The no-touch saphenous vein for coronary artery bypass grafting maintains a patency, after 16 years, comparable to the left internal thoracic artery: A randomized trial

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ABSTRACT

Objectives: This study investigates whether the no-touch (NT) vein graft, at a mean time of 16 years, maintains a significantly higher patency rate than conventional (C) vein grafts and still has patency comparable to that of the left internal thoracic artery (LITA).

Methods: A total of 156 patients accepted for coronary artery bypass grafting were randomly allocated to 1 of 3 groups. In the C group, the saphenous vein (SV) was stripped and distended. In the intermediate group, the SV was stripped but not distended. In the NT group, the SV was neither stripped nor distended, but rather harvested with a fat pedicle. This study is an angiographic follow-up of the C and NT groups, at a mean time of 16 years postoperatively.

Results: Fifty-four patients were included (C group = 27; NT group = 27). In all, 72 and 75 vein grafts were completed in groups C and NT, respectively. Crude SV graft patency was 64% in the C group versus 83% in the NT group ($P = .03$), which was similar to the patency of the LITA (88%). The harvesting technique had a major impact on the patency with a hazard ratio for occlusion of 1.83 for the C group ($P = .04$).

Conclusions: Harvesting the SV with the NT technique conferred, at a mean time of 16 years, a significantly higher patency than the conventional technique that was still comparable to that of the LITA. (J Thorac Cardiovasc Surg 2015;150:880-8)
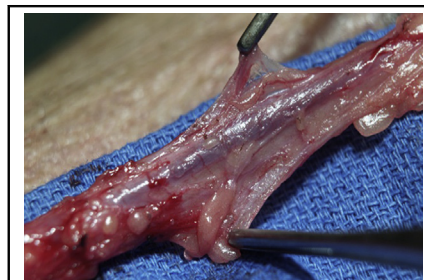
The no-touch saphenous vein, showing the pedicle and the vaso vasorum.

Central Message

The no-touch saphenous vein should be included in the arsenal of conduits for coronary artery bypass grafting.

Perspective

Harvesting the SV with the NT technique maintains, after 16 years postoperatively, a significantly better patency rate than conventionally harvested veins, and it is still comparable to that of the LITA. After these encouraging results, more cardiac surgeons may consider using the NT technique in harvesting SV grafts.

Ischemic heart disease remains one of the leading causes of death worldwide.[1] Coronary artery bypass grafting (CABG) is considered the best treatment in many cases,[2,3] and its success depends on the long-term patency rate of the conduits. Greater use of arterial grafts has been advocated because of their long-term patency compared with the high incidence of early graft occlusion, progressive intimal hyperplasia, and late graft atherosclerosis with the use of saphenous vein (SV) grafts.[4] However, arterial grafts are associated with limitations, such as an increased incidence of mediastinitis, particularly when using bilateral internal thoracic arteries in patients with diabetes mellitus,[5,6] poorer results when bypassing target vessels with stenosis <70%,[7] spasms that are common in free arterial grafts,[8] and the risk of ischemia after removal of arterial grafts.[9]

In many centers, the SV accounts for up to 80% of all grafts used in CABG. Consequently, the SV remains an indispensable conduit in CABG, and its long-term patency is one of the most crucial challenges in cardiovascular surgery. However, various studies have shown that damage to

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Abbreviations and Acronyms

C   = conventional
CABG = coronary artery bypass grafting
CI   = confidence interval
HR   = hazard ratio
LAD   = left anterior descending
LITA = left internal thoracic artery
NT   = no-touch
SV   = saphenous vein

vessels during surgical preparation influences graft patency.[10] Here, SVs are conventionally harvested by stripping them from their surrounding tissues, which commonly causes graft spasm, and then dilating them with normal saline or blood to overcome this spasm. This is a known cause of vessel wall damage.[11] Since the beginning of the 1990s, we have been using a technique for SV preparation in which the vein is harvested with a pedicle of surrounding tissue: the "no-touch (NT) technique." This technique has been shown to reduce the risk of spasm and the need for dilatation[12] and therefore preserve vessel wall integrity. With this background, a randomized trial was initiated in 1993, to compare 3 harvesting techniques. The angiographic assessments of graft patency that were conducted at a mean time of 1.5 and 8.5 years postoperatively demonstrated a significantly better patency rate for the NT group.[13,14] The primary aim of this longitudinal trial is to examine whether the NT vein grafts still maintain a significantly higher patency rate than conventional vein grafts; the secondary aim is to determine whether this patency is still comparable to that of the left internal thoracic artery (LITA) at a mean time of 16 years.

