The impact of a second arterial graft on 5-year outcomes after coronary artery bypass grafting in the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery Trial and Registry

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ABSTRACT

Objective: Despite various evidence supporting the advantages of multiple arterial grafting, inconsistencies in use of the procedure have resulted in high variability in the acceptance and practice of arterial grafting. The purpose of this study was to assess the effects of an arterial versus venous second grafts on outcomes at 5-year follow-up in the coronary artery bypass grafting population from the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) trial.

Methods: Patients (n = 1419) with an arterial graft to the left anterior descending artery and ≥ 1 other graft were included and divided according to the second graft's type: 2nd-graft-arterial group (n = 456) and 2nd-graft-venous group (n = 963). Five-year outcomes were compared between subgroups. Event rates were estimated with Kaplan-Meier analyses. Propensity-score matching was used, to control for selection bias due to nonrandom group assignment in a 1:1 manner, resulting in 432 pairs with balanced baseline characteristics.

Results: In unmatched groups, the 2nd-graft-arterial group had significantly lower rates of death (8.9% vs 13.1%; $P = .02$), and composite safety endpoint of death/stroke/myocardial infarction (13.3% vs 18.7%; $P = .02$), compared with the 2nd-graft-venous group. The rate of major adverse cardiac or cerebrovascular events was similar between groups (22.9% vs 25.5%; $P = .30$), because it includes the rate of repeat revascularization (12.6% in the 2nd-graft-arterial group vs 9.6% in the 2nd-graft-venous group; $P = .10$). After propensity-score matching, no statistically significant differences were found between groups.

Conclusions: This study reveals comparable 5-year outcomes with arterial and venous conduits as second grafts after an arterial graft anastomosed to the left anterior descending artery. This study demonstrates the multi-institutional variation in patient selection and operator technique with regard to arterial revascularization, although extended follow-up beyond 5 years is required to estimate its impact on long-term outcomes.

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Event rates of death and repeat revascularization before and after propensity matching.

Central Message

The choice of a second graft, in addition to the left internal mammary artery, should favor arterial conduits, when feasible.

Perspective

The main findings of this multicenter study highlight: (1) bias toward selecting arterial conduits; (2) technique variability in arterial grafting; and (3) comparable midterm clinical outcomes of use of arterial versus venous conduits as second grafts. These results support current clinical practice but require longer follow-up before definitive recommendations can be made.

See Editorial page 452.

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CK-MB	= creatinine kinase-MB
IMA	= internal mammary artery
LAD	= left anterior descending
MACCE	= major adverse cardiac or cerebrovascular events
SYNTAX	= Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery

Supplemental material is available online.

The left internal mammary artery graft (IMA) to the left anterior descending (LAD) artery is regarded as the “gold standard” for coronary artery bypass grafting (CABG).¹⁻⁴ The success of this procedure encouraged the use of multiple or total arterial grafting, in an attempt to increase the benefits of long-term graft patency and improve survival, by multiplying the number of conduits that have endothelial secretory properties.⁵ Numerous observational studies and meta-analyses documented the benefit of certain types and compositions of arterial grafts, such as the radial artery or use of both IMAs.^{6,7} However, bilateral IMA grafting has been associated with increased risk of sternal wound infection, and radial artery usage has been associated with an increased tendency toward spasm of the graft.^{8,9}

The impact of a second arterial graft on long-term outcome has not been conclusively proven by large randomized trials, and this uncertainty results in a low adoption rate of multiple arterial grafting,^{10,11} ranging from <4% to 31.5%. The objective of this study was to assess the effect of using a second arterial graft, on 5-year outcomes in patients who underwent CABG in the SYNTAX (Synergy Between PCI With TAXUS and Cardiac Surgery) trial and registry.

METHODS**Study Design**

The analysis of this study is based on the CABG population within the multinational-multicenter SYNTAX trial, which consisted of 897 patients randomized to CABG, and an additional 649 patients in the CABG registry who underwent 5-year follow-up.¹² The current study examines the “as-treated” CABG cohort (n = 1510). Patients with no arterial graft to the LAD artery (n = 72), and patients in whom only 1 graft was used

(n = 17), were excluded, resulting in a CABG population of 1419 patients. Overall 5-year follow-up was available for 1322 patients (93.2%).

