - LIMA-LAD + SVG-Diag/Cx/RCA	- Overall survival and survival free from cardiac-related mortality after isolated CABG - MACCEs (MACCEs: defined as cardiac death, myocardial infarction, need for repeated percutaneous intervention or surgical revascularization on grafted vessels, stroke).	101 months	
Kunihara et al. ^[14] (2018)	Observational retrospective	Japan	1995-2001	Number of patients; - Before propensity: 123 - After propensity: 104 Type of Grafts: - LITA-LAD (implanted in sequential fashion if additional Diagonal branches) + RA in a T-graft-RCA/LCx Harvesting technique: - Arterial conduit: skeletonized - SVG: standard open fashion Type of CABG: - Conventional mild hypothermic (34° C) cardiopulmonary bypass	Number of patients; - Before propensity: 123 - After propensity: 104 Type of Grafts: - LITA – LAD + SVG – RCA/LCx	- Long term survival after first time, isolated CABG - Long term MACCE (MACCE was defined as cardiac, death, recurrent angina, myocardial infarction, or repeat revascularization by either PCI or CABG, stroke).	134±53 months	
Tatoulis et al. ^[8] (2016)	Observational retrospective	Australia and New Zealand	2001-2012	Number of patients; - Before propensity: 3795 - After patients: 2017 Type of grafts: - LITA, RITA, RA, (T-Y graft: 20.7%). Harvesting technique: - ITA: skeletonized or semi-skeletonized - RA: open atraumatic technique - SVG: open technique Type of CABG: - On pump CABG - Off pump CABG: used in 8.4% of cases, predominantly for ascending aorta atheroma.	Number of patients; - Before propensity: 7847 - After propensity: 1967 Type of grafts: - LITA, RITA, RA, (T-Y graft: 4.2%), SVG.	- All-cause late mortality >30 days after surgery after first time isolated CABG - 30-day mortality, DSWI, postoperative myocardial infarction, low cardiac output, stroke, return to the operating room for bleeding, new onset renal failure requiring hemofiltration, and septicemia	4.5±3.1 years	

Table 1. Continued

Author	Study type	Country	Study period	Number of patients, type of grafts, harvesting technique, type of CABG		Outcome of interest reported	Mean follow-up
				TAR	Non-TAR		
Pevni et al. ^[7] (2016)	Observational retrospective	Israel	1996-2010	Number of patients: - Before propensity: 964 - After propensity: 490 Type of grafts: - BITA (most to left coronary system): in-situ BITA or RITA-LITA (composite T grafting) - rGEA/RA- (RCA if stenosis >80%)	Number of patients: - Before propensity: 564 - After propensity: 490 Type of grafts: - SITA+SVG-(RCA if stenosis < 80%) Harvesting technique: - ITA: skeletonized - RA/rGEA/SVG: N/A Type of CABG: - Standard cardiopulmonary bypass - Off-pump CABG: BITA; 109 (22.2), SITA; 119 (24.3)	- Long-term survival - Early mortality, perioperative myocardial infarct (defined by the appearance of new Q waves on the electrocardiogram associated with elevated levels of creatine phosphokinase-myocardial band fraction greater than 50 mU/mL), sternal wound infection, postoperative CVA (CVA was defined as a new permanent neurologic deficit and computed tomographic evidence of cerebral infarction).	12.2±4.3 years
Lin et al. ^[15] (2013)	Observational retrospective	USA	1997-2001	Number of patients: 260 - Type of grafts: LITA-LAD+RA Harvesting Technique: - RA: open conventional - ITA/SVG: N/A Type of CABG: - CABG was performed with cardiopulmonary bypass - Off-pump procedures were performed when the aorta was heavily diseased.	Number of patients: 260 - Type of grafts: LITA-LAD+SVG	- Long term survival after first-time isolated CABG for diabetic patients in subgroup analysis	9.4 years
Buxton et al. ^[16] (2012)	Observational retrospective	Australia	1996-2008	Number of patients: - Before propensity: 246 - After propensity: 103 Type of grafts: - BITA - BITA+RA - SITA+RA - SITA+Bilateral RA - BITA+Bilateral RA	Number of patients: - Before propensity: 154 - After propensity: 103 Type of grafts: - SITA+Vein - Single RA+Vein, - BITA+Vein - Bilateral RA+Vein - SITA+Single RA+Vein - BITA+Single RA+Vein - SITA+Bilateral RA+Vein - BITA+Bilateral RA+Vein Harvesting technique: N/A Type of CABG: with cardiopulmonary bypass	- Six major early postoperative events (in-hospital mortality, myocardial infarction, stroke, new renal failure, postoperative atrial fibrillation and harvest site infection) - Long-term survival after primary isolated CABG	7.8±3.7 years

