Comparison of free arterial and saphenous vein grafting in outcomes after coronary bypass surgery

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ABSTRACT

Objectives. The goal of this study was to examine whether the use of free arterial grafts could reduce the need for repeated revascularization and all-cause mortality in patients undergoing coronary artery grafting. Design. The cohort study included 17,354 consecutive adults with isolated coronary artery grafting from 2000 to 2016 in three cardiac surgery centers. Data were obtained from the Western Denmark Heart Registry. Propensity matching with 24 factors was used to establish comparable groups of patients receiving either vein grafts (n = 1019) or free arterial grafts (n = 1019) for outcome analysis. Results. The need for repeated revascularization and all-cause mortality was similar in both graft groups at 10 years of follow-up. Creatine-Kinase MB Isoenzyme >100 μg/L increased the risk of repeated revascularization rate after 1, 5 and 10 years. Conclusions. Long-term outcomes in revascularization and survival are comparable after free arterial or saphenous vein grafting.

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CABG; arterial grafting; venous grafting; long-term mortality; revascularization rate

Introduction

Coronary artery bypass grafting (CABG) remains the primary treatment in high-risk patients with severe left main coronary artery disease, severe triple coronary vessel disease, poor ventricular function and diabetes mellitus [1]. Due to superior patency, more than 90% of CABG patients receive the pedicle of the left internal mammary artery (LIMA) as the first conduit [2,3]. However, most patients have multivessel disease and require a supplement with venous grafts (saphenous vein grafts [SVG]), free arterial grafts, that is, radial artery (RA) or the right internal mammary artery (RIMA).

Since 1970 SVG have been the most popular supplemental grafts in CABG [4,5] as easy to use and in abundance. However, a disadvantage of SVG is an increased possibility of the development of atherosclerosis, causing declining patency with time and a possible reduced long-term outcome [6]. The positive results achieved with LIMA increased interest in other supplemental arterial grafts, such as RA, initially showing satisfactory early and midterm RA patency compared with SVG and RIMA [7,8]. The choice of the vascular conduit is an important element in patient survival and the latest 2018 ESC/EACTS guidelines advocate for multiple arterial grafting due to suboptimal SVG patency rates for non-LAD targets [9]. Despite this, the SV is used for up to 80% of all grafts in many centers [10].

We aimed to examine the effect of free arterial grafts and SVG in patients subjected to isolated CABG to evaluate the optimal grafting strategy, with the hypothesis that free arterial grafts will reduce the need for repeated revascularization and all-cause mortality.

Material and methods

Aiming at a minimal 3-year observation time, the primary cohort consisted of all consecutive adults undergoing CABG between 2000 and 2016 in the three cardiac surgery centers (Aalborg, Odense and Aarhus University Hospitals), reporting to the Western Denmark Heart Registry (WDHR). WDHR is a mandatory internet-based registry of all cardiac procedures in the western part of Denmark. Registration is completed by the attending surgeon, anesthesiologist and perfusionist. Individuals were identified by the unique Central Personal Registration (CPR) number assigned to all people, who have been or are currently residing in Denmark. The Danish Civil Registration System (DCRS) contains basic personal information, civil and vital status including the date of death of citizens with a valid CPR number. The WDHR is updated daily and thus contains information on all patients with a valid CPR number. The study was approved by the Danish Data Protection Agency (1-16-02-830-17). Written consent is not required for registry-based studies according to Danish legislation.
Patient population

We found 20,061 eligible procedures where patients underwent isolated CABG. Patients with isolated RIMA or LIMA grafting, missing required information, dying within 36 h after surgery and unknown graft types were excluded. Following, the final cohort was CABG with the pedicle of LIMA and/or RIMA and supplemental free arterial grafts or SVG, including single or sequential, skeletonized or no-touch grafts, independently of the urgency, with a total of 17,354 procedures, of which 1082 received a free arterial graft (Figure 1).