All patients received an artery to the LAD artery. After this step was completed, the cohort was divided into 2 groups: a 2nd-graft-arterial group, with patients who received ≥ 1 arterial graft in addition to an artery to the LAD artery; and a 2nd-graft-venous group, with patients who received only venous grafts in addition to an artery to the LAD artery.

Coronary Artery Bypass Grafting Surgery

No limitations were imposed on the CABG technique, although strong recommendations were made to use complete revascularization and arterial revascularization, especially in patients aged <70 years.¹³ Complete revascularization was defined as bypassing all lesions with $\geq 50\%$ stenosis in vessels of ≥ 1.5 mm in diameter, as defined during the heart team conference.¹⁴ Further specifications included use of pedicled left or right IMA for the LAD artery and/or diagonal branches whenever feasible, and use of another mammary artery or arterial grafts for the remaining vessels.

Definitions

The primary outcomes for the SYNTAX trial have been defined previously. This subset analysis used the same outcome definitions: The primary composite endpoint of major adverse cardiac or cerebrovascular events (MACCE) included all-cause death, myocardial infarction, stroke, and repeat revascularization. The secondary endpoints consisted of the composite safety endpoint of all-cause death/stroke/myocardial infarction, as well as all the individual components of MACCE. Stroke was defined as focal neurologic deficits of central origin lasting >72 hours, resulting in permanent brain damage or body impairment.

Myocardial infarction was defined in relation to intervention status as follows: (1) after allocation but before treatment: Q-wave new pathologic Q-waves in ≥ 2 leads, lasting ≥ 0.04 seconds, with creatine kinase-MB (CK-MB) levels above normal and non-Q-wave myocardial infarction (elevation of CK levels to >2 times the upper limit of normal, with positive CK-MB, or elevation of CK levels to >2 times the upper limit of normal without new Q-waves if no baseline CK-MB was available); (2) <7 days after intervention: new Q-waves and either peak CK-MB/total CK >10%, or plasma level of CK-MB 5 times the upper limit of normal; and (3) ≥ 7 days after intervention: new Q-waves or peak CK-MB/total CK >10%, or plasma level of either CK or CK-MB 5 times the upper limit of normal. Repeat revascularization was defined as any CABG or percutaneous coronary intervention after the initial surgical treatment. Graft occlusion was defined as clinical presentation of acute coronary syndrome with confirmed occlusion within and/or adjacent to a previous graft during the follow-up period, and/or Q-wave myocardial infarction in the treated vessel territory within 30 days of the index procedure.

Statistical Methods

Continuous variables are given as mean $\pm$ SD, and compared using the Student *t* test. Discrete variables were expressed as counts and percentages, and comparisons between groups were done with χ^2 analysis or the Fisher exact test, as appropriate. Kaplan-Meier estimates were used to assess cumulative event-free rates, and differences between groups were analyzed using the log-rank test.

Propensity score-adjusted analysis was used to control for selection bias caused by nonrandom group assignment. The propensity score was calculated using nonparsimonious logistic regression with 2nd-graft-arterial or 2nd-graft-venous as the binominal dependent variable. The probability of being assigned to 1 of the 2 groups was calculated based on 18 pre-procedural variables (Appendix 1).

Correlations between variables were explored and used as interaction terms when the correlation was found to be significant. The c-statistic was used to assess the predictive ability of the model (c = 0.688, 95%

confidence interval = 0.658-0.718). Two groups were selected, using 1:1 propensity-score matching with a caliper width of 0.2 of the logit of the estimated propensity score, which resulted in 432 matched pairs (maximum caliper = 0.185 between matched patients).¹⁵

To further improve precision of the matching, the propensity score was additionally used in a 1:2 manner, resulting in groups of 337:674 patients.¹⁶ However, results were similar to those for the 1:1 matched groups, and only the analyses from the 1:1 matched groups is reported, because of a higher number of matched groups. Comparisons between the matched groups were done using the McNemar test and the paired-sample *t* test or Wilcoxon signed-rank test when appropriate. Absolute standardized differences were computed for all measured covariates and found to be <10%, suggesting considerable covariate balance across the groups.¹⁷ Missing values were imputed using multiple imputations, with the assumption of missing data being random.

