DOI: 10.1111/jocs.14359

ORIGINAL ARTICLE

JOURNAL OF CARDIAC SURGERY WILEY

Intraoperative graft flow profiles in coronary artery bypass surgery: A meta-analysis

Manuela Silva MD[1,3] | Lisa Q Rong MD[2] | Ajita Naik MD[1] | Mohamed Rahouma MD[1] | Irbaz Hameed MD[1] | Bryce Robinson MD[1] | Yongle Ruan MD[1] | Yuan Jiang MD[1] | Anas W Abed MD[1] | Leonard N Girardi MD[1] | Mario Gaudino MD[1]

[1]Department of Cardiothoracic Surgery, Weill Cornell Medicine, New York, New York

[2]Department of Anesthesiology, Weill Cornell Medicine, New York, New York

[3]Department of Cardiothoracic Surgery, Hospital Santa Marta - CHULC, Lisbon, Portugal

Correspondence
Mario Gaudino, MD, Department of Cardiothoracic Surgery, Weill Cornell Medicine, 525 East 68th Street, New York, NY 10065.
Email: mfg9004@med.cornell.edu

Abstract

Background: Conduits used in coronary artery bypass artery grafting (CABG) have different properties and flow profiles. We compared intraoperative mean graft flow (MGF) between arterial and venous conduits, off-pump CABG (OPCABG) and on-pump CABG (ONCABG) procedures, skeletonized and pedicled internal mammary artery (IMA) grafts, and pulsatility index (PI) between OPCABG and ONCABG, in pairwise meta-analyses.

Methods: Following a systematic literature search, all studies comparing MGF in arterial and venous grafts, were included. The primary endpoint was comparison of pooled MGF between arterial and venous grafts. Secondary endpoints were comparisons of pooled MGF in OPCABG vs ONCABG, anastomosed skeletonized vs pedicled IMA grafts, free skeletonized vs pedicled IMA grafts and PI in OPCABG versus ONCABG.

Results: A total of 25 studies with 4443 patients were included. Compared with venous grafts, arterial grafts had lower MGF (standardized mean difference [SMD], −0.28; 95% confidence interval [CI, −0.34; −0.22]; $P < .001$). OPCABG was associated with significantly lower MGF compared to ONCABG (SMD, −0.29; 95% CI, −0.50; −0.08]; $P = .01$). No differences were found in MGF between skeletonized vs pedicled IMA after anastomosis (SMD, 0.32; 95%CI [−0.08; 0.71]; $P = .11$) or in free flow (SMD, 0.76; 95%CI [−0.14; 1.65]; $P = .10$). No difference was found in PI between OPCABG and ONCABG. At meta-regression, age was associated with higher MGF, while OPCABG was associated with lower MGF.

Conclusions: Intraoperative flow of venous conduits is higher than that of arterial grafts. Compared to OPCABG surgery, graft flow is higher in ONCABG. In skeletonized and pedicled IMA conduits, no difference in flow profiles was found.

KEYWORDS
coronary artery bypass grafting, graft flow, transit time flow measurement

1 | INTRODUCTION

Conduits used in coronary artery bypass grafting (CABG) have distinctive flow profiles. Compared to venous grafts, arterial grafts can adapt to different demands of blood supply, due to their functional and histological properties.[1] Graft flow is a major determinant postoperative conduit patency[2] and an inverse relationship between graft flow and intimal proliferation has been reported.[3]

Measurement of the intraoperative graft flow and associated variables allow assessment of early graft function and help