Perioperative management

All medications were paused before the surgery except beta-blocking agents. Since 2013 acetylsalicylic acid was continued until the day before surgery and before that in all patients with the acute coronary syndrome (ACS). Other antiplatelet therapies were discontinued 5 days before surgery, but patients with recent percutaneous intervention (PCI) perioperatively received low-molecular-weight heparin (LMWH) Dalteparin. Oral anticoagulant treatment was discontinued 2–3 days before the surgery and in the case of vitamin K-antagonists, the anticoagulation effect was controlled by measurement of the International Normalized Ratio (INR) and corrected when needed.

General anesthesia and invasive hemodynamic monitoring were used in all patients. CABG was done off-pump or with extracorporeal circulation (ECC) at the discretion of the attending surgeon. Routine cardio-protective strategies were used at all centers. The decision about pharmacological support and transfusions was primarily made by the attending anesthetist. None of the centers have detailed guidelines or algorithms for perioperative medical treatment. Vasodilation with nitroglycerine infusion was administered for the first 12 h, especially in RA graft-patients, at the discretion of the surgeon.

Lifelong low-dose antiplatelet therapy with acetylsalicylic acid was reestablished on the first postoperative day. LMWH was administered for the first five postoperative days. In the presence of preoperative ACS or recent PCI, the treatment was supplemented with the previous antiplatelet agents, after discontinuing LMWH. In patients receiving RA graft peroral nitroglycerine or calcium antagonists were administered for at least 3 months postoperatively.

Surgical technique

A median sternotomy was performed on all patients. Free artery or vein utilization was at the discretion of the surgeon. RA harvesting was performed via a full forearm incision. Skeletonized SV was harvested directly through an incision over the vein along the medial leg and in 2011 a “no-touch” SV harvesting technique was implemented in one center. The SV/RA was stored at room temperature in a storage solution consisting of 60 mL blood, 1000 IU heparin and 60 mg Papaverine. RA or SV were used for coronary artery grafting as a single or sequential graft. The mean flow (mL/min) of the grafts was measured (Transit time; Medistim, Norway) after completion of all anastomoses. Perioperative surgical graft correction due to low flow was at the discretion of the surgeon.

Outcomes

The primary outcomes were all-cause mortality along with a need for revascularization during 10 years of follow up. Revascularization was defined as a new CABG or PCI after discharge from the primary operation.

The secondary outcomes were in-hospital complications, such as central nervous system impairment, new dialysis, arrhythmias, Creatine-kinase MB isoenzyme (CKMB) level >100 μg/L, and myocardial infarction. Postoperative myocardial infarction was defined if any of the following were detected: increased CKMB > 100 μg/L and/or a new pathological Q-wave or new left bundle branch block, angiographically documented occlusion or imaging evidence of new loss of viable myocardium.

Statistical analysis

We used a 1:1 ratio propensity score matching to attenuate the differences between groups and reduce the risk of confounding bias and the non-random assignment of patients in the grafting groups. After propensity matching, two comparable groups (with 1019 patients in each) were formed. The included covariates were primarily based on EuroSCORE I/II [11] together with surgical, graft factors and department (Table 1). After randomized ranking of the
### Table 1. Frequencies of factors and covariates before and after propensity score match.

