Saphenous vein versus right internal thoracic artery as a Y-composite graft: Five-year angiographic and clinical results of a randomized trial

Min-Seok Kim, MD, PhD,[a] Ho Young Hwang, MD, PhD,[a] Jun Sung Kim, MD,[a] Se Jin Oh, MD, PhD,[a] Myoung-jin Jang, PhD,[b] and Ki-Bong Kim, MD, PhD[a]

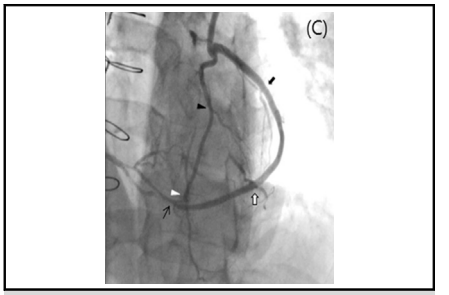
ABSTRACT

Objectives: We compared the 5-year graft occlusion rates and midterm clinical outcomes of saphenous vein composite grafts with those of right internal thoracic artery composite grafts in patients who were enrolled in the SAphenous VEin versus Right Internal Thoracic Artery as a Y-Composite Graft trial.

Methods: Of 224 eligible patients with multivessel coronary artery disease who were randomized to undergo off-pump revascularization using the saphenous vein (saphenous vein group, n = 112) or right internal thoracic artery (right internal thoracic artery group, n = 112) as Y-composite grafts based on the in situ left internal thoracic artery from September 2008 to October 2011, 219 patients (saphenous vein group, n = 109; right internal thoracic artery group, n = 110) entered the analysis. A third limb conduit to lengthen the graft limb for complete revascularization was used in 47 patients (saphenous vein group vs right internal thoracic artery group, 8 vs 39). Postoperative 5-year (61.7 ± 5.2 months) angiograms were performed in 186 patients (84.9%; saphenous vein group = 95; right internal thoracic artery group = 91). Follow-up was complete in 97.7% (214/219) of patients with a median follow-up of 80.7 months.

Results: The overall graft occlusion rate was 3.6% at 5 years (3.5% in the saphenous vein group vs 3.7% in the right internal thoracic artery group, $P = .910$). The 5-year occlusion rate of the second limb conduits in the saphenous vein group was 4.3% and was noninferior to that of the right internal thoracic artery group (2.4%) within the 95% 2-sided confidence interval of −1.4% to 5.2% ($P < .001$ for noninferiority). No statistically significant differences were found in the overall survival ($P = .439$) and the freedom from major adverse cardiac and cerebrovascular event rates ($P = .354$) at 5 and 8 years between the 2 groups.

Conclusions: The saphenous vein composite grafts were noninferior to the right internal thoracic artery composite grafts in terms of 5-year graft occlusion rates and midterm clinical outcomes. (J Thorac Cardiovasc Surg 2018;156:1424-33)



Patent SV Y-composite graft based on the left ITA at 5-year angiography.

Central Message

The SV composite grafts were noninferior to the RITA composite grafts in terms of 5-year graft occlusion rates and midterm clinical outcomes.

Perspective

In the present extended SAVE RITA trial, the occlusion rate and clinical results of minimally manipulated SV composite grafts showed no statistically significant differences compared with those of RITA composite grafts.

See Editorial Commentary page 1434.

See Editorial page 1408.

Although the saphenous vein (SV) is still a widely used conduit for coronary artery bypass grafting (CABG), it has disadvantages of declining patency with time and resulting worse clinical outcomes compared with patency and

Scanning this QR code will take you to a supplemental video, figure, and table. To view the AATS Annual Meeting Webcast, see the URL next to the webcast thumbnail.

From the [a]Department of Thoracic and Cardiovascular Surgery, and [b]Medical Research Collaborating Center, Seoul National University Hospital, Seoul, Korea.

ClinicalTrials.gov ID of the SAVE RITA trial: NCT01051986

Date and number of Institutional Review Board approval of the SAVE RITA trial: September 4, 2008, H-0803-024-237. Date and number of Institutional Review Board approval for this follow-up study: April 17, 2017, H-1704-045-844.

Read at the 97th Annual Meeting of The American Association for Thoracic Surgery, Boston, Massachusetts, April 29-May 3, 2017.

Received for publication Sept 24, 2017; revisions received April 7, 2018; accepted for publication April 10, 2018; available ahead of print July 6, 2018.

Address for reprints: Ki-Bong Kim, MD, PhD, Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea (E-mail: kimkb@snu.ac.kr).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2018.04.123

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
ITA = internal thoracic artery
ITT = intention-to-treat
MACCE = major adverse cardiac and cerebrovascular events
MDCT = multidetector computed tomography
OPCAB = off-pump coronary artery bypass grafting
PP = per protocol
RITA = right internal thoracic artery
SAVE RITA = SAphenous VEin versus Right Internal Thoracic Artery as a Y-Composite Graft
SV = saphenous vein

outcomes of the internal thoracic artery (ITA) conduit.[1] In a long-term review of aortocoronary SV bypass grafts, Fitzgibbon and colleagues[2] showed that SV patency was 75% at 5 years and 50% at 15 years or more postoperatively. Recent randomized trials also have demonstrated unsatisfactory patency rates for aortocoronary SV bypass grafts harvested with conventional methods: Patency rates were 86.4% at 5 years and 81.4% at 7.7 years.[3,4] To overcome the limitations of SV conduits, we have suggested that revascularization using a minimally manipulated SV harvesting technique and using an SV conduit as a composite graft based on the left ITA may have comparable early results when compared with revascularization using a right ITA (RITA) composite graft.[5,6]

The aim of the present study was to compare 5-year occlusion rates and midterm clinical outcomes in patient groups enrolled in the SAphenous VEin versus Right Internal Thoracic Artery as a Y-composite graft (SAVE RITA) trial, which was designed to compare the SV with the RITA when each was used as a Y-composite graft based on the in situ left ITA in patients undergoing CABG.

MATERIALS AND METHODS

The SAVE RITA trial was a randomized, controlled, open-label clinical trial with a primary end point of the 1-year angiographic patency rate of distal anastomoses performed with a side-arm composite graft (SV or RITA) (ClinicalTrials.gov identifier:NCT01051986). The institutional review board approved the SAVE RITA trial study protocol (approval no. H-0803-024-237), and all study patients provided informed consent. For this follow-up study, the study protocol was reviewed by the Institutional Review Board and approved as a minimal risk retrospective study (approval no. H-1704-045-844) that did not require individual consent based on the institutional guidelines for waiving consent.

