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Endoscopic versus Open Vein-Graft Harvesting in Coronary-Artery Bypass Surgery

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ABSTRACT

BACKGROUND

Vein-graft harvesting with the use of endoscopy (endoscopic harvesting) is a technique that is widely used to reduce postoperative wound complications after coronary-artery bypass grafting (CABG), but the long-term effects on the rate of vein-graft failure and on clinical outcomes are unknown.

METHODS

We studied the outcomes in patients who underwent endoscopic harvesting (1753 patients) as compared with those who underwent graft harvesting under direct vision, termed open harvesting (1247 patients), in a secondary analysis of 3000 patients undergoing CABG. The method of graft harvesting was determined by the surgeon. Vein-graft failure was defined as stenosis of at least 75% of the diameter of the graft on angiography 12 to 18 months after surgery (data were available in an angiographic subgroup of 1817 patients and 4290 grafts). Clinical outcomes included death, myocardial infarction, and repeat revascularization. Generalized estimating equations were used to adjust for baseline covariates associated with vein-graft failure and to account for the potential correlation between grafts within a patient. Cox proportional-hazards modeling was used to assess long-term clinical outcomes.

RESULTS

The baseline characteristics were similar between patients who underwent endoscopic harvesting and those who underwent open harvesting. Patients who underwent endoscopic harvesting had higher rates of vein-graft failure at 12 to 18 months than patients who underwent open harvesting (46.7% vs. 38.0%, $P<0.001$). At 3 years, endoscopic harvesting was also associated with higher rates of death, myocardial infarction, or repeat revascularization (20.2% vs. 17.4%; adjusted hazard ratio, 1.22; 95% confidence interval [CI], 1.01 to 1.47; $P=0.04$), death or myocardial infarction (9.3% vs. 7.6%; adjusted hazard ratio, 1.38; 95% CI, 1.07 to 1.77; $P=0.01$), and death (7.4% vs. 5.8%; adjusted hazard ratio, 1.52; 95% CI, 1.13 to 2.04; $P=0.005$).

CONCLUSIONS

Endoscopic vein-graft harvesting is independently associated with vein-graft failure and adverse clinical outcomes. Randomized clinical trials are needed to further evaluate the safety and effectiveness of this harvesting technique.

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Coronary-artery bypass grafting (CABG) is one of the most commonly performed surgical procedures and improves the clinical outcomes in appropriately selected patients.[1,2] Despite increased use of an arterial conduit, the greater saphenous vein remains the conduit that is used most often in CABG.[1]

Traditionally, the saphenous vein is harvested under direct vision (open harvesting) with the help of linear incisions along the course of the vein. This approach is associated with discomfort and the risk of complications, including edema, hematoma, delayed healing, cellulitis, and wound dehiscence.[3-7]

Endoscopic vein-graft harvesting, a procedure that was developed to eliminate the need for the long incisions associated with open harvesting, reduces the risk of wound infection and other complications, lessens postoperative pain, shortens the patient's length of stay in the hospital, and leads to greater patient satisfaction.[8-18] Little is known, however, about the effect of endoscopic harvesting on long-term graft patency or on clinical outcomes. The objectives of this study were to assess the effect of endoscopic vein-graft harvesting on vein-graft failure as assessed by angiography 12 to 18 months after CABG and on clinical outcomes at 3 years.

Methods

Study Population

We conducted these analyses with the use of the database from the Project of Ex-vivo Vein Graft Engineering via Transfection IV trial (PREVENT IV; ClinicalTrials.gov number, NCT00042081). The design and main results of the PREVENT IV trial have been published previously.[19,20] PREVENT IV was a phase 3, multicenter, randomized, double-blind, placebo-controlled trial of ex vivo treatment of vein grafts with the E2F transcription factor decoy, edifoligide, in patients undergoing CABG. The trial was conducted at 107 sites in the United States, and more than 3000 patients were enrolled in 2002 and 2003. Patients were eligible for inclusion in the study if they were 18 to 80 years of age and were undergoing a first isolated CABG with at least two planned vein-graft implantations. The first 2400 patients were in an angiographic cohort and were scheduled to return for angiographic assessment 12 to 18 months after surgery. Major exclusion criteria were previous cardiac surgery or planned concomitant valve surgery, a nonatherosclerotic cause of coronary-artery disease, and a coexisting illness that made survival for 5 years unlikely. The institutional review board at each site approved the PREVENT IV trial protocol, and all patients gave written informed consent. The primary outcome was the composite of death or vein-graft failure as assessed by quantitative coronary angiography 12 to 18 months after surgery. All patients have been followed for the clinical outcomes of death, myocardial infarction, and repeat revascularization. The 3-year follow-up has been completed.