| Factors                             | Pre-match  |  | p-Value  | After match |  | p-Value  |
|-------------------------------------|------------|------------|-----------|-------------|------------|-----------|
| Procedures                         | 16,272     | 1082       | .060      | 1019        | 1019       | .270*     |
| EuroSCORE                          | 4 (2–6)    | 4 (2–6)    | <.0001    | 4 (2–6)     | 4 (2–6)    | .854*     |
| Age                                | 67 (60–73) | 66 (57–72) | <.0001    | 65 (57–72)  | 66 (57–72) | .830      |
| Female                             | 3091 (19.0)| 227 (21.0) | .010      | 228 (21.8)  | 218 (21.4) | .830      |
| Chronic obstructive lung disease   | 1577 (9.7) | 106 (9.8)  | .912      | 86 (8.4)    | 102 (10.0) | .221      |
| Extracardiac artheriopathy         | 1901 (11.7)| 167 (15.4) | .0002     | 156 (15.3)  | 161 (15.8) | .760      |
| Poor mobility                      | 1078 (6.6) | 52 (4.8)   | .019      | 56 (5.5)    | 51 (5.0)   | .620      |
| Previous cardiac surgery           | 343 (2.1)  | 48 (4.4)   | <.0001    | 39 (3.8)    | 45 (4.4)   | .504      |
| s-Creatinine >200                  | 318 (2.0)  | 19 (1.8)   | .670      | 24 (2.4)    | 17 (1.7)   | .270      |
| Critical preoperative state        | 560 (3.4)  | 18 (16.6)  | .0016     | 16 (1.6)    | 18 (1.8)   | .730      |
| Unstable angina                    | 2623 (16.1)| 177 (16.4) | .836      | 173 (17.0)  | 172 (16.9) | .953      |
| Myocardial Infarction <90 days     | 4472 (27.5)| 298 (27.5) | .967      | 252 (24.7)  | 273 (26.8) | .288      |
| Pulmonary hypertension             | 339 (2.1)  | 14 (1.3)   | .075      | 17 (1.7)    | 13 (1.3)   | .462      |
| Acute surgery                      | 1194 (7.3) | 90 (8.3)   | .233      | 75 (7.3)    | 81 (7.9)   | .617      |
| Insulin treated Diabetes           | 1116 (6.9) | 78 (7.2)   | .661      | 65 (6.4)    | 73 (7.2)   | .481      |
| Off-pump surgery                   | 1404 (8.8) | 280 (25.9) | <.0001    | 240 (23.6)  | 234 (23.0) | .753      |
| Left ventricular ejection fraction  |            |            |           |             |            |           |
| LVEF < 30                           | 1312 (8.1) | 67 (6.2)   | .007      | 61 (6.0)    | 63 (6.2)   | .719      |
| LVEF = 30–50                        | 8601 (52.9)| 620 (57.3) |           | 606 (59.4)  | 588 (57.7) |           |
| LVEF > 50                           | 6358 (39.1)| 395 (36.5) |           | 352 (34.5)  | 368 (36.1) |           |
| Department                          |            |            |           |             |            |           |
| Department A                        | 6112 (37.5)| 328 (30.3) | <.0001    | 330 (32.4)  | 325 (32.0) | .924      |
| Department B                        | 6525 (40.1)| 214 (19.8) |           | 207 (20.3)  | 214 (21.0) |           |
| Department C                        | 3625 (22.3)| 540 (49.9) |           | 482 (47.3)  | 480 (47.1) |           |
| Number left                         | 2 (2–3)    | 2 (2–3)    | .100      | 2 (2–3)     | 2 (2–3)    | .696*     |
| Number right                        | 0 (0–1)    | 0 (0–1)    | .307      | 0 (0–1)     | 0 (0–1)    | .557*     |
| LIMA left                           | 14,933 (91.8)| 1017 (94.0)| .0095     | 958 (94.0)  | 954 (93.6) | .713      |
| RIMA right                          | 122 (0.7)  | 133 (12.3) | <.0001    | 84 (8.2)    | 84 (8.2)   | 1.0       |
| LIMA + RIMA left                    | 197 (1.2)  | 32 (3.0)   | <.0001    | 37 (3.6)    | 30 (2.9)   | .329      |
| LIMA/RIMA sequential               | 227 (1.4)  | 129 (11.9) | <.0001    | 100 (9.8)   | 101 (9.9)  | .941      |

*Median (IQR), Wilcoxon’s-test paired samples, the rest Numbers (percentage); χ²-test. LIMA: left internal mammary artery; RIMA: right internal mammary artery.

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**Figure 2.** Standardized differences of criteria, before and after propensity match. The included covariates were primarily EuroSCORE I/II criteria combined with graft data. COLD: chronic obstructive lung disease; Mi: myocardial infarction; LVEF: left ventricular ejection fraction.
patients, the propensity score-matched analysis was carried out, aiming to match each patient receiving free arterial grafts to a patient receiving SVG using the nearest neighbor matching without replacement within a maximum caliper range of ±0.025 [12]. Standard crude and adjusted conditional regression analyses were used for the investigation of the outcomes. Categorical data were analyzed with Chi-square test or McNemar test where appropriate longitudinal data were added with Wilcoxon’s paired test. The adjustment factors were perioperative constrictors, perioperative inotropes, year of procedure (3 groups) and transfusion of red blood cells (RBC) (units 0–9).