Statistical analysis was performed on the imputed datasets and verified with complete case analyses without imputations, which yielded similar results. A *P* value of <.05 was considered to be statistically significant for all analyses. Statistical analyses were performed using SPSS, version 20.0, statistical software (SPSS Inc, Chicago, Ill). Propensity-score matching was performed using SAS, version 9.3, software (Cary, NC).

RESULTS

Population and Coronary Artery Bypass Grafting Characteristics

The risk profile of patients in the 2nd-graft-arterial group, compared with the 2nd-graft-venous group was lower (Table 1), comprising younger (62.3 ± 9.7 vs 66.4 ± 9.2 , respectively; $P < .001$) patients with lower logistic euroSCOREs (European System for Cardiac Operative Risk Evaluation) (2.9 ± 2.9 vs 4.3 ± 4.7 , respectively; $P < .001$). The groups were comparable in terms of complexity of coronary artery disease as described by the SYNTAX score (32.2 ± 12.9 and 33.2 ± 12.8 , respectively; $P = .16$), although the 2nd-graft-arterial group, as opposed to the 2nd-graft-venous group, had a lower presence of diffuse/small-vessel disease (21.4% vs 27.3%; $P = .02$) and chronic total occlusions (31.7% vs 38.8%; $P = .01$).

No differences were found in the mean number of distal anastomoses, number of grafts per patient, or completeness of revascularization between the 2 groups (Table 2). A higher rate of off-pump CABG in the 2nd-graft-arterial group (21.9% vs 13.9% in the 2nd-graft-venous group; $P < .001$). Bypass time and cross-clamp time were significantly longer in the 2nd-graft-arterial group. The mean postprocedure hospital stay was longer in the 2nd-graft-arterial group (9.8 ± 8.6 vs 8.5 ± 6.2 ; $P = .004$).

In the 2nd-graft-arterial group, the left IMA was used to bypass the LAD artery in 82.2% of cases, whereas in 16.9% of cases, the right IMA, and in 0.9% of cases, the radial artery was used for the LAD target, with the left IMA still used for a more-distant anastomosis. In the 2nd-graft-venous group, in 99.6% of cases, the left IMA was used for an anastomosis to the LAD artery. Based on the lesion classification used in the SYNTAX score, a generalized model of the graft type distribution, per location of the distal anastomosis, is presented (Table 3).

In the 2nd-graft-arterial group, venous grafts were used as well, when the available arterial grafts were deemed insufficient to achieve the required revascularization. The configuration of grafts in the 2nd-graft-arterial group was: left IMA + radial artery in 25.2%; bilateral IMA in 58.3%; and bilateral IMA + radial artery in 15.8%. Total arterial revascularization was performed in 47.6% of patients (Figure 1).

Incidence of Major Adverse Cardiac or Cerebrovascular Events and Components

At 5-year follow-up, the incidence of MACCE in the whole CABG cohort was 25.7%. The incidence of MACCE did not differ significantly between the 2nd-graft-arterial and the 2nd-graft-venous groups (22.9% vs 25.1%, respectively; $P = .30$) (Table 4). Within the 2nd-graft-arterial group, no difference in long-term outcomes was found in patients with the left versus right IMA anastomosed to the LAD artery (data not shown).

However, in the 2nd-graft-arterial group, the cumulative incidence of the composite safety endpoint was lower (13.3% vs 18.7%; $P = .017$), as well as the all-cause death rate (8.9% vs 13.1%; $P = .024$) (Figure 2). The frequencies of stroke, myocardial infarction, and graft occlusion were similar between the groups. A trend for higher repeat revascularization rate was observed in the 2nd-graft-arterial group (12.6% vs 9.6% in the 2nd-graft-venous group, $P = .10$), mainly owing to repeat percutaneous coronary intervention revascularization (Figure 3).