Study Design

The study design of the SAVE RITA trial has been described.[5] Patients (aged 40-75 years) who were scheduled to undergo off-pump CABG (OPCAB) for multivessel coronary artery disease using a Y-composite graft based on the in situ left ITA were evaluated for eligibility. The exclusion criteria included ineligible Y-composite graft revascularization, an unavailable RITA or SV, left ventricular dysfunction (ejection fraction ≤25%), chronic renal failure requiring renal replacement therapy, previous

TABLE 1. Baseline characteristics, risk factors, and operative data of the study patients

	ITT population				PP population			
	Total (n = 224)	SV group (n = 112)	RITA group (n = 112)	*P**	Total (n = 219)	SV group (n = 109)	RITA group (n = 110)	*P**
Age (y), median (IQR)	63.5 (57.5, 70)	64 (59, 70)	63 (56, 69.5)	.574	64 (57, 70)	64 (59, 70)	63.5 (56, 70)	.725
Female, n (%)	50 (22.3)	29 (25.9)	21 (18.8)	.199	48 (21.9)	27 (24.8)	21 (19.1)	.310
Risk factors, n (%)								
Smoking	112 (50.0)	58 (51.8)	54 (48.2)	.593	109 (49.8)	57 (52.3)	52 (47.3)	.457
Hypertension	156 (69.6)	80 (71.4)	76 (67.9)	.561	153 (69.9)	79 (72.5)	74 (67.3)	.401
Diabetes mellitus	97 (43.3)	46 (41.1)	51 (45.5)	.500	96 (43.8)	45 (41.3)	51 (46.4)	.449
Dyslipidemia	91 (40.6)	52 (46.4)	39 (34.8)	.077	89 (40.6)	50 (45.9)	39 (35.5)	.117
Overweight (BMI ≥25)	104 (46.4)	52 (46.4)	52 (46.4)	1.000	102 (46.6)	51 (46.8)	51 (46.4)	.950
History of stroke	31 (13.8)	13 (11.6)	18 (16.1)	.333	31 (14.2)	13 (11.9)	18 (16.4)	.346
Unstable angina	165 (73.7)	83 (74.1)	82 (73.2)	.879	163 (74.4)	82 (75.2)	81 (73.6)	.787
LMD with or without peripheral disease	85 (37.9)	42 (37.5)	43 (38.4)	.890	85 (38.8)	42 (38.5)	43 (39.1)	.932
3-vessel disease with or without LMD	179 (79.9)	89 (79.5)	90 (80.4)	.868	175 (79.9)	87 (79.8)	88 (80.0)	.973
LVEF by TTE (%), median (IQR)	58 (52.5, 64)	58 (53.5, 65)	57 (50, 63)	.115	58 (52, 64)	58 (54, 65)	57 (50, 63)	.136
No. of distal anastomoses, median (IQR)								
Per patient	4 (3, 4)	4 (3, 4)	4 (3, 4)	.657	4 (3, 4)	4 (3, 4)	4 (3, 4)	.779
Per the LITA	1 (1, 1)	1 (1, 1)	1 (1, 1)	.717	1 (1, 1)	1 (1, 1)	1 (1, 1)	.580
Per the second conduit	2 (2, 2.5)	2 (2, 3)	2 (1, 2)	.003	2 (2, 3)	2 (2, 3)	2 (1, 2)	.002
Per the third conduit	0 (0, 0)	0 (0, 0)	0 (0, 1)	<.001	0 (0, 0)	0 (0, 0)	0 (0, 1)	<.001

ITT, Intention-to-treat; *PP*, per protocol; *SV*, saphenous vein; *RITA*, right internal thoracic artery; *IQR*, interquartile range; *BMI*, body mass index; *LMD*, left main disease; *LVEF*, left ventricular ejection fraction; *TTE*, transthoracic echocardiography; *LITA*, left internal thoracic artery. **P* values were obtained from Wilcoxon rank-sum tests for continuous variables and from chi-square tests for categoric variables.

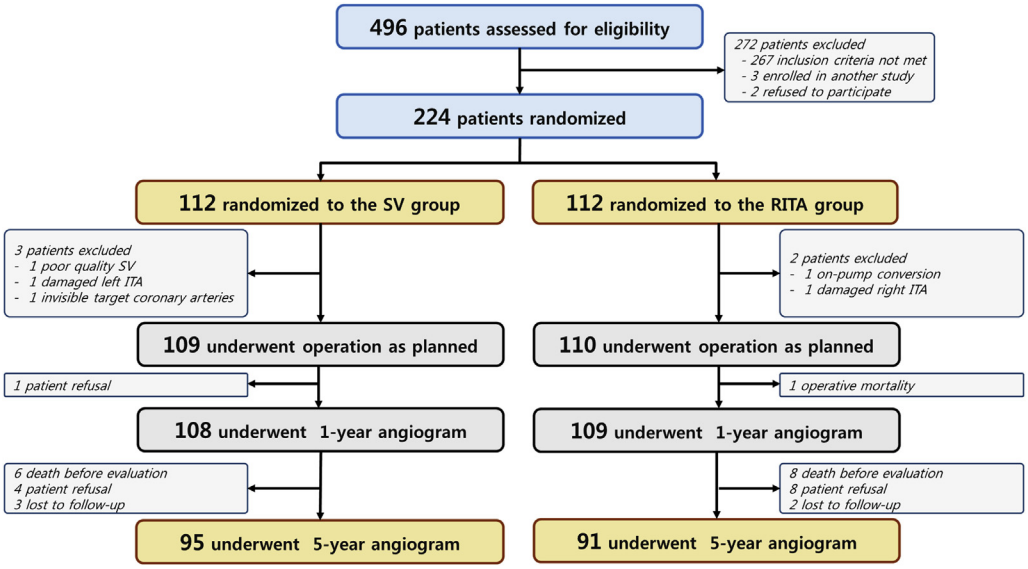


FIGURE 1. Summary flow diagram of participants. *SV*, Saphenous vein; *RITA*, right internal thoracic artery; *ITA*, internal thoracic artery.

cardiac surgery, emergency operation, or a medical history such as malignant disease that might limit the possibility of midterm follow-up.

Of 511 patients who had undergone first-time isolated CABG from September 2008 to October 2011, 496 patients scheduled to undergo OPCAB were assessed for eligibility. The 224 eligible patients who were expected to receive a left ITA-based Y-composite graft for complete revascularization were assigned randomly to 1 of 2 study groups in a 1:1 manner, depending on the second limb conduit used for construction of the Y-composite graft: the SV Y-composite graft (SV group, n = 112) or the free RITA Y-composite graft (RITA group, n = 112). Randomization was performed with a web-based block randomization method with randomly determined block sizes of 4 and 6. Of the 224 patients, 219 (SV group = 109; RITA group = 110) received intervention as specified earlier (Table 1 and Figure 1).

