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Original research

Patency of skeletonized versus pedicled internal thoracic artery in coronary bypass graft surgery: A systematic review, meta-analysis and meta-regression

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HIGHLIGHTS

- As for patency, skeletonized ITA seems to be non-inferior in comparison to pedicled ITA after CABG.
- In sensitivity analysis, no difference regarding left or right ITA was also observed.
- The meta-regression identified no modulating factors that could have influenced the results.

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ABSTRACT

Background: It is suggested that the skeletonization harvesting technique influences the patency rates of internal thoracic artery (ITA) after coronary artery bypass graft (CABG) surgery in comparison to conventional (pedicled) harvesting. We conducted a meta-analysis to determine whether there is any difference between skeletonized versus pedicled ITA in terms of patency after CABG.

Methods: We performed a systematic-review using MEDLINE, EMBASE, CENTRAL/CCTR, SciELO, LILACS, Google Scholar and reference lists of relevant articles to search for studies that performed angiographic evaluation within the first two years after CABG between these two groups until December 2013. The principal summary measures were odds ratio (OR) with 95% Confidence Interval (CI) and *P* values (statistically significant when <0.05). The OR's were combined across studies using weighted DerSimonian–Laird random effects model and weighted Mantel–Haenszel fixed effects. Meta-analysis, sensitivity analysis and meta-regression were completed using the software Comprehensive Meta-Analysis version 2 (Biostat Inc., Englewood, New Jersey).

Results: Five studies involving 1764 evaluated conduits (1145 skeletonized; 619 pedicled) met the eligibility criteria. There was no evidence for important heterogeneity of effects among the studies. The overall OR (95% CI) for graft occlusion showed no statistical significant difference between groups (fixed effect model: OR 1.351, 95% CI 0.408 to 4.471, $P = 0.801$; random effect model: OR 1.351, 95% CI 0.408 to 4.471, $P = 0.801$). In sensitivity analysis, no difference regarding to left or right ITA was also observed. In meta-regression, we observed no statistically significant coefficients for graft occlusion and proportion of female, diabetics, renal failure, age, off-pump surgery or urgency, which means that the effect is not modulated by these factors.

Conclusion: In terms of patency, skeletonized ITA appears to be non-inferior in comparison to pedicled ITA after CABG.

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1. Introduction

1.1. Rationale

Sternal wound infection (SWI) is a recognized and important complication of coronary artery bypass graft (CABG) surgery [1]. The most serious manifestation of an SWI is mediastinitis, which extends the previous anatomical classification to the risk of sepsis. It is well known that an infection of the mediastinum can be severe and potentially lethal [2].

It is suggested that the method of internal thoracic artery (ITA) harvesting influences the incidence of postoperative SWI [3–5]. There are two established harvesting techniques: pedicled and skeletonized ITAs. Whereas the pedicled technique dissects the artery away from the sternum with its accompanying veins, fascia, adipose tissue, and lymphatics generating a pedicled graft, skeletonization requires the ITA to be dissected free of all surrounding tissue, solely yielding the artery [3].

We performed a meta-analysis [6] with 4817 patients from 22 studies, demonstrating that skeletonized ITA really appears to reduce the incidence of postoperative SWI in comparison to pedicled ITA after CABG.

Despite our study, many surgeons concern about the patency of skeletonized ITA in comparison to pedicled ITA, taking into consideration that the skeletonization technique may induce damage to the vessel wall, endothelial dysfunction, loss of the vasa vasorum (which might lead to ischemia in the media layer), inducing to detrimental effects on the integrity of ITA.

Our meta-analysis attempts to determine if there is any difference between skeletonized and pedicled ITA in terms of conduit patency.

1.2. Objectives

We performed a meta-analysis and meta-regression of studies to compare skeletonized versus pedicled ITA during CABG, according to *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses (PRISMA) statement [7].

2. Methods

2.1. Eligibility criteria

Using PICOS (*P*opulation, *I*ntervention, *C*omparison, *O*utcome, *S*tudy design) strategy, studies were considered if: (1) population comprised patients undergoing CABG; (2) compared outcomes between skeletonized versus pedicled ITA; (3) outcomes studied included those which reported data regarding postoperative angiography within the first two years after CABG; (4) were prospective or retrospective or non-randomized studies or randomized controlled trials.

2.2. Information sources

The following databases were used (until December 2013): MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL/CCTR), ClinicalTrials.gov, SciELO (Scientific Electronic Library Online), LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde – The Latin American and Caribbean Health Sciences), Google Scholar and reference lists of relevant articles.