TAR: Total arterial revascularization; LIMA: Left internal mammary artery; LAD: Left anterior descending; RIMA: Right internal mammary artery; RA: Radial artery; Diag: Diagonal; Cx: Circumflex; RCA: Right coronary artery; SVG: Saphenous vein graft; ITA: Internal thoracic artery; N/A: Not applicable; MACCEs: Major adverse cardiac and cerebrovascular events; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass; LCx: Left circumflex; PCI: Percutaneous coronary intervention; BITA: Bilateral internal thoracic arteries; RITA: Right internal thoracic artery; LITA: Left internal thoracic artery; SITA: Single internal thoracic artery; CVA: Cerebrovascular accident; rGEA: Right gastroepiploic artery.

several studies^[10-13] were excluded for reasons such as not involving diabetic patients, not comparing TAR, or focusing on different primary outcomes. Ultimately, six studies^[4,7,8,14-16] published between January 2003 and October 2023 were included in the final analysis. The six studies covered a total of 15,336 patients, of which 6,006 patients underwent TAR-CABG and 9,330 patients underwent non-TAR-CABG. The study characteristics and patient characteristics are outlined in Table 1 and [Supplementary Table 1](#).

Primary outcome

Survival rate

Long-term survival rate was reported in six studies. The heterogeneity was observed to be high among the studies ($I^2=65\%$). Due to the high heterogeneity, a random-effects model was used for analysis. Sensitivity analysis using the leave-one-out method was conducted. The result indicated that TAR had a higher survival rate than non-TAR, indicating a statistically significant difference (IRR=0.85, 95% CI: 0.74-0.98, $p=0.02$) (Figure 2).

Secondary outcomes

Cerebrovascular accident

Only four studies reported CVA. The heterogeneity was observed to be high among the studies ($I^2=61\%$).

Therefore, a random-effects model was used for analysis. Sensitivity analysis using the leave-one-out method was conducted. The result showed no significant difference in early occurrence of CVA between TAR and non-TAR groups (OR=1.14, 95% CI: 0.46-2.80, $p=0.78$) (Figure 3).

Mortality rate

Early mortality rate was reported in four studies. The heterogeneity was observed to be low among the studies ($I^2=0\%$). Due to the low heterogeneity, a fixed-effects model was used for analysis. Sensitivity analysis using the leave-one-out method was conducted. The result showed no significant difference in early mortality rate between TAR and non-TAR groups (OR=0.90, 95% CI: 0.59-1.37, $p=0.62$) (Figure 4).

Myocardial infarction

Among all included studies, four reported MI in the early-term. The heterogeneity was observed to be low among the studies ($I^2=0\%$). Therefore, a fixed-effects model was used for analysis. Sensitivity analysis using the leave-one-out method was conducted. The result showed that TAR had lower MI events than non-TAR group, indicating a statistically significant difference (OR=0.45, 95% CI: 0.22-0.92, $p=0.03$) (Figure 5).