Operative Strategies

The basic surgical procedures and principles of OPCAB have been described.[5] The left and right ITAs were both harvested using a skeletonization technique. The SV was harvested from a lower leg. The manipulation and tension of the SV during harvest were minimized, and manual intraluminal dilatation was avoided. Immediately after the second limb conduit (SV or RITA) was harvested, it was anastomosed to the left ITA to construct a Y-composite graft. The left anterior descending coronary artery territory was revascularized first by using the left ITA while the second limb conduit was dilated spontaneously by the native flow and pressure of the left ITA. The left circumflex coronary artery territory was revascularized and then the right coronary artery territory. A sequential anastomotic technique using each side arm of the Y-composite graft was used when more than 2 coronary arterial anastomoses were needed. When

TABLE 2. Angiographic patency rates of distal anastomoses

	ITT population				
	Total	SV group	RITA group	Difference (%, 95% CI)	*P*
1-y occlusion rates, % (n/total)*	(n = 222)	(n = 111)	(n = 111)		
Overall grafts	2.7% (21/788)	2.6% (10/392)	2.8% (11/396)	−0.2 (−2.5, 2.0)	.843
Grafts using the LITA	0% (0/271)	0% (0/137)	0% (0/134)	–	–
Grafts using the second conduit	2.7% (12/450)	2.9% (7/242)	2.4% (5/208)	0.5 (−2.5, 3.5)	.747
Grafts using the third conduit	13.4% (9/67)	23.1% (3/13)	11.1% (6/54)	12.0 (−12.4, 36.4)	.336
1-y occlusion rates, % (total)†	(n = 224)	(n = 112)	(n = 112)		
Overall grafts	2.7% (795)	2.6% (396)	2.8% (399)	−0.2 (−2.4, 2.0)	.857
Grafts using the LITA	0% (273)	0% (138)	0% (135)	–	–
Grafts using the second conduit	2.7% (455)	2.9% (245)	2.4% (210)	0.5 (−2.4, 3.5)	.735
Grafts using the third conduit	13.4% (67)	23.1% (13)	11.1% (54)	12.0 (−13.3, 37.3)	.354
5-y occlusion rates, % (total)†	(n = 224)	(n = 112)	(n = 112)		
Overall grafts	4.2% (795)	4.7% (396)	3.6% (399)	1.1 (−1.7, 4.0)	.429
Grafts using the LITA	0.8% (273)	1.6% (138)	0% (135)	1.6 (−0.6, 3.7)	.156
Grafts using the second conduit	3.9% (455)	5.1% (245)	2.4% (210)	2.7 (−0.8, 6.2)	.128
Grafts using the third conduit	19.7% (67)	30.8% (13)	17.0% (54)	13.7 (−14.4, 41.9)	.339

ITT, Intention-to-treat; *PP*, per protocol; *SV*, saphenous vein; *RITA*, right internal thoracic artery; *CI*, confidence interval; *LITA*, left internal thoracic artery. *Occlusion rates of the conduits were calculated in patients who underwent 1-year angiograms. †Cumulative incidences of graft occlusion were estimated using the nonparametric method with noncardiac death as a competing risk.

the length of 1 or both limb conduits of the Y graft did not reach the target vessels because of an insufficient length, an additional SV segment from the other lower leg (a third limb conduit) was harvested to lengthen the graft limb (left ITA or second limb conduit [SV or RITA]) into an I-shape. The average number of distal anastomoses per patient (SV vs RITA group, 3.6 ± 0.9 vs 3.6 ± 0.8, $P = .904$) and per the left ITA (SV vs RITA group, 1.2 ± 0.4 vs 1.2 ± 0.5, $P = .542$) was similar between the 2 groups. The number of distal anastomoses in the 3 coronary artery territories also was similar between the 2 groups, as reported in our earlier analysis.[6] However, the number of distal anastomoses using the second limb conduit was smaller in the RITA group than in the SV group (1.9 ± 0.7 vs 2.2 ± 0.8, $P = .001$), and the third limb conduit was needed more frequently in the RITA group than in the SV group (n = 39 vs 8, $P < .001$).

Patients were given heparin to maintain an activated clotting time of more than 300 seconds. All patients took aspirin until the day of surgery and resumed it as soon as possible after surgery, usually at 1 day postoperatively. If the patient had a high blood level of low-density lipoprotein cholesterol (>100 mg/dL), drug therapy was initiated.

Evaluation of End Points

The primary end point measurement of the SAVE RITA trial was the 1-year patency rate of the second limb conduits (SV or RITA). In the present study, the primary end point was the 5-year occlusion rate of the second limb conduits, and the secondary end points were midterm clinical outcomes, including overall survival and rates of freedom from cardiac death and major adverse cardiac and cerebrovascular events (MACCE). The graft patency was graded in the manner described by Fitzgibbon and colleagues.[2] Grades A (excellent graft) and B (fair) were treated as patent. Grade O anastomosis, which included stenosis of 75% or more of the grafted coronary artery or a totally occluded graft, was treated as occluded. Cardiac death was defined as any death related to cardiac events, including sudden death during the follow-up period. MACCE included cardiac death, nonfatal acute myocardial infarction, coronary reintervention (including redo-CABG), and cerebrovascular accident. Both coronary angiograms and multidetector computed tomography (MDCT) angiograms initially were blind-reviewed in consensus by 2 specialists in each study. All patients who underwent 5-year evaluations also had undergone coronary angiography early and 1 year after surgery. If a 5-year MDCT suggested occluded or stenotic grafts when compared with the patient's 1-year angiogram, a coronary angiogram also was performed to confirm the status of graft patency and consensus was reached with cardiologists. The corresponding author of this study also reviewed all of the angiograms.

Follow-up

All of the 1-year (12.8 ± 2.4 months) patency rates were evaluated by coronary angiograms in 217 (99.1%; SV group = 108; RITA group = 109) of 219 patients who received allocated intervention. Two patients were excluded from the 1-year angiographic evaluation: One patient died in the early postoperative period, and 1 patient refused to undergo the angiographic examination. The 5-year (61.7 ± 5.2 months) evaluations were performed in 186 patients (84.9%) by coronary angiograms (n = 99: SV group = 80, RITA group = 19) or MDCT (n = 87: SV group = 15, RITA group = 72). We recommended that the patients, particularly the SV group, be evaluated by coronary angiograms because the coronary angiogram is currently the gold standard for graft patency evaluation. Patients who were reluctant to perform coronary angiographic evaluation received MDCT angiography as an alternative evaluation method. Thirty-three patients (15.1%) were excluded from the 5-year angiographic evaluation: A total of 15 patients died (1 in the early postoperative period and 14 during the follow-up period); 13 patients refused to undergo the 5-year angiographic follow-up examination; and 5 patients were lost to follow-up (Figure 1). The patients underwent regular postoperative follow-up examinations through the outpatient clinic at 3- or 4-month intervals and were interviewed by telephone for confirmation of their condition if the last clinic visit had not been conducted as scheduled. The clinical and angiographic follow-up examinations were closed on December 31, 2016. The follow-up data were complete in 97.7% (214/219) of patients with a median follow-up duration of 80.7 months (69.3-99.2 months).

Statistical Analysis

The SAVE RITA study was designed to have 80% power to detect 1-year patency rates of 93% in the SV versus 95% in the RITA grafts, with a 1-sided type I error of 2.5% and a noninferiority margin of −8%.