Propensity-Matched Groups

Based on the propensity score, we were able to create 1:1-matched pairs, a total of 432. No significant differences were found between groups after matching (Table 1), and the absolute standardized differences were <10% for all variables (Figure E1).

The incidence of MACCE and its individual components was similar between the groups after matching (Table 4). The 2nd-graft-arterial and 2nd-graft-venous groups were no longer significantly different in the incidence of the composite safety endpoint (13.5% vs 15.0%, respectively; $P = .56$) or all-cause death (9.1% vs 9.5%, respectively; $P = .84$) (Figure 2), or in any of the individual components (Figure 3).

DISCUSSION

This study shows that in the unmatched group analysis, there was a significant difference in favor of arterial grafts, with lower rates of the composite safety endpoint, and improved survival at 5-year follow-up. However, after propensity matching, no benefit was derived from arterial grafting.

The long-term outcome is considered to be dependent on the endurance of the coronary artery bypass, which is in fact

TABLE 1. Baseline characteristics

Characteristics	Unmatched groups			Groups matched by propensity score		
	2nd-graft-arterial (n = 456)	2nd-graft-venous (n = 963)	P value	2nd-graft arterial (n = 432)	2nd-graft venous (n = 432)	P value
Age (y)	62.3 ± 9.7	66.4 ± 9.2	<.001	63.0 ± 9.1	62.8 ± 9.4	.51
Gender, female	13.5 (61)	22.1 (213)	<.001	14.1 (61)	16.7 (72)	.31
Coronary risk factors						
Family history of CAD	29.5 (127)	28.4 (261)	.66	29.6 (120)	31.9 (132)	.70
Hypertension	74.7 (336)	75.0 (714)	.89	75.2 (325)	73.4 (317)	.57
Hyperlipidemia	78.9 (355)	76.3 (723)	.28	78.9 (341)	79.6 (344)	.87
Diabetes mellitus	25.2 (115)	29.8 (287)	.07	26.4 (114)	24.5 (106)	.56
Smoking history	26.0 (118)	20.6 (197)	.02	24.2 (104)	23.5 (101)	.83
Perioperative risk factors						
Previous MI	27.1 (125)	35.6 (337)	.004	28.5 (123)	28.0 (121)	.94