Study Outcomes

Patients returned to their enrolling center for follow-up angiographic assessment. Vein-graft failure was defined as stenosis of at least 75% of the diameter of the graft. All angiograms were analyzed at a core laboratory (PERFUSE Angiographic Core Laboratory, Boston); the laboratory personnel who analyzed the angiograms were unaware of the harvesting technique used.

Clinical events, including death, myocardial infarction, and revascularization, were assessed annually through mail and telephone contact with the patients.[19] In the case of patients who reported events, medical records were collected, and the events were adjudicated by an independent clinical-events committee with the use of prespecified criteria. Myocardial infarctions that occurred after the index CABG were classified as spontaneous (if the MB fraction of creatine kinase was more than 2 times the upper limit of the normal range or if there were new Q-waves), occurring in association with a percutaneous coronary intervention (PCI) (if the MB fraction of creatine kinase was more than 3 times the upper limit of the normal range or if there were new Q-waves after PCI), or occurring in association with a second CABG (if the MB fraction was more than 10 times the upper limit of the normal range or more than 5 times the upper limit of the normal range with new Q-waves after CABG). Both PCI and repeat CABG were adjudicated as revascularization events.

Statistical Analysis

Baseline characteristics and medication use are summarized as frequencies and percentages in the case of categorical variables and as medians with interquartile ranges in the case of continu-

ous variables. Patients were classified according to the technique used for vein-graft harvesting: endoscopic or open. Fifty patients in whom both endoscopic and open harvesting techniques were used were included in the analyses as part of the endoscopic-harvesting group. Patients whose records did not indicate which harvesting technique was used (14 patients) were excluded from these analyses.

Differences in baseline characteristics and medication use between patients who underwent endoscopic harvesting and those who underwent open harvesting were assessed with the use of the Wilcoxon rank-sum test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. All statistical tests were two-tailed, and P values of less than 0.05 were considered to indicate statistical significance.

Vein-graft failure was evaluated both according to patient and according to graft. Logistic-regression analysis was used to assess graft-failure outcomes per patient. The analysis was adjusted for the patient's weight, the duration of the surgery, the quality of the worst graft (good, fair, or poor, as assessed by the surgeon), the quality of the worst target artery (good, fair, or poor, as assessed by the surgeon), and the use of a composite or noncomposite graft. For outcomes per graft, generalized estimating equations were used to adjust for the correlation between grafts within a patient.[21-23] The analysis was also adjusted for the patient's weight, the duration of the surgery, the quality of the graft, the quality of the target artery, and composite or noncomposite graft.

Cumulative event rates for the clinical outcomes were calculated with the use of the Kaplan–Meier method. Analyses of outcomes adjusted for covariates were assessed with the use of the Cox proportional-hazards model. Covariates included in the final model were age, sex, race (white or nonwhite), worst target-artery quality, history or no history of congestive heart failure, New York Heart Association (NYHA) class, creatinine clearance, recent myocardial infarction (within 30 days before enrollment) or no recent myocardial infarction, body-mass index, history or no history of hypertension, smoking status (nonsmoker, former smoker, or current smoker), and presence or absence of lung disease, diabetes, and peripheral vascular disease. Because the choice of harvesting technique was made by the patient's surgeon, we used a robust sandwich estimate to adjust for the correlation among patients within sites and to correct the estimates of standard errors.[24]

We performed a number of sensitivity analyses. First, we assessed the outcomes with patients who underwent both endoscopic and open harvesting included in the open-harvesting group. Second, we developed a propensity score for endoscopic harvesting that included baseline variables other than the enrolling center. No variable other than the enrolling center, however, was significantly associated with the use of endoscopic harvesting. We nevertheless included this propensity score with and without the enrolling center as a covariate in the models for vein-graft failure and clinical outcomes. Since some sites enrolled very few patients, the model for vein-graft failure was limited to centers that enrolled at least 20 patients. Third, we assessed the association between endoscopic harvesting and clinical outcomes in an analysis that was limited to the cohort of patients who underwent angiographic follow-up. Fourth, we assessed the association between endoscopic harvesting and both angiographic and clinical outcomes, after adjusting for the center, among patients at centers where both endoscopic and open harvesting were performed. Finally, we limited the clinical outcome to death, myocardial infarction, or revascularization associated with vein-graft failure in order to exclude revascularization procedures that were not associated with vein-graft failure.