Postoperative drainages (mL) were added with Wilcoxon’s paired test. The adjusted odds ratios were estimated and described using the Kaplan–Meier plot. No substantial difference was seen between the graft types in the need for revascularization at any point during the short or long-term observations nor in all-cause mortality during 10 years (Table 3), which was further demonstrated with Kaplan-Meier’s survival curves, indicating a non-significant higher survival probability in SVG patients during the 10 years (Figure 3). Postoperative CK-MB >100 µg/L precipitated higher revascularization rates after 1, 5 and 10 years (Figure 4).

### Discussion

We could not demonstrate a difference in the need for repeated revascularization and all-cause mortality between free arterial grafts and SVG, used as a supplemental conduit in CAGB surgery after a 10 years follow-up period. A recent review of randomized controlled trials and meta-analysis showed better patency of arterial conduits, but no clear evidence of better clinical outcomes after arterial versus SVG grafting [13]. The most likely explanation for our findings might be that SVG is not as sensitive to stenosis-degree of

### Table 2. Per- and post-operative outcomes divided on graft types.

| Outcomes                  | Vein  | Free arterial | p-Value |
|---------------------------|-------|---------------|---------|
| Patients                  | 1019  | 1019          |         |
| Per-operative             |       |               |         |
| Anti-arrhythmia drugs     | 3.3%  | 2.6%          | .392a   |
| Pacemaker (any use)       | 58.1% | 64.3%         | .002a   |
| Vasodilators              | 41.1% | 47.9%         | .002a   |
| Post-operative            |       |               |         |
| Postoperative drainage    | 770 (475–1198) | 700 (475–1058) | .101b   |
| CK-MB level (Ui/L)        | 20 (12–32) | 18 (11–28)    | .018b   |
| Anti-arrhythmia drugs     | 10.9% | 10.5%         | 1.0a    |
| Pacemaker (any use)       | 43.8% | 46.9%         | .182a   |

### Table 3. Fractions and odd-ratios (95% confidence limits) of postoperative in-hospital events together with long-term outcomes divided into graft types.

| Outcome                  | Vein     | Free arterial | p-Value | Crude OR | Adjusted OR |
|--------------------------|----------|---------------|---------|----------|-------------|
| Stroke                   | 14 (1.5) | 13 (1.4)      | .839    | 0.85 (0.38–1.88) | 0.77 (0.29–2.05) |
| New dialysis             | 11 (1.2) | 24 (2.5)      | .020    | 2.56 (1.18–5.52) | 2.81 (0.84–9.32) |
| Arrhythmia               | 261 (27.0) | 323 (32.7)   | .007    | 1.33 (1.08–1.62) | 1.32 (1.07–1.63) |
| CK-MB >100               | 33 (4.2) | 27 (3.3)      | .883    | 0.91 (0.51–1.63) | 0.95 (0.45–1.98) |
| Myocardial infarction    | 48 (4.9) | 48 (4.9)      | .834    | 1.07 (0.71–1.61) | 1.17 (0.74–1.85) |
| Re-exploration bleeding  | 38 (3.9) | 52 (5.3)      | .193    | 1.36 (0.89–2.09) | 0.89 (0.37–2.16) |
| 30-days                  | 9 (0.9)  | 18 (1.8)      | .112    | 2.00 (0.89–4.45) | 4.01 (0.57–27.9) |
| 6-months                 | 23 (2.3) | 31 (3.0)      | .332    | 1.36 (0.79–2.36) | 1.61 (0.75–3.45) |
| 1-year                   | 33 (3.3) | 37 (3.6)      | .716    | 1.13 (0.70–1.81) | 1.07 (0.59–1.95) |
| 5-years                  | 64 (6.8) | 75 (8.3)      | .275    | 1.22 (0.88–1.70) | 1.42 (0.97–2.07) |
| 10-years                 | 88 (11.6) | 97 (13.7)    | .314    | 1.16 (0.89–1.50) | 1.26 (0.94–1.68) |
| Mortality                |          |               |         |          |             |
| 30-days                  | 10 (1.0) | 19 (1.9)      | .136    | 1.90 (0.88–4.08) | 1.16 (0.39–6.92) |
| 6-months                 | 28 (2.7) | 32 (3.1)      | .699    | 1.14 (0.60–1.90) | 1.23 (0.61–2.52) |
| 1-year                   | 39 (3.8) | 40 (3.9)      | 1.0     | 1.02 (0.66–1.60) | 1.15 (0.64–2.06) |
| 5-years                  | 135 (14.3) | 135 (14.8)  | 1.0     | 1.00 (0.77–1.29) | 1.05 (0.78–1.41) |
| 10-years                 | 241 (31.9) | 232 (32.7)   | .876    | 0.98 (0.80–2.10) | 1.04 (0.83–1.31) |