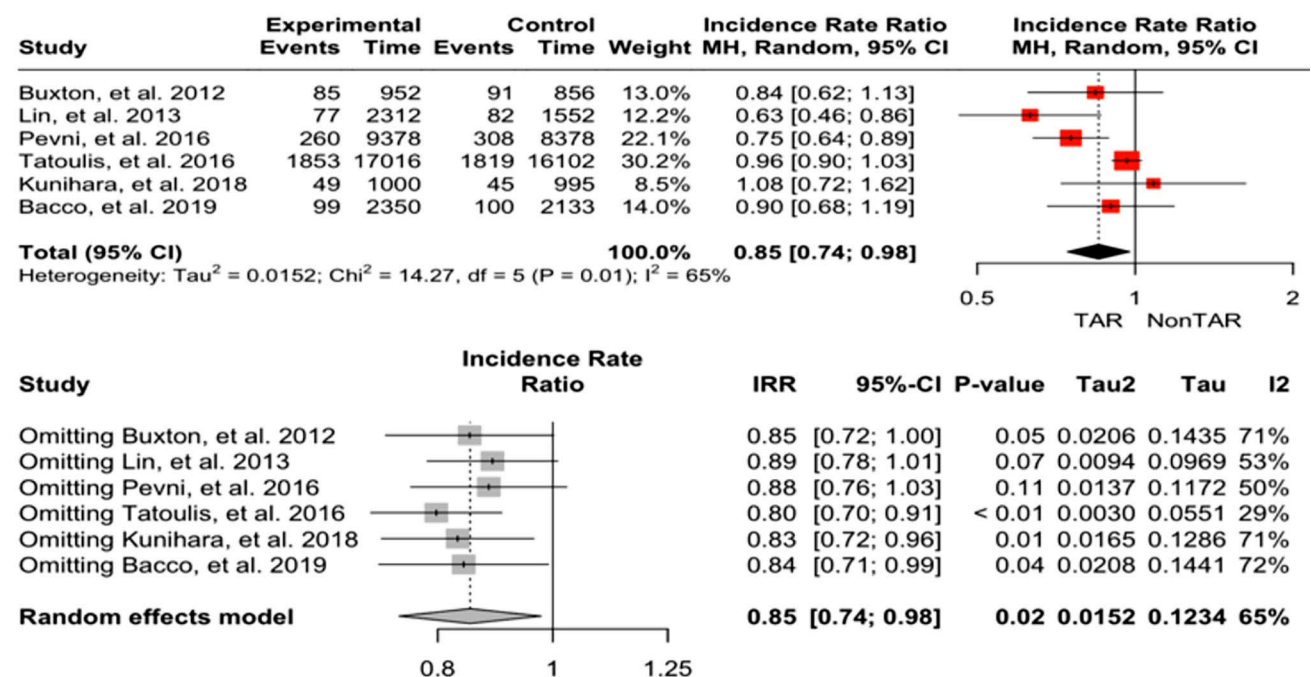


Figure 2. Forest plot random model and sensitivity analysis survival.

MH: Mantel-Haenszel method; CI: Confidence interval; TAR: Total arterial revascularization; IRR: Incidence rate ratio; Tau: Tau-squared (τ^2).