RESULTS

STUDY POPULATION

Of the 3014 patients enrolled in the PREVENT IV trial, 1753 underwent endoscopic harvesting and 1247 underwent only open harvesting. At the time of this analysis, 2913 patients (97.1%) had completed 3-year follow-up evaluations. Among the 2400 patients enrolled in the angiographic cohort, angiographic follow-up was completed in 1817 patients (75.7%; total number of vein grafts assessed, 4290). The median time to angiographic follow-up was 12.6 months (interquartile range, 12.2 to 13.4).

BASELINE CHARACTERISTICS

The baseline characteristics of the patients who underwent endoscopic vein-graft harvesting were generally similar to those of the patients who un-

Table 1. Baseline Characteristics and Medications Used 30 Days or More after Vein-Graft Harvesting, According to Harvesting Technique.*

Characteristic	Total (N=3000)	Open Harvesting (N=1247)	Endoscopic Harvesting (N=1753)	P Value
Age — yr				0.57
Median	64	64	63	
Interquartile range	56–71	56–71	56–70	
Male sex — no. (%)	2373 (79.1)	981 (78.7)	1392 (79.4)	0.62
Race or ethnic group — no. (%)†				<0.001
White	2730 (91.0)	1127 (90.4)	1603 (91.4)	
Black	139 (4.6)	44 (3.5)	95 (5.4)	
Asian	29 (1.0)	11 (0.9)	18 (1.0)	
Hispanic	72 (2.4)	50 (4.0)	22 (1.3)	
Native American	13 (0.4)	10 (0.8)	3 (0.2)	
Other	17 (0.6)	5 (0.4)	12 (0.7)	
Weight — kg				0.05
Median	87.9	86.5	88.4	
Interquartile range	76.3–100.0	76.0–99.3	77.0–100.0	
Height — cm				0.23
Median	175	175	174	
Interquartile range	167.6–180.0	167.6–180.3	167.6–180.0	
Body-mass index‡				0.02
Median	28.8	28.5	29.1	
Interquartile range	26.0–32.6	25.8–32.2	26.1–32.9	
Blood pressure — mm Hg				
Systolic				0.20
Median	134	132	134	
Interquartile range	120–149	120–148	120–150	
Diastolic				0.08
Median	75	74	75	
Interquartile range	67–82	66–81	68–82	
Heart rate — beats/min				0.37
Median	70	70	70	
Interquartile range	62–80	61–80	62–80	
Current NYHA class — no./total no. (%)				<0.001
I	1191/2969 (40.1)	434/1233 (35.2)	757/1736 (43.6)	
II	989/2969 (33.3)	439/1233 (35.6)	550/1736 (31.7)	
III	536/2969 (18.1)	260/1233 (21.1)	276/1736 (15.9)	
IV	253/2969 (8.5)	100/1233 (8.1)	153/1736 (8.8)	
Hypertension — no. (%)	2250 (75.0)	905 (72.6)	1345 (76.7)	0.01
History of diabetes — no. (%)	1132 (37.7)	468 (37.5)	664 (37.9)	0.85
Hypercholesterolemia — no. (%)§	2290 (76.4)	935 (75.0)	1355 (77.3)	0.13
Prior myocardial infarction — no. (%)	1267 (42.2)	511 (41.0)	756 (43.1)	0.24
Prior stroke — no. (%)	163 (5.4)	62 (5.0)	101 (5.8)	0.35

Table 1. (Continued.)