Statistics: fractions: McNemar-test; crude/adjusted: conditional regression analysis with 95% confidence limits. Adjustment factors: perioperative vasoconstrictors and inotropes, year group (3 groups) and red blood cell transfusion (10 groups, units 0–9+).
the target vessel as free arterial grafts [14,15]. Alternatively, SVG patency has improved following greater use of guideline-based medical therapy, like aspirin, statins, beta-blockers and angiotensin-converting-enzyme-inhibitors, thus reducing the risk of SVGs failure [5]. Another reason for an improved SVGs patency could be the grafting technique. Dreifaldt and colleagues completed a randomized trial, where they demonstrated a very high angiographic patency rate of no-touch SVG compared to RA grafts [16]. However, this can only partly explain our results as only one center operates with a no-touch technique.

It is assumed that free arterial grafts demonstrate better patency and outcomes, if preparations for surgery have been done optimally regarding the proper choice of indications for arterial grafting, correct selection of artery harvesting technique, established optimal artery preparation together with target-vessel location and stenosis degree [14]. A review of 6 randomized trials comparing RA and SV as a second conduit, found that RA had a significantly lower rate of myocardial infarction and repeated revascularization and thus a better patency rate at the 5-years follow-up [17]. Our findings also demonstrate a significantly, although clinically unimportant, lower postoperative CKMB level using free arterial grafts. Crude data shows a higher incidence of in-hospital dialysis and arrhythmias in the free arterial group, but the finding was not persistent after adjustment.

Our findings of higher postoperative CKMB (>100 μg/L) being associated with a higher revascularization rate are not surprising. Local or global myocardial ischemia [18] may lead to myocardial necrosis and thus increase levels of CKMB. Ischemia and/or myocardial necrosis likely determine a higher revascularization rate and further, a high CKMB release might be an important predictor for graft occlusion [19].

**Strengths and limitations**

The primary strength of the study is the large cohort with prospectively reported data from a multi-institutional design. The detailed complete long-term follow-up data on all CABG patients during the 17-year period allow a robust estimation of the outcomes. In order to compensate for the time factor, time was included as an adjustment factor.

Our study has intrinsic limitations. As a register-based design, we cannot reject that additional effects of missing covariates and the lack of randomization, potentially increase the risk of confounding. However, propensity matching by adjusting a large number of covariates attenuates the differences and diminishes confounding, but despite the comprehensive covariate adjustment, the possibility of uncontrolled confounding remains. The imbalance in numbers between the two groups before matching has to be
considered, but almost all arterial grafts were included in the propensity match and the random numbering further diminishes the risk.

Yet another significant limitation was the fact that the causes of death are unknown. Due to the long observation time, the death rate may be independent of cardiac factors. However, the risk of repeated revascularization within the 10 years observation period without statistically significant differences can be used as an indicator of graft patency.