2.3. Search

We conducted the search using Medical Subject Heading (MeSH) terms ('skeletonized' OR 'skeletonization') AND ('pedicled' OR 'pedunculated' OR 'in situ') AND ('arteries, mammary' OR 'artery, mammary' OR 'mammary artery' OR 'internal mammary artery' OR 'arteries, internal mammary' OR 'artery, internal mammary' OR 'internal mammary arteries' OR 'mammary arteries' OR 'mammary arteries, internal' OR 'mammary artery, internal' OR 'internal thoracic artery' OR 'arteries, internal thoracic' OR 'artery, internal thoracic' OR 'internal thoracic arteries' OR 'thoracic arteries, internal' OR 'thoracic artery, internal') AND ('coronary artery bypass graft' OR 'coronary artery bypass grafting' OR 'coronary artery bypass surgery' OR 'coronary bypass surgery' OR 'coronary artery bypass graft surgery' OR 'coronary artery bypass' OR 'coronary bypass').

2.4. Study selection

The following steps were done: (1) identification of titles of records through databases searching; (2) removal of duplicates; (3) screening and selection of abstracts; (4) assessment for eligibility through full-text articles; (5) final inclusion in study.

One reviewer followed the steps 1 to 3. Two independent reviewers followed step 4 and selected studies. Inclusion or exclusion of studies was decided unanimously. When there was disagreement, a third reviewer took the final decision.

2.5. Data items

The endpoints were Odds Ratio (OR) for graft occlusion after CABG using skeletonized versus pedicled ITA.

2.6. Data collection process

Two independent reviewers extracted the data. When there was disagreement about data, a third reviewer (the first author) checked the data and took the final decision about it. From each study, we extracted patient characteristics, study design, and outcomes (number of events and number of total groups).

2.7. Risk of bias in individual studies

Included studies were assessed for the following characteristics: (1) sequence generation, (2) allocation concealment, (3) blinding, (4) incomplete outcome data, (5) selective outcome reporting, and (6) other sources of bias. Taking these characteristics into account, the papers were classified into A (low risk of bias), B (moderate risk of bias) or C (high risk of bias).

Two independent reviewers assessed risk of bias. Agreement between the 2 reviewers was assessed using kappa statistics for full text screening, and rating of relevance and risk of bias. When there was disagreement about risk of bias, a third reviewer (the first author) checked the data and took the final decision about it.

2.8. Summary measures

The principal summary measures were OR's with 95% Confidence Interval (CI) and *P* values (considered statistically significant when <0.05). The meta-analysis was completed using the software Comprehensive Meta-Analysis version 2 (Biostat Inc., Englewood, New Jersey).

2.9. Synthesis of results

Forest plots were generated for graphical presentations for clinical outcomes and we performed the I^2 test and Chi^2 test for assessment of heterogeneity across the studies [8]. Each study was summarized by the OR for skeletonized ITA compared to pedicled

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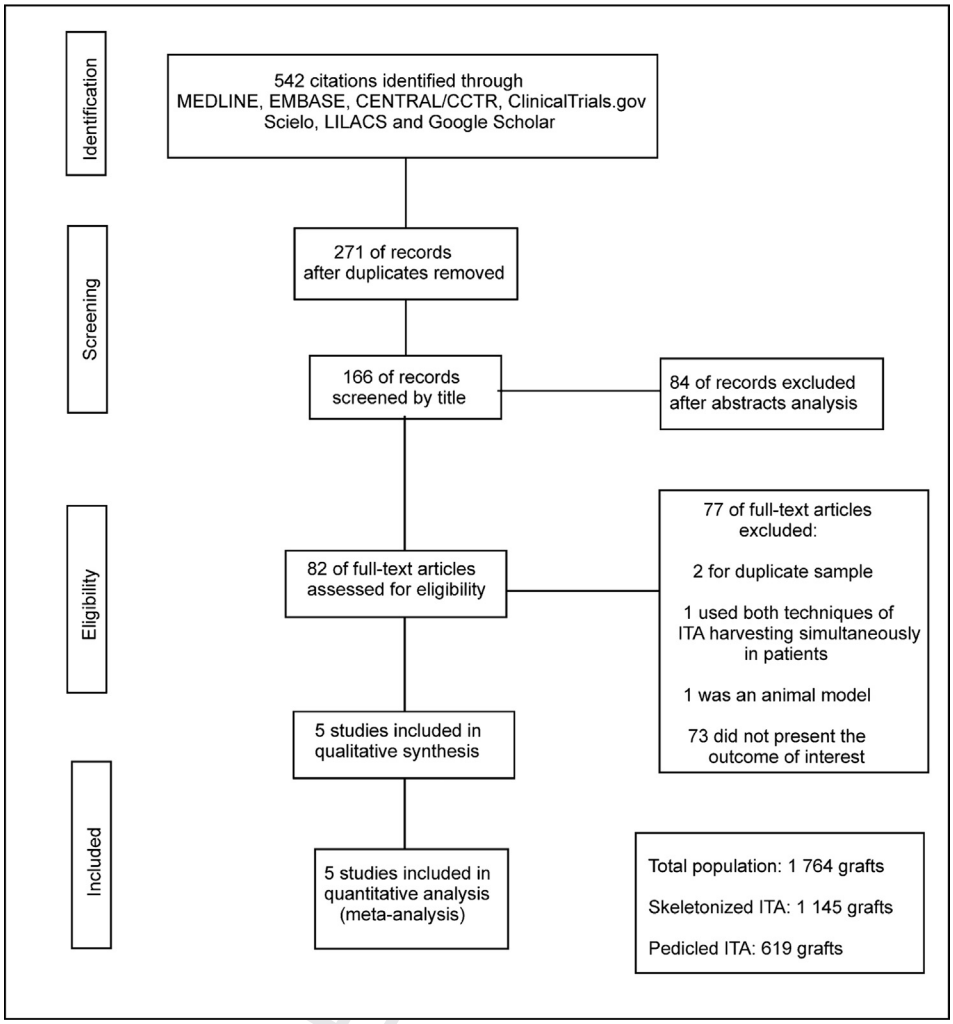