TABLE 1 Details of the included studies

Author/year	Study type	Study period	Hospital name	Country	Procedure performed	Grafts compared	Flow measurement technique
Amin et al 2019[10]	R	2015-2017	Oxford University Hospitals Trust	UK	Arterial vs venous/ONCABG vs OPCABG	LIMA, RIMA, RA, SVG	TTFM
Balacumaraswami et al 2008[8]	P	2003-2004	John Radcliffe Hospital	UK	Arterial vs venous/ONCABG vs OPCABG	IMA, RA, SVG	TTFM
Boodhwani et al 2006[11]	RCT	2003-2005	University of Ottawa Heart Institute	Canada	Skeletonized vs pedicled IMA/ anastomosed and free graft flow	LIMA, RIMA	TTFM
Cerqueira et al 2012[12]	R	2010	Bahia Foundation of Cardiology	Brazil	ONCABG vs OPCABG	LIMA	TTFM
Cetin et al 2006[13]	R	2000-2003	West German Heart Center Essen, University Hospital	Germany	Arterial vs venous	LIMA, SVG	TTFM
D'Ancona et al 2000[14]	P	1997-1998	Kaleida Health Systems and the State University of New York at Buffalo	USA	Arterial vs venous	IMA, SVG	TTFM
Hassanein et al 2005[15]	R	1999-2003	Heart Institute Lahr/Baden	Germany	Arterial vs venous/ONCABG vs OPCABG	IMA, RA, SVG	TTFM
Hirotani et al 2001[16]	R	1996-2000	Tokyo Saiseikai Central Hospital,	Japan	Arterial vs venous	IMA, LIMA, RIMA, SVG	TTFM
Kieser et al 2010[17]	P	2004-2007	University of Calgary	Canada	Arterial vs venous	LIMA, RIMA, RA, IEA, SVG	TTFM
Kjaergard et al 2004[18]	R	2000-2004	University of Copenhagen	Denmark	Arterial vs venous/ONCABG vs OPCABG	LIMA, SVG	TTFM
Leong et al 2005[19]	P	2001-2002	National University of Singapore	Singapore	Arterial vs venous/ONCABG vs OPCABG	LIMA, SVG	TTFM
Nakajima et al 2019[20]	R	2007 - 2015	International Medical Center Saitama Medical University	Japan	Arterial vs venous	GEA, SVG	TTFM
Reineke et al 2012[21]	P	-	University Hospital Bern	Switzerland	Arterial vs venous	LIMA, RIMA, SVG	TTFM
Sanisoglu et al 2003[22]	P	1999	Florence Nightingale Hospital	Turkey	Arterial vs venous	LIMA, SVG	TTFM
Santarpino et al 2009[23]	P	2003-2007	Magna Graecia University of Catanzaro	Italy	Arterial vs venous/ONCABG vs OPCABG	RA, SVG	TTFM
Schmitz et al 2003[24]	R	2000-2001	University of Bonn	Germany	ONCABG vs OPCABG	LIMA, RIMA, SVG	TTFM
Seetharama Bhat et al 2019[25]	P	2014-2018	Sri Jayadeva Institute of Cardiovascular Sciences and Research	India	Arterial vs venous	LIMA, SVG	TTFM
Takami and Ina 2002[26]	R	-	Kasugai Municipal Hospital,	Japan	Skeletonized vs pedicled anastomosed IMA	LIMA	TTFM
Walpoth et al 2008[27]	P	-	University Hospital Bern	Switzerland	Arterial vs venous	IMA, SVG	TTFM

(Continues)

TABLE 1 (Continued)

Author/year	Study type	Study period	Hospital name	Country	Procedure performed	Grafts compared	Flow measurement technique
Castro et al 2005[28]	RCT	2003	Hospital de Clínicas	Brazil	Skeletonized vs pedicled IMA free flow	LIMA	Graded plastic receptacle
Chaudhri et al 2016[29]	RCT	2013	Armed Forces Institute of Cardiology and National Institute of Heart Diseases	Pakistan	Skeletonized vs pedicled IMA free flow	LIMA	Container
Kandemir et al 2007[30]	RCT	2006	Karaelmas University	Turkey	Skeletonized vs pedicled IMA free flow	LIMA	Capacity
Mannacio et al 2011[31]	RCT	2004-2007	University of Naples Federico II	Italy	Skeletonized vs pedicled IMA/ anastomosed and free flow	LIMA	TTFM
Walpoth et al 1996[5]	RCT	-	Department of Thoracic and Cardiovascular Surgery	Switzerland	Skeletonized vs pedicled IMA/ anastomosed and free flow	LIMA	TTFM
Wendler et al 1999[32]	R	1997-1998	University Hospital Homburg	Germany	Skeletonized vs pedicled IMA free flow	LIMA, RIMA	Container