TABLE 2. Continued

PP population				
Total	**SV group**	**RITA group**	**Difference (%, 95% CI)**	***P***
(n = 217)	(n = 108)	(n = 109)		
2.3% (18/772)	1.8% (7/383)	2.8% (11/389)	−1.0 (−3.1, 1.1)	.356
0% (0/265)	0% (0/134)	0% (0/131)	–	–
2.5% (11/448)	2.5% (6/240)	2.4% (5/208)	0.1 (−2.8, 3.0)	.948
11.9% (7/59)	11.1% (1/9)	12% (6/50)	−0.9 (−23.3, 21.5)	.938
(n = 219)	(n = 109)	(n = 110)		
2.3% (779)	1.8% (382)	2.8% (392)	−1.0 (−3.1, 1.1)	.365
0% (267)	0% (135)	0% (132)	–	–
2.4% (453)	2.5% (243)	2.4% (210)	0.1 (−2.7, 3.0)	.935
11.9% (59)	11.1% (9)	12% (50)	−0.9 (−24.5, 22.7)	.941
(n = 219)	(n = 109)	(n = 110)		
3.6% (779)	3.5% (382)	3.7% (392)	−0.2 (−2.8, 2.5)	.910
0.8% (267)	1.6% (135)	0% (132)	1.6 (−0.6, 3.8)	.156
3.4% (453)	4.3% (243)	2.4% (210)	1.9 (−1.4, 5.2)	.264
17.3% (59)	11.1% (9)	18.4% (50)	−7.3 (−31.7, 17.1)	.556

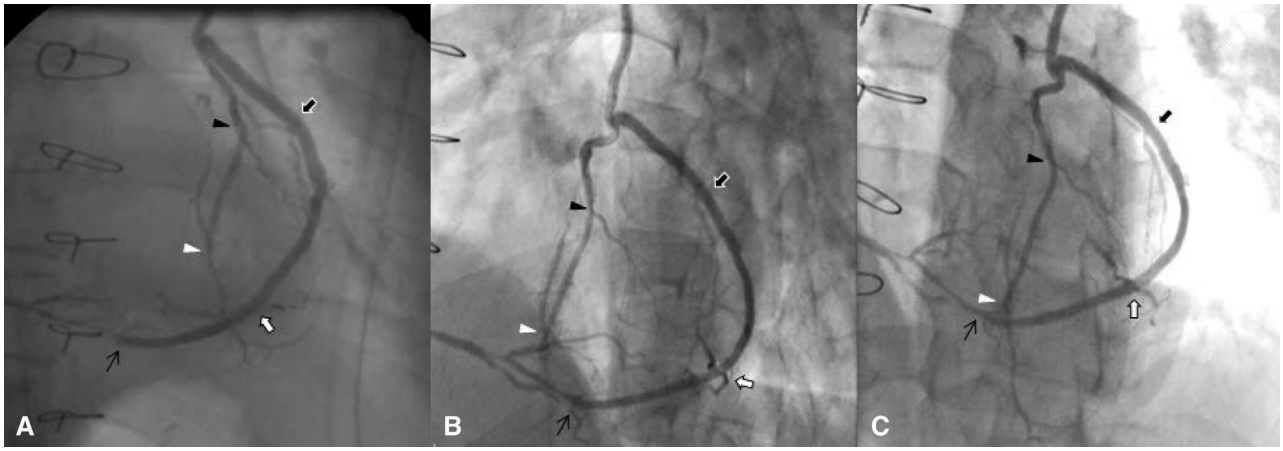


FIGURE 2. Patent SV Y-composite grafts based on the in situ left ITA at (A) early postoperative, (B) 1-year, and (C) 5-year angiographies in a 54-year-old male patient. The in situ left ITA was anastomosed to the second diagonal (*black arrowheads*) and left anterior descending coronary arteries (*white arrowheads*), and the SV was anastomosed to the first diagonal (*black arrows*) and distal obtuse marginal (*white arrows*) and right posterolateral coronary arteries (*black thin arrows*) using a sequential anastomotic technique.

We previously showed that the SV composite grafts were noninferior to the RITA composite grafts in terms of the 1-year patency rates.[6] In the present study, the study period was extended to record the 5-year occlusion rates. The null hypothesis was that the SV conduit was inferior to the RITA conduit based on the 5-year occlusion rate, with a noninferiority margin of 8%.

Statistical analysis was performed with the Statistical Package for Social Sciences software package, version 20 (SPSS, Inc, Chicago, Ill) or R version 3.4.1. Continuous data were expressed as the mean ± standard deviation for normally distributed variables or as medians (interquartile ranges) for non-normally distributed variables according to the Kolmogorov–Smirnov test, and categoric data were expressed as count (percentage). The unit of analysis was an anastomosis, under the assumption that the anastomoses would be independent from each other in each patient. Categoric variables were compared using the chi-square test except when more than 20% of expected counts were less than 5, when the Fisher exact test was used. Comparisons between continuous variables were made using Student *t* test for normally distributed data or Wilcoxon rank-sum test for non-normally distributed data according to the Kolmogorov–Smirnov test. Cumulative incidence of graft occlusion with death as a competing risk was estimated by the nonparametric method with R software (cmprsk package). For 5-year cumulative incidence of graft occlusion, confidence intervals for group difference and *P* value for noninferiority tests with a noninferiority margin of 8% were calculated using a z-statistics test for binary and time to event outcomes.[7] Overall survival and freedom from MACCE were analyzed using Kaplan–Meier survival curves, and comparisons between the 2 groups were performed using the log-rank test. Competing risk analyses for incidence of MACCE were also performed with noncardiac death as a competing risk, not as a censoring event. Cumulative incidence of MACCE with noncardiac death as a competing risk was estimated, and those of 2 groups were compared by using Gray's test.[8] Analyses were performed on both intention-to-treat (ITT) and per protocol (PP) populations. The ITT population included all randomized participants, and the PP population included patients who were randomized and received allocated intervention. The analyses for anastomotic qualities and subgroup analysis for coronary artery territories were performed among the PP population who underwent 5-year angiograms. To account for the different proportion of evaluation method between groups in assessing the 5-year occlusion, mixed-effects logistic regression models were used for repeated measures of graft occlusion at 1 year and 5 years. Adjusted odds ratio of 2 groups for occlusion was obtained from the mixed-effects models with time-to-angiogram and type of investigation as fixed effects and each graft as random effects.

RESULTS

Five-Year Postoperative Angiographic Results

In the PP population, the cumulative occlusion rate of overall grafts was 3.6% at 5 years postoperatively (3.5% in the SV group vs 3.7% in the RITA group; $P = .910$). The 5-year occlusion rates of the distal anastomoses using the left ITA were 1.6% in the SV group and 0% in the RITA group, respectively ($P = .156$). The 5-year occlusion rates of the distal anastomoses using the second limb conduit were 4.3% in the SV group and 2.4% in the RITA group ($P = .264$), a difference of 1.9% (95% confidence interval, −1.4 to 5.2). The upper confidence limit was smaller than the noninferiority margin of 8% with $P < .001$ of the noninferiority in the 5-year occlusion rate of the SV to the RITA. In patients who needed a third limb SV conduit, the 5-year occlusion rates were evaluated in 40 of 47 patients, and 10 of 52 distal anastomoses that used third limb SV conduits were occluded including 9 occlusions in the right coronary artery territories. The 5-year occlusion rate of the third limb SV conduit showed no statistical difference between the 2 groups ($P = .556$). The overall 5-year occlusion rate of the distal anastomoses that used a third limb SV conduit was 17.3%, which was significantly higher than that of the distal anastomoses that used a second limb SV conduit (4.3%, $P = .012$) (Table 2 and Figure 2).