Previous CHF	2.2 (10)	6.6 (63)	<.001	2.3 (10)	1.6 (7)	.58
Unstable angina	25.2 (115)	25.4 (245)	.96	25.2 (102)	26.6 (115)	.71
Critical pre-procedural state	0.4 (2)	1.9 (18)	.03	0.5 (2)	0.2 (1)	>.99
PAD	10.7 (49)	12.4 (119)	.38	11.1 (48)	10.6 (46)	.91
Carotid artery disease	9.9 (45)	9.6 (92)	.85	10.0 (43)	9.5 (41)	.91
CVA/TIA	8.4 (38)	9.0 (86)	.67	7.9 (34)	8.3 (36)	.90
COPD	7.5 (34)	8.7 (84)	.42	7.6 (33)	6.7 (29)	.70
Renal impairment	1.1 (5)	1.8 (17)	.49	1.2 (5)	1.2 (5)	>.99
BMI	27.8 ± 4.2	28 ± 4.6	.46	27.9 ± 4.3	27.6 ± 4.2	.31
Parsonnet score	6.6 ± 5.7	9.3 ± 7.1	<.001	6.8 ± 5.8	6.6 ± 5.7	.56
EuroSCORE (additive)	3.1 ± 2.4	4.1 ± 2.7	<.001	3.2 ± 2.4	3.2 ± 2.3	.89
EuroSCORE (logistic)	2.9 ± 2.9	4.3 ± 4.7	<.001	2.9 ± 2.9	2.9 ± 2.8	.75
Cardiac variables						
Angina assessment						
Stable angina	56.0 (260)	61.4 (592)	.10	58.3 (252)	59.3 (256)	.84
Unstable angina	25.2 (115)	25.4 (245)	.96	25.2 (102)	26.6 (115)	.71
Silent ischemia	10.3 (47)	7.5 (72)	.07	9.3 (40)	7.2 (31)	.32
No angina	7.5 (34)	5.6 (54)	.18	7.2 (31)	6.9 (30)	>.99
Impaired LVEF (<50% EF)	15.1 (69)	26.0 (250)	<.001	16.0 (69)	16.2 (70)	>.99
Coronary complexity						
Left dominance	14.0 (64)	16.3 (157)	.28	14.6 (63)	16.2 (70)	.58
Diffuse/small VD	21.3 (97)	27.1 (261)	.02	21.8 (94)	23.4 (101)	.61
LM disease, any	39.5 (180)	43.3 (417)	.17	40.3 (174)	39.1 (169)	.78
3VD	79.2 (361)	76.1 (732)	.20	78.7 (340)	79.6 (344)	.81
LM disease only	4.2 (19)	3.0 (29)	.40	4.2 (18)	3.0 (13)	.46
LM + 1VD	6.4 (29)	7.2 (69)	.56	6.7 (29)	6.9 (30)	>.99
LM + 2VD	9.0 (41)	12.1 (116)	.06	9.0 (39)	8.8 (38)	>.99
LM + 3VD	20.0 (91)	21.1 (203)	.54	20.4 (88)	20.4 (88)	>.99
2VD only	1.3 (6)	1.6 (15)	.73	1.4 (6)	1.6 (7)	>.99
3VD only	59.2 (270)	55.1 (530)	.10	58.3 (252)	59.3 (256)	.84
Any chronic total occlusion	31.7 (143)	38.7 (368)	.01	33.1 (143)	33.6 (145)	.94
Number of coronary lesions/patient	4.4 ± 1.8	4.4 ± 1.8	.99	4.35 ± 1.7	4.36 ± 1.7	.96
SYNTAX score	32.2 ± 12.9	33.2 ± 12.8	.16	32.4 ± 12.8	32.1 ± 11.9	.89