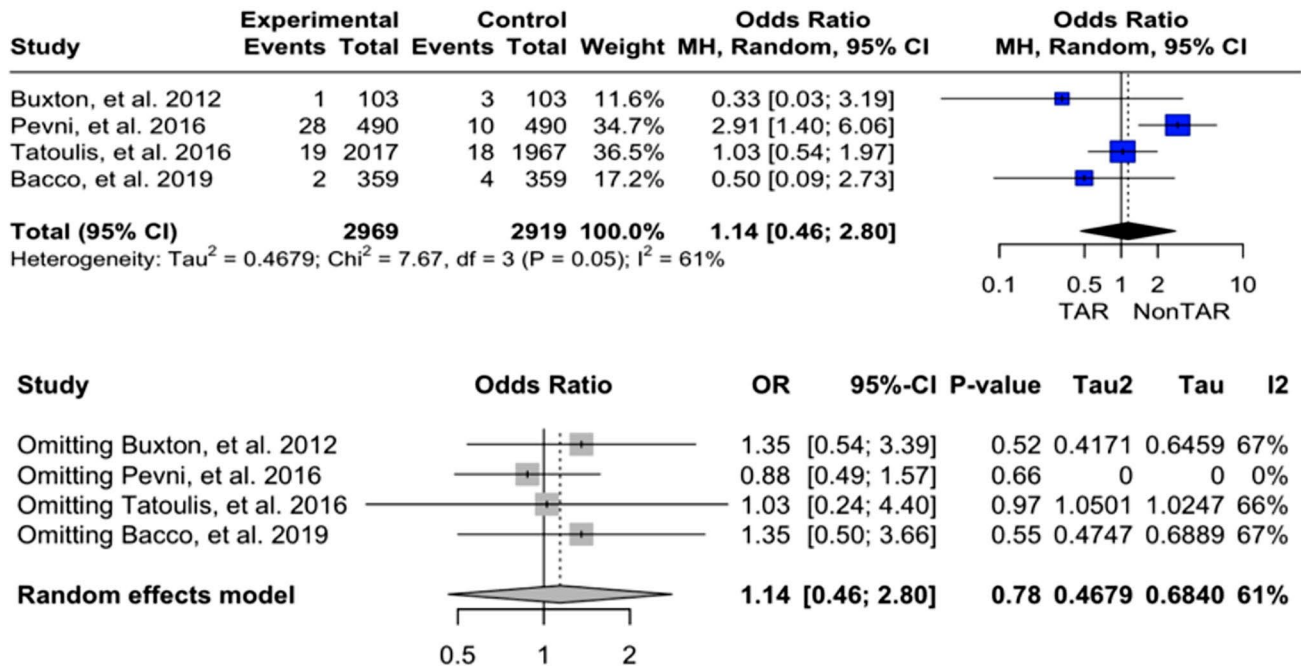


Figure 3. Forest plot random model and sensitivity analysis cerebrovascular accident.
MH: Mantel-Haenszel method; CI: Confidence interval; TAR: Total arterial revascularization; OR: Odds ratio; Tau: Tau-squared (τ^2).

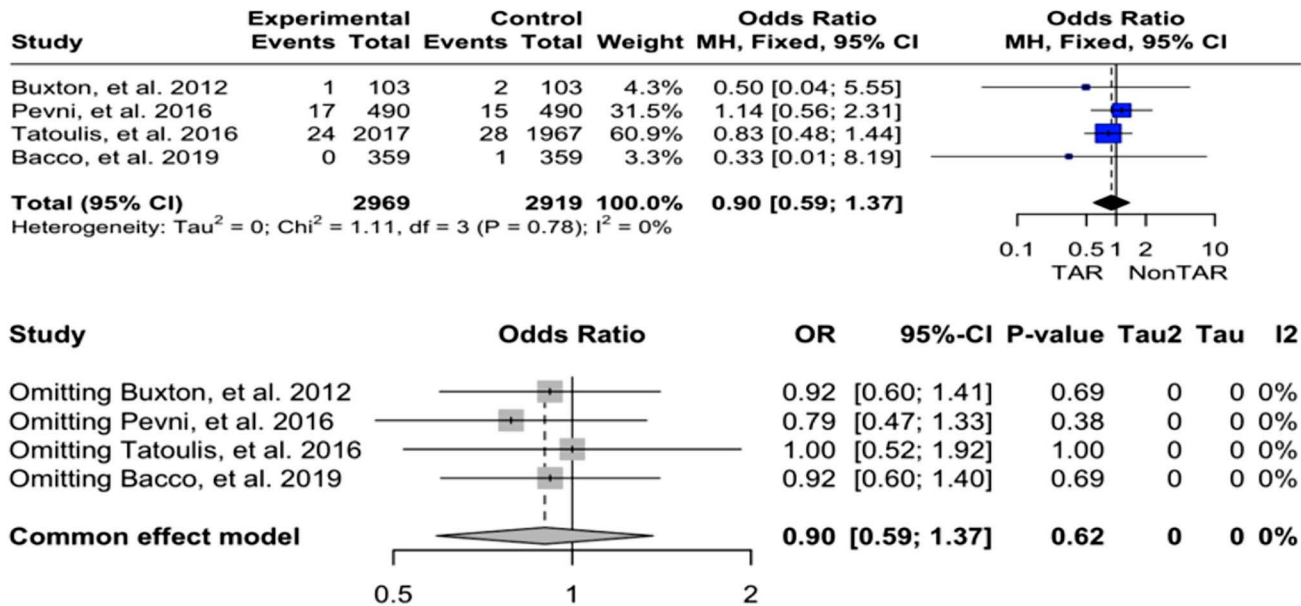


Figure 4. Forest plot fixed model and sensitivity analysis mortality rate.
MH: Mantel-Haenszel method; CI: Confidence interval; TAR: Total arterial revascularization; OR: Odds ratio; Tau: Tau-squared (τ^2).