The proportions of grades A, B, and O of the left ITA grafts and the second limb conduits were not statistically different between the 2 groups at 5 years postoperatively (Table 3). When the second limb conduit patency rates were compared according to the target coronary artery

TABLE 3. Comparison of the anastomotic qualities between the saphenous vein and right internal thoracic artery groups at 5-year angiography

Conduits	Fitzgibbon grade	SV group (n = 95)	RITA group (n = 91)	*P*
LITA				.408*
	A	97.4% (114/117)	98.1% (106/108)	
	B	0.9% (1/117)	1.9% (2/108)	
	O	1.7% (2/117)	0% (0/108)	
Second limb conduit (SV or RITA)				.116*
	A	92.5% (198/214)	96.5% (167/173)	
	B	2.8% (6/214)	1.2% (2/173)	
	O	4.7% (10/214)	2.3% (4/173)	

Data presented as % (n/total). *SV*, Saphenous vein; *RITA*, right internal thoracic artery; *LITA*, left internal thoracic artery. **P* value using linear by linear association.

territories, no statistically significant differences were found in the patency rates between the 2 groups (Table 4). Results from mixed-effects logistic regression models showed no significant difference between the 2 groups after adjusting the different evaluation methods (OR [95% confidence interval], 0.83 [0.35-1.97] for overall grafts and 1.05 [0.27-4.1] for grafts using the second conduit) (Table E1).

Overall Survival and Freedom From Cardiac Death

One operative death occurred in the RITA group. Late deaths occurred in 14 patients: 6 in the SV group (2 strokes, 1 cardiac death, 1 pneumonia, 1 accident, and 1 natural cause) and 8 in the RITA group (4 malignancies, 2 natural causes, 1 stroke, and 1 cardiac death). The overall survivals at 5 and 8 years of the ITT population were 94.2% and 93.1%, respectively, and the overall survivals at 5 and 8 years of the PP population were 94.0% and 92.9%, respectively. There was no statistically significant difference between the 2 groups (ITT population, $P = .429$; PP population, $P = .439$) (Figure 3). The rates of freedom from cardiac death also were similar between the 2 groups (ITT population, $P = .989$; PP population, $P = .994$).

Freedom From Major Adverse Cardiac and Cerebrovascular Events

During the study period, 13 patients (4 in the SV group; 9 in the RITA group) experienced angina recurrence that required angiographic examinations. In the SV group, percutaneous coronary intervention was performed in 3 patients (1 with conduit occlusion and 2 with native disease progression), and redo OPCAB was performed in 1 patient for native disease progression. In the RITA group, percutaneous coronary intervention was performed in 9 patients (5 with native disease progression and 4 with conduit occlusion). The overall freedom from reintervention rates at 5 and 8 years postoperatively were 95.8% and 92.4%, respectively. The overall freedom from reintervention rates at 5 and 8 years in the ITT population were 95.9% and 92.6%, respectively, and those of the PP population were 95.8% and 92.4%, respectively, without statistically significant differences between the 2 groups (ITT population, 96.3% and 96.3% in SV group vs 95.4% and 88.8% in RITA group, $P = .152$; PP population, 96.2% and 96.2% in SV group vs 95.3% and 88.5% in RITA group, $P = .155$). Five patients (3 in SV group; 2 in RITA group) experienced stroke events during the follow-up period. One patient in the SV group died of a fatal complication during the 1-year angiogram, and 1 patient in the RITA group experienced sudden cardiac death during the follow-up period. The freedom from MACCE rates at 5 and 8 years in the ITT population were 92.7% and 89.5%, respectively, and those in the PP population were 93.0% and 88.3%, respectively, without statistically significant differences between the 2 groups (ITT population, 92.7% and 92.7% in SV group vs 92.7% and 86.2% in RITA group, $P = .346$; PP population, 92.5% and 92.5% in SV group vs 92.5% and 85.9% in RITA group, $P = .354$) (Figure 4). The cumulative incidence of MACCE was compared between the 2 groups using competing risk analysis, considering noncardiac death as the competing risk (Figure E1). No significant difference was found between the 2 groups (ITT population, $P = .370$; PP population, $P = .379$).

TABLE 4. Comparison of 5-year patency rates for distal anastomoses performed with the second limb conduits between the saphenous veins and right internal thoracic arteries according to coronary artery territories

	SV group (n = 95)	RITA group (n = 91)	*P*
Total	95.3% (204/214)	97.7% (169/173)	.278*
LAD territory	93.2% (41/44)	100% (35/35)	.127†
LCX territory	99.1% (107/108)	97.0% (96/99)	.351†
RCA territory	90.3% (56/62)	97.4% (38/39)	.244†
P	.619‡	.484‡	–

Data presented as % (n/total). *SV*, Saphenous vein; *RITA*, right thoracic artery; *LAD*, left anterior descending coronary artery; *LCX*, left circumflex coronary artery; *RCA*, right coronary artery. **P* value using chi-square test for inequality. †*P* value using Fisher exact test for inequality. ‡*P* value using linear by linear association.

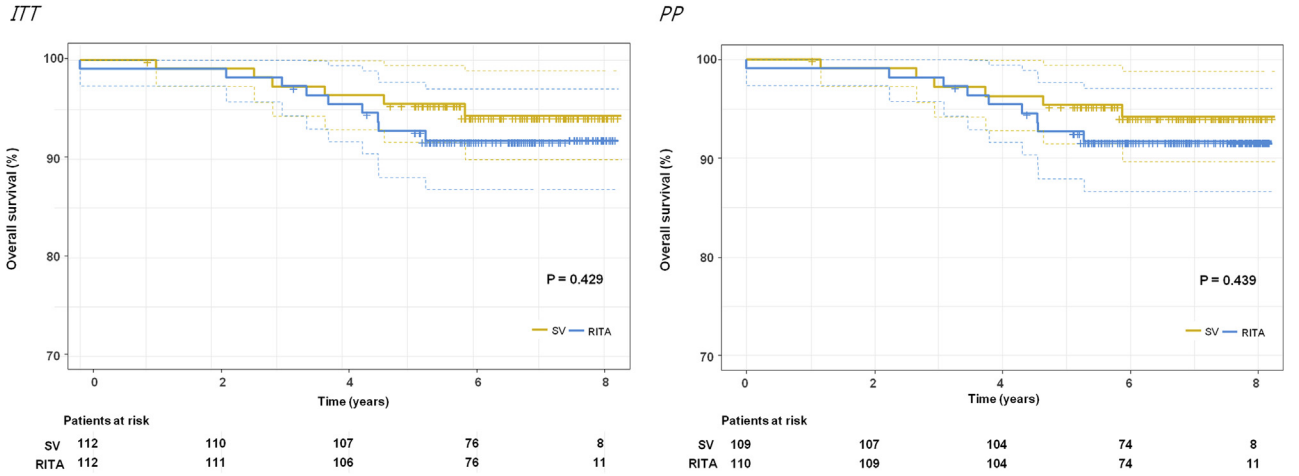


FIGURE 3. Comparison of the overall survival between the SV and RITA groups. *ITT*, Intention-to-treat; *SV*, saphenous vein; *RITA*, right internal thoracic artery; *PP*, per protocol.

