

CORRESPONDENCE



Endoscopic versus Open Vein-Graft Harvesting

TO THE EDITOR: Lopes and colleagues (July 16 issue)¹ report data on vein-graft harvesting techniques from the Project of Ex-vivo Vein Graft Engineering via Transfection IV (PREVENT IV) study and conclude that endoscopic vein-graft harvesting, as compared with open harvesting, is independently associated with increased vein-graft failure and adverse outcomes.

In another analysis from the same study,² off-pump and on-pump coronary-artery bypass grafting (CABG) were compared. An interesting finding was that with endoscopically harvested grafts, the probability of graft failure was significantly higher in the off-pump group than in the on-pump group (odds ratio, 1.78 vs. 1.27). In addition, vein grafts of poor or fair quality (as compared with those of good quality) had a significantly higher rate of failure with off-pump than with on-pump CABG. The failure rate of left internal thoracic artery grafts was about 8%, as compared with a failure rate of about 25% for vein grafts. The failure rate of grafts to the left anterior descending artery was much lower than that of grafts to the right coronary artery and circumflex arteries.

The study by Lopes et al. does not adjust for the use of off-pump CABG or of left internal thoracic artery grafts. Furthermore, there is no information on the quality of the veins or of the target vessels. These are major omissions that may have an effect on the results and conclusions of the study.

Sary F. Aranki, M.D.

Barry Shopnick, P.A.-C.

Brigham and Women's Hospital
Boston, MA
saranki@partners.org

1. Lopes RD, Hafley GE, Allen KB, et al. Endoscopic versus open vein-graft harvesting in coronary-artery bypass surgery. *N Engl J Med* 2009;361:235-44.

2. Magee MJ, Alexander JH, Hafley G, et al. Coronary artery

bypass graft failure after on-pump and off-pump coronary artery bypass: findings from PREVENT IV. *Ann Thorac Surg* 2008; 85:494-500.

TO THE EDITOR: Limitations of the post hoc, retrospective analysis of PREVENT IV data by Lopes et al. preclude a definitive attribution of negative outcomes to endoscopic vein-graft harvesting, rather than to confounding factors. First, the study design did not include randomization and standardization to compare the outcomes of harvesting techniques. In addition, the majority of patients were enrolled when the technology and operator training and experience with respect to endoscopic vein-graft harvesting were in their infancy. There have since been great advances in technology and in operator experience; more than 80% of saphenous veins harvested in the United States are now procured endoscopically. Administration of heparin before the procedure has also been shown to significantly improve early graft patency.¹

Endoscopic vein-graft harvesting has represented a major advance in CABG surgery, and numerous studies² have shown significant reductions in wound infections, pain, and costs and improved patient satisfaction. Randomized trials^{3,4} and our clinical experience have not identified the adverse clinical outcomes reported by Lopes et al. We disagree that endoscopic vein-graft harvesting is independently related to more adverse cardiac outcomes. Endoscopic vein-graft harvest-

THIS WEEK'S LETTERS

- 1907 Endoscopic versus Open Vein-Graft Harvesting
- 1910 Perioperative Safety and Bariatric Surgery
- 1912 Dosing Tamiflu Oral Suspension in Children

ing has provided and continues to provide substantial benefit for patients undergoing CABG.

Mark W. Connolly, M.D.

