Endoscopic versus Open Saphenous Vein Harvest in Patients Undergoing CABG, an Angiographically Measured Graft Patency Comparison

M. Brooke Barone
Pacific University

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Abstract
Background: Endoscopic vein harvest (EVH) was introduced in 1996 as an alternative to open vein harvest (OVH) for coronary artery bypass graft (CABG) surgeries utilizing the saphenous vein. EVH has been shown to decrease post operative pain, wound complications, and length of hospital stay. Although EVH has become the preferred method of saphenous vein harvest, the effect of EVH on graft patency has not been well studied. A study published in the New England Journal of Medicine in 2009 concluded that EVH was independently linked to increased morbidity and decreased graft patency. This surprising conclusion was not endorsed by the cardiothoracic community. Much debate about the effect of EVH on graft patency has ensued, however, surgical practice appears to have remained unchanged. The potential harm of EVH must be weighed against its proven benefits in the light of the large number of patients that undergo EVH annually as the predominant mode of saphenous vein harvest.

Methods: An exhaustive literature search was performed using OVID, Web of knowledge, EBMR, CINAHL, and clinicaltrials.gov with the following search terms: coronary artery bypass graft, endoscopy, saphenous vein, graft occlusion, and vascular patency. Three studies were identified; two randomized controlled trials and one retrospective cohort study. Several trials examining graft patency in comparing EVH to OVH that utilized clinical outcomes (such as myocardial infarction, revascularization, stroke or death) as surrogate endpoints were excluded.

Results: Of the three included studies, two studies determined that there was no statistical significance in occlusion rates when comparing EVH to OVH grafts. One study, referenced above, did determine statistically significant higher occlusion rates in EVH grafts as compared to OVH grafts.

Conclusion: Further research is needed to adequately explore the relationship between EVH and graft patency associated morbidity. Such research would need to address many confounding variables while including a large sample population with angiography patency measurements at predetermined time points. The limited state of current research has failed to demonstrate statistically significant harm that may otherwise persuade the Society for Thoracic Surgery to ignore the important proven benefits of EVH over OVH. At this juncture, EVH remains the predominant method of saphenous vein harvest for patients undergoing CABG surgery.

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coronary artery bypass graft, endoscopy, saphenous vein, graft occlusion, and vascular patency
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Endoscopic versus Open Saphenous Vein Harvest in Patients Undergoing CABG, an Angiographically Measured Graft Patency Comparison

M. Brooke Barone

A Clinical Graduate Project Submitted to the Faculty of the School of Physician Assistant Studies Pacific University Hillsboro, OR

For the Masters of Science Degree, August 14, 2010

Clinical Graduate Project Coordinators: Annjanette Sommers MS, PA-C & Rob Rosenow PharmD, OD
Biography

Brooke Barone grew up in rural Oregon with an interest in medicine that was fostered by her mother, a critical care nurse. At the age of 18 she was able to observe an open-heart surgery, an experience that marked the beginning of her fascination with cardiology. After completing her undergraduate degree in Anthropology and Social Science, she completed a short stint in the Peace Corp in Paraguay, South America. This experience inspired her to become involved with providing care to underserved populations. Soon after her return from Paraguay, she began volunteering at the Essential Health Clinic in Hillsboro, Oregon while working in the Surgical ICU at OHSU. She worked with many amazing physician assistants both at OHSU and the Essential Health Clinic who served as inspiring examples of a dynamic profession. After graduation from PA school Brooke plans on staying in the Pacific Northwest to pursue a career in cardiothoracic surgery or family medicine.
Abstract

**Background:** Endoscopic vein harvest (EVH) was introduced in 1996 as an alternative to open vein harvest (OVH) for coronary artery bypass graft (CABG) surgeries utilizing the saphenous vein. EVH has been shown to decrease post operative pain, wound complications, and length of hospital stay. Although EVH has become the preferred method of saphenous vein harvest, the effect of EVH on graft patency has not been well studied. A study published in the New England Journal of Medicine in 2009 concluded that EVH was independently linked to increased morbidity and decreased graft patency. This surprising conclusion was not endorsed by the cardiothoracic community. Much debate about the effect of EVH on graft patency has ensued, however, surgical practice appears to have remained unchanged. The potential harm of EVH must be weighed against its proven benefits in the light of the large number of patients that undergo EVH annually as the predominant mode of saphenous vein harvest.

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**Conclusion:** Further research is needed to adequately explore the relationship between EVH and graft patency associated morbidity. Such research would need to address many confounding variables while including a large sample population with angiography patency measurements at predetermined time points. The limited state of current research has failed to demonstrate statistically significant harm that may otherwise persuade the Society for Thoracic Surgery to ignore the important proven benefits of EVH over OVH. At this juncture, EVH remains the predominant method of saphenous vein harvest for patients undergoing CABG surgery.

**Keywords:** coronary artery bypass graft, endoscopy, saphenous vein, graft occlusion, and vascular patency
Acknowledgements

To my family, for their unconditional support.

To mom, your shining example of determination and drive has inspired me to fulfill my dreams, thank you.
# Table of Contents

Biography ........................................................................................................... 2
Abstract ............................................................................................................. 3
Acknowledgements ............................................................................................. 4
Table of Contents ............................................................................................... 5
List of Tables ....................................................................................................... 6
List of Abbreviations ........................................................................................... 7
Background .......................................................................................................... 8
Methods ............................................................................................................... 10
Results .................................................................................................................. 11
Discussion and Recommendations ..................................................................... 14
Conclusion .......................................................................................................... 19
References ......................................................................................................... 21
Tables ................................................................................................................. 23
List of Tables

Table I: Summary of Reviewed Articles
Table II: Validity Score
Table III: Summary of Findings
List of Abbreviations

EVH.................................................................Endoscopic Vein Harvest
OVH.....................................................................Open Vein Harvest
CABG...............................................................Coronary Artery Bypass Graft surgery
SV........................................................................Saphenous Vein
LV.......................................................................Left Ventricle
COPD.................................................................Chronic Obstructive Pulmonary Disease
Endoscopic versus Open Saphenous Vein Harvest in Patients Undergoing CABG, an Angiographically Measured Graft Patency Comparison

BACKGROUND:

A recent article in the New England Journal of Medicine (NEJM) rapidly gained the attention of the cardiothoracic community. Lopes et al\(^1\) concluded that endoscopic vein harvest (EVH) of the saphenous vein for coronary artery bypass graft (CABG) surgery lead to decreased graft patency and increased morbidity when compared to saphenous veins harvested by the conventional open vein harvest (OVH) technique.\(^1\) This surprising conclusion sparked a lively discussion among the cardiothoracic community regarding saphenous vein harvest methods and potential subsequent effects on graft patency. Despite the conclusion of Lopes et al\(^1\), EVH continues to be the predominant method of saphenous vein harvest for CABG surgeries.\(^2\) This dichotomy sparked a systematic literature review of current evidence.

EVH was introduced in 1996, to reduce the morbidity associated with OVH wound complications in patients undergoing CABG with utilization of the saphenous vein.\(^3\) In addition to decreased wound complications, EVH has been shown to decrease length of hospital stay and decrease postoperative incisional leg pain.\(^4,5\)

Despite the clearly advantageous patient outcomes associated with EVH, the effect of EVH on long-term graft patency is not yet clear. Early studies microscopically evaluated vein samples and reported acute endothelial changes in veins harvested with EVH. These changes were generally attributed to the manipulation of the endoscope during EVH. For that reason, there was concern that these acute endothelial changes associated with EVH may poorly effect graft quality and therefore graft patency. However, a separate study comparing intraoperative vein specimens harvested by both techniques showed similar medial smooth-muscle and endothelial function,\(^6,7\) suggesting that vein
quality at the time of anastomoses may in fact be similar between the two techniques. Therefore, harvest method may have less of an acute histological effect on vein quality than was previously thought.