Values are shown as mean ± SD (n) or % (n/N), unless otherwise noted. CAD, Coronary artery disease; MI, myocardial infarction; CHF, cardiac heart failure; PAD, peripheral artery disease; CVA/TIA, cerebrovascular attack/transient ischemic attack; COPD, chronic obstructive pulmonary disease; BMI, body mass index; euroSCORE, European System for Cardiac Operative Risk Evaluation; LVEF, left ventricular ejection fraction; EF, ejection fraction; LM, left main; VD, vessel disease; SYNTAX, Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery.

a complex combination of techniques to match a certain graft type with its appropriate target vessel. Although technically more demanding, and with a slightly higher risk of sternal wound complications, the use of bilateral IMAs with pedicled or skeletonized harvesting has been

associated with fewer repeated cardiac events, a lower rate of repeated revascularization, and a higher survival rate.¹⁸ A meta-analysis comparing bilateral IMA and single IMA grafting revealed a survival benefit of bilateral IMA grafting in studies with a mean period of follow-up of

TABLE 2. Surgical characteristics

Characteristics	Unmatched groups			Groups matched by propensity score		
	2nd-graft-arterial (n = 456)	2nd-graft-venous (n = 963)	P value	2nd-graft-arterial (n = 432)	2nd-graft-venous (n = 432)	P value
Number of distal anastomoses per patient	3.36 ± 0.9	3.42 ± 0.9	.25	3.36 ± 0.9	3.45 ± 0.9	.12
2	15.7	15.4	.89	16.4	14.1	.39
3	44.8	40.3	.11	43.8	40.0	.31
4	28.9	33.2	.11	29.2	34.7	.10
5	10.6	11.2	.75	10.6	11.1	.91
Number of grafts per patient	2.8 ± 0.7	2.8 ± 0.8	.27	2.8 ± 0.8	2.9 ± 0.7	.13
2	32.9	35.8	.28	32.2	34.3	.56
3	55.4	46.1	.001	54.4	45.8	.019
4	11.7	18.1	.002	13.0	19.9	.010
Distal anastomosis from Y graft	26.7	2.1	<.001	26.6	2.3	<.001
Distal anastomosis from jump-graft	35.1	36.3	.67	35.9	36.8	.83
Off-pump CABG	21.9	13.9	<.001	21.5	13.9	.005
Cardioplegia use						
Blood cardioplegia	49.9	45.5	.096	50.5	46.3	.26
Crystalloid cardioplegia	24.5	38.6	<.001	24.3	38.7	<.001
Complete revascularization	67.5	70.6	.25	67.6	70.1	.46
Bypass time (min)	92.7 ± 31.7	87.8 ± 35.9	.03	92.1 ± 31.4	86.5 ± 37.4	.043
Cross-clamp time (min)	62.3 ± 24.6	55.9 ± 35.7	.004	62.1 ± 24.6	54.3 ± 27.0	.001
Postprocedure hospital stay (d)	9.8 ± 8.6	8.5 ± 6.2	.004	9.9 ± 8.8	8.3 ± 6.6	.003
Medication at discharge						
Aspirin	91.7	86.9	.009	92.6	86.3	.004
Thienopyridine derivative	19.5	17.1	.27	19.2	17.1	.47
Coumadin derivative	4.6	9.3	.002	4.9	9.3	.017
Statins	72.1	71.1	.69	72.5	72.2	>.99
Calcium-channel antagonists	24.1	17.9	.006	23.4	16.7	.015

Values are shown as mean ± SD, or %, unless otherwise noted. CABG, Coronary artery bypass graft.

≥9 years.¹⁹ In case the right, in addition to the left, IMA is not feasible or desired, arterial grafting using the radial artery may be an alternative. Many studies claim improved graft patency and survival rate related to radial artery use, but results from randomized controlled trials are rather controversial.²⁰⁻²²

Total arterial grafting is the next step in achieving adequate revascularization with maximum benefit for each target vessel. Several observational studies on total arterial revascularization describe perioperative mortality and morbidity rates similar to those with conventional CABG, with long-term results favoring total arterial

revascularization.²³⁻²⁵ A recent multicenter analysis comparing total arterial revascularization with single IMA showed a significant survival benefit over a period of 15 years.²⁵ After adjustments for selection bias of older and more-unstable patients in the single IMA group, improved long-term survival was evident with total arterial revascularization. When differentiated by type and distal target-vessel, patency seems to be translated into the long-term outcomes, according to the combination of grafts used.²⁶

Many of the published studies in favor of arterial grafting, whether regarding an additional IMA, a radial

TABLE 3. Distribution of conduits by location of distal anastomosis

	2nd-graft-arterial group (n = 456)							2nd-graft-venous group (n = 963)						
	LAD	Diag	LCxA	OMA	PLA	RCA	PDA	LAD	Diag	LCxA	OMA	PLA	RCA	PDA
LIMA	82.2	3.1	3.2	12.3	2.2	0.4	—	99.6	1.3	—	—	—	—	—
RIMA	16.9	0.2	5.5	34.9	6.6	10.1	3.5	0.3	—	—	—	—	—	—
RA	0.9	—	3.9	22.2	6.8	5.7	11.4	0.1	—	—	—	—	—	—
SV	—	0.2	2.0	8.3	7.0	17.5	21.7	—	2.6	—	—	—	—	—
Total	100	3.5	14.6	77.7	22.6	32.7	36.0	100	3.9	10.1	77.8	23.6	41.8%	30.7%

Values are given as %. An anatomic description of the specific locations of distal anastomosis is provided in Figure E1. LAD, Left anterior descending; Diag, diagonal; LCxA, left circumflex artery; OMA, obtuse marginal artery; PLA, postero-lateral artery; RCA, right coronary artery; PDA, posterior descending artery; LIMA, left internal mammary artery; RIMA, right internal mammary artery; RA, radial artery; SV, saphenous vein.