METHODS
Study Design
Details of this longitudinal, angiographic, single-center randomized clinical trial have been described previously.[13,14] Briefly, 156 patients were enrolled from 1993 to 1997. Patients were randomly allocated, using a block-randomization technique, into 3 groups of 52 patients each, according to 3 SV harvesting techniques. In summary, in group C (conventional), the vein was stripped of its surrounding tissue and manually distended with saline before grafting. In the intermediate group, the vein was stripped but not distended; and in group NT, it was neither stripped nor distended. The NT grafts were allowed to passively dilate when attached to the arterial cannula. All patients were to receive a LITA to the left anterior descending (LAD) artery. The SV was harvested by the same senior surgeon in all of the cases. The first 2 follow-ups were performed at 1.5 years and 8.5 years and have been published previously.[13,14] All patients in the C and NT groups who were initially randomized, and were alive at a mean time of 16 years, were asked to participate in a clinical and computed tomography angiographic assessment. The local ethics committee approved a third follow-up, and patients were included after informed consent. Exclusion criteria were allergy to contrast media, impaired renal function, or inability to conduct the study according to protocol.

Twenty-seven patients in each group underwent computed tomography angiographic assessment. Figure 1 shows the flowchart of the follow-up. The cause of death was established from the Swedish death registry. In addition, we managed to retrieve postmortem samples of vein grafts from both groups, including the LITA for macroscopic analysis, after informed consent was obtained from the relatives. Clinical evaluation was performed, which included history, physical examination, blood sampling (complete blood count, renal function, and lipid profile), a health-related quality-of-life questionnaire (EQ-5D), and echocardiography; the results are published separately.[15] The intermediate group was not included in the last 2 follow-ups, owing to financial limitations and relevance—the patency of the intermediate group was inferior to both the C and NT arms at earlier assessment.[13]

Angiography
The first 2 follow-ups (at 1.5 years and 8.5 years) were performed with conventional coronary angiography. The third follow-up occurred at a mean time of 16 years (range 14-18 years) and was performed with computed tomographic angiography, due to the less-invasive nature of the technique and its reliability in estimating graft occlusion.[16,17]

The electrocardiogram-gated computed tomographic angiography examinations were performed with a Somatom Flash dual-source CT scanner (Siemens, Erlangen, Germany). All subjects received 0.25 mg of nitroglycerin sublingually, and those with a heart frequency >70 beats/minute and no contraindications were also given up to 10 mg of Metoprolol (Seloken injection, 1 mg/ml; AstraZeneca, Hamilton, OH) intravenously before the examination. Contrast media (60-70 ml) (Iomeron; 400 mg/ml, Bracco, Milan, Italy) was administered with a pressure injector at a flow rate of 6 ml/second, followed by a bolus of 60-ml saline. When LITA had been used for bypass, scanning started at the left subclavian artery and ended at the base of the heart; otherwise, scanning started below the aortic arch. The images were reviewed at a Siemens Syngo Multimodality Workplace workstation.

All images were independently reviewed by 2 thoracic radiologists who were blinded to group assignment. Disagreements were resolved by consensus. Where possible, the studies were compared with reports and images from previous coronary angiographies. A graft was judged as occluded when the graft was not opacified by contrast media. A graft stenosis was judged as significant when the narrowing of the lumen diameter was >50% relative to the adjacent parts of the vessel.