Although histological examination is useful in assessing vein conduit quality, vein quality is only one of many factors that may contribute to long-term graft patency. Other confounding variables include patient characteristics, such as age, sex, and gender. Additional intraoperative factors beyond method of vein harvest may also affect graft patency. These may include the administration of heparin prior to vein harvest, and harvesting technician experience. Finally, although postoperative care of patients undergoing CABG, whether EVH or OVH, will likely be similar at each institution, differences in postoperative medication administration could also affect graft patency. Because many different factors affect graft patency, establishing a causative relationship between vein harvest method and graft failure requires a clinical trial that also examines the aforementioned confounding variables and utilizes an objective endpoint measurement such as graft measurements via coronary angiography.

The purpose of this study is to systematically review recent literature regarding endoscopic vein harvest (EVH) versus open vein harvest (OVH) in CABG patients with regard to angiographic outcome. In patients undergoing CABG is there a decrease in angiographically measured graft patency when the saphenous vein is harvested endoscopically rather than by the traditional open method? The potential harm of EVH must be evaluated in the light of the large number of patients that undergo EVH annually as the predominant mode of saphenous vein harvest.

**General Operative Technique Background**

Open harvest of the saphenous vein (OVH) is accomplished with a single long incision that stretches from the thigh to the medial malleous. The saphenous vein is removed as the incision progresses, while branches are clipped. In contrast, EVH involves a small, 2-3cm incision at or above the knee. This is used to identify and isolate the saphenous vein. A subcutaneous retractor and/or
endoscope is introduced into the subcutaneous tissue and advanced toward the groin or down towards the medial malleolus, as venous side branches are identified and clipped or cauterized. A second, .5cm incision may be made near the distal end of the endoscope to secure the vein for removal. Many different brands of equipment exist for EVH, and carbon dioxide insufflation is frequently used to improve the visualization of the vein during harvest. EVH is technician and device dependant, thus as with many other surgical techniques, it takes practice to master. A 2005 study found that veins harvested with EVH required a significantly greater number of repairs as compared to OVH, these repairs have generally been attributed to the learning curve associated with mastering the EVH technique. It is unknown how these repairs affect graft patency.

METHODS:

An exhaustive literature search was performed using OVID, Web of knowledge, EBMR, CINAHL, and clinicaltrials.gov with the following search terms: coronary artery bypass graft, endoscopy, saphenous vein, graft occlusion, and vascular patency. The initial articles were carefully reviewed to see if they met the inclusion criteria, and a secondary review of the bibliographies was conducted. In addition, a prospective and retrospective works cited search of articles included in this systematic review was completed.

Eligibility criteria:

Studies were limited to only include those which compared EVH and OVH procedures in patients undergoing CABG and addressed angiographic measurements of graft patency. EVH was defined as harvest of the great saphenous vein using endoscopic instruments. OVH was defined as harvest of the saphenous vein using a continuous skin incision or several smaller incisions, known as a “bridging” technique. One meta-analysis and one systematic review were excluded for review purposes, however their bibliographic works were utilized in obtaining articles for inclusion in the systematic review. Several trials examining graft patency in comparing EVH to OVH that utilized
clinical outcomes (such as myocardial infarction, revascularization, stroke or death) as surrogate endpoints were excluded.

Three studies were identified; two randomized controlled trials and one retrospective cohort study (see Table I). The three articles were assessed for quality and validity using an original scoring tool. Points were awarded for prospective randomization to either EVH or OVH, for utilizing radiologists that were blinded to harvest method when reviewing the angiographic films, for describing the quality of vein graft and technique/experience of harvesting technician in methods, and for a large sample population size (see Table II).

RESULTS:

The literature search identified three studies meeting eligibility criteria; two randomized controlled trials and one retrospective cohort study. Table III summarizes the demographics and results of these studies.