FIGURE 1. The diagram shows the use of arterial and venous grafts in relation to placement of distal anastomoses. The percentage of arterial grafts is shown in red, and of venous grafts in blue. LCx, Left circumflex artery; LAD, left anterior descending; Diag, diagonal; RCA, right coronary artery; OM, obtuse marginal artery; PDA, posterior descending artery; PL, postero-lateral artery.

artery, or both, are based on single-center experiences, implying a particular decision algorithm, followed by a preferred CABG technique. The results of the present study must be seen in the light of a multicenter CABG cohort with complex coronary disease, for whom revascularization was performed according to the personal experience of the surgeon, and local practices. The result was a high level of heterogeneity of CABG techniques, which shows varying opinion of the best “graft-target match” across centers.

The success of arterial grafting often is explained by the physiologic properties of the graft and the local anatomic characteristics of the anastomosis, but in the clinical setting, a surgeon’s technique and experience may be of equal or greater importance for the long-term patency rates. For

each individual, complex coronary disease requires a compromise between conduit type, complex grafting, and completeness of revascularization.²⁷ Recommendations have been made regarding the issues described, but they vary among centers, and their impact on outcome remains unknown. Variations in acceptance, experience, and approach relating to use of multiple arterial conduits could explain why the benefits of arterial grafting are diminished when analyzed at this multinational multicenter scale.

Despite the fact that the left-IMA-to-LAD-artery procedure is considered the gold standard, only 82.2% of the patients in the 2nd-graft-arterial group received this procedure; the rest received another artery to LAD artery (16.9% right IMA; 0.9% radial artery). One should judge these rates as a compromise between grafts in the context of multiple arterial grafting, while acknowledging that grafting of the left IMA to the LAD artery is not 100% achievable, even with single artery use.²⁸

The differences found in favor of arterial grafting in the unmatched groups analyses can be explained by the lower risk profile of patients who received a second arterial graft as opposed to a venous graft. This finding was not surprising, given that arterial grafting is technically more demanding, which translates into longer bypass time and cross-clamp time, and automatically precludes higher-risk patients from receiving more arterial grafts.

Additionally, patients in the 2nd-graft-arterial group had a longer postprocedure hospital stay, which could be seen as an indicator of other complications, not evaluated by the primary or secondary endpoints of the present study. Although arterial grafting in general does not increase perioperative risk,^{29,30} in other studies, the use of bilateral IMA grafts has been associated with a higher incidence of sternal wound infections,⁸ resulting in longer postprocedure hospital stays.

Contrary to our expectations, no difference was found in the repeat revascularization rate between the groups. In both

TABLE 4. Incidence of major adverse cardiac and cerebrovascular events at 5-year follow-up

Variable	Cumulative incidence Kaplan-Meier analysis					
	Unmatched groups			Groups matched by propensity score		
	2nd-graft-arterial (n = 456)	2nd-graft-venous (n = 963)	P value	2nd-graft-arterial (n = 432)	2nd-graft-venous (n = 432)	P value
MACCE	22.9	25.5	.30	23.3	21.4	.56
Death/Stroke/MI	13.3	18.7	.017	13.5	15.0	.56
Death	8.9	13.1	.024	9.1	9.5	.84
Stroke	3.2	4.8	.19	2.9	3.2	.82
MI	2.9	3.9	.38	2.8	4.5	.20
Revascularization	12.6	9.6	.10	13.0	9.3	.12
PCI revascularization	11.8	9.1	.14	12.1	8.8	.16
CABG revascularization	0.9	0.7	.77	0.9	0.9	.99
Graft occlusion	3.2	4.3	.42	3.4	3.9	.68

Values are given as %, unless otherwise noted. MACCE, Major adverse cardiac and cerebrovascular event; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

FIGURE 2. Kaplan-Meier cumulative event curves at 5-year follow-up. Event rates and comparisons are depicted for: all-cause death in the (A) unmatched groups, and (B) matched groups; and for repeat revascularization in the (C) unmatched groups, and (D) matched groups.