STATISTICAL ANALYSIS
Statistical analysis was performed on 127, 101, and 72 C grafts at the 1.5-year, 8.5-year, and 16-year assessments, respectively, and 124, 101, and 75 NT grafts at the same assessment periods. An outcome with 2 states (ie, patency or occlusion) was analyzed with Cox proportional hazard regression models, regarding time to occlusion, and with a multilevel logistic regression model for patency when data for patency was given in 2-by-2 tables stratified by type of graft (single or sequential) and harvesting technique. The main predictor variables were the 2 harvesting techniques: C and NT. Additional predictor variables for the Cox regression were examined individually; those expected to have a significant relationship to the outcome, and those that had an uneven distribution across the 2 harvesting techniques, were selected and used in the final model. For the Cox regression, the observations from the 1.5-year assessment, 8.5-year assessment, and final 16-year assessment were analyzed together, thus combining all available information in 1 model.
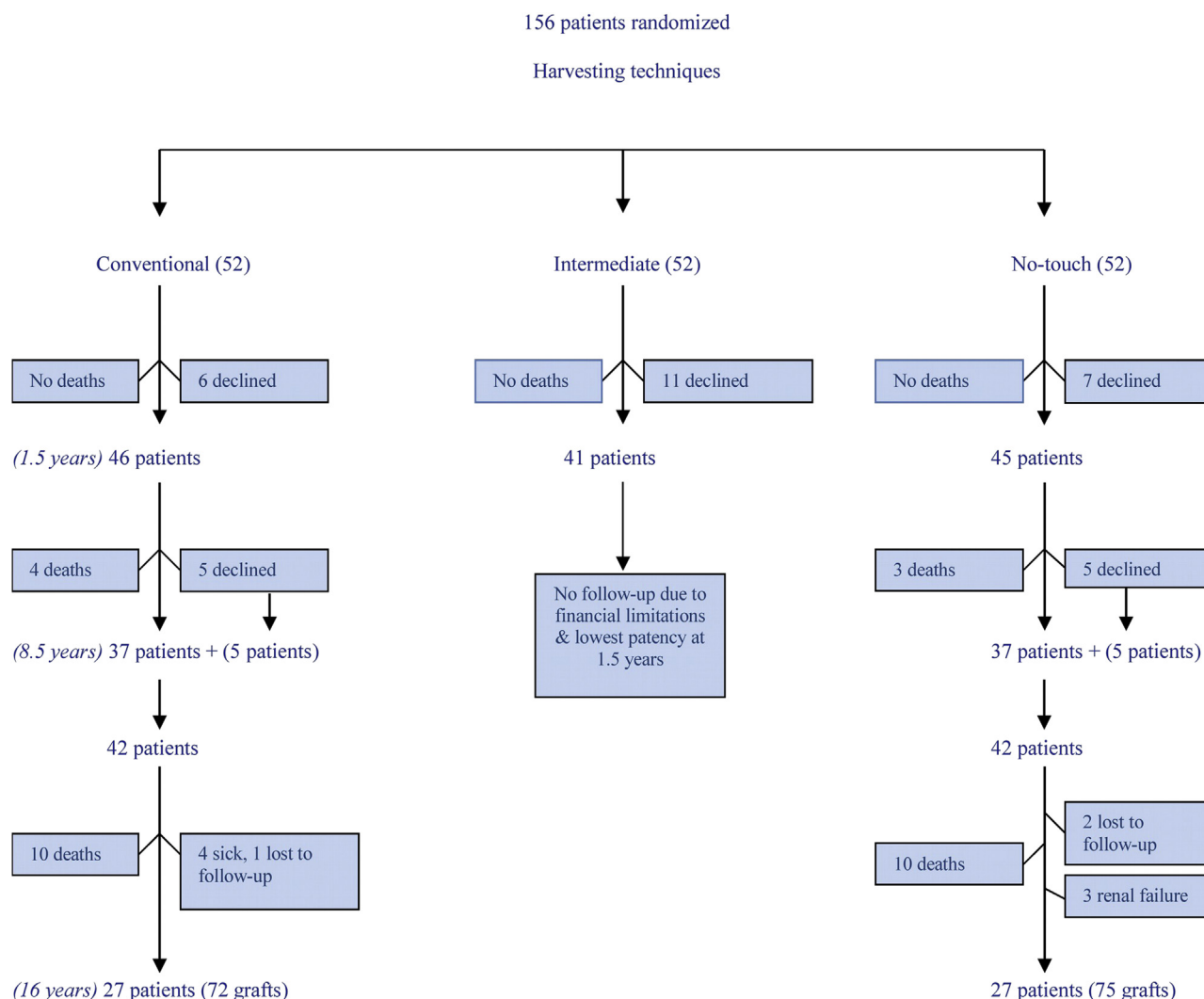
156 patients randomized

Harvesting techniques

Conventional (52)   Intermediate (52)   No-touch (52)

| No deaths | 6 declined | | No deaths | 11 declined | | No deaths | 7 declined |

(1.5 years) 46 patients   41 patients   45 patients

| 4 deaths | 5 declined | | 3 deaths | 5 declined |

(8.5 years) 37 patients + (5 patients)   No follow-up due to financial limitations & lowest patency at 1.5 years   37 patients + (5 patients)

42 patients   42 patients

| 10 deaths | 4 sick, 1 lost to follow-up | | 10 deaths | 2 lost to follow-up |
| | | | | 3 renal failure |

(16 years) 27 patients (72 grafts)   27 patients (75 grafts)

FIGURE 1. Flowchart of the longitudinal follow-up.

From the dates for surgery and assessments (year-month-day), the time-to-event in number of days was calculated. For occlusion, the time when occlusion actually took place was estimated to be the midpoint of the 2 assessments before and after the reported occlusion. As this is an estimate of the actual time of occlusion, sensitivity analyses using randomly generated dates were performed to evaluate the influence of date of occlusion on the estimates from the regression model. For patency, the dates of the assessments were used.

Additionally, multilevel logistic regression was applied at each separate assessment to focus on the actual percentage of patency. In this model, the patient was defined as level 1, and the graft as level 2, and this was done to allow for multiple grafts per patient. Multiple grafts per patient might introduce dependencies between the observations. We corrected for clustered observations in the calculation of *P* values and confidence intervals (CIs), with each patient

forming a separate cluster, and this correction was done in all analyses. The outcome parameter of interest in the Cox regression is the hazard ratio (HR), and in this analysis, all HRs >1.0 indicate an increased risk of occlusion. Before reaching the final model, we examined the possibility that the additional predictor variables had significant interactions with the main predictor variable, ie, the harvesting technique. The basic assumption of the Cox proportional hazard regression, that of proportional hazards, was tested based on Schoenfeld residuals.[18] For those predictor variables that did not fulfill the proportionality assumptions, stratified analyses were done.