Fig. 1. Flow diagram of studies included in data search.

ITA. The OR's were combined across studies using weighted DerSimonian–Laird random effects model [9] and weighted fixed effects model using the Mantel–Haenszel model [10]. The models were weighted by number of events in each study to show how much each study contributed in the analysis.

2.10. Risk of bias across studies

To assess publication bias, a funnel plot was generated, being statistically assessed by Begg and Mazumdar's test [11] and Egger's test [12].

2.11. Sensitivity analysis

We performed subgroup analysis involving use of left ITA or right ITA to establish whether there was any difference regarding the ITA side.

2.12. Meta-regression analysis

Meta-regression analyses were performed to determine whether the effects of skeletonized ITA were modulated by prespecified factors. Meta-regression graphs describe the effect of

Table 1
Study characteristics and risk of bias (internal validity).

Study	SKT/PED patients (*n*)	SKT/PED evaluated conduits (*n*)	Study design	Selection bias	Performance bias	Attrition bias	Detection bias	Multivariable adjustment for possible confounders
Mannacio [13]	100/100	196/194	P, R, NM	A	B	A	B	Probably adequate
Kai [14]	162/23	274/46	NP, NR, NM	B	B	A	B	Probably adequate
Hirose [15]	115/99	195/77	P, NR, M	B	B	A	B	Probably adequate
Amano [16]	131/112	214/160	P, NR, NM	B	B	A	B	Probable adequate
Calafiore [17]	842/304	266/142	P, NR, M	B	B	A	B	Probably adequate

A: risk of bias is low; B: risk of bias is moderate; C: risk of bias is high; D: incomplete reporting; P: prospective; NP: non-prospective; R: randomized; NR: non-randomized; M: multicenter; NM: non-multicenter.

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Table 2
Preoperative characteristics of patients.

Study	SKT/PED female (%)	SKT/PED hypertension (%)	SKT/PED diabetes (%)	SKT/PED smoking (%)	SKT/PED dyslipidemia (%)	SKT/PED age (Mean ± SD)
Mannacio [13]	29/32	39/34	24/21	NA	44/41	67.0 ± 15/65.0 ± 12
Kai [14]	43.2/53.2	64.2/52.2	100/100	NA	53.1/60.9	66.9 ± 8.5/62.3 ± 9.2*
Hirose [15]	33.0/21.2	69.6/59.6	100/100	40.0/44.4	50.4/46.5	64.7 ± 8.3/63.6 ± 9.1
Amano [16]	22.1/28.6	64.9/65.2	55.0/48.2	45.8/50.0	44.3/54.5	65.9 ± 8.9/65.8 ± 8.9
Calafiore [17]	16.0/7.9*	NA	26.5/13.1*	NA	NA	62.0 ± 9.2/59.8 ± 8.2*

SKT – skeletonized ITA; PED – pedicled ITA; SD – standard deviation; NA – non-available; *$P < 0.05$.

skeletonized ITA on the outcome (plotted as a log OR on the *y*-axis) as a function of a given factor (plotted as a mean or proportion of that factor on the *x*-axis). Meta-regression coefficients show the estimated increase in log OR per unit increase in the covariate. Since log OR > 0 corresponds to OR > 1 and log OR < 0 corresponds to OR < 1, a negative coefficient would indicate that as a given factor increases, the OR decreases.