Characteristic	Total (N=3000)	Open Harvesting (N=1247)	Endoscopic Harvesting (N=1753)	P Value
Renal failure — no. (%)	65 (2.2)	25 (2.0)	40 (2.3)	0.61
Peripheral vascular disease — no. (%)	368 (12.3)	156 (12.5)	212 (12.1)	0.73
Prior PCI — no. (%)	776 (25.9)	345 (27.7)	431 (24.6)	0.06
Pacemaker implantation — no. (%)	35 (1.2)	20 (1.6)	15 (0.9)	0.06
Smoking status — no. (%)				0.18
Nonsmoker	938 (31.3)	413 (33.1)	525 (29.9)	
Former smoker	1373 (45.8)	557 (44.7)	816 (46.5)	
Current smoker	689 (23.0)	277 (22.2)	412 (23.5)	
Creatinine clearance — ml/min				0.10
Median	88.5	86.9	89.6	
Interquartile range	69.6–112.0	69.2–109.6	69.8–113.6	
Total creatine kinase¶				0.01
Median	0.4	0.4	0.4	
Interquartile range	0.3–0.7	0.2–0.7	0.3–0.7	
MB fraction of creatine kinase¶				0.04
Median	0.4	0.4	0.3	
Interquartile range	0.2–0.8	0.2–0.9	0.2–0.8	
Medications — no./total no. (%)				
Aspirin	2693/2976 (90.5)	1123/1240 (90.6)	1570/1736 (90.4)	0.91
Clopidogrel	652/2976 (21.9)	215/1240 (17.3)	437/1736 (25.2)	<0.001
ACE inhibitor	1066/2977 (35.8)	446/1240 (36.0)	620/1737 (35.7)	0.88
Angiotensin-receptor blocker	199/2977 (6.7)	84/1240 (6.8)	115/1737 (6.6)	0.87
Beta-blocker	2345/2977 (78.8)	969/1240 (78.1)	1376/1737 (79.2)	0.48
Nitrate	200/2976 (6.7)	71/1239 (5.7)	129/1737 (7.4)	0.07
Diuretic	842/2976 (28.3)	359/1239 (29.0)	483/1737 (27.8)	0.49
Statin	2171/2977 (72.9)	888/1240 (71.6)	1283/1737 (73.9)	0.17
Other lipid-lowering drug	291/2977 (9.8)	128/1240 (10.3)	163/1737 (9.4)	0.40
Corticosteroid	74/2977 (2.5)	31/1240 (2.5)	43/1737 (2.5)	0.97

* ACE denotes angiotensin-converting enzyme, NYHA New York Heart Association, and PCI percutaneous coronary intervention.
† Race or ethnic group was self-reported.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.
§ Data were missing for one patient in the endoscopic-harvesting group.
¶ Total creatine kinase and MB fraction of creatine kinase are expressed as ratios of the values to the upper limit of the normal range.

derwent open harvesting. However, there were fewer Hispanic patients, more black patients, and a higher prevalence of hypertension in the endoscopic-harvesting group than in the open-harvesting group; in addition, patients who underwent endoscopic harvesting had a higher median body-mass index than those who underwent open harvesting (Table 1). In the angiographic cohort, patients who underwent endoscopic harvesting, as compared with those who underwent open harvesting, had higher median creatinine clearance values (91 ml per minute vs. 87 ml per minute, P=0.04) and were less likely to have advanced heart failure (NYHA class III or IV, 22% vs. 30%; P<0.001).

Table 2. Angiographic Outcomes, According to Vein-Graft Harvesting Technique.*

Outcome†	Total	Open Harvesting	Endoscopic Harvesting	Odds Ratio (95% CI)	P Value
Patients					
Total no.	1817	822	995		
Vein-graft failure (%)	42.8	38.0	46.7	1.45 (1.20–1.76)	<0.001
Vein-graft occlusion (%)	38.6	33.8	42.6	1.47 (1.20–1.79)	<0.001
Grafts					
Total no.	4290	1969	2321		
Vein-graft failure (%)	25.1	22.6	27.2	1.34 (1.14–1.59)	<0.001
Vein-graft occlusion (%)	22.0	19.4	24.2	1.39 (1.17–1.66)	<0.001

* The odds ratios and P values were calculated with the use of adjusted logistic-regression models in the case of the per-patient analysis and with the use of generalized estimating equations in the case of the per-graft analysis. The models for patients were adjusted for weight, duration of surgery, worst graft quality, worst target-artery quality, and use of composite or noncomposite grafts. The models for grafts were adjusted for weight, duration of surgery, graft quality, target-artery quality, and composite or noncomposite graft.

† Vein-graft failure was determined to have occurred if there was stenosis of at least 75% of the diameter of the graft.

There was substantial variation in the rates of the use of the endoscopic-harvesting technique among the 107 centers that participated in the PREVENT IV trial, with a median rate of 60% (interquartile range, 4 to 100). Similar secondary-prevention regimens were used in the two groups, except that clopidogrel was used more frequently in patients who underwent endoscopic harvesting than in those who underwent open harvesting (Table 1).