Comparisons with LITA: With the aim of investigating noninferiority and equivalence of the SV techniques with LITA, the approach recommended by Fleming[19] and Christensen[20] was used. Results are shown as confidence intervals (CI) for the differences in patency rates between the investigated techniques (LITA–SV). The margins of

TABLE 1. Baseline demographics and clinical characteristics at 16 years

Characteristics	Conventional (C)	No-touch (NT)
No. of patients (n)	27	27
Mean age (y), female/male	74/71	73/78
Female/male (n)	4/23	2/25
Body mass index ≥25	23 (85)	21 (78)
Family history of ischemic heart disease	19 (70)	14 (52)
Smoking	4 (15)	3 (11)
Hypertension	18 (67)	15 (56)
Diabetes mellitus	8 (30)	10 (37)
Hyperlipidemia	25 (93)	26 (96)
Beta blockers	18 (67)	20 (74)
Calcium inhibitors	7 (26)	7 (26)
ASA	25 (93)	26 (96)
Warfarin	1 (4)	1 (4)
Clopidogrel	1 (4)	1 (4)
Statins	24 (89)	26 (96)
Nitrates	6 (22)	4 (15)
Diuretics	3 (11)	6 (22)
ACE inhibitors or AII blockers	17 (63)	11 (41)
Digitalis	1 (4)	0
Oral diabetic medication only	3 (11)	3 (11)
Insulin diabetic medication only	0	3 (11)
Oral and insulin diabetic medication	5 (19)	4 (15)

Values are n (%), unless otherwise indicated. *ASA,* Acetyle salicylic acid; *ACE,* angiotensin-converting enzyme.

equivalence and noninferiority were set to 10 and 15 percentage units. Through these CIs, possible equivalences between LITA and the different vein grafts can be visualized. Confidence intervals that are completely included within the margins of equivalence show no rejection of the equivalence hypothesis; CIs that include the ''0-line'' but reach outside the margins of equivalence are inconclusive (the reasons for which can be low statistical power for a small data set); and CIs that do not include the ''0-line'' reject equivalence. The confidence level was set to 90%; thus, equivalence is evaluated at this level, and noninferiority can be deduced from the upper 90% CI level, referred to as the one-sided 95% CI for noninferiority. Computations were performed with STATA, version 12 (StatSoft, Inc, Tulsa, Okla).

RESULTS

Of the 46 and 45 patients in the C and NT groups, respectively, which were included in the first follow up at 1.5 years, 27 were included in the conventional group and 27 in the NT group at a mean time of 16 years (range 14-18 years). In Table 1, the baseline characteristics of the 54 late angiographic patients are shown. The 2 groups had fairly similar data regarding risk factors and medical treatment.

From the original 104 patients, 14 in the C (27%) and 13 (25%) in the NT groups have died since the start of the

study. Seven patients were excluded for medical reasons (4 for strokes and dementia; 3 because of renal failure); and 3 were lost to follow-up. Six cardiac-related deaths (12%) occurred in group C, and 4 (8%) with the NT technique (myocardial infarctions and heart failure). The noncardiac deaths in group C were: 4 cancer, 1 renal failure, 1 pneumonia, 1 lung fibrosis, and 1 drowning. In the NT group, the noncardiac causes were cancer (6), ruptured abdominal aortic aneurysm (1), stroke (1), and septicemia (1).

Postmortem biopsies were collected in patients from both groups that died 8 years, 9 years, 12 years, and 18 years postoperatively. Representative macroscopic sections are shown in Figure 2. In the C vessels, there was considerable necrotic and friable tissue, as well as a diffuse atherosclerotic process. The atherosclerotic process in NT grafts was less pronounced, more localized, and organized.

In the C group, there were 72 grafts (63 single, 9 sequential), whereas the NT group had 75 grafts (67 single, 8 sequential). The sequential grafts were considered totally occluded, even if partially patent to ≥1 coronary arteries. The ratio of patency to total number of grafts for the 2 surgical techniques was tested with multilevel logistic regression; the sequential grafts were compared using Fisher's exact test, owing to the small numbers and cells with no occluded grafts (Table 2). Data from all 3 follow-ups (1.5 years, 8.5 years, and 16 years) were included in the analysis. The total patency after a mean time of 16 years in the C group was 64% (46 of 72), and in the NT technique group 83% (62 of 75); *P* = .03. The single grafts had a patency of 65% (41 of 63) in the C group versus 82% (55 of 67) in the NT technique group, *P* = .06; whereas the sequential grafts showed a patency of 56% (5 of 9) in the C group and 87% (7 of 8) in the NT technique group, *P* = .29. Graft patency according to distal anastomosis was 65% (54 of 83) in the C group versus 83% (69 of 83), *P* = .01. In the C group, 37% (10 of 27) of patients had no SV grafts occluded, whereas in the group who had the NT technique, it was 63% (17 of 27). Three grafts had a significant stenosis (>50% and not stented) in the C group versus 2 grafts in the NT technique group; 2 other grafts in C, and 4 in the NT technique group had been stented and were still patent at the time of the examination.