DISCUSSION

The present study of the extended SAVE RITA trial demonstrated 3 main findings. First, the 5-year occlusion rate of the SV used as a Y-composite graft based on the in situ left ITA was noninferior to that of the RITA composite graft. Second, the clinical results of OPCAB using SV composite grafts showed no statistically significant differences compared with those of OPCAB using RITA composite grafts up to 8 years after surgery in terms of overall survival and MACCE-free survival. Third, the third SV conduit needed to extend the second limb conduit revealed a significantly higher occlusion rate compared with the SV conduit used as a second limb conduit.

The initial selection of the conduits that have superior patency rates is one of the important factors in improved long-term clinical outcomes of patients undergoing CABG.[2,9] Although the SV is still a widely used conduit, it has shown the disadvantage of declining patency with time.[1] Recent randomized studies also have demonstrated unsatisfactory patency rates for SV conduits.[3,4] However, those previous studies examined the patency rates of aortocoronary SV bypass grafts that were harvested with conventional methods.

Of revascularization strategies, construction of arterial composite grafts based on the in situ left ITA has been demonstrated to be a safe and efficient method for revascularization.[10-12] Total arterial revascularization using arterial composite grafts based on the ITA was also the preferred method for revascularization in the mid-2000s at our institute. However, the SV was used as a second graft when an additional arterial conduit was not available or as a third graft when arterial conduits were too short to reach target vessels. The use of SV composite

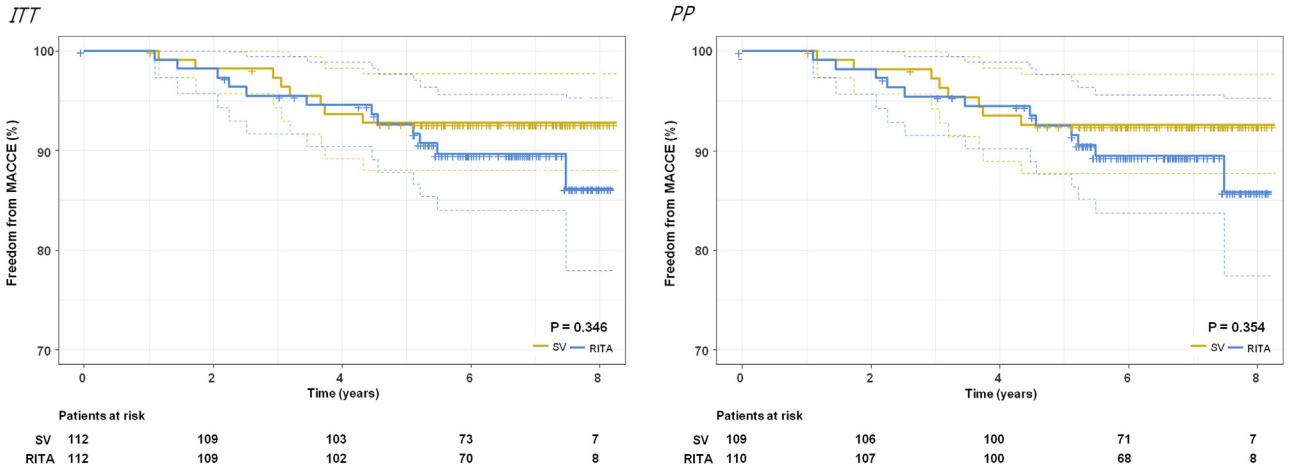
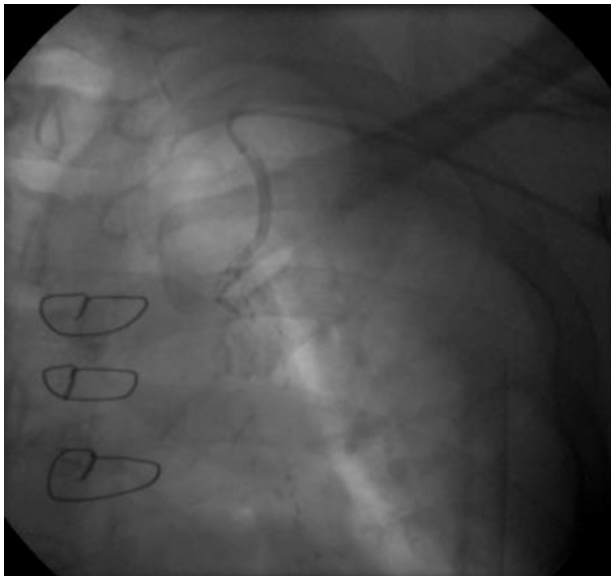
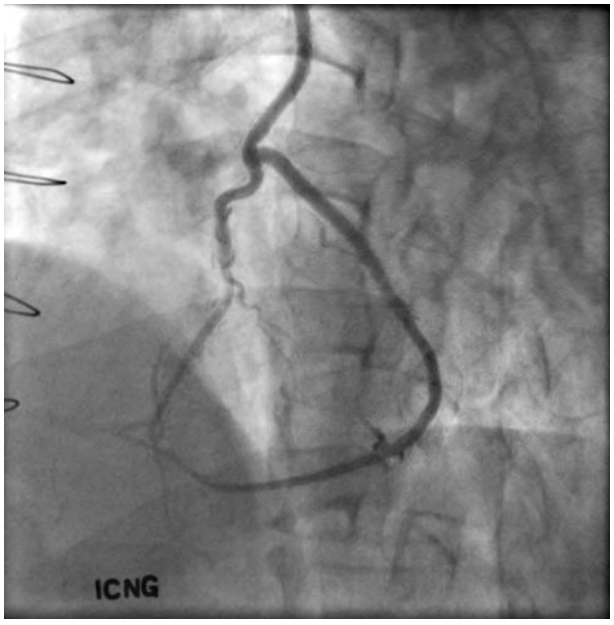


FIGURE 4. Comparison of freedom from MACCE between the SV and RITA groups. *MACCE*, Major adverse cardiac and cerebrovascular events; *ITT*, intention-to-treat; *PP*, per protocol; *SV*, saphenous vein; *RITA*, right internal thoracic artery.