The pre-determined modulating factors to be examined were: sex, age, diabetes, renal failure, off-pump surgery and urgency. Sex was represented as the proportion of females in the study. Age was represented as the mean age of the patients participating in the study. Diabetes was represented as the proportion of diabetics (insulin dependent or non-insulin dependent) in the study. Renal failure was represented as the proportion of patients with renal failure undergoing conservative treatment or those on dialysis. Off-pump surgery was represented as the proportion of patients operated without cardiopulmonary bypass. Urgency was represented as the proportion of patients undergoing CABG in non-elective scenario.

3. Results

3.1. Study selection

A total of 542 citations were identified, of which 82 studies were potentially relevant and retrieved as full-text. Five [13–17]

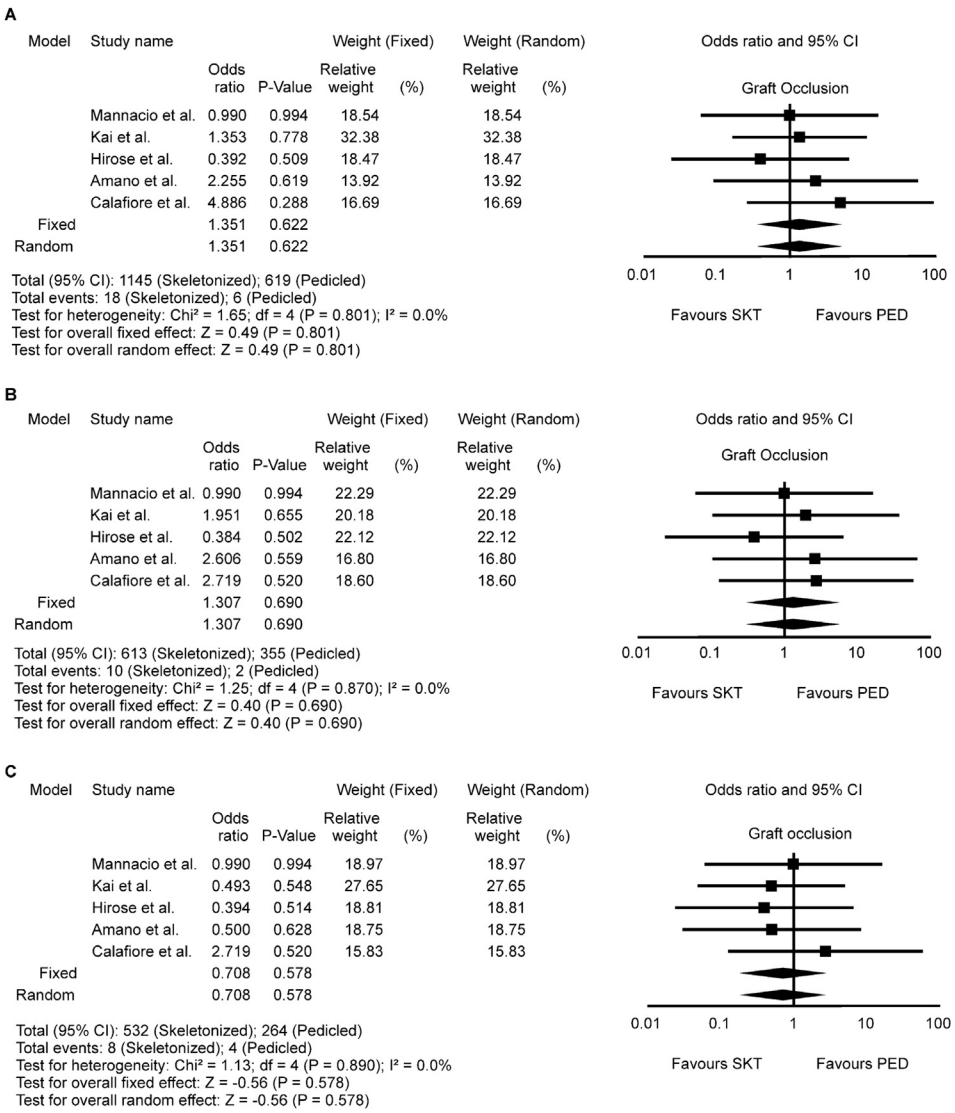


Fig. 2. Odds ratio and conclusions plot of graft occlusion associated with skeletonized versus pedicled ITA. *A – All conduits; *B – Left ITA conduits; *C – Right ITA conduits.