Sternal wound infection

Of all included studies, four reported about SWI. The heterogeneity was observed to be low among the studies ($I^2=0\%$). Due to the low heterogeneity,

a fixed-effects model was used for analysis. Sensitivity analysis using the leave-one-out method was conducted. The result showed no significant difference in SWI between TAR and non-TAR

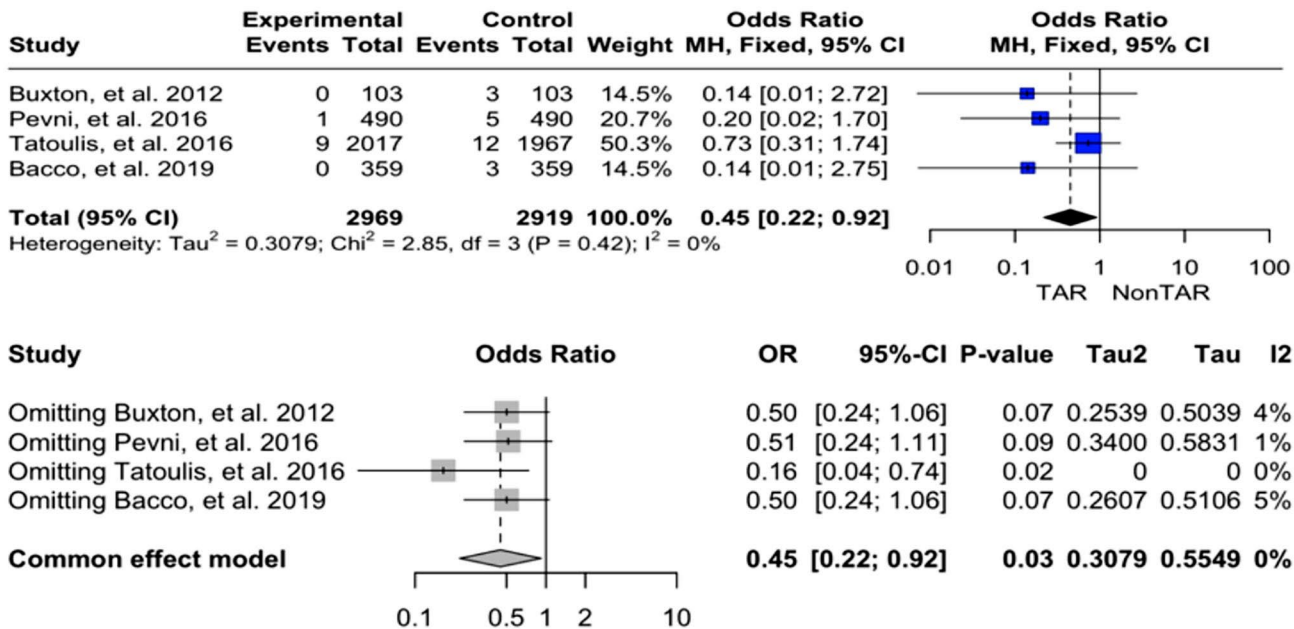


Figure 5. Forest plot fixed model and sensitivity analysis myocardial infarct.
MH: Mantel-Haenszel method; CI: Confidence interval; TAR: Total arterial revascularization; OR: Odds ratio; Tau: Tau-squared (τ^2).