St. Michael's Medical Center
Newark, NJ
mconnolly@smmc.nj.org

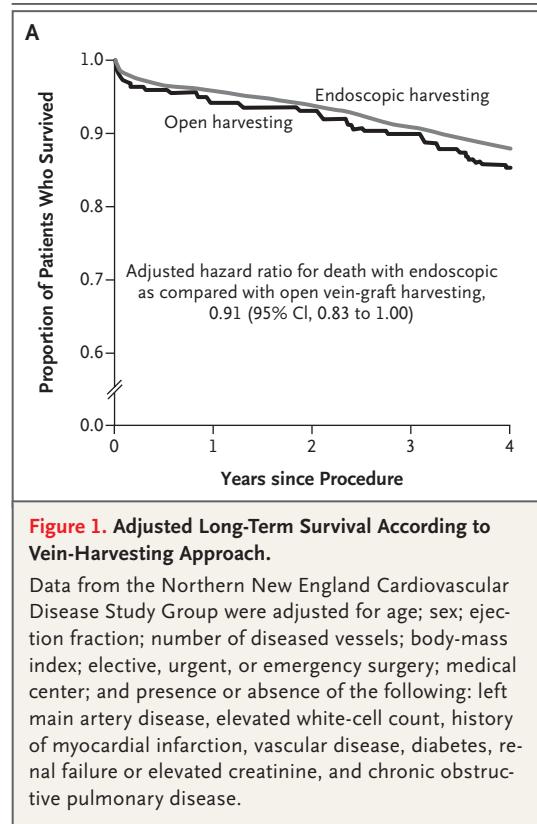
Robert S. Poston, M.D.

Boston University Medical Center
Boston, MA

1. Poston R, Desai P. Heparin administration prior to endoscopic vein harvest limits clot retention and improves graft patency. Presented at the Annual Scientific Meeting of the International Society of Minimally Invasive Cardiothoracic Surgery, San Francisco, June 3–6, 2009. abstract.
2. Cheng D, Allen KB, Cohn W, et al. Endoscopic vein harvest in coronary artery bypass grafting surgery: a meta-analysis of randomized trials and controlled trials. *Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery* 2005;1:61-74.
3. Yun KL, Wu Y, Aharonian V, et al. Randomized trial of endoscopic versus open vein harvest for coronary artery bypass grafting: six-month patency rates. *J Thorac Cardiovasc Surg* 2005;129:496-503.
4. Allen KB, Heimansohn DA, Robison RJ, Schier JJ, Griffith GL, Fitzgerald EB. Influence of endoscopic versus traditional saphenectomy on event-free survival: five-year follow-up of a prospective randomized trial. *Heart Surg Forum* 2003;6:E143-E145.

TO THE EDITOR: Lopes et al. found significantly higher rates of death, myocardial infarction, or repeat revascularization 3 years after primary, isolated CABG when an endoscopic approach as compared with an open approach for harvesting the saphenous vein was used.

The Northern New England Cardiovascular Disease Study Group is a voluntary, regional consortium of all eight medical centers at which cardiac surgery and interventional cardiology are performed in Vermont, New Hampshire, and Maine. From 2001 through 2008, a total of 15,497 CABG procedures were performed (66.2% with endoscopy) in our region. The vein-harvesting approach was determined at the discretion of the surgeon. After adjustment for baseline characteristics and medical center, endoscopic harvesting was not significantly associated with diminished survival within 4 years after the index procedure (hazard ratio for death, 0.91; 95% confidence interval [CI], 0.83 to 1.00) (Fig. 1). Endoscopic harvesting insignificantly increased the risk of repeat revascularization (hazard ratio, 1.08; 95% CI, 0.95 to 1.24). These findings were consistent across medical centers and years of observation. The risk of an in-hospital Q-wave myocardial infarction did not differ significantly between patients who underwent open vein-graft harvest-



ing and those who underwent endoscopic harvesting (0.5% and 0.6%, respectively; $P=1.00$).

Our regional experience suggests that the risk of an in-hospital myocardial infarction, the need for repeat revascularization, and long-term mortality are not affected by the vein-harvesting approach during isolated CABG surgery.