unmatched and matched analysis, a trend was found toward higher incidence of repeat revascularization in the 2nd-graft-arterial group, mostly because of percutaneous coronary intervention revascularization. The higher rate of off-pump procedures in the 2nd-graft-arterial group may have played a role; it has been associated with increased repeat revascularization rates. Additional analysis failed to show off-pump CABG to be a confounder of arterial grafting, in relation to reintervention, in our study. This result suggests that arterial grafting to a non-LAD target has its own additional risk for revascularization that resides in both intrinsic features and technical difficulty. Nevertheless, these results are a cumulative measure of the grafts' effects on repeat revascularization, because both arterial and venous grafts were used to achieve revascularization in the 2nd-graft-arterial group. Although the current use of statins and aspirin after CABG improves venous graft patency,^{31,32} the infrequent administration of

calcium-channel blockers could negatively influence patency in arterial grafts.^{33,34}

We may conclude only that proving an advantage of arterial grafting is rather difficult in a trial comparing percutaneous coronary intervention with CABG, such as SYNTAX. Long-term results supported by the randomized Arterial Revascularisation Trial trial are still awaited, to define the role of bilateral IMA when it is deployed to the LAD artery and the next left-sided target-vessel, with the remaining lesions treated with venous or radial artery grafts.³⁵ Meanwhile, our study provides evidence that midterm results are not influenced by the choice of a second graft, provided that the LAD artery is bypassed by an arterial conduit.

Study Limitations

Despite being based on data from the multinational SYNTAX trial, the present study is a post hoc analysis

FIGURE 3. Kaplan-Meier cumulative event curves at 5-year follow-up. Event rates and comparisons are depicted for: PCI repeat revascularization in the (A) unmatched and (B) matched groups; MI in the (C) unmatched and (D) matched groups; and graft occlusion in the (E) unmatched and (F) matched groups. *PCI*, Percutaneous coronary intervention; *MI*, myocardial infarction.

that compels careful consideration of the results, because patients were not randomized between the groups who had an arterial versus a venous second graft. Another limitation of the study is that the degree of stenosis in the target vessel was not accounted for; which has particular implications in the case of arterial grafting. Angiography

was not systematically performed to assess graft patency, and the associated repeated revascularization is rather a subjective measure, because it describes graft patency within the limit of clinical significance. Furthermore, studies have suggested that the benefit of arterial grafts is seen in particular with follow-up of >10 years.³⁶ Therefore,

a 5-year follow-up period may be too short to reach the point where the difference in patency significantly influences survival.

CONCLUSIONS

In the CABG population from the SYNTAX trial and registry, the use of a second arterial versus venous graft did not result in a survival benefit at 5-year follow-up in a propensity-matched cohort. This study demonstrates the multi-institutional variation that occurs in patient selection and operator technique with regard to arterial revascularization, although extended follow-up beyond 5 years is required to estimate its impact on long-term outcomes.

Conflict of Interest Statement

Dr Dawkins is a full-time employee of Boston Scientific Corporation. Dr Feldman has received fees for consulting or serving on advisory boards, from Boston Scientific Corporation. All other authors have nothing to disclose with regard to commercial support.

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Key Words: coronary artery bypass, arterial graft, venous graft, SYNTAX

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APPENDIX 1. VARIABLES ENTERED IN THE MULTIVARIATE ANALYSIS

The variables entered in the multivariate analysis are: age, gender, medically treated diabetes mellitus, body mass index, smoking, hypertension, hyperlipidemia, previous myocardial infarction, previous cardiac heart failure,

unstable angina, previous cerebrovascular attack/transient ischemic attack, peripheral vessel disease, renal impairment, critical pre-procedural state, impaired left ventricular ejection fraction, diffuse disease, any total occlusion, and number of lesions per patient.

FIGURE E1. Love plot for absolute standardized differences before and after propensity-score matching. *BMI*, Body mass index; *Fam HCAD*, familial history of coronary artery disease; *MI*, myocardial infarction; *CHF*, cardiac heart failure; *PAD*, peripheral artery disease; *CaAD*, carotid artery disease; *CVA/TIA*, cerebrovascular attack/transient ischemic attack; *COPD*, chronic obstructive pulmonary disease; *LVEF*, left ventricular ejection fraction; *LM*, left main; *VD*, vessel disease; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *SYNTAX*, Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery.