ORIGINAL ARTICLE

Randomized Trial of Endoscopic or Open Vein-Graft Harvesting for Coronary-Artery Bypass

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ABSTRACT

BACKGROUND

The saphenous-vein graft is the most common conduit for coronary-artery bypass grafting (CABG). The influence of the vein-graft harvesting technique on long-term clinical outcomes has not been well characterized.

METHODS

We randomly assigned patients undergoing CABG at 16 Veterans Affairs cardiac surgery centers to either open or endoscopic vein-graft harvesting. The primary outcome was a composite of major adverse cardiac events, including death from any cause, nonfatal myocardial infarction, and repeat revascularization. Leg-wound complications were also evaluated.

RESULTS

A total of 1150 patients underwent randomization. Over a median follow-up of 2.78 years, the primary outcome occurred in 89 patients (15.5%) in the open-harvest group and 80 patients (13.9%) in the endoscopic-harvest group (hazard ratio, 1.12; 95% confidence interval [CI], 0.83 to 1.51; P=0.47). A total of 46 patients (8.0%) in the open-harvest group and 37 patients (6.4%) in the endoscopic-harvest group died (hazard ratio, 1.25; 95% CI, 0.81 to 1.92); myocardial infarctions occurred in 34 patients (5.9%) in the open-harvest group and 27 patients (4.7%) in the endoscopic-harvest group (hazard ratio, 1.27; 95% CI, 0.77 to 2.11), and revascularization occurred in 35 patients (6.1%) in the open-harvest group and 31 patients (5.4%) in the endoscopic-harvest group (hazard ratio, 1.14; 95% CI, 0.70 to 1.85). Leg-wound infections occurred in 18 patients (3.1%) in the open-harvest group and in 8 patients (1.4%) in the endoscopic-harvest group (relative risk, 2.26; 95% CI, 0.99 to 5.15).

CONCLUSIONS

Among patients undergoing CABG, we did not find a significant difference between open vein-graft harvesting and endoscopic vein-graft harvesting in the risk of major adverse cardiac events. (Funded by the Cooperative Studies Program, Office of Research and Development, Department of Veterans Affairs; REGROUP ClinicalTrials.gov number, NCT01850082.)

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*A complete list of the REGROUP Trial Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Despite evidence favoring the use of multiple arterial conduits for coronary-artery bypass grafting (CABG), the greater saphenous vein remains the most commonly used conduit worldwide because of its ready availability and ease of use.[1,2] The two main limitations of vein grafts in myocardial revascularization are the high rates of graft failure, leading to a graft patency of approximately 60% at 10 years, and the risk of harvest-site complications (e.g., infections and pain).[3-5]

Endoscopic vein-graft harvesting is a minimally invasive technique designed to reduce the rate of harvest-site complications. Endoscopic vein-graft harvesting technology was first introduced clinically in the mid-1990s and is currently being used in more than 90% of CABG cases in the United States.[6,7] Although the effectiveness of the endoscopic technique in reducing the incidence of leg-wound healing complications is well established, the evidence for its safety is derived from randomized trials of relatively small size, with short follow-up times and limited statistical power to evaluate major adverse cardiac events.[8,9] Furthermore, vein-graft patency has been consistently lower with endoscopic harvesting than with nonendoscopic harvesting, possibly because of mechanical factors during procurement (e.g., overstretch injury) performed by inexperienced endoscopic harvesters.[10,11] One particularly troubling observational study described both lower graft patency and a near doubling of mortality 18 months after CABG with endoscopic as compared with open vein-graft harvesting.[12] In the Randomized Endovein Graft Prospective (REGROUP) trial, we assessed the clinical outcomes of open or endoscopic vein-graft harvesting in CABG surgery in a multicenter, randomized trial.

Methods

Trial Design and Oversight

We conducted a randomized, intention-to-treat, multicenter trial funded by the Cooperative Studies Program of the Department of Veterans Affairs. The rationale and design of the trial have been published previously.[13] Cardiac surgery programs at Veterans Affairs medical centers with expertise in performing endoscopic vein-graft harvesting were eligible to participate. An executive committee was responsible for trial oversight. The trial was approved by the institutional review board at each participating center. Patients gave written informed consent before participation. The authors vouch for the accuracy and completeness of the data and the analyses and for the fidelity of the trial to the protocol, which is available with the full text of this article at NEJM.org.