Abbreviations: IEA, inferior epigastric artery; IMA, internal mammary artery; LAD, left anterior descending artery; LIMA, left internal mammary artery; ONCABG, on-pump coronary artery bypass artery grafting; OPCABG, off-pump coronary artery bypass artery grafting; P, prospective; R, retrospective; RA, radial artery; RCT, randomized clinical trial; RIMA, right internal mammary artery; SVG, saphenous vein graft; TTFM, transit time flowmeter.

prevent graft failure, and reduce perioperative morbidity and mortality.[4,5]

Multiple techniques for assessing flow have been proposed,[6] but the most common technique is transit time flow measurement (TTFM).[7] TTFM measures mean graft flow (MGF) in addition to providing a flow waveform and derived values such as a pulsatility index (PI).[8] The European guidelines for myocardial revascularization have recommended its use since 2010, and according to the current 2018 update, the routine intraoperative graft flow measurement is a Class IIa Level B recommendation.[9]

We performed a meta-analysis comparing arterial and venous grafts flow during CABG using TTFM. We also compared graft flow in off-pump CABG (OPCABG) and on-pump CABG (ONCABG) procedures, as well as in the internal mammary artery (IMA) flow according to the harvesting technique.

2 | METHODS

2.1 | Search strategy and study selection

A medical librarian (MD) performed comprehensive searches to identify contemporary randomized trials and observational studies on graft flow in adult CABG series. Searches were run on 15 August 2019 in the following databases: Ovid MEDLINE (All; 1946 to 13 August, 2019); Ovid EMBASE (1974 to present); and the cochrane library (Wiley). The full search strategy for Ovid MEDLINE is available in Table S1.

2.2 | Study selection and data extraction

Searches throughout the databases yielded 5776 results. Titles and abstracts were reviewed based on the pre-defined inclusion/exclusion criteria. Articles were considered for inclusion if they were in English, observational or randomized trials comparing MGF between arterial and venous grafts, OPCABG and on-pump, and skeletonized and pedicled IMA grafts, in patients with CABG. Animal studies, case reports, conference presentations, editorials, expert opinions, studies reporting postoperative flow characteristics were excluded.

For the second round of eligibility screening, full text was pulled for the selected studies. The bibliography of all studies and any previously published relevant meta-analyses were also searched to identify articles. The full preferred reporting items for systematic reviews and meta-analyses flow diagram outlining the study selection process is available in Figure S1. All studies were reviewed by two independent investigators (MS and AN) and disagreements were resolved by the senior author (MG). For overlapping studies, the largest series were included.

Two authors (MS and AN) performed data extraction independently, and the extracted data were verified by a third investigator (YR) for accuracy. Variables extracted were study variables (study year, period, country, comparison arms, sample size), procedure-related variables (preoperative intra-aortic balloon pumpMand urgency of procedure; Table 1), and patient variables (age, sex, body