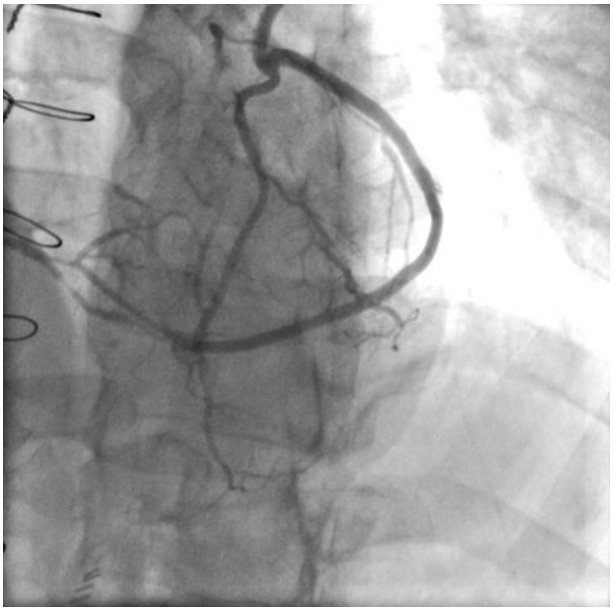
VIDEO 1. Patent SV Y-composite grafts based on the in situ left ITA at early postoperative angiography in a 54-year-old male patient. The in situ left ITA was anastomosed to the second diagonal and left anterior descending coronary arteries, and the SV was anastomosed to the first diagonal and distal obtuse marginal and right posterolateral coronary arteries using a sequential anastomotic technique. Video available at: https://www.jtcvs.org/article/S0022-5223(18)31492-2/fulltext.



VIDEO 2. Patent SV Y-composite grafts based on the in situ left ITA at 1-year angiography. Video available at: https://www.jtcvs.org/article/S0022-5223(18)31492-2/fulltext.

graft based on the left ITA has produced conflicting results. One study demonstrated suboptimal short-term patency results in patients who received an SV composite graft,[13] whereas other studies demonstrated comparable hemodynamic characteristics and early patency results between the SV and arterial composite grafts.[14,15] In our previous study, the SV composite grafts showed a 1-year patency rate similar to that of arterial composite grafts.[15] The equivalent patency rate of SV composite grafts to that of arterial composite grafts was shown to continue at 5 years postoperatively.[16] Impressed by the excellent patency results of the SV composite graft, we designed a randomized clinical trial, the SAVE RITA trial, to evaluate the noninferiority of the SV compared with the RITA as a Y-composite graft based on the left ITA.[5] The SAVE RITA trial demonstrated that the SV composite grafts were noninferior to the RITA composite grafts in terms of 1-year patency rates, the primary end point of the trial (Videos 1 and 2).[6] In the present examination of the extended SAVE RITA trial, the occlusion rate of the SV Y-composite graft was noninferior to that of the RITA composite graft at 5 years postoperatively (Video 3). There also were no significant differences in freedom from cardiac death and freedom from MACCE rates up to 8 years postoperatively between the 2 groups. In the SAVE RITA trial, the SV was harvested using a minimal manipulation technique because of its efficacy in preserving the venous endothelial layer and was used as a second limb conduit to construct the Y-composite graft.[17] The theoretical advantages of using the SV composite graft over an aortocoronary bypass graft include the following: (1) The SV conduit anastomosed to the side of the left ITA is exposed to less circulatory stress than a conduit anastomosed to the ascending aorta; (2) the SV composite graft is exposed continuously to endothelial-protective substances, such as nitric oxide produced from the left ITA; (3) complications such as embolic stroke and aortic dissection could be reduced by avoiding aortic clamping for proximal anastomosis; and (4) the length of the SV is preserved compared with aortocoronary SV grafts, because the SV from a lower leg will be sufficient for complete revascularization in most patients with multivessel coronary artery disease.[6,18-20] The SV composite graft was found to undergo a negative remodeling during the first postoperative year.[21] The additional benefits of using SV composite grafts compared with bilateral ITA composite grafts are that the RITA is reserved in the event of possible later redo CABG and that the risk of perioperative morbidity, such as sternal infection, is decreased.[6]

In the present study, an additional SV segment was harvested to lengthen the conduit when the length of 1 or both arms of the Y graft was not sufficient for complete revascularization. The third limb conduit to lengthen the graft limb was needed more frequently in the RITA group than in the SV group. The overall occlusion rate of the third limb SV conduit was significantly higher than that of the second limb SV conduit at 5 years postoperatively. An



VIDEO 3. Patent SV Y-composite grafts based on the in situ left ITA at 5-year angiography. Serial postoperative angiograms demonstrated patent SV conduit with significantly decreased diameter and patent in situ ITA with increased diameter during postoperative 5 years. Video available at: https://www.jtcvs.org/article/S0022-5223(18)31492-2/fulltext.

additional surgical manipulation to lengthen the graft limb may have affected the significantly higher occlusion rate of the third limb SV conduit, although this requires further investigation.

Study Limitations

The present study had limitations that must be recognized. First, although the SAVE RITA trial was prospective, randomized, and controlled, it was not a multicenter study and it had an institutional factor. Second, the 5-year occlusion rate and midterm clinical outcomes with a median follow-up duration of 80.7 months may not provide sufficient data to reach a definite conclusion on the noninferiority of the SV composite graft compared with the RITA composite graft. The sample size of this study is also small for comparison of clinical outcomes. Larger studies with long-term angiographic and clinical follow-up may be needed. Third, the 5-year graft patency evaluation was not performed in 18 patients among the surviving patients (18 of 203 as treated patients, 8.9%) at the 5-year follow-up. In addition, MDCT instead of coronary angiography was performed in 46.8% (87/186) of patients, although the diagnostic efficacy of computed tomographic angiography has been demonstrated as excellent,[22] and our results showed no significant difference in the occlusion rate between the 2 groups after adjusting the different evaluation methods. Fourth, a third SV conduit was used to lengthen the graft limb for complete revascularization in 47 patients. This additional conduit could be a possible confounder, although none of the second conduits extended by a third conduit were occluded.

CONCLUSIONS

The SV composite grafts were noninferior to the RITA composite grafts in terms of 5-year graft occlusion rate. Midterm clinical results of OPCAB using SV composite grafts were similar to those of OPCAB using RITA composite grafts up to 8 years after surgery.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/17AM/2017-05-01/RM311/05-01-17_Room311_1430_Kim.mp4.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

References

1. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery. *J Am Coll Cardiol*. 2011;58:e123-210.
2. Fitzgibbon GM, Kafka HP, Leach AJ, Keon WJ, Hooper GD, Burton JR. 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*. 1996;28:616-26.
3. Collins P, Webb CM, Chong CF, Moat NE, Radial Artery Versus Saphenous Vein Patency (RSVP) Trial Investigators. Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. *Circulation*. 2008;117:2859-64.
4. Deb S, Cohen EA, Singh SK, Une D, Laupacis A, Fremes SE. Radial artery and saphenous vein patency more than 5 years after coronary artery bypass surgery: results from RAPS (radial artery patency study). *J Am Coll Cardiol*. 2012;60:28-35.
5. Hwang HY, Kim JS, Oh SJ, Kim K-B. A randomized comparison of the saphenous vein versus right internal thoracic artery as a Y-composite graft (SAVE RITA) trial: early results. *J Thorac Cardiovasc Surg*. 2012;144:1027-35.
6. Kim K-B, Hwang HY, Hahn S, Kim JS, Oh SJ. A randomized comparison of the saphenous vein versus right internal thoracic artery as a Y-composite graft (SAVE RITA) trial: one-year angiographic results and mid-term clinical outcomes. *J Thorac Cardiovasc Surg*. 2014;148:901-8.
7. da Silva GT, Logan BR, Klein JP. Methods for equivalence and non-inferiority testing. *Biol Blood Marrow Transplant*. 2008;15:120-7.
8. Gray RJ. A Class of K-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat*. 1988;16:1141-54.
9. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal thoracic artery grafts: effects on survival over a 15-year period. *N Engl J Med*. 1996;334:216-9.
10. Muneretto C, Bisleri G, Negri A, Manfredi J, Metra M, Nodari S, et al. Total arterial myocardial revascularization with composite grafts improves results of coronary surgery in elderly: a prospective randomized comparison with conventional coronary artery bypass surgery. *Circulation*. 2003;108(Suppl II):II-29-II-33.