Patient Population

Patients undergoing elective or urgent CABG with cardiopulmonary bypass and cardioplegic arrest and a decision to use at least one vein graft underwent screening for enrollment. Inclusion criteria were an age of 18 years or older and planned elective or urgent (but not emergency) CABG with the use of the median sternotomy approach and a plan to use at least one saphenous vein graft as a conduit. Exclusion criteria were a planned valve procedure in combination with CABG, the presence of moderate or severe valve disease, the presence of hemodynamic instability or cardiogenic shock, enrollment in another therapeutic or interventional study, planned off-pump CABG, a life expectancy of less than 1 year, a history of venous stripping or ligation in the legs, and an inability to provide informed consent.

The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score was used to quantify the severity of coronary-artery disease for each trial participant.[14] The SYNTAX score reflects a comprehensive angiographic assessment of the coronary vasculature, with a score of 22 or less indicating low anatomical complexity, scores of 23 to 32 indicating intermediate anatomical complexity, and scores of more than 32 indicating high anatomical complexity (0 is the lowest score, and there is no upper limit).

Vein-Graft Harvesting Experience and Techniques

Only expert endoscopic vein-graft harvesters (e.g., surgeons or physician assistants but not trainees) were invited to participate in the trial. Participating harvesters provided information on their experience (certified by the principal investigator at the site) and had to receive approval to participate from an ad hoc committee chaired by a senior physician assistant in the field of endoscopic harvesting. Minimum expertise was defined as experience with more than 100 endoscopic

vein harvesting cases with a certified low (<5%) conversion rate to open harvesting, as part of an established endoscopic vein harvesting program with more than 2 years of experience, as well as similar levels of experience with the open approach.[15]

The use of any endoscopic vein harvesting device approved by the Food and Drug Administration was allowed in the trial; the equipment was purchased by the participating hospitals. Best-practice endoscopic harvesting was recommended; the surgical technique is described in the Supplementary Appendix, available at NEJM.org.[13] Open harvesting was performed according to the preference at each site. Guideline-directed medical therapy for secondary prevention of cardiovascular events was recommended as described in the Supplementary Appendix.[16]

RANDOMIZATION AND FOLLOW-UP

Before randomization, an experienced vein harvester was identified and assigned to the case. Patients were then randomly assigned to either endoscopic or open vein-graft harvesting, in a 1:1 ratio, by means of a telephone call to the Cooperative Studies Program Coordinating Center in Perry Point, Maryland, with the use of an automated system. A block randomization scheme with a random sequence of block sizes was used to ensure a balanced distribution of participants assigned to each harvester and within each medical center. Unless the patient had an urgent medical condition, surgery was scheduled to occur at the earliest possible date on the basis of the availability of the expert harvester and other circumstances at the center.

Participants were actively followed for a minimum of 1 year. Assessments were collected by site research personnel using in-clinic visits, telephone calls, or medical chart review. Assessments occurred at baseline, during surgery, after surgery, at discharge (or 30 days after surgery, if the patient was still hospitalized), at 6 weeks, and every 3 months thereafter until the end of the active follow-up phase and the beginning of the passive follow-up phase (for 2 additional years).

TRIAL OUTCOMES

The primary outcome was defined as the first occurrence of a major adverse cardiac event (a composite of death from any cause, nonfatal myocardial infarction, or repeat revascularization) in a time-to-event analysis over the active follow-up period of the trial. The primary composite outcome and the individual components of that outcome (as defined in the Supplementary Appendix) were identified and adjudicated. A clinical-events committee consisting of cardiologists and cardiac surgeons, all of whom were unaware of the treatment assignments, reviewed and adjudicated all major adverse cardiac events, with differences reconciled appropriately. The clinical-events committee further assigned causes of death as cardiac, noncardiac, or unknown on the basis of a review of data from medical records both inside and outside the Veterans Health Administration.