Lawrence J. Dacey, M.D., M.S.
Dartmouth-Hitchcock Medical Center
Lebanon, NH

John H. Braxton, M.D.
Maine Medical Center
Portland, ME

Donald S. Likosky, Ph.D.
Dartmouth Medical School
Hanover, NH
likosky@dartmouth.edu

for the Northern New England Cardiovascular Disease Study Group

TO THE EDITOR: Given the high stakes of potential misinterpretation of the evidence, this study should be placed in the context of all available evidence. Multiple randomized trials in which there are similar characteristics between groups

at baselines have shown unequivocally that endoscopic as compared with open harvesting significantly improves patient outcomes, including reduced pain, sensory–neural decline, perioperative complications, infection, and the need for surgical reintervention and improved mobility and patient satisfaction — all without adverse effects on graft failure and survival in the near term.^{1,2} One randomized trial with a 5-year follow-up period showed no significant difference in event-free survival.³

The difference between the findings in these randomized trials and the conclusions of the study by Lopes et al. regarding the increased risk of death or adverse cardiac events highlights the risk of focusing on only one single retrospective analysis that does not adequately take into consideration important prognostic differences (e.g., the proportion of patients undergoing on-pump versus off-pump bypass or difference in clopidogrel use between the open-harvesting group and the endoscopic-harvesting group). The results in the study by Lopes et al. were significantly different across institutions, suggesting that there were important differences in surgical technique, operator experience, and devices used. More important, the vein-harvesting technique was not the basis for randomization, and unrecognized confounding variables could have been unaccounted for. This study highlights the potential for risk associated with endoscopic harvesting with respect to medium-term graft patency; this is a hypothesis that should be tested by additional and longer-term prospective, randomized, controlled trials.

Davy Cheng, M.D.
Janet Martin, Pharm.D.

University of Western Ontario
London, ON, Canada

Francis D. Ferdinand, M.D.

Lankenau Hospital
Wynnewood, PA

1. Cheng D, Allen KB, Cohn W, et al. Endoscopic vein harvest in coronary artery bypass grafting surgery: a meta-analysis of randomized trials and controlled trials. *Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery* 2005; 1:61-74.
2. Allen KB, Cheng D, Cohn W, et al. Endoscopic vascular harvest in coronary bypass grafting surgery: a consensus statement of the International Society of Minimally Invasive Cardiothoracic Surgery (ISMICS) 2005. *Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery* 2005;1:51-60.
3. Allen KB, Heimansohn DA, Robison RJ, Schier JJ, Griffith GL, Fitzgerald EB. Influence of endoscopic versus traditional

saphenectomy on event-free survival: five-year follow-up of a prospective randomized trial. *Heart Surg Forum* 2003;6:E143-E145.

THE AUTHORS REPLY: As noted in our article, the major limitation of our analyses of endoscopic versus open vein-graft harvesting is that the study was not randomized. In response to Aranki and Shopnick: angiographic outcomes were adjusted for vein-graft quality and target-artery quality, and clinical outcomes for target-artery quality. Cardio-pulmonary bypass and internal thoracic-artery grafts were included as candidate variables; however, owing to the lack of statistical significance, they were not included in the final models. Forcing these variables into the models does not change the association between endoscopic harvesting and vein-graft failure (odds ratio, 1.44; 95% CI, 1.18 to 1.75; $P < 0.001$), the composite of death, myocardial infarction, or revascularization (hazard ratio, 1.20; 95% CI, 0.99 to 1.44; $P = 0.06$), or total mortality (hazard ratio, 1.51; 95% CI, 1.13 to 2.02; $P = 0.006$). As noted by Cheng et al., clopidogrel use differed between patients who underwent endoscopic harvesting and those who underwent open harvesting. It is often considered to be inappropriate to adjust for post-baseline variables; however, when clopidogrel use is included in the models, the relation between endoscopic harvesting and outcomes is unchanged. Ultimately, statistical adjustment is inherently limited, and the only way to definitively assess the relation between harvesting technique and outcome is through randomized clinical trials.

We agree with Connolly and Poston that endoscopic-harvesting techniques have changed since 2002–2003; however, to our knowledge, the effects of these changes on clinical outcomes have not been evaluated. We also agree that multiple studies have shown the short-term benefits of endoscopic harvesting over open harvesting. These short-term beneficial effects were not assessed in PREVENT IV¹ and, in our view, the current literature is of inadequate size² and duration of follow-up to assess the effect of endoscopic harvesting on clinically important long-term outcomes after coronary-artery bypass surgery.