11. Hwang HY, Cho KR, Kim K-B. Equivalency of right internal thoracic artery and right gastroepioloic artery composite grafts: five-year outcomes. *Ann Thorac Surg*. 2013;96:2061-8.
12. Navia DO, Vrancic M, Piccinini F, Camporrotondo M, Dorsa A, Espinoza J, et al. Myocardial revascularization exclusively with bilateral internal thoracic arteries in T-graft configuration: effects on late survival. *Ann Thorac Surg*. 2016;101:1775-81.
13. Gaudino M, Alessandrini F, Pragliola C, Luciani N, Trani C, Burzotta F, et al. Composite Y internal thoracic artery-saphenous vein grafts: short-term angiographic results and vasoreactive profile. *J Thorac Cardiovasc Surg*. 2004;127:1139-44.
14. Glineur D, Boodhwani M, Poncelet A, Kerchove LD, Etienne PY, Noirhomme P, et al. Comparison of fractional flow reserve of composite Y-grafts with saphenous vein or right internal thoracic arteries. *J Thorac Cardiovasc Surg*. 2010;140:639-45.
15. Hwang HY, Kim JS, Kim K-B. Angiographic equivalency of off-pump saphenous vein and arterial composite grafts at one year. *Ann Thorac Surg*. 2010;90:516-21.
16. Hwang HY, Lee J-H, Han JW, Kim K-B. Equivalency of saphenous vein and arterial composite grafts: 5-year angiography and midterm clinical follow-up. *Ann Thorac Surg*. 2016;102:580-8.
17. Hwang HY, Kim M-A, Seo JW, Kim K-B. Endothelial preservation of the minimally manipulated saphenous vein composite graft: histologic and immunohistochemical study. *J Thorac Cardiovasc Surg*. 2012;144:690-6.
18. Tedoriya T, Kawasuji M, Sakakibara N, Ueyama K, Watanabe Y. Pressure characteristics in arterial grafts for coronary bypass surgery. *Cardiovasc Surg*. 1995;3:381-5.
19. Tsui JCS, Souza DSR, Filbey D, Bomfim V, Dashwood MR. Preserved endothelial integrity and nitric oxide synthase in saphenous vein grafts harvested by a 'no-touch' technique. *Br J Surg*. 2001;88:1209-15.
20. Gaudino M, Toesca A, Maggiano N, Pragliola C, Possati G. Localization of nitric oxide synthase type III in the internal thoracic and radial arteries and the great saphenous vein: a comparative immunohistochemical study. *J Thorac Cardiovasc Surg*. 2003;125:1510-5.
21. Hwang HY, Koo B-K, Oh SJ, Kim K-B. Morphologic changes of the saphenous vein y-composite graft based on the left internal thoracic artery: 1-year intravascular ultrasound study. *J Thorac Cardiovasc Surg*. 2015;149:487-93.
22. Kahn R, Rawal S, Eisenberg MJ. Transitioning from 16-slice to 64-slice multidetector computed tomography for the assessment of coronary artery disease: are we really making progress? *Can J Cardiol*. 2009;25:533-42.

Key Words: coronary artery bypass grafting, internal thoracic artery, patency, saphenous vein

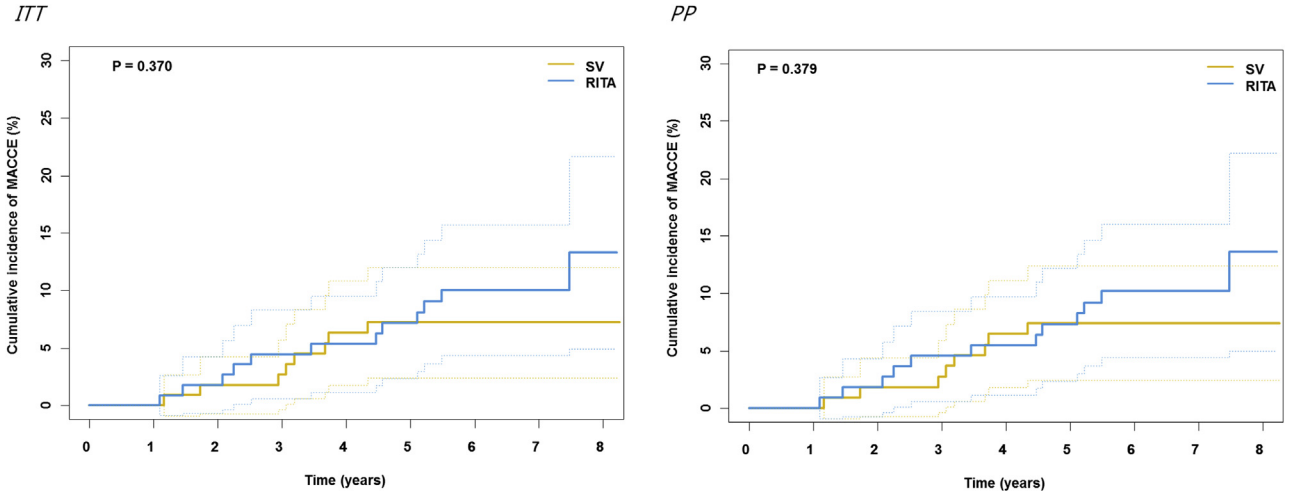


FIGURE E1. Comparison of cumulative incidence of MACCE between the SV and RITA groups using competing risk analysis, considering noncardiac death as the competing risk. *ITT*, Intention-to-treat; *MACCE*, major adverse cardiac and cerebrovascular events; *PP*, per protocol; *SV*, saphenous vein; *RITA*, right internal thoracic artery.

TABLE E1. Odds ratio of graft occlusion using mixed-effects logistic regression models

	Overall grafts		Grafts using the second conduit	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
SV vs RITA (reference)	0.83 (0.35-1.97)	.673	1.05 (0.27-4.1)	.943
Evaluation method (CAG vs MDCT)	1.93 (0.78-4.74)	.153	2.91 (0.69-12.3)	.146
Time of angiogram (5 y vs 1 y)	1.72 (0.92-3.21)	.090	1.60 (0.68-3.81)	.283

OR, Odds ratio; *CI*, confidence interval; *SV*, saphenous vein; *RITA*, right internal thoracic artery; *CAG*, coronary angiography; *MDCT*, multidetector computed tomography.