**Conclusion**

Our study demonstrates that free arterial graft equals SVG, with no significant differences in outcomes. Higher postoperative CKMB levels are significantly associated with repeated revascularization rate in free arterial grafts and SVG for 10 years. The revascularization rates call for new studies focusing on cause analysis.

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**References**

[1] Rehman SM, Yi G, Taggart DP. The radial artery: current concepts on its use in coronary artery revascularization. Ann Thorac Surg. 2013;96(5):1900–1909.

[2] Schwann TA, Hashim SW, Badour S, et al. Equipoise between radial artery and right internal thoracic artery as the second arterial conduit in left internal thoracic artery-based coronary artery bypass graft surgery: a multi-institutional study. Eur J Cardiothorac Surg. 2016;49(1):188–195.

[3] Schwann TA, Tranbaugh RF, Dimitrova KR, et al. Time-varying survival benefit of radial artery versus vein grafting: a multi-institutional analysis. Ann Thorac Surg. 2014;97(4):1328–1334.

[4] Gaudino M, Puskas JD, Di Franco A, et al. Three arterial grafts improve late survival. A meta-analysis of propensity-matched studies. Circulation. 2017;135(11):1036–1044.

[5] Janiec M, Dimberg A, Shafti TZN, et al. No improvements in long-term outcome after coronary artery bypass grafting with arterial grafts as a second conduit: a Swedish Nationwide Registry Study. Eur J Cardiothorac Surg. 2018;53(2):448–454.

[6] Tranbaugh RF, Schwann TA, Swistel DG, et al. Coronary artery bypass graft surgery using the radial artery, right internal thoracic artery, or saphenous vein as the second conduit. Ann Thorac Surg. 2017;104(2):553–559.

[7] Collins P, Webb CM, Chong CF, et al. Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. Circulation. 2008;117(22):2859–2866.

[8] Gaudino M, Benedetto U, Fremez S, et al. Radial-artery or saphenous-vein grafts in coronary-artery bypass surgery. N Engl J Med. 2018;378(22):2069–2077.

[9] Sousa-Uva M, Neumann F-J, Ahlsson A, et al. 2018 ESC/ EACTS guidelines on myocardial revascularization. Eur J Cardiothorac Surg. 2019;55(1):4–90.

[10] Samano N, Dashwood M, Souza D. No-touch vein grafts and the destiny of venous revascularization in coronary artery bypass grafting—a 25th anniversary perspective. Ann Cardiothorac Surg. 2018;7(5):681–685.

[11] Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. Eur J Cardiothorac Surg. 2012;41(4):734–735.

[12] Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. J Thorac Cardiovasc Surg. 2007;134(5):1128–1135.

[13] Affronti A, Ruel M, Gaudino MFL. Multiarterial coronary artery bypass grafting: is the radial artery fulfilling the unkept promise of the right internal thoracic artery? Curr Opin Cardiol. 2019;34(6):628–636.

[14] Leonard JR, Abouarab AA, Tam DY, et al. The radial artery: results and technical considerations. J Card Surg. 2018;33(5):213–218.

[15] Ruttmann E, Dietl M, Feuchtner GM, et al. Long-term clinical outcome and graft patency of radial artery and saphenous vein grafts in multiple arterial revascularization. J Thorac Cardiovasc Surg. 2019;158(2):442–450.

[16] Dreifaldt M, Mannion JD, Bodin L, et al. The no-touch saphenous vein as the preferred second conduit for coronary artery bypass grafting. Ann Thorac Surg. 2013;96(1):105–111.

[17] Schwann TA, Zacharias A, Riordan CJ, et al. Sequential radial artery grafts in multivessel coronary artery bypass graft surgery: 10-year survival and angiography results. Ann Thorac Surg. 2009;88(1):31–39.

[18] Overgaard CB, Dzavik V. Inotropes and vasopressors: review of physiology and clinical use in cardiovascular disease. Circulation. 2008;118(10):1047–1056.

[19] Niclauss L. Techniques and standards in intraoperative graft verification by transit time flow measurement after coronary artery bypass graft surgery: a critical review. Eur J Cardiothorac Surg. 2017;51(1):26–33.