A secondary outcome included major adverse cardiac events at 1 year after surgery. Additional secondary outcomes of major adverse cardiac events at 3 years after surgery and time to major adverse cardiac events over the combined (active and passive) follow-up period have not yet been assessed, because the trial is currently in the passive follow-up period.

Several tertiary and post hoc outcomes were also assessed. The severity of incisional leg pain was assessed at the time of discharge and at approximately 6 weeks after surgery. Leg wounds were also evaluated with the ASEPSIS criteria, which are described in the Supplementary Appendix.[17] The ASEPSIS criteria include Likert-scale scores for the presence of erythema, serous exudates, purulent exudates, and separation of tissues, as well as assessments of the use of therapeutic interventions including antibiotic treatment, drainage, débridement, and prolongation of the hospital stay. In a post hoc analysis, leg wound infections were adjudicated according to the Centers for Disease Control and Prevention criteria as described in the Supplementary Appendix.[18] Quality of life was assessed at baseline, 6 weeks, and 1 year with the use of the Veterans RAND 12-item health survey (VR-12) and the Seattle Angina Questionnaire.[19]

STATISTICAL ANALYSIS

We calculated that we would need a total sample of 1150 patients; details are provided in the Supplementary Appendix. Survival-analysis techniques were used to analyze the time to major adverse cardiac events (the primary outcome). Kaplan–Meier nonparametric survival estimates were used to evaluate the unadjusted effect of vein harvest-

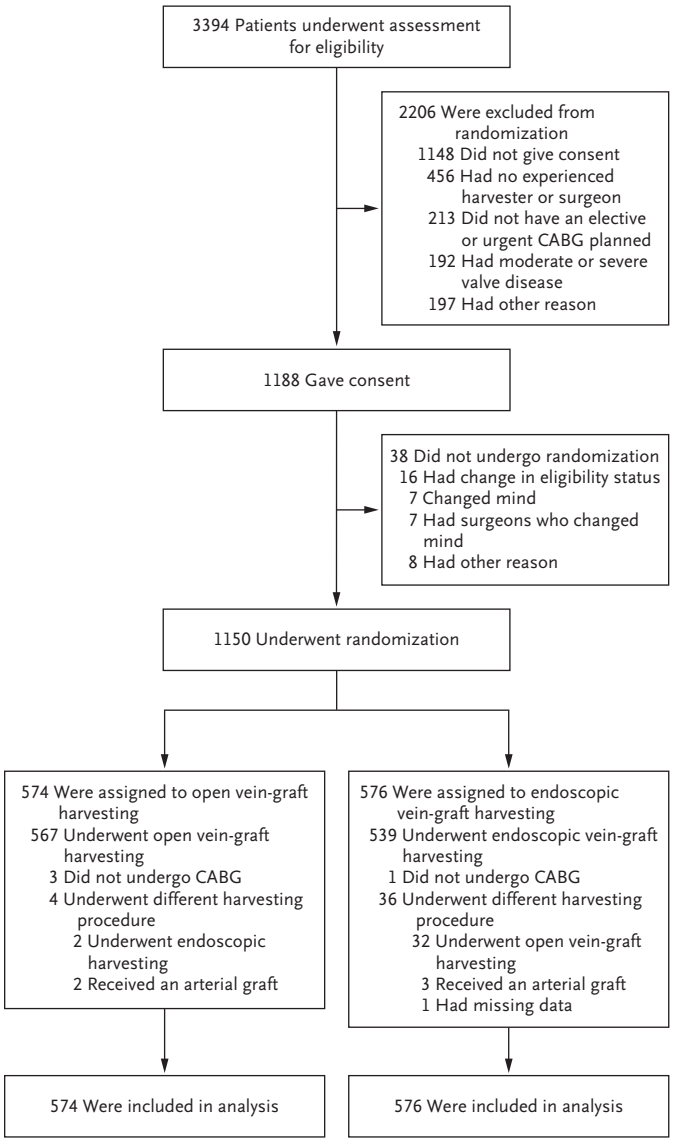

Figure 1. Enrollment and Randomization.
CABG denotes coronary-artery bypass grafting.