TABLE 2 Summary of outcomes

Outcome	Comparison arms	Studies	Number of grafts	Standardized mean difference effect estimate (95%CI; *P*) value	Heterogeneity (I_2 [*P*] value)	Tau2
Mean graft flow	Arterial vs venous[a,b]	15	5503	RE: −0.20 (−0.56; 0.16); *P* = .27	96.4%; *P* < .001	0.45
				FE: −0.28 (−0.34; −0.22); *P* < .001		
	OPCABG vs ONCABG	8	5041	RE: −0.29 (−0.50; −0.08); *P* = .01	87.6%; *P* < .001	0.07
				FE: −0.31 (−0.38; −0.25); *P* < .001		
	Skeletonized vs pedicled	4	381	RE: 0.32 −0.08; 0.71); *P* = .11	64.3%; *P* = .04	0.10
				FE: 0.39 (0.19; 0.60); *P* < .001		
IMA free flow	Skeletonized vs pedicled	7	693	RE: 0.76 −0.14; 1.65); *P* = .10	96.4%; *P* < .001	1.39
				FE: 0.38 (0.22; 0.54); *P* < .001		
Pulsatility index	OPCABG vs ONCABG	4	2469	RE: 0.05 −0.13; 0.24); *P* = .59	66.0%; *P* = .03	0.02
				FE: 0.13 (0.05; 0.21); *P* < .001		

Note: Not all studies reported IMA subgroups (three studies reported IMA as a whole group).
Abbreviations: CABG, coronary artery bypass artery grafting; 95%CI, 95% confidence interval; FE, fixed effect; IMA, internal mammary artery; LIMA, left internal mammary artery; MGF, mean graft flow; ONCABG, on-pump CABG; OPCABG, off-pump CABG; RA, radial artery; RE, random effect; SVG, saphenous vein graft; SMD, standardized mean difference.
[a]Arterial grafts: IMA, RA, gastroepiploic artery (GEA) and inferior epigastric artery (IEA).
[b]Not enough studies of GEA or IEA for individualized analysis.

mass index, diabetes, hypertension, dyslipidemia, smoking history, left ventricular ejection fraction, and history of myocardial infarction, cerebrovascular accident, peripheral vascular disease, chronic obstructive pulmonary disease, renal failure, atrial fibrillation; Table S2).

The quality of the included studies was assessed using the Newcastle-Ottawa scale for observational studies (Table S3) and the Cochrane Collaboration's tool for assessing risk of bias in randomized trials studies (Table S4).[33,34]

2.3 | Outcomes and effects summary

The primary comparison was pooled MGF in arterial vs venous grafts. Secondary endpoints were pooled MGF in OPCABG vs ONCABG; (a) pooled MGF in skeletonized vs pedicled anastomosed IMA; (b) pooled MGF in skeletonized vs pedicled free IMA grafts, and (c) PI in OPCABG vs ONCABG (Table 2).

2.4 | Meta-analysis

Continuous variables were expressed as mean (standard deviation) while categorical variables were reported as percentages (%). Standardized mean difference (SMD) with 95% confidence interval (95%CI) was used to estimate the effect for continuous outcomes and was calculated by DerSimonian-Laird (inverse variance) method.[35] Fixed and random effects model were used.

Sensitivity analysis using “leave-one-out analysis” was performed for the primary outcome. Meta-regression was used to explore the effects of age, male gender, left internal mammary artery grafts, radial artery grafts and OPCABG surgery on MGF (Table 3).

TABLE 3 Meta-regression for the primary outcome (arterial vs venous mean graft flow). Positive beta (regression coefficient) corresponds to higher standardized mean difference with higher covariate, while negative beta reflects lower SMD with higher covariate

Variables	Beta ± SD (*P*) value
Mean age	0.10 ± 0.04; 0.01
Male gender	−0.03 ± 0.03; 0.38
Left internal mammary artery (%)	0.02 ± 0.02; 0.44
Radial artery (%)	0.03 ± 0.02; 0.20
Off-pump CABG (%)	−0.02 ± 0.01; 0.04

Abbreviations: CABG, coronary artery bypass grafting; OPCABG, off-pump CABG; SD, standard deviation.

Statistical significance was set at the two-tailed 0.05 level. Hypothesis testing for statistical homogeneity was based on the Cochran Q test with I^2 values of 0% to 25%, 26% to 50%, and 51% to 100% representing low, moderate, and high heterogeneity, respectively.[36] Meta and metafor packages in R (version 3.3.3R Project for Statistical Computing) were used for the analyses.