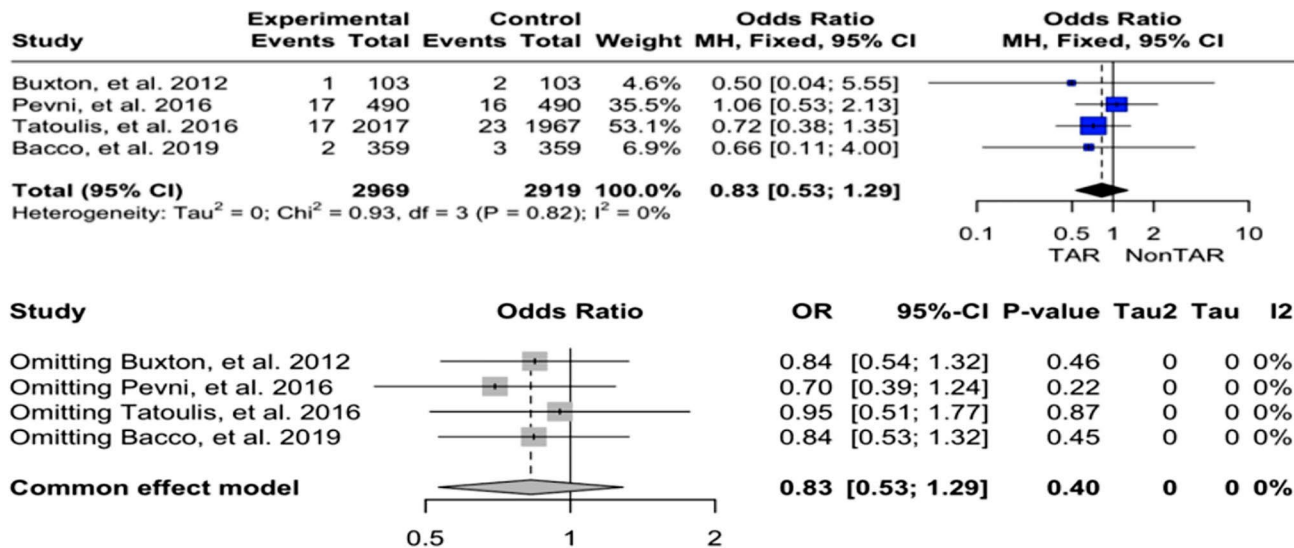


Figure 6. Forest plot fixed model and sensitivity analysis sternal wound infection.
MH: Mantel-Haenszel method; CI: Confidence interval; TAR: Total arterial revascularization; OR: Odds ratio; Tau: Tau-squared (τ^2).

groups (OR=0.83, 95% CI: 0.53-1.29, $p=0.40$) (Figure 6).

Publication BIAS assessment

The funnel plot for all studies comparing TAR and non-TAR across all outcomes is shown in [Supplementary Figure 1](#). The visual appearance of

funnel plot indicates asymmetry, suggesting potential publication bias. To assess publication bias more rigorously, the Trim & Fill method was applied. The results of this analysis indicated that additional studies need to be filled to correct for potential publication bias.

DISCUSSION

Diabetes mellitus is recognized as a significant risk factor for cardiovascular diseases, often presenting with more severe coronary artery disease (CAD), including multi-vessel disease (MVD), aggressive atherosclerosis, diffuse coronary lesions, smaller coronary vessels, and more extensive disease.^[17-19] Diabetes is also associated with an increased mortality risk from heart disease and a higher likelihood of undergoing any type of surgical intervention compared to the non-diabetic population.^[19,20] A study showed that a previous diagnosis of diabetes was an independent risk factor for increased postoperative morbidities, including SWI, renal failure, extended hospital stay, readmission with MI and in-hospital mortality after CABG surgery.^[21]

Considering the multi-center Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial results, CABG is suggested over percutaneous coronary intervention (PCI) as the preferred treatment for diabetic patients.^[17] Except in rare circumstances, general patients should receive at least one arterial graft, preferably the left internal mammary artery (LIMA) to left anterior descending artery (LAD), as LIMA has been shown to be superior to saphenous vein graft (SVG) in terms of freedom from angina, long-term patency and survival.^[22-24] Studies have confirmed that using more than two artery conduits is associated with decreased mortality or improved long-term survival. It is the development tendency of CABG to preferably use arterial conduits to take the place of SVG and gradually achieve multi-arterial and even TAR.^[25] Of note, TAR has shown to be feasible and achievable in most patients with three-vessel CAD,^[26] particularly in diabetics involving the LAD, and is favored over PCI to decrease mortality and reduce the need for repeat revascularizations (1A recommendation).^[16]