The results from the Northern New England Cardiovascular Disease Study Group cited by Dacey et al. are important and are different from those observed in PREVENT IV. Exploration of

the differences between these observational data sets might provide insights to further refine endoscopic-harvesting techniques. We look forward to seeing these data published in the peer-reviewed literature.

Our analysis has identified an important potential area for quality improvement in cardiac surgery, and further observational and randomized evaluations are called for. The medical community and regulatory agencies should continually assess whether technological changes in medical devices should be implemented only after an analysis of randomized outcome data or can be implemented on the basis of observational or anecdotal information. Data collected in professional registries³ and more efficient clinical trials should enable us to reduce the substantial uncertainty that currently exists regarding the balance of benefit and risk of many therapies.⁴ Further research on endoscopic harvesting should focus on improving the technique so that patients can benefit from the short-term advan-

tages without any detriment to long-term clinical outcomes.

Renato D. Lopes, M.D., Ph.D.

John H. Alexander, M.D., M.H.S.

Duke Clinical Research Institute

Durham, NC

john.h.alexander@duke.edu

T. Bruce Ferguson, M.D.

East Carolina University

Greenville, NC

1. Alexander JH, Hafley G, Harrington RA, et al. Efficacy and safety of edifoligide, an E2F transcription factor decoy, for prevention of vein graft failure following coronary artery bypass graft surgery. *JAMA* 2005;294:2446-54.

2. Allen KB, Heimansohn DA, Robison RJ, Schier JJ, Griffith GL, Fitzgerald EB. Influence of endoscopic versus traditional saphenectomy on event-free survival: five-year follow-up of a prospective randomized trial. *Heart Surg Forum* 2003;6:E143-E145.

3. STS Adult Cardiac Surgery Database. Chicago: Society of Thoracic Surgeons, 2008. (Accessed October 15, 2009, at http://www.sts.org/documents/pdf/ndb/2008_Harvest2_Executive-Summary.pdf.)

4. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA* 2009;301:831-41. [Erratum, *JAMA* 2009;301:1544.]

Perioperative Safety and Bariatric Surgery

TO THE EDITOR: Flum and colleagues (July 30 issue)¹ report on the Longitudinal Assessment of Bariatric Surgery (LABS) consortium study (LABS-1) in which the rate of the composite adverse outcome by 30 days after bariatric surgery was greater among the patients who underwent laparoscopic Roux-en-Y gastric bypass than among the patients who underwent laparoscopic adjustable gastric banding, after controlling for coexisting conditions. However, there is a potential for confounding by indication inherent in nonrandomized studies. Given the beneficial effects of Roux-en-Y gastric bypass on the remission of diabetes, patients with more severe diabetes are probably more likely to undergo Roux-en-Y gastric bypass than laparoscopic adjustable gastric banding. The mechanism of adjustment for diabetes in this study seems vulnerable to residual confounding by indication (or, as some authors have suggested, “confounding by severity”²). The stratum of “insulin use” encompasses a wide range of diabetes severity, and among patients

receiving insulin, those with more severe diabetes may be more likely to undergo Roux-en-Y gastric bypass than laparoscopic adjustable gastric banding. Given the important role that glycemic control plays in determining postoperative outcomes,³ both investigators and the medical community should be cautious in interpreting these results as representing inherent risks of the procedures themselves.

Marion L. Vetter, M.D., R.D.

Christopher L. Vinnard, M.D., M.P.H.

Thomas A. Wadden, Ph.D.

University of Pennsylvania School of Medicine

Philadelphia, PA

marion.vetter@uphs.upenn.edu

1. Flum DR, Belle Sh, King WC, et al. Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med* 2009; 361:445-54.

2. Salas M, Hofman A, Stricker BH. Confounding by indication: an example of variation in the use of epidemiologic terminology. *Am J Epidemiol* 1999;149:981-3.

3. Ramos M, Khalpey Z, Lipsitz, et al. Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. *Ann Surg* 2008;248:585-91.