Coronary artery and vein graft characteristics that might influence long-term graft patency are shown in Table 3. The patency of vein grafts anastomosed to target coronaries <2 mm in diameter was 65% (28 of 43) in the C group and 86% (49 of 57) in the NT group. Eleven percent of the veins in the C group were considered to have poor quality at surgery, showing either varicose or fibrotic changes, compared with 24% in the NT group. The proportion of vein grafts with poor quality still patent after 16 years was 38% (3 of 8) in the C group and 89% (16 of 18) in the NT group. The patency of vein grafts with a flow rate of ≤40 ml/minutes was 55% (18 of 33) in the C group versus 81% (29 of 36)
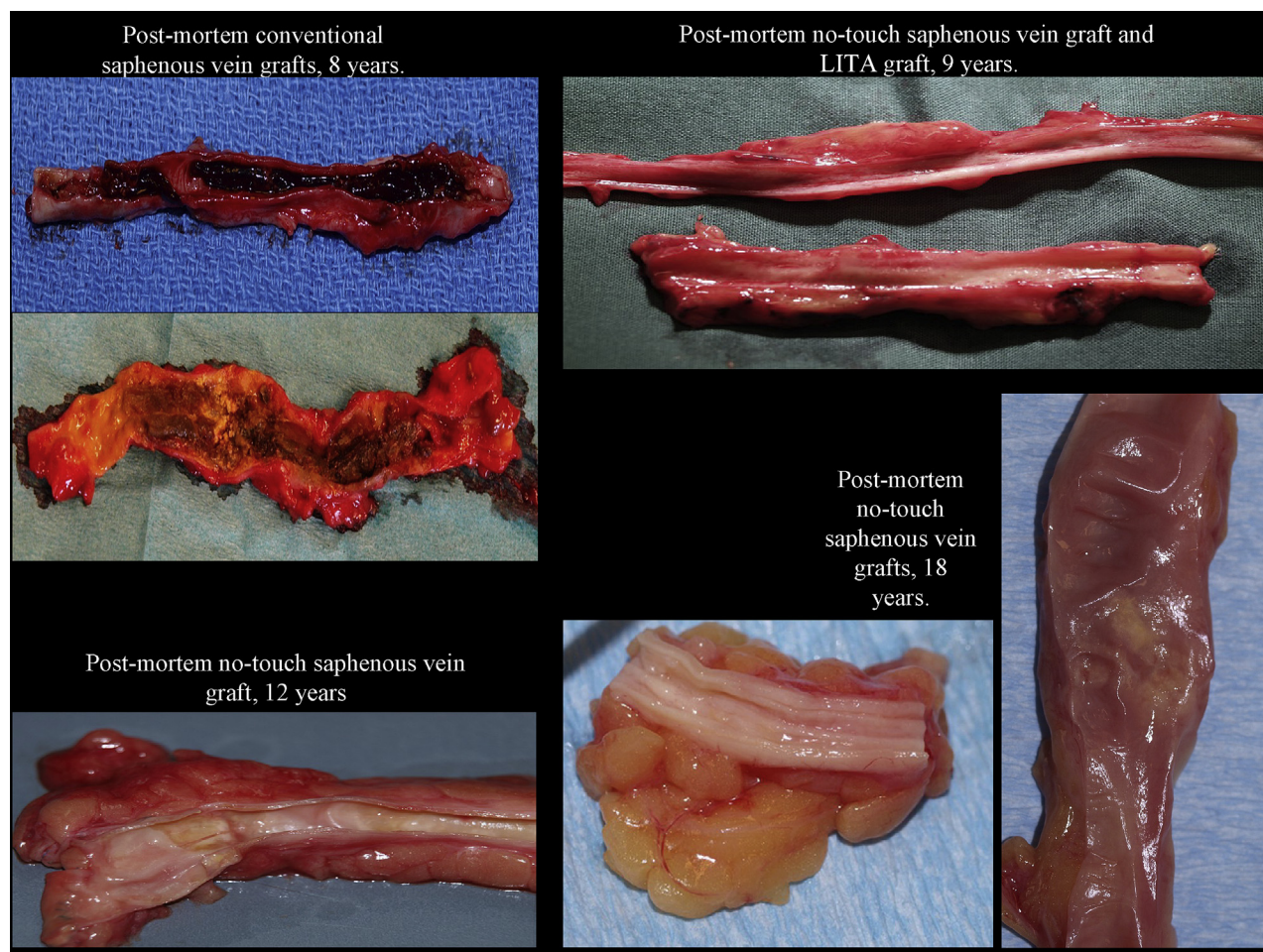
FIGURE 2. Postmortem biopsies at 8 years, 9 years, 12 years, and 18 years postoperatively. *LITA*, Left internal thoracic artery.