This review provides that long-term survival rate of TAR is significantly higher compared to non-TAR in diabetic patients undergoing CABG. In previous study by Liao *et al.*,^[9] TAR was associated with a higher rate of long-term overall survival in diabetic patients compared to conventional surgical revascularization with LIMA plus SVG. Conversely, a study by Urso *et al.*,^[27] according to meta-regression analysis, suggested a greater long-term survival benefit of TAR in diabetic patients but without statistical significance. In a single-institution 20-year

study by Momin *et al.*,^[28] TAR utilizing bilateral internal mammary artery (BIMA) and RA was associated with a significantly superior long-term survival rate. Another multicenter cohort study by Ren *et al.*^[29] demonstrated that patients undergoing TAR had a significantly lower risk of late death compared to patients undergoing multiple arterial grafting (MAG) with SVG. A Recent study also by Ren *et al.*^[44] demonstrated patient receiving exclusively arterial grafts experienced enhanced survival benefits compared to those receiving MAG with supplementary SVGs, except in patient with low LVEF (<30%), the difference was not statistically significant. According to the European Society of Cardiology and European Association for Cardio-Thoracic Surgery (ESC/EACTS) 2018 guidelines, the arterial revascularization trial reported that using BIMA could improve 10-year survival compared to SIMA in the general population, but survival outcomes specifically for diabetic patients have not been reported.^[24]

Theoretically, better graft patency and beneficial metabolic effects on the recipient coronary arteries can lead to survival benefits, particularly in diabetic patients with advanced atherosclerosis and impaired endothelial function.^[9] Arterial conduits, such as LIMA, BIMA and RA, exhibit superior patency compared to SVG, resulting in better long-term survival.^[30] The progressive failure of SVGs is attributed to accelerated atherosclerosis, whereas arterial grafts do not experience the same progression, thereby enhancing long-term durability and protecting native vessels from atherosclerosis.^[31] The protective effect of arterial grafts on disease progression in patients undergoing CABG may stem from the active endothelium of these grafts. These metabolically active grafts produce vasoactive substances and endothelial progenitor cells, which may help defend native vessels against atherosclerosis. Specifically, RA and LIMA grafting demonstrate a strong protective effect against the progression of native CAD, and the use of multiple arterial grafts may contribute to improved survival in patients undergoing revascularization.^[30]

Perioperative MI (PMI) refers to MI occurs during or shortly after surgical procedure, typically within 48 to 72 h postoperatively.^[32,33] It is a complication which adversely affects the prognosis of patients, with reported incidence between 2 and 10% and its pathophysiology may be different from the traditional instability of atherosclerotic plaque.^[32] It can be related to a significant adverse outcome,

such graft-related complications including early graft failure and coronary artery thrombosis, as well as non-graft-related factors like preoperative ischemic injuries. Technical errors during surgery and graft spasm are common causes of PMI.^[33] In this review, TAR demonstrates a significantly lower incidence of MI compared to non-TAR. A meta-analysis by Yanagawa et al.^[1] which compared TAR with conventional CABG and also evaluated the use of two arterial grafts found significant reductions in PMI, stroke, and hospital mortality in unmatched studies. Several factors may contribute to graft spasm during CABG, including mechanical stimulation during graft harvesting, hypothermia, pharmacological stimulation such as alpha-adrenoceptor agonists, and the use of cardiopulmonary bypass (CPB), which can increase endothelin concentrations.^[34]

Using BIMA as conduit in diabetic patients are risk factors for developing SWI, sternal wound complication, sternal dehiscence or mediastinitis.^[18,24,35] A study by Obed et al.^[36] reported early postoperative incidence of adverse events such as neurological complications (stroke, transient ischemic attack [TIA]), deep SWI, respective harvesting site infections, and prolonged ventilation (>48 h) was not statistically different in TAR and aortocoronary venous bypass.^[36] Another study by Urso et al.^[27] found that TAR had a significantly higher risk of deep SWI compared to those in the non-TAR group, with a relative risk (RR) of 1.29 (95% CI: 1.08-1.55; $p=0.005$; $I^2=0.0\%$). Although deep SWI were more frequently observed in the TAR group, this review indicates that the incidence of SWIs in the early term does not differ significantly between TAR and non-TAR groups.