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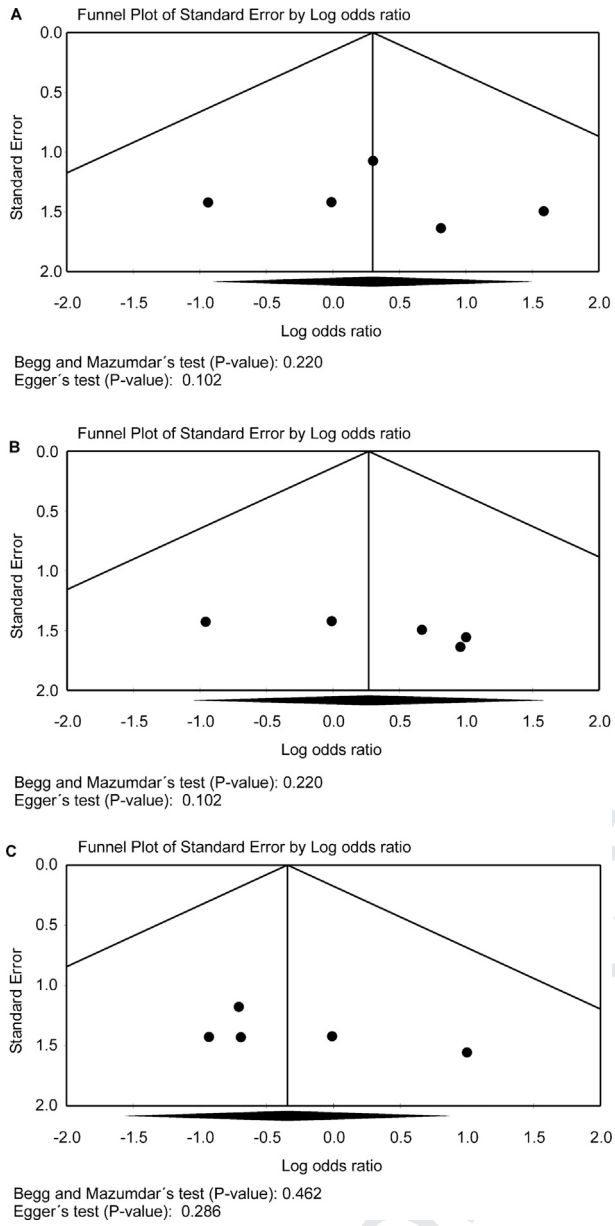


Fig. 3. Publication bias analysis by funnel plot graphic for graft occlusion. *A – All conduits; *B – Left ITA conduits; *C – Right ITA conduits.

publications fulfilled our eligibility criteria. Interobserver reliability of study relevance was excellent (Kappa = 0.87). Agreement for decisions related to study validity was very good (Kappa = 0.83). The search strategy can be seen in Fig. 1.

3.2. Study characteristics

Characteristics of each study are shown in Table 1. A total of 1764 conduits were studied being 1145 skeletonized ITA and 619 pedicled ITA, including the years 1999–2011, being 4 prospective (80%), one randomized (20%), two multicenter (40%). All studies used a multivariable adjustment for possible confounders. Informations not shown in Table 1, but noteworthy, is that all studies consisted of patients whose bypass grafts were evaluated within the first year after surgery as a routine part of the study. The overall internal validity was considered moderate risk of bias. The preoperative characteristics of patients are described in Table 2. We must make some important remarks regarding the postoperative assessment of the ITA. The quality of the anastomosis and conduit was graded in all the studies (except for Hirose et al. [15]) according to Fitzgibbon and colleagues [18]. Briefly, according to the latter, grade A stands for excellent graft patency, grade B for graft stenosis more than 50%, and grade O for occlusion. In our study, only those grafts that had a grade O were considered as "non-patent". Regarding the method of postoperative assessment of the ITA, except for Mannaccio et al. (whose final angiographic evaluation was performed by 64-slice multidetector computed tomography.), all of studies used the catheterization.

3.3. Synthesis of results

The OR of graft occlusion in the skeletonized ITA group compared with pedicled ITA group in each study is reported in Fig. 2A. There was no evidence for important heterogeneity of treatment effect among the studies for graft occlusion. The overall OR (95% confidence interval) of graft occlusion showed no statistical significant difference between groups (SKT 1.5% vs PED 1.0%; fixed effect model: OR 1.351, 95% CI 0.408 to 4.471, $P = 0.801$; random effect model: OR 1.351, 95% CI 0.408 to 4.471, $P = 0.801$).

3.4. Risk of bias across studies

Funnel plot analysis (Fig. 3A–C) disclosed symmetry around the axis for the treatment effect in graft occlusion outcome, which means we probably do not have publication bias related to this endpoint.

3.5. Sensitivity analysis

The OR of graft occlusion in the skeletonized left ITA group compared with pedicled left ITA group in each study is reported in Fig. 2B. There was no evidence for important heterogeneity of treatment effect among the studies for graft occlusion. The overall OR (95% confidence interval) of graft occlusion showed no statistical significant difference between groups (SKT 1.6% vs PED 0.6%; fixed effect model: OR 1.307, 95% CI 0.351 to 4.870, $P = 0.690$; random effect model: OR 1.307, 95% CI 0.351 to 4.870, $P = 0.690$).

The OR of graft occlusion in the skeletonized right ITA group compared with pedicled right ITA group in each study is reported in Fig. 2C. There was no evidence for important heterogeneity of treatment effect among the studies for graft occlusion. The overall OR (95% confidence interval) of graft occlusion showed no statistical significant difference between groups (SKT 1.5% vs PED 1.5%; fixed effect model: OR 0.708, 95% CI 0.211 to 2.384, $P = 0.578$; random effect model: OR 0.708, 95% CI 0.211 to 2.384, $P = 0.578$).

3.6. Meta-regression analysis

Meta-regression coefficients were not statistically significant for graft occlusion and proportion of females, diabetes, renal failure, off-pump surgery, urgency or age. It means that none of these evaluated factors have any modulation influence on the final effect. See Fig. 4.

4. Discussion

4.1. Summary of evidence

The results of this meta-analysis demonstrate that there was no statistical significant difference against skeletonized ITA compared to pedicled ITA in risk for graft occlusion, being the summary measures free from the influence of heterogeneity of the effects or

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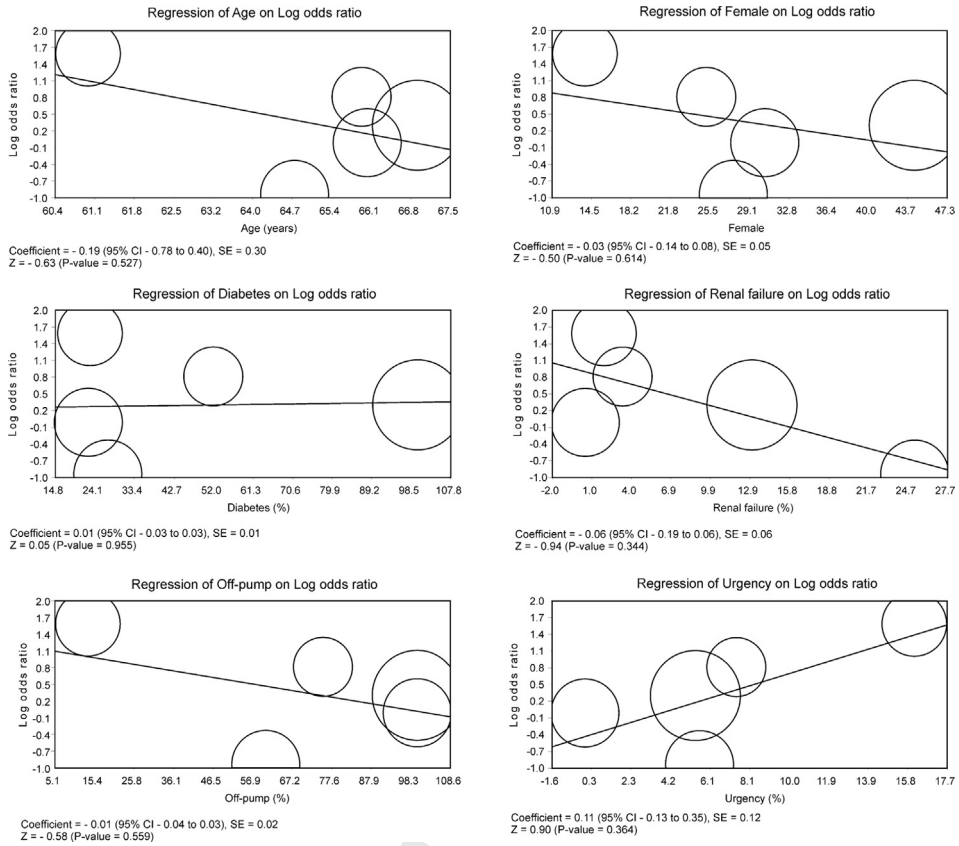


Fig. 4. Meta-regression analysis by representative plots.

publication bias. In sensitivity analysis, there was no difference against skeletonized ITA compared to pedicled ITA regardless of the harvested side. Meta-regression did not demonstrate any influence of proportion of females, diabetes, renal failure, off-pump surgery, urgency or age.

4.2. Considerations about this meta-analysis

To our knowledge, this is the first meta-analysis of studies performed to date regarding patency of skeletonized ITA versus pedicled ITA, providing incremental value by demonstrating that skeletonized ITA is not inferior to pedicled ITA on this aspect, deserving our attention concerning to daily surgical practice.

Skeletonization is certainly more traumatic for the arterial wall than pedicled preparation, and the possibility that mechanical peeling of the adventitia combined with the repeated stretching may affect the ITA integrity has never been clearly denied. In our meta-analysis, we showed that patency between the two harvesting techniques are similar, therefore, maybe the concern of some surgeons is unnecessary, although rational and relied on the possibility of endothelial dysfunction, ischemia of media layer and damage to adventitia. Our findings may be explained by laboratorial research of other authors.

Gaudino et al. [19] showed preservation of the endothelium in the skeletonized ITA by an immunohistochemical technique. Deja et al. [20] demonstrated that skeletonization did not damage endothelial function on acetylcholine-induced arterial relaxation and skeletonized ITA presented a higher blood flow in comparison to pedicled ITA. Noera et al. [21] showed that blood effusion in adventitia of skeletonized ITA was maintained after harvesting and did not present impaired morphology, histology and tissue viability. Ueda et al. [22], in a canine model study, showed that the structural and functional integrity of the endothelial cells in skeletonized ITA was similar to that of pedicled ITA, taking into consideration quantitative analyses with immunohistochemical staining of eNOS (endothelial nitric oxide synthase), which was not different in both groups.

An interesting finding of Ueda et al. [22] was there were significantly more microvessels positive for VWF (von Willebrand factor) in the adventitia of skeletonized ITA in comparison to pedicled ITA, which means more thrombogenesis and/or neovascularization. They also showed that the proliferation of smooth muscle cells in the media was minimal, as in normal vessels. These results suggested that the loss of vasa vasorum did not induce ischemia or remodeling in the media and neovascularization in the adventitia did not induce proliferation in media layer.

As we can see, our meta-analysis shows that the patency of skeletonized ITA is not inferior to pedicled ITA, and the laboratorial studies give us good reasons to think that the similar patency observed in the studies is due to maintained endothelial functional, non proliferation of smooth cells and ability of adventitia for recovering.

4.3. Risk of bias and limitations

This meta-analysis included data from nonrandomized and/or observational studies, which reflects the “real world”, but they are limited by treatment bias, confounders, and a tendency to overestimate treatment effects. Patient selection alters outcome and thus makes nonrandomized studies obviously less robust.

Although it was not observed important statistical heterogeneity among studies, the differences in terms of operative

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technique and volume may have led to an influence of clinical heterogeneity not capable of perception by meta-analysis.

There are inherent limitations with meta-analyses, including the use of cumulative data from summary estimates. Patient data were gathered from published data, not from individual patient follow-up. Access to individual patient data would have enabled us to conduct further subgroup analysis and propensity analysis to account for differences between the treatment groups.

4.4. Future perspectives

Because the findings support a potential benefit from a specific harvesting method and as part of the regular curriculum in cardiovascular surgery, we recommend that skeletonization technique should become a mandatory part of learning to cardiovascular surgery residents. The results of this study suggest the need for a large-scale (with a calculated probabilistic sample size), multicenter, prospective, randomized trial of skeletonized versus pedicled ITA grafts to verify whether there is not indeed any difference in the patency of grafts.

5. Conclusions

In terms of patency, skeletonized ITA appears to be non-inferior in comparison to pedicled ITA after CABG.

Ethical approval

This work is a meta-analysis involving other works already published in the literature. There is no need of ethical approval.

Author contribution

All the authors participated in the study design and writing.
And also:
Michel Sá – data analysis/statistics.
Paulo Ferraz – data analysis/statistics.
Rodrigo Escobar – data collections/data extraction/data assessment.
Eliobas Nunes – data collections/data extraction/data assessment.
Pablo Lustosa – data collections/data extraction/data assessment.
Frederico Vasconcelos – data collections/data extraction/data assessment.
Ricardo Lima – data analysis/assessment of data.

Conflicts of interest

The authors have no conflicts of interest.