in the NT group. In the C group, the patency rate according to the segment of the vein was 73% (19 of 26), 62% (16 of 26), and 55% (11 of 20) regarding the distal (lower leg), medial (knee), and proximal (thigh) segments of the veins, respectively. In the NT group, the patency rate was 78% (21 of 27), 81% (22 of 27), and 90% (19 of 21) for the distal, medial, and proximal segments of the veins, respectively. Thus, the C group shows decreasing patency rates comparing distal, medial, and proximal segments, whereas the NT group shows increasing patency, with the proximal segments even showing a statistically significant advantage compared with those of the C group, $P = .02$.

A Cox proportional hazard regression model for analysis of time to occlusion was performed without and with allowance of additional explanatory factors other than the harvesting technique (graft flow, coronary artery diameter, and harvest region). Data from 1.5 years, 8.5 years, and 16 years follow-up were included (Table 4). After

TABLE 2. Ratio of number of patent grafts to total number of grafts for the 2 surgical techniques at 3 follow-up timepoints

	Follow-up								
	Conventional			No-touch			Group difference in % patency*		
Variable (y)	1.5	8.5	16	1.5	8.5	16	1.5	8.5	16
No. of patients	46	37	27	45	37	27			
Grafts									
Single	96/107 (90)	68/87 (78)	41/63 (65)	103/109 (94)	78/87 (90)	55/67 (82)	0.23	0.05	0.06
Sequential	16/20 (80)	10/14 (71)	5/9 (56)	15/15 (100)	14/14 (100)	7/8 (87)	0.12	0.10	0.29
All	112/127 (89)	78/101 (77)	46/72 (64)	118/124 (95)	92/101 (91)	62/75 (83)	0.08	0.01	0.03

Values in parentheses are %. *Tested with multilevel logistic regression, except for sequential grafts, for which Fisher's exact test had to be used because of small numbers and cells with no occluded grafts.

TABLE 3. Coronary artery and vein graft characteristics in the 2 randomized study groups

| | Follow-up years | | | | | |
| | Conventional group | | | No-touch group | | |
	1.5	8.5	16	1.5	8.5	16
Grafts (n)	127	101	72	124	101	75
Graft flow (ml/min)						
≤40	48/56 (86)	37/50 (74)	18/33 (55)	56/61 (92)	44/46 (96)	29/36 (81)
>40	64/71 (90)	41/51 (80)	28/39 (72)	62/63 (98)	48/55 (87)	33/39 (85)
Coronary artery diameter (mm)						
<2.0	66/78 (85)	47/64 (73)	28/43 (65)	89/94 (95)	73/78 (94)	49/57 (86)
≥2.0	46/49 (94)	31/37 (84)	18/29 (62)	29/30 (97)	19/23 (83)	13/18 (72)
Artery quality						
Good	93/106 (88)	66/84 (79)	42/63 (67)	100/106 (94)	77/86 (90)	52/64 (81)
Mildly calcified	16/17 (94)	10/14 (71)	4/8	10/10	8/8 (100)	7/8
Moderately calcified	1/2	1/2	0/1	8/8	7/7	3/3
Occluded (TEA)	2/2	1/1	0/0	0/0	0/0	0/0
Venous quality						
Good	106/116 (91)	74/90 (82)	43/64 (67)	88/91 (97)	68/74 (92)	46/57 (81)
Poor	6/11 (55)	4/11 (36)	3/8 (38)	30/33 (91)	24/27 (89)	16/18 (89)
Saphenous vein						
Distal	42/45 (93)	29/36 (81)	19/26 (73)	43/45 (96)	35/37 (95)	21/27 (78)
Medial	40/45 (89)	28/36 (78)	16/26 (62)	42/45 (93)	32/37 (87)	22/27 (81)
Proximal	30/37 (81)	21/29 (72)	11/20 (55)	33/34 (97)	25/27 (93)	19/21 (90)
Coronary system						
CX	41/47 (87)	28/39 (72)	18/29 (62)	44/47 (94)	33/36 (92)	21/27 (78)
DIAG	31/36 (86)	21/29 (72)	11/18 (61)	35/38 (92)	31/32 (97)	21/24 (88)
LAD	2/2	0/0	1/1	1/1	1/1	0/0
Right	14/16 (87)	10/12 (83)	7/11	13/13 (100)	6/10	4/7
PDA	24/26 (92)	19/21 (91)	9/13 (69)	25/25 (100)	21/22 (95)	16/17 (94)

Values are the number of patent grafts divided by total number of grafts, for follow-ups at 1.5 years, 8.5 years, and 16 years. Ratios (patent/total) supplemented with percentages for subgroups with >20 grafts altogether, ie, the conventional and no-touch harvesting techniques combined. Values in parentheses are %, unless otherwise indicated. *TEA*, Thromboendarterectomy; *CX*, circumflex; *DIAG*, diagonal; *LAD*, left anterior descending; *PDA*, posterior descending artery.

adjustment was made for multiple grafts within patients, the vein-harvesting technique was found to be a major factor in determining the probability of occlusion, with an HR of 1.83 (95% CI 1.01-3.32), $P = .04$ for the C technique versus the NT technique (HR >1.0 indicated higher probability of occlusion). The harvesting technique was particularly important for the SV of poor quality (HR 5.8 [95% CI

1.17-28.79], $P = .03$) and the SV harvested from the thigh (HR 4.86 [95% CI 1.29-18.23]), $P = .02$.