3 | RESULTS

3.1 | Study and patient characteristics

A total of 337 studies were retrieved of which 25 studies with 4443 patients met our inclusion criteria. There were 19 observational studies and 6 randomized trials. Four studies were from Germany, three from Japan and Switzerland each, and the rest from other countries (Table 1).

The number of patients in the individual studies ranged from 20 to 896. The mean age ranged from 52.0 to 75.2 years. Males ranged from 65.0% to 92.4%. The details of patient characteristics are presented in Table S2. Quality assessment of included studies is shown in Table S3 and Table S4.

3.2 | Meta-analysis

3.2.1 | Primary outcome

Mean graft flow

The detailed results of the pairwise meta-analysis are summarized in Table 2.

3.2.2 | Arterial vs venous grafts

Arterial grafts had a lower MGF than venous grafts (SMD between venous and arterial grafts −0.28; 95%CI [−0.34; −0.22]; *P* < .001). (Figure 1 and Table 2)

3.2.3 | Secondary outcomes

1. Comparison of MGF by type of surgery (OPCABG vs ONCABG)
   OPCABG was associated with lower MGF than ONCABG (SMD, −0.29; 95%CI [−0.50; −0.08]; *P* = .01; Table 2; Figure S2).
2. Comparison of MGF in skeletonized vs pedicled anastomosed IMA
   There was no difference in MGF between skeletonized and pedicled IMA grafts (SMD, 0.32; 95%CI [−0.08; 0.71]; *P* = .11; Table 2; Figure S3).
3. Comparison of MGF in skeletonized vs pedicled free IMA
   There was no difference in free flow between skeletonized and pedicled IMA grafts (SMD, 0.76; 95%CI [−0.14; 1.65]; *P* = .10; Table 2; Figure S4).
4. Comparison of PI by type of surgery (OPCABG vs ONCABG)

There was no difference in PI between OPCABG and ONCABG (SMD, 0.05; 95%CI [−0.13; 0.24]; *P* = .59; Figures S5).

Leave-one-out analysis confirmed the solidity of the primary outcome (Figure S6).

3.3 | Meta-regression

At meta-regression, age (Beta=0.10 ± 0.04; *P* = .01) was associated with higher MGF, while OPCABG (Beta = −0.02 ± 0.01; *P* = .04) was associated with lower MGF.

4 | DISCUSSION

Our meta-analysis showed that arterial grafts have a lower MGF than venous grafts. While there was no difference in MGF between different IMA harvesting techniques, OPCABG was associated with lower MGF compared to ONCABG. No difference was found in PI between both types of surgery.

Previous individual studies have analyzed the influence of intraoperative graft flow measurement on predicting graft failure.[7,37,38] However, an objective estimate of the flows in different conduits has not been pooled in a meta-analysis. Our findings are consistent with previous observational studies. Amin et al[10] reported an overall lower MGF in arterial conduits, compared with venous grafts (43.6 ± 31.4 vs 48.2 ± 33.6 mL/min; *P*-value .11). Cetin et al[13] showed that MGF graft flow was lower in LITA grafts than in venous grafts (41.6 ± 2.3 vs 45.8 ± 2 mL/min). Similarly, Balacumaraswami et al[34] found a higher flow in veins compared to radial grafts supplying the same myocardial territory.

Schmitz et al[24] suggested that flow in OPCABG should be expected to be lower since the vasodilatory effect of ischemia and

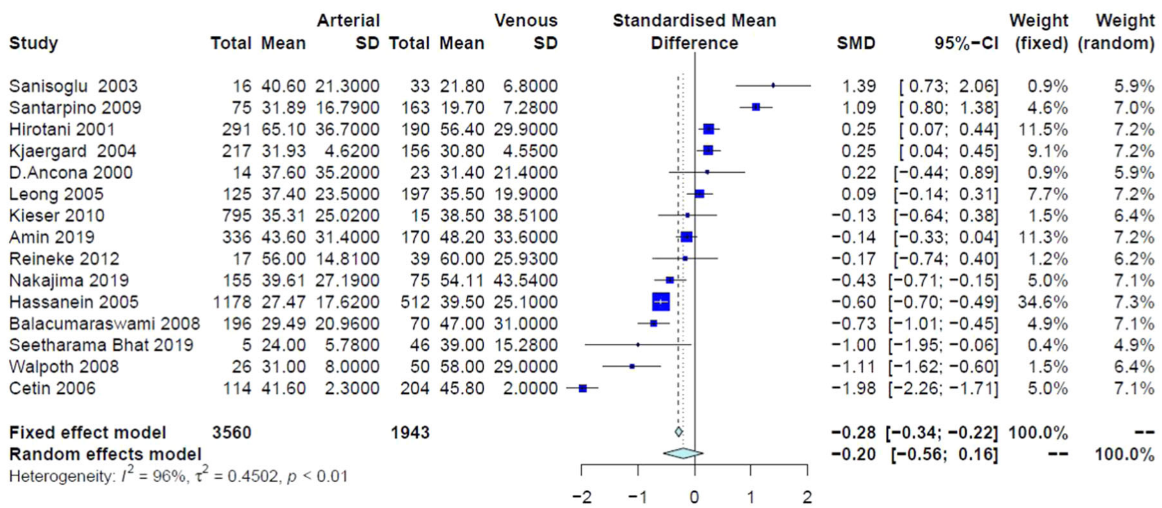

FIGURE 1 Forest plot showing standardized mean difference (SMD) of mean graft flow in arterial vs venous grafts. CI, confidence interval; SD, standard deviation

acidosis induced by arresting the heart is absent.[8,39,40] Moreover, a lower graft flow can be related to the use of vasoconstrictors to control hemodynamics during heart positioning. We found grafts in OPCABG to have lower MGF than in ONCABG. Amin et al[10] found comparable values for PI in the crude comparison, irrespective of surgical technique. In our analysis, no difference was found in PI between OPCABG and ONCABG.

Several studies have highlighted advantages of skeletonized IMA compared to pedicled, namely, improved early blood flow[26,31,41,42] and more pronounced vasodilator action of papaverine.[29,42] In a randomized study by Mannacio et al,[31] skeletonized IMA was found to have a superior free flow (55.1 ± 24.5 pedicled group vs 63.8 ± 31.3 mL/minute skeletonized group; $P = .02$), as well as a greater postanastomotic mean flow (30.31 ± 3.2 mL/minute vs 25.4 ± 11.1 mL/minute; $P = .0005$). Boodhwani et al,[11] however, could not find an increased flow with skeletonization, probably as a result of vasospasm, and IMA flow was also similar after anastomosis. Similarly, no differences in IMA free flow and anastomosed MGF were found in our study.

Our study shares the usual limitations of meta-analyses of observational studies. The included studies applied different surgical techniques and perioperative protocol. There was moderate to high heterogeneity, although leave-one-out sensitivity analysis confirmed the solidity of results.

In conclusion, the intraoperative flow of venous conduits is higher than that of arterial grafts. Compared to OPCABG surgery, graft flow is higher in ONCABG. In skeletonized and pedicled IMA conduits, no difference in flow profiles was found.

ORCID

Lisa Q Rong http://orcid.org/0000-0003-0982-7154
Ajita Naik http://orcid.org/0000-0001-7398-4643
Mario Gaudino http://orcid.org/0000-0003-4680-0815

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Silva M, Rong LQ, Naik A, et al. Intraoperative graft flow profiles in coronary artery bypass surgery: A meta-analysis. *J Card Surg*. 2020;35:279–285. https://doi.org/10.1111/jocs.14359