ing technique on major adverse cardiac events. Tests of differences of the survival-function estimates across strata (open and endoscopic harvest) were performed with the log-rank test. Multivariable survival analyses applying a Cox proportional-hazards regression model were performed to investigate the effect of vein harvesting technique on the primary outcome, with adjustment for other potentially influential baseline characteristics. A Wei–Lin–Weissfeld model was used to compare multiple times to events (recurrent events) between the groups during active follow-up. Pearson's chi-square analysis was used to compare the rate of major adverse cardiac events between the groups during the first year of follow-up.

A type I error rate of 0.025 was used for the primary outcome to account for the alpha error assigned to three interim analyses (as described in the Supplementary Appendix). No adjustment for multiplicity of testing was made; therefore, P values are not reported for outcomes other than the primary outcome. Confidence intervals were two-sided with a 95% confidence level and were not adjusted for multiplicity; therefore, inferences drawn from these intervals regarding secondary and tertiary outcomes may not be reproducible. All statistical analyses were conducted with the use of SAS statistical software, version 9.4 (SAS Institute).

RESULTS

PATIENTS AND TREATMENT

From March 2014 through April 2017, we enrolled 1188 patients at 16 Veterans Affairs cardiac surgery centers in the United States. Of the 1150 patients who underwent randomization, 574 were assigned to open vein-graft harvesting and 576 to endoscopic vein-graft harvesting (Fig. 1). The groups were balanced with regard to age, sex, smoking status, race or ethnic group, body-mass index, and coexisting conditions (Table 1). Medical therapy at baseline and during follow-up is shown in Table S1 in the Supplementary Appendix.

Characteristics of the surgical procedures and the patients are described in Table 2. The mean (±SD) SYNTAX score was 28.5±11.5 (median, 27). No site used the open "no touch" vein harvesting technique.[20] The mean vein harvesting time was 61.4±28.7 minutes in the open-harvest group and 57.5±24.4 minutes in the endoscopic-harvest group. Conversion to open harvesting occurred in 5.6% of the patients who had been randomly assigned to the endoscopic-harvest group (Table 2). A few protocol violations occurred: in 0.5% of the cases, CABG was performed off pump, and in 0.3% of the cases, combined CABG and valve surgery was performed.

PRIMARY AND SECONDARY OUTCOMES

The active follow-up period ended in April 2018. The median follow-up duration was 2.78 years (interquartile range, 1.99 to 3.48). During active follow-up, the primary composite outcome of major adverse cardiac events occurred in 89 patients

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Open Harvesting (N=574)	Endoscopic Harvesting (N=576)	All Patients (N=1150)
Age — yr†	66.6±7.1	66.2±6.7	66.4±6.9
Male sex — no./total no. (%)	571/574 (99.5)	572/575 (99.5)	1143/1149 (99.5)
Smoking status — no. (%)			
Lifelong nonsmoker	123 (21.4)	137 (23.8)	260 (22.6)
Current smoker	151 (26.3)	164 (28.5)	315 (27.4)
Former smoker	296 (51.6)	274 (47.6)	570 (49.6)
Missing data	4 (0.7)	1 (0.2)	5 (0.4)
Race or ethnic group — no. (%)‡			
White, not of Hispanic origin	484 (84.3)	490 (85.1)	974 (84.7)
Missing data	0	1 (0.2)	1 (0.1)
Body-mass index§	30.6±5.2	30.3±5.2	30.4±5.2
Diabetes — no. (%)			
No history of diabetes	277 (48.3)	295 (51.2)	572 (49.7)
Insulin-dependent diabetes	137 (23.9)	125 (21.7)	262 (22.8)
Non–insulin-dependent diabetes	160 (27.9)	155 (26.9)	315 (27.4)
Missing data	0	1 (0.2)	1 (0.1)
Hypertension — no./total no. (%)	515/574 (89.7)	521/575 (90.6)	1036/1149 (90.2)
Hyperlipidemia — no./total no. (%)	502/574 (87.5)	491/575 (85.4)	993/1149 (86.4)
Peripheral vascular disease — no./total no. (%)	80/574 (13.9)	80/575 (13.9)	160/1149 (13.9)
Previous stroke — no./total no. (%)	48/574 (8.4)	48/575 (8.3)	96/1149 (8.4)
Previous myocardial infarction — no./total no. (%)	207/573 (36.1)	219/575 (38.1)	426/1148 (37.1)
Previous PCI — no./total no. (%)	158/574 (27.5)	160/575 (27.8)	318/1149 (27.7)
NYHA functional class — no. (%)¶			
No heart failure	285 (49.7)	284 (49.3)	569 (49.5)
Class I	68 (11.8)	60 (10.4)	128 (11.1)
Class II	151 (26.3)	167 (29.0)	318 (27.7)
Class III	65 (11.3)	54 (9.4)	119 (10.3)
Class IV	4 (0.7)	4 (0.7)	8 (0.7)
Missing data	1 (0.2)	7 (1.2)	8 (0.7)
CCS angina class — no. (%)‖			
No angina present on admission	57 (9.9)	57 (9.9)	114 (9.9)
Class I	92 (16.0)	82 (14.2)	174 (15.1)
Class II	224 (39.0)	238 (41.3)	462 (40.2)
Class III	130 (22.6)	141 (24.5)	271 (23.6)
Class IV	46 (8.0)	35 (6.1)	81 (7.0)
Missing data	25 (4.4)	23 (4.0)	48 (4.2)

* Plus–minus values are means ±SD. Percentages may not total 100 because of rounding. No significant differences were found between groups for any baseline characteristic (P<0.05). PCI denotes percutaneous coronary intervention.
† Data on age were missing for one patient in the endoscopic-harvest group.
‡ Race and ethnic group were reported by the patient.
§ The body-mass index is the weight in kilograms divided by the square of the height in meters. Data were missing for two patients in the endoscopic-harvest group and one patient in the open-harvest group.
¶ New York Heart Association (NYHA) functional class indicates the severity of heart failure, with higher class numbers indicating greater severity.
‖ Canadian Cardiovascular Society (CCS) angina class indicates the severity of angina, with higher class numbers indicating greater severity.

(15.5%) in the open-harvest group and 80 patients (13.9%) in the endoscopic-harvest group (hazard ratio, 1.12; 95% confidence interval [CI], 0.83 to 1.51; P=0.47) (Fig. 2 and Table 3, and Fig. S1 in the Supplementary Appendix). A total of 46 patients (8.0%) in the open-harvest group and 37 patients (6.4%) in the endoscopic-harvest group died (hazard ratio, 1.25; 95% CI, 0.81 to 1.92) (Fig. S2 in the Supplementary Appendix). Causes of death were adjudicated as cardiac, not cardiac, or unknown; these data are provided in Table S2 in the Supplementary Appendix. Myocardial infarction occurred in 34 patients (5.9%) in the open-harvest group and 27 patients (4.7%) in the endoscopic-harvest group (hazard ratio, 1.27; 95% CI, 0.77 to 2.11), and repeat revascu-

Table 2. Characteristics of the Surgical Procedures and the Patients.*

Characteristic	Open Harvesting (N=574)	Endoscopic Harvesting (N=576)	All Patients (N=1150)	P Value
No. of days from randomization to surgery	0.1±2.4	0.0±0.0	0.1±1.7	0.06
Status of index CABG procedure — no. (%)				0.56
Elective	423 (73.7)	415 (72.0)	838 (72.9)	
Urgent	151 (26.3)	160 (27.8)	311 (27.0)	
Missing data	0	1 (0.2)	1 (0.1)	
Combined CABG plus mitral-valve repair — no. (%)	1 (0.2)	2 (0.3)	3 (0.3)	>0.99
Coronary artery disease territories — no. (%)				0.11
Single-vessel disease	12 (2.1)	4 (0.7)	16 (1.4)	
Double-vessel disease	119 (20.7)	129 (22.4)	248 (21.6)	
Triple-vessel disease	443 (77.2)	442 (76.7)	885 (77.0)	
Missing data	0	1 (0.2)	1 (0.1)	
Left main coronary artery disease — no./total no. (%)†	168/572 (29.4)	187/575 (32.5)	355/1147 (31.0)	0.25
SYNTAX score — no. (%)‡				0.83
<22	166 (28.9)	164 (28.5)	330 (28.7)	
22–32	218 (38.0)	228 (39.6)	446 (38.8)	
>32	188 (32.8)	181 (31.4)	369 (32.1)	
Missing data	2 (0.3)	3 (0.5)	5 (0.4)	
Ejection fraction — %§	54.4±9.3	53.7±10.4	54.0±9.9	0.59
No. of grafts per patient¶	3.1±0.8	3.2±0.8	3.1±0.8	0.63
Bilateral internal thoracic artery grafts used — no./total no. (%)	55/571 (9.6)	63/574 (11.0)	118/1145 (10.3)	0.45
Radial artery graft used — no./total no. (%)	6/571 (1.1)	7/574 (1.2)	13/1145 (1.1)	0.79
Off-pump procedure performed — no. (%)	5 (0.9)	1 (0.2)	6 (0.5)	0.12
STS predicted risk of death — %‖	0.97±0.87	0.92±0.85	0.94±0.86	0.73
VASQIP predicted risk of death — %**	0.98±0.88	1.01±1.00	0.99±0.95	0.82
Vein harvesting time — min††	61.4±28.7	57.5±24.4	59.4±26.7	0.01
Cross-clamp time — min‡‡	75.5±31.7	76.6±29.8	76.1±30.7	0.39
Cardiopulmonary bypass time — min§§	107.9±36.4	108.8±35.2	108.4±35.8	0.65
Endoscopic harvesting device type — no. (%)				
Maquet Vasoview	—	548 (95.1)	—	—
Terumo Virtuosaph	—	24 (4.2)	—	—
Missing data	—	4 (0.7)	—	—
Endoscopic harvesting conversion to open harvesting — no. (%)	—	32 (5.6)	—	—

Table 2. (Continued.)

Characteristic	Open Harvesting (N = 574)	Endoscopic Harvesting (N = 576)	All Patients (N = 1150)	P Value
Reason for conversion				
Bleeding	—	6 (18.8)	—	—
Unacceptable duration of endoscopic procedure	—	3 (9.4)	—	—
Insufficient amount of usable vein from endoscopic procedure	—	7 (21.9)	—	—
Harvester unable to locate vein	—	5 (15.6)	—	—
Other	—	11 (34.4)	—	—
Need for procedure to harvest additional conduit after successful endoscopic harvesting — no. (%)	—	4 (0.7)	—	—

* Plus–minus values are means ±SD. CABG denotes coronary-artery bypass grafting.
† Patients with 50% or greater stenosis of the left main coronary artery were included.
‡ The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score reflects a comprehensive angiographic assessment of the coronary vasculature; scores of 22 or less indicate low anatomical complexity, scores of 23 to 32 indicate intermediate anatomical complexity, and scores higher than 32 indicate high anatomical complexity (0 is the lowest score, and there is no upper limit).
§ Data on ejection fraction were missing for 4 patients in the open-harvest group and 3 patients in the endoscopic-harvest group.
¶ Data on number of grafts for were missing for 3 patients in the open-harvest group and 2 patients in the endoscopic-harvest group.
‖ The Society of Thoracic Surgeons (STS) predicted risk of death indicates the risk of operative death based on the adult cardiac surgery database maintained by the STS in the United States. Data were missing for 2 patients in the open-harvest group and 1 patient in the endoscopic-harvest group.
** The Veterans Affairs Surgical Quality Improvement Project (VASQIP) predicted risk of death indicates the risk of operative death and is maintained by the Department of Veterans Affairs National Surgery Office with the use of its database. Data were missing for 1 patient in the open-harvest group and 3 patients in the endoscopic-harvest group.
†† Data on vein harvesting time were missing for 6 patients in the open-harvest group and 3 patients in the endoscopic-harvest group.
‡‡ Data on cross-clamp time were missing for 24 patients in the open-harvest group and 16 patients in the endoscopic-harvest group.
§§ Data on cardiopulmonary bypass time were missing for 8 patients in the open-harvest group and 3 patients in the endoscopic-harvest group.

larization occurred in 35 patients (6.1%) in the open-harvest group and 31 patients (5.4%) in the endoscopic-harvest group (hazard ratio, 1.14; 95% CI, 0.70 to 1.85).

A multivariable Cox proportional-hazards regression model with adjustment for potentially influential baseline demographic and clinical characteristics of the patients showed no significant difference in risk according to the type of vein harvesting (Table S3 in the Supplementary Appendix). In an analysis of recurrent major cardiac events after open as compared with endoscopic harvesting, the hazard ratio was 1.29 (95% CI, 1.00 to 1.68) (Table S4 in the Supplementary Appendix). The 1-year rate of major adverse cardiac events was 8.2% for open harvesting and 7.8% for endoscopic harvesting. The results of competing-risks analyses for myocardial infarction, repeat revascularization, and the composite of myocardial infarction or complete revascularization were similar to those of the primary analyses and are shown in Table S5 in the Supplementary Appendix.

TERTIARY OUTCOMES

Leg-wound infections occurred in 18 patients (3.1%) in the open-harvest group and in 8 patients (1.4%) in the endoscopic-harvest group (absolute difference, 1.7 percentage points; relative risk, 2.26; 95% CI, 0.99 to 5.15). Data on the timing of leg-wound infections are shown in Table S6 in the Supplementary Appendix. Incisional leg pain had little or no effect on functioning at 6 weeks after surgery in 62.2% of the patients in the open-harvest group, as compared with 79.1% of those in the endoscopic-harvest group (relative risk, 0.79; 95% CI, 0.73 to 0.85) (Table S7 in the Supplementary Appendix). There was no significant difference in quality of life between the groups as assessed with either the VR-12 survey or the Seattle Angina Questionnaire (Tables S8 through S14 in the Supplementary Appendix).

Antibiotics were administered at follow-up to 14.4% of the patients in the open-harvest group and in 4.6% of the patients in the endoscopic-harvest group (relative risk, 3.15; 95% CI, 2.06 to 4.82). The percentage of patients who received a

Table 3. Major Adverse Cardiac Events during Active Follow-up.

Event	Open Harvesting (N = 574)	Endoscopic Harvesting (N = 576)	Hazard Ratio (95% CI)
	number of patients (percent)		
Primary outcome: death from any cause, nonfatal myocardial infarction, or repeat revascularization	89 (15.5)	80 (13.9)	1.12 (0.83–1.51)*
Death from any cause	46 (8.0)	37 (6.4)	1.25 (0.81–1.92)
Myocardial infarction	34 (5.9)	27 (4.7)	1.27 (0.77–2.11)
Repeat revascularization	35 (6.1)	31 (5.4)	1.14 (0.70–1.85)

* P=0.47 in the unadjusted Cox proportional-hazards model for the primary composite outcome.

visit from a nurse to dress the leg wound at home after discharge from the hospital was 3.7% in the open-harvest group as compared with 1.2% in the endoscopic-harvest group (relative risk 3.03; 95% CI, 1.30 to 7.08). Additional components of the ASEPSIS criteria for wound status are shown in Table S15 in the Supplementary Appendix. Data on the experience of individual vein harvesters, as well as trial outcomes according to center and harvester, are provided in Tables S16 through S19 in the Supplementary Appendix.

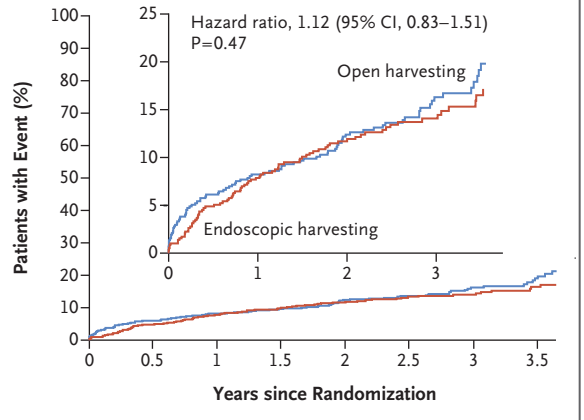

Figure 2. Composite Outcome of Death from Any Cause, Myocardial Infarction, or Repeat Revascularization during the Active Follow-up Period.
The inset shows the same data on an enlarged y axis.

DISCUSSION

In this trial, in which vein-graft harvesting for CABG was performed by operators with documented experience, we did not find any significant difference between open and endoscopic vein-graft harvesting in the rate of major adverse cardiac events over a median follow-up of 2.78 years. We found a trend toward lower rates of major adverse cardiac events in association with the endoscopic technique when recurrent events were compared between the two treatment groups, although longer-term follow-up will be necessary to determine whether this finding is persistent. Endoscopic harvesting resulted in better harvest-site healing than did the open approach, a finding consistent with previous observations.

The conflicting findings regarding the safety profile of endoscopic harvesting that were published during 2009 through 2012, as well as our own data from a preplanned analysis of the Randomized On/Off Bypass (ROOBY) trial, led to the launch of the REGROUP trial in 2013.[12,21-23] An important feature of our trial design is the required high level of expertise of the vein harvesters, for both endoscopic and open harvesting, a characteristic that has not always been a part of previous trial designs.[12,21] In fact, a well-founded criticism of previous trials of endoscopic vein-graft harvesting was the lack of information on expertise. The learning curve for vein-graft harvesting is steep, and proficiency is required for good outcomes. Inexperienced operators may cause unnecessary stretching and trauma to the vein graft during harvesting, leading

to endothelial injury and possible early vein-graft failure.[24-26]

The results of our trial are consistent with those of a large observational study involving Medicare patients who underwent CABG at 934 surgical centers participating in the Society of Thoracic Surgeons national database; in that study no significant difference in the long-term rates of major adverse cardiac outcomes were found in association with endoscopic as compared with open vein-graft harvesting.[21] The safety concern raised by a retrospective analysis of the Project of Ex-vivo Vein Graft Engineering via Transfection IV (PREVENT IV) trial[12] may be explained by the lack of information on the experience of the endoscopic vein-graft harvesters. Because less experienced harvesters were allowed to participate in their trial, the quality of the conduits could have been compromised, contributing to accelerated vein-graft failure and worse clinical outcomes.

Limitations of our trial included the absence of an imaging evaluation of graft patency. Consequently, some subclinical events may have been overlooked. However, graft patency is an imperfect surrogate for clinical events, and since there was no signal of superior clinical outcomes with open harvesting and a trend toward a lower rate of recurrent events with endoscopic harvesting, it is unlikely that subclinical events related to graft patency would have altered the overall trial results. The trial focused on experienced harvesters, and its results may not apply to other populations. The open "no touch" technique of vein-graft harvesting was not practiced at any site in the study, and therefore the results reflect only outcomes associated with the more traditional technique of open harvesting.[20] The results reflect experience in a predominantly male population of patients. Off-pump CABG was excluded because of evidence of lower graft patency with this approach; therefore, the results of our trial apply to the on-pump technique with cardioplegic arrest, which remains the most common form of CABG.[27,28]

In conclusion, our trial did not show a significant difference between endoscopic and open vein-graft harvesting in the rate of major adverse cardiac events among patients undergoing CABG surgery during a follow-up period with a median duration of 2.78 years. The rate of wound complications was lower in the endoscopic-harvest group than in the open-harvest group. Further studies are needed to establish standards for harvester expertise to ensure the safety of patients and effectiveness of the procedure.

The views and opinions expressed herein are those of the authors and do not necessarily represent that of the Department of Veterans Affairs or the U.S. government.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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APPENDIX

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