The total numbers of LITAs examined in this follow-up were 83, 68, and 48 at the 3 assessments, with almost identical distributions on the NT and C groups; that is, 42 versus 41, 34 versus 34, and 25 versus 23. All LITAs except 1 were anastomosed to the LAD artery. The overall patency at the

TABLE 4. Cox proportional hazard regression models for analysis of time to occlusion, at 16 years' follow-up

| | Single-factor model* | | Multifactor model* | |
Saphenous vein grafts	HR with 95% CI	P value	HR with 95% CI	P value
All data				
C vs NT; n = 251	1.83 (1.03-3.26)	.04	1.83 (1.01-3.32)	.04
Analysis in strata by venous quality and location of saphenous vein				
Good venous quality, C vs NT, n = 207	1.47 (0.75-2.85)	.26	1.41 (0.71-2.83)	.33
Inferior venous quality, C vs NT, n = 44	6.92 (2.77-17.29)	<.001	5.80 (1.17-28.79)	.03
Distal location, C vs NT, n = 90	1.51 (0.61-3.72)	.37	1.42 (0.57-3.53)	.45
Medial location, C vs NT, n = 90	1.36 (0.59-3.13)	.47	1.42 (0.56-3.58)	.45
Proximal location, C vs NT, n = 71	4.20 (1.17-15.09)	.03	4.86 (1.29-18.23)	.02

Outcome parameter is HR with 95% CI, adjusted for multiple grafts per patient. Single-factor and multifactor models showing HR for C group, with NT as a reference group, thus HR >1.0 indicates higher risk for occlusion for the C group. The number of grafts is given by n. *HR*, Hazard ratio; *CI*, confidence interval; *C*, conventional; *NT*, no-touch. *Single-factor model includes only group (C/NT) as regressor; multifactor models include group (C/NT) as well as graft flow, coronary artery diameter, and location of saphenous vein. All included factors fulfill the proportionality assumption of the Cox proportional hazard model.

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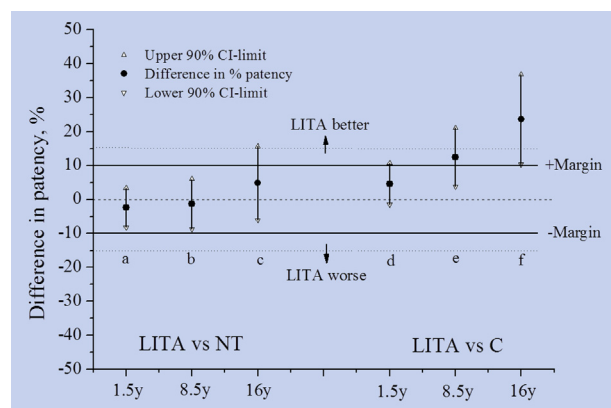
FIGURE 3. Differences in patency LITA-NT, LITA-C at 1.5 years, 8.5 years, and 16 years. The 6 confidence intervals (a-f) and the margins of 10 and 15 percentage units are the basis for comparing LITA with SV, with respect to potential equivalence and noninferiority (see text). *CI*, Confidence interval; *LITA*, left internal thoracic artery; *NT*, no touch; *C*, conventional.

16-year follow-up was 88% (42 of 48), a figure that was only slightly lower than those for 1.5 years (77 of 83 [93%]) and 8.5 years (61 of 68 [90%]). Figure 3 shows the differences in patency between LITA and the 2 SV-based techniques at the 3 assessments, supplemented with 90% CIs. With a margin of equivalence of 10 percentage units, the hypothesis of equivalence (at the 90% CI level) for NT with LITA is not rejected at the 1.5-year and 8.5-year follow-up; for the follow-up at 16 years, a nonconclusive result is obtained for this much smaller data set. The same conclusions are obtained at the 95% level if a noninferiority approach is taken. For the C group, a borderline result with respect to not rejecting the hypothesis of equivalence at the 1.5-year follow-up is found, but this is rejected at the 8.5-year follow-up and the 16-year follow-up. With the margin set at 15 percentage units, the hypotheses of equivalence and noninferiority are not rejected for NT at any of the follow-ups. The results for the C group are the same as with the stricter margins.