In this review, no significant differences in early mortality rates were observed between the TAR and non-TAR groups. These findings are in line with those reported by Urso et al.^[27] and Buxton et al.^[37] Specifically, Urso et al.^[27] found no significant difference in 30-day mortality between TAR and non-TAR groups (RR: 0.88; 95% CI: 0.73-1.05; $p=0.14$; $I^2=0.0\%$), while Buxton et al.^[37] reported that, after propensity score matching, there was no statistically significant difference in 30-day mortality between TAR (0.8%) and SIMA + SVG (1.3%). The most significant independent predictors of mortality following CABG surgery include the surgical technique (off-pump or on-pump), chest re-exploration, redo surgery, and preoperative dialysis.^[38]

Cerebrovascular accident was typically known as any new neurological deficit lasting >24 h.^[39-41] Cerebrovascular accident or mostly mentioned as stroke is a devastating complication of both CABG surgery and PCI, another neurological dysfunction following CABG can manifest as encephalopathy or postoperative cognitive dysfunction.^[39-41] The pathogenesis of stroke is multifactorial and it is important to assess the etiology in three distinct time periods: (i) Intraoperative stroke: Thromboembolism and hypoperfusion, (ii) Early postoperative stroke: The majority of strokes related to CABG occur during the first seven postoperative days and are related to arrhythmias and hemodynamic instability, (iii) Late stroke (beyond 7 days): Late stroke is largely predicted by the overall atherosclerotic risk profile of patients.^[39] Embolization of atheromatous debris from the aorta is likely to occur during the cannulation of the aorta (aortic cross-clamping) for CPB, when the aortic clamp is applied or released, or during proximal graft anastomoses with a side-biting clamp.^[40-42] Increased duration of cross-clamp and CPB times, along with cerebral hypoperfusion, have been associated with higher rates of neurological complications.^[42] El-Gharabawy et al.^[43] reported that the TAR technique was more favorable compared to the conventional method, as it resulted in shorter CPB times and ischemia times. Similarly, Obed et al.^[36] found that patients undergoing TAR had significantly shorter operation times, ventilation times, aortic cross-clamp times, and CPB times. Yet, this review provides no significant differences between TAR and non-TAR in CVA events, although TAR is associated with shorter operation and CPB times, suggesting a potentially reduced risk profile.

This study suggests that TAR for diabetic patients leads to improved survival rates and a reduced risk of MI, highlighting its potential as a superior revascularization strategy compared to conventional methods. Clinicians should be encouraged to assess the feasibility of TAR for diabetic patients more rigorously and integrate it into standard practice guidelines. Future research should continue to explore the mechanisms by which TAR confers these benefits and identify specific patient subgroups that may derive the most significant advantage from this approach. For future research, patient groups should be stratified based on clinical factors like medication use, glycated hemoglobin (HbA1c) levels, conduit types used to assess how these variables impact TAR outcomes. In meta-analyses, conducting subgroup analyses is advised to manage heterogeneity and improve the precision of the findings. This approach

may help refine patient selection criteria and enhance personalized treatment strategies, ultimately leading to better tailored and more effective therapeutic interventions for diabetic patients undergoing CABG.

However, this meta-analysis has several limitations. First, the analysis may be subject to bias inherent in the observational study design used for the analyzed populations. Although propensity score matching is employed to adjust for risk profiles, it remains an imperfect tool. Second, analyzing TAR is challenging due to the diverse revascularization strategies it encompasses. Third, the statistical significance may be influenced by the limited number of studies included in the analysis. Fourth, the Trim & Fill method suggested adding more studies to address publication bias, but we were unable to identify additional studies comparing TAR and non-TAR specifically in diabetic patients.

In conclusion, this review provides that total arterial revascularization is significantly associated with higher survival rate and lower myocardial infarction events compared to non-total arterial revascularization in diabetic patients undergoing coronary artery bypass grafting without a significant difference in early mortality rate, sternal wound infection and cerebrovascular accidents between the two groups.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study conception and design, analysis and interpretation of results: E.F.W., W.A.G.; Literature search, data extraction: E.F.W., H.R.A., W.A.G.; Draft manuscript preparation: E.F.W., H.R.A.; Critical revision of the manuscript: W.A.G., N.U.D., M.P.

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