VEIN-GRAFT FAILURE AND CLINICAL OUTCOMES

There were significantly higher rates of vein-graft failure and occlusion among patients who underwent endoscopic harvesting and among the grafts harvested with the use of an endoscopic technique than among patients who underwent open harvesting and among grafts harvested with an open technique (Table 2). Over the 3-year follow-up period, patients who had undergone endoscopic harvesting, as compared with those who had undergone open harvesting, had a higher rate of death, myocardial infarction, or revascularization (20.2% vs. 17.4%; adjusted hazard ratio, 1.22; 95% confidence interval [CI] 1.01 to 1.47; P=0.04), a higher rate of death or myocardial infarction (9.3% vs. 7.6%; adjusted hazard ratio, 1.38; 95% CI, 1.07 to 1.77; P=0.01), and a higher rate of death (7.4% vs. 5.8%; adjusted hazard ratio, 1.52; 95% CI, 1.13 to 2.04; P=0.005) (Table 3). These differences did not become apparent for 12 to 18 months after surgery (Fig. 1 and 2). There was no interaction between treatment with edifoligide and endoscopic harvesting for any of these outcomes.

SENSITIVITY ANALYSES

The angiographic and clinical outcomes were similar when the 50 patients who had both endoscopic and open harvesting were included in the open-harvesting group instead of in the endoscopic-harvesting group (data not shown). After inclusion of the propensity score for undergoing endoscopic harvesting (C-index for the propensity-score model, 0.55) in the models, endoscopic harvesting, as compared with open harvesting, remained significantly associated with higher rates of vein-graft failure (adjusted odds ratio, 1.35; 95% CI, 1.15 to 1.60; P<0.001) and the composite of death, myocardial infarction, or revascularization (adjusted hazard ratio, 1.26; 95% CI, 1.04 to 1.53; P=0.02). After inclusion of the propensity score for undergoing endoscopic harvesting and the enrolling center as covariates, endoscopic harvesting remained significantly associated with a higher rate of death, myocardial infarction, or revascularization (adjusted hazard ratio, 1.41; 95% CI, 1.06 to 1.89; P=0.02). When the clinical outcome was assessed only in the subgroup of patients who underwent angiographic follow-up assessment, the risk of death, myocardial infarction, or revascularization remained higher in the endoscopic-harvesting group than in the open-harvesting group (adjusted hazard ratio 1.34; 95% CI, 1.07 to 1.69; P=0.01). The association between endoscopic harvesting and the composite clinical outcome among patients whose surgery was performed at sites where both endoscopic and open harvesting were performed remained significant (ad-

Table 3. Major Adverse Cardiac Events at 3 Years of Follow-up, According to Vein-Graft Harvesting Technique.*

Event	Total (N=3000)	Open Harvesting (N=1247)	Endoscopic Harvesting (N=1753)	Hazard Ratio with Endoscopic Harvesting (95% CI)	P Value
Death, myocardial infarction, or revascularization				1.22 (1.01–1.47)	0.04
No. of events	564	214	350		
Kaplan–Meier estimate of 3-year event rate (%)†	19.0	17.4	20.2		
Death or myocardial infarction				1.38 (1.07–1.77)	0.01
No. of events	255	93	162		
Kaplan–Meier estimate of 3-year event rate (%)†	8.6	7.6	9.3		
Death				1.52 (1.13–2.04)	0.005
No. of events	199	71	128		
Kaplan–Meier estimate of 3-year event rate (%)†	6.7	5.8	7.4		

* The hazard ratios and P values were calculated with the use of Cox proportional-hazards models. The models were adjusted for age, sex, race or ethnic group, worst target-artery quality, enrolling center, history or no history of congestive heart failure, New York Heart Association class, creatinine clearance, recent myocardial infarction (within 30 days before enrollment) or no recent myocardial infarction, body-mass index, history or no history of hypertension, smoking status (nonsmoker, former smoker, or current smoker), and presence or absence of lung disease, diabetes, and peripheral vascular disease.

† The event rate was not adjusted for covariates.

justed hazard ratio, 1.30; 95% CI, 1.02 to 1.66; P=0.03); however, the association between endoscopic harvesting and vein-graft failure was no longer significant (adjusted odds ratio, 1.18; 95% CI, 0.92 to 1.52; P=0.19). Finally, the association between endoscopic harvesting and the composite of death, myocardial infarction, or revascularization with vein-graft failure remained significant (adjusted hazard ratio, 1.26; 95% CI, 1.05 to 1.52; P=0.01).

DISCUSSION

In this study, we investigated the association of endoscopic harvesting with graft patency and long-term clinical outcomes. We found that, as compared with patients who underwent open harvesting, patients who underwent endoscopic harvesting had higher rates of vein-graft failure 12 to 18 months after CABG and, more important, also had significantly worse clinical outcomes at 3 years, including higher mortality.

Open vein-graft harvesting is associated with a risk of serious complications and discomfort. Endoscopic vein-graft harvesting was introduced in 1996 as an alternative to open harvesting in order to reduce the risk of complications.[8] On the basis of its demonstrated advantages, endoscopic harvesting has now become the predominant mode of graft harvesting at many surgical centers.[8,10-18] Contemporary data from the Society of Thoracic Surgery National Database show that in 2008 endoscopic harvesting was used in approximately 70% of CABG surgeries performed in the United States.[25]

In 2005, the International Society for Minimally Invasive Cardiothoracic Surgery published a consensus statement on the use of endoscopic versus open harvesting in CABG.[1] On the basis of reports of similar rates of major adverse cardiac events, angiographic patency at 6 months, and quality of the harvested conduit with the two techniques in both randomized and nonrandomized trials, the members of the consensus committee suggested that either endoscopic harvesting or open harvesting can be used. However, they recommended that endoscopic harvesting be the standard of care in order to reduce wound-related complications, improve patient satisfaction, and decrease postoperative pain, length of stay in the hospital, and use of outpatient wound-management resources.

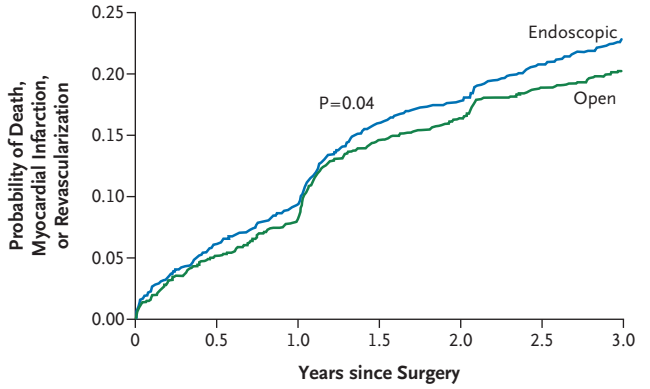

Figure 1. Adjusted Kaplan–Meier Curves for the Composite of Death, Myocardial Infarction, or Revascularization after Endoscopic or Open-Graft Harvesting.

Most studies that have shown that endoscopic harvesting has advantages over the open technique had short-term follow-up, were not randomized, or did not evaluate clinically important outcomes. In a large randomized trial, Yun and colleagues compared the effect of endoscopic harvesting with that of open harvesting on graft patency at 6 months among 200 patients undergoing CABG.[15] A total of 72% of the patients (73 patients who underwent endoscopic harvesting and 71 who underwent open harvesting) had angiographic follow-up assessments. Although the rate of graft occlusion was higher with endoscopic harvesting than with open harvesting (21.7% vs. 17.6%), endoscopic harvesting was not a significant predictor of graft occlusion in a multivariate analysis (odds ratio, 1.15; 95% CI, 0.65 to 2.05; P=0.63). In a randomized trial in which 112 patients were followed for 5 years after CABG, the rate of freedom from death, myocardial infarction, and recurrent ischemia was similar with endoscopic harvesting and open harvesting (75% and 74%, respectively; P=0.85).[26]

In 2005, a meta-analysis of randomized studies (13 studies, with a total of 1319 patients) and nonrandomized studies (23 studies, with 8313 patients) showed that with endoscopic harvesting as compared with open harvesting, there was a significant reduction in the number of wound complications (odds ratio, 0.31; 95% CI, 0.23 to 0.41) and wound infections (odds ratio, 0.23; 95% CI, 0.20 to 0.53).[18] However, the rates were similar between endoscopic harvesting and open harvesting with respect to postoperative myocardial infarction (odds ratio, 1.02; 95% CI, 0.58 to 1.78), stroke (odds ratio, 1.01; 95% CI, 0.17 to 5.97), reintervention for ischemia or recurrence of angina (odds ratio, 1.06; 95% CI, 0.38 to 2.96), and death (odds ratio, 0.71; 95% CI, 0.34 to 1.48). All but one study in this meta-analysis had short-term follow-up (4 to 6 weeks).

Although the patients in our analysis were not randomly assigned to endoscopic or open harvesting, our findings suggest that there may be an important increase in graft failure and adverse clinical outcomes in patients who undergo endoscopic harvesting. The difference in clinical outcomes in our study did not become apparent until almost a year after the CABG. This observation may explain why previous studies with shorter follow-up failed to detect differences between the two techniques. Thus, this study highlights the need for randomized clinical trials with long-term follow-up of clinically relevant outcomes to compare these two approaches to vein harvesting.

Histologic studies, performed with the use of light and scanning electron microscopy, have shown that the integrity of the vessels is the same at the time of surgery, whether endoscopic harvesting or open harvesting is used.[11,27-31] In addition, no differences between the two techniques in the degree of endothelial damage have been seen on electron microscopy.[32-34] In a randomized study that compared endoscopic harvesting with open harvesting in 44 patients, Black et al. found that the two techniques were associated with similar medial smooth-muscle and endothelial function.[35] A recent, small, prospective study in which multiphoton imaging, immunofluorescence assessment, and biochemical techniques were used showed that both the structure and the functional viability of saphenous-vein endothelium are preserved more effectively with open harvesting than with endoscopic harvesting in patients undergoing CABG.[36] These recent data support our findings and may explain the worse long-term clinical outcomes with endoscopic harvesting. Caution should be used when interpreting these histologic studies because they examined acute histologic features of the vein and may not reflect the effects of endoscopic harvesting on long-term histologic findings in the vein. There is no standard vein-preparation solution used in clinical practice;

whether the preparation solution might influence vein patency and long-term outcomes is unknown. A plausible explanation for our findings is that endoscopic harvesting is more traumatic to the vein, leading to accelerated atherosclerosis and worse long-term patency and clinical outcomes. Open harvesting, though more invasive and associated with more wound complications, may be less traumatic to the vein and could result in a better conduit.

Our study was not randomized, and unmeasured confounders between patients who underwent endoscopic harvesting and those who underwent open harvesting could explain our findings. However, we did adjust for differences in prognostically important variables. At the time of the PREVENT IV trial, at least two different endoscopic devices for harvesting the vein were commercially available. These devices use different techniques to harvest the vein, and these differences could have played a role in our findings. Unfortunately, we did not collect information regarding the type of device used. In addition, for both the endoscopic-harvesting group and the open-harvesting group, we were not able to account for the effect of the level of experience of, or the volume of procedures performed by, the practitioner who harvested the veins, since these data were not collected in the PREVENT IV trial. Previous studies, however, have shown that in current practice, graft harvesting is overwhelmingly performed by nonphysician practitioners.[7,37] We developed a propensity score for endoscopic harvesting; however, information on variables other than the enrolling center that might have influenced the decision to use endoscopic harvesting was not collected. Finally, although no interaction with edifoligide treatment was observed, it is possible that procedures unique to the PREVENT IV trial[19] influenced our results.

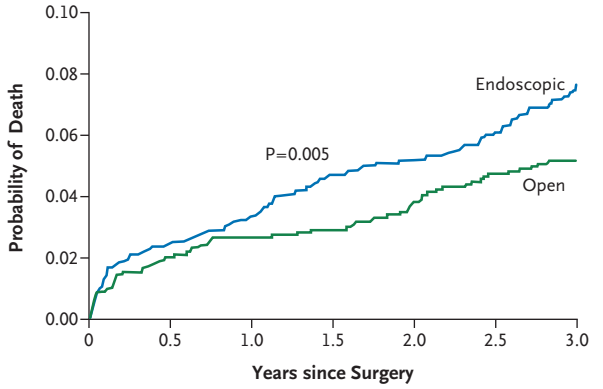

Figure 2. Adjusted Kaplan–Meier Curves for Death after Endoscopic or Open-Graft Harvesting.

In conclusion, our study shows that in patients undergoing CABG, endoscopic harvesting is an independent predictor of vein-graft failure and is associated with worse clinical outcomes, including higher mortality, than is open harvesting. The mechanism behind these findings requires further investigation, and randomized clinical trials evaluating the effect of endoscopic harvesting on long-term angiographic and clinical outcomes are needed. Until further data are available, the increased risk of worse outcomes with endoscopic harvesting should be weighed against its known short-term benefits.

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