DISCUSSION

The main message of this study is that the technique of harvesting the SV for CABG plays a crucial role in the long-term outcome of vein grafts. This unique longitudinal randomized trial has followed a group of patients who underwent CABG, evaluating them at 1.5 years, 8.5 years, and now 16 years, postoperatively. The NT vein grafts maintain a patency rate that is significantly better than that of the conventionally harvested veins, and is comparable to that of the LITA.

We additionally observed that the NT veins maintained a somewhat similar patency, independent of the harvesting site, and that the NT veins harvested from the thigh (proximal) had a significantly higher patency than that of the C veins harvested from the thigh. This difference is important to consider in patients who have impaired distal circulation, because the risk of wound complications is higher in the leg, requiring the vein grafts to be harvested from the thighs. In addition, this factor is important when developing an endoscopic harvesting technique for NT grafts, in which the harvesting is often from the thigh.

Previous studies have shown that the predictors for long-term patency of vein grafts are distal runoff, target vessel quality, and diameter and quality of the grafts.[4,21] In our study, these factors seemed to have a greater impact on the patency of the C grafts, as opposed to the NT grafts. Despite randomization, the NT group had a greater proportion of poor quality veins (11% in the C group vs 24% in the NT group) and a higher percentage of smaller target vessels (60% in the C group vs 76% in the NT group). Another important aspect of this study is that the patency of conventional grafts was considerably higher (64%), compared with previous reports[22-24] of a 10-year patency rate between 40% and 60%. This difference could be due to the fact that most of the published reports were based on small retrospective studies of selected groups of patients and that most of the C veins in our study were of good quality.

We are aware of a single-center randomized clinical trial comparing a LITA to the SV for LAD artery bypass, which demonstrated improved survival, event-free survival, and graft patency in the LITA group.[25] In addition, we agree with the general consensus that the use of a LITA for the LAD artery is the gold standard in CABG surgery. However, Chow and colleagues[26] showed that a LITA used to bypass vessels other than the LAD artery had a significantly lower patency compared with a LITA connected to the LAD artery.

Despite the fact that the patency rate of the LITA in our study was higher than that of the NT vein (88% vs 83%, respectively), after a mean time of 16 years, they still were comparable (Figure 3).[19,20] Taking into consideration the fact that the LITAs were anastomosed to the LAD artery, as was the SV to smaller target vessels, and that arterial grafts are more sensitive to the degree of stenosis and competitive flow, we think it is fairly reasonable to assume that the NT SV might have had a higher patency rate if it were anastomosed to the LAD artery.[22] This possibility is currently being investigated in a separate trial (clinicaltrials.gov: NCT02339857).

Several mechanisms seem to be behind the success of NT vein grafts: the decreased risk of graft spasm and the associated requirement for graft dilatation limits endothelial cell loss and resultant long-term damage.[27,28] Other aspects are the preservation of the vasa vasorum, which allows retrograde blood flow from the graft lumen to perfuse through the vein wall, thereby decreasing transmural ischemic damage, and preservation of endothelial nitric

oxide synthase,[29] which is known to decrease intimal hyperplasia, subsequent atherosclerosis, and long-term graft failure.[30] Furthermore, the perivascular tissue may act as a natural external stent, reducing the neointimal and medial thickening of the vein graft,[31,32] and preventing it from kinking, which is especially important when using sequential grafts.

An intravascular ultrasound series showed a 4-fold increase of grafts with considerable intimal hyperplasia, and a 2-fold increase in grafts with plaques of atherosclerosis in C grafts rather than in NT grafts.[33] This increase has been noticed in our postmortem studies as well, in which the C grafts showed diffuse atherosclerotic changes, whereas the changes in the NT grafts were more localized (Figure 2).

Limitations

The low number of patients in this study is an obvious limitation, and therefore, a larger randomized multicenter trial is needed to confirm some of the results. A multicenter trial is currently underway (SUPERIOR-SVG, clinicaltrials.gov: NCT01047449) comparing the NT harvesting technique with the C technique.

Concerns have been raised about the issue of increased leg-wound complications. A recently published study showed that functional leg recovery was similar between the C and NT harvesting techniques 12 months after surgery.[10]

This technique is associated with a learning curve, but improved efficiency with experience is the norm. Good preparation preoperatively is a key factor in reducing some of these concerns, namely, mapping of the SV with ultrasonographic imaging, to assess the quality and size of the vein, as well as mark its course. This process has been shown to reduce the size of the scar and the harvest time, in addition to minimizing unnecessary incisions.[34] However, a minimally invasive endoscopic technique for harvesting the NT vein grafts is crucial to further reduce these risks.[35]

CONCLUSIONS

The SV can still be considered a reliable conduit for CABG. This study is the first to demonstrate that the use of an SV graft to non-LAD targets can provide patency comparable to that of LITA for LAD artery, at a mean follow-up of 16 years postoperatively. However, to achieve such results, the SV should be harvested using the NT technique.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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

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