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References

[1] T.C. Horan, M. Andrus, M.A. Dudeck, CDC/NHSN surveillance definition of health care: associated infection and criteria for specific types of infections in the acute care setting, Am. J. Infect. Control 36 (2008) 309–332.
[2] M.C. Gib, J.S. Alvarez, O.C.B. Wender, Mediastinitis: mortality rate comparing single-stage surgical approach and preconditioning of wound, Rev. Bras. Cir. Cardiovasc. 28 (2) (2013) 200–207.
[3] M.P. Sá, E.F. Soares, C.A. Santos, O.J. Figueiredo, R.O. Lima, R.R. Escobar, et al., Risk factors for mediastinitis after coronary artery bypass grafting surgery, Rev. Bras. Cir. Cardiovasc. 26 (2011) 27–35.
[4] M.P. Sá, E.F. Soares, C.A. Santos, O.J. Figueiredo, R.O. Lima, R.R. Escobar, et al., Skeletonized left internal thoracic artery is associated with lower rates of mediastinitis in diabetic patients, Rev. Bras. Cir. Cardiovasc. 26 (2011) 183–189.
[5] M.P. Sá, C.A. Santos, O.J. Figueiredo, R.O. Lima, P.E. Ferraz, A.M. Soares, et al., Skeletonized left internal thoracic artery is associated with lower rates of mediastinitis in elderly patients, Rev. Bras. Cir. Cardiovasc. 26 (2011) 617–623.
[6] M.P.B.O. Sá, P.E. Ferraz, R.R. Escobar, F.P. Vasconcelos, A.A. Ferraz, D.M. Braile, et al., Skeletonized versus pedicled internal thoracic artery and risk of sternal wound infection after coronary bypass surgery: meta-analysis and meta-regression of 4817 patients, Interact. Cardiovasc. Thorac. Surg. 16 (2013) 849–857.
[7] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, Ann. Intern. Med. 151 (2009) 264–269.
[8] J.P. Higgins, S.G. Thompson, J.J. Deeks, D.G. Altman, Measuring inconsistency in meta-analyses, BMJ 327 (2003) 557–560.
[9] R. DerSimonian, R. Kacker, Random-effects model for meta-analysis of clinical trials: an update, Contemp. Clin. Trials 28 (2007) 105–114.
[10] J. Lau, J.P. Ioannidis, C.H. Schmid, Quantitative synthesis in systematic reviews, Ann. Intern. Med. 127 (1997) 820–826.
[11] C.B. Begg, M. Mazumdar, Operating characteristics of a rank correlation test for publication bias, Biometrics 50 (1994) 1088–1101.
[12] M. Egger, G. Davey Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, BMJ 315 (1997) 629–634.
[13] V. Mannacio, L. Tommaso, V. Amicis, P. Stassano, C. Vosa, Randomized flow capacity comparison of skeletonized and pedicled left internal mammary artery, Ann. Thorac. Surg. 91 (2011) 24–30.
[14] M. Kai, M. Hanyu, Y. Soga, T. Nomoto, J. Nakano, T. Matsuo, et al., Off-pump coronary artery bypass grafting with skeletonized bilateral internal thoracic arteries in insulin-dependent diabetics, Ann. Thorac. Surg. 84 (2007) 32–36.
[15] H. Hirose, A. Amano, S. Takanashi, A. Takahashi, Skeletonized bilateral internal mammary artery grafting for patients with diabetes, Interact. Cardiovasc. Thorac. Surg. 2 (2003) 287–292.
[16] A. Amano, A. Takahashi, H. Hirose, Skeletonized radial artery grafting: improved angiographic results, Ann. Thorac. Surg. 73 (2002) 1880–1887.
[17] A.M. Calafiore, G. Vitolla, A.L. Iaco, C. Fino, G. Di Giammarco, F. Marchesani, et al., Bilateral internal mammary artery grafting: midterm results of pedicled versus skeletonized conduits, Ann. Thorac. Surg. 67 (1999) 1637–1642.
[18] G.M. Fitzgibbon, H.P. Kafka, A.J. Leach, W.J. Keon, G.D. Hooper, J.R. Burton, Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years, J. Am. Coll. Cardiol. 28 (1996) 616–626.
[19] M. Gaudino, A. Toesca, S.L. Nori, F. Glieca, G. Possati, Effect of skeletonization of the internal thoracic artery on vessel wall integrity, Ann. Thorac. Surg. 68 (1999) 1623–1627.
[20] M.A. Deja, S. Wos, K.S. Golba, P. Zurek, W. Domaradzki, R. Bachowski, et al., Intraoperative and laboratory evaluation of skeletonized versus pedicled internal thoracic artery, Ann. Thorac. Surg. 68 (1999) 2164–2168.
[21] G. Noera, P. Pensa, R. Lodi, M. Lamarra, B. Biagi, P. Guelfi, Influence of different harvesting techniques on the arterial wall of internal mammary artery graft: microscopic analysis, Thorac. Cardiovasc. Surg. 41 (1997) 16–20.
[22] T. Ueda, S. Taniguchi, T. Kawata, K. Mizuguchi, M. Nakajima, A. Yoshioka, Does skeletonization compromise the integrity of internal thoracic artery grafts? Ann. Thorac. Surg. 125 (2003) 638–641.

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