Perrault et al9

A prospective randomized trial done by Perrault et al9 in 2004, included 40 adult patients undergoing a routine CABG, on or off pump, requiring ≥1 saphenous vein (SV) grafts. Patient characteristics were similar prior to randomization, including; age, sex, episodes of unstable angina, hypertension, chronic obstructive pulmonary disease (COPD), diabetes, 3-vessel disease, 2-vessel disease, and left ventricular (LV) ejection fraction. The Vasoview system was used for EVH, it is unknown how much prior experience the technician performing the EVH had before the study. The quality of conduit, target vessel, and target vessel distribution is also unknown. A coronary angiographic evaluation was performed on 27 OVH grafts and 32 EVH grafts one to nine months after surgery. No statistical significance (p=.973, OVH 14.8% EVH 15.6%) of occlusion of saphenous vein grafts were found and no statistical significance of hemodynamically significant stenosis (p=.280, OVH 3.7% EVH 0%) were found (see Table III).
A 2005 randomized trial done by Yun et al$^5$ included 200 adult patients undergoing a routine CABG on pump requiring $\geq 1$ SV grafts. Patient characteristics were similar prior to randomization including; age, sex, smoking history, hypertension, myocardial infarction, congestive heart failure, diabetes mellitus, peripheral vascular disease, carotid disease, stroke, and the designation of the New York Heart Association class (I-IV).

The Vasoview system was used for EVH, one physician assistant was utilized for each EVH surgery with case documentation of the PA’s prior EVH experience. The quality of each vein conduit was assessed intraoperatively by noting the conduit diameter and the number of conduit repairs needed. Additionally, target vessel atherosclerotic disease severity was assessed intraoperatively. No significant differences were detected in the severity of target vessel disease or size, vein graft size or quality, or graft flow rates between the two groups.

Coronary angiography was performed six months postoperatively on 166 EVH grafts and 170 OVH grafts. Overall graft occlusion rates at six months were 21.7% for EVH and 17.6% for OVH. Significant disease ($>50\%$ stenosis) was noted in an additional 10.2% of EVH grafts and 12.4% of OVH grafts (see Table III). A univariate analysis determined no significant difference in occlusion and disease rates in EVH as compared to OVH ($p=.584$). A multivariable logistic regression found EVH to not be a significant factor for graft occlusion or disease (adjusted OR 1.15 [95% CI, 0.65-2.05] $p=.594$). According to this study significant predictors for vein graft occlusion were congestive heart failure, vein graft to the diagonal territory, and larger vein graft size. Conversely, higher vein graft flow demonstrated a protective effect on the grafts.

A recent (2009) retrospective cohort study by Lopes et al$^1$ examined patients who were randomized into the PREVENT IV trial, a phase-III, multicenter, randomized double-blind placebo-
controlled trial of ex vivo treatment of autologous vein grafts with edifoligide in patients undergoing initial CABG surgery\textsuperscript{10} on or off pump. Three thousand patients were enrolled at 107 sites in the United States. These patients were randomized to placebo or edifoligide, and the first 2400 patients were enrolled in coronary angiography cohort to evaluate graft patency 12-18 months following surgery. Inclusion criteria for the PREVENT IV trial were patients 18-80 years old, who were undergoing a first isolated CABG with at least two planned vein-graft implantations. This trial included patients undergoing routine, urgent and emergent CABG procedures utilizing either EVH or OVH methods for saphenous vein harvest, occurring on or off pump. The enrolling center’s operating surgeon decided which method of harvest to utilize on a case by case basis.

Patient characteristics of the PREVENT trial were significantly different in that there was an increased proportion of African Americans (p<0.001), hypertensive patients (p=.01), patients with increased body mass index (p=.02), and fewer Hispanic patients (p<0.001) in the EVH cohort as compared to OVH.\textsuperscript{1} Other baseline patient characteristics between the groups did not demonstrate statistical significance.\textsuperscript{1}

Intraoperative technician experience with EVH was not recorded, nor was the type of EVH device utilized. The quality of the target vessel was recorded intraoperatively as assessed by the operating surgeon, however, vein conduit quality was not recorded.

Coronary angiography was performed 12-18 months after surgery for 1817 patients. 2321 EVH grafts were analyzed and 1969 OVH grafts were analyzed. Overall graft failure was 27.2\% for EVH and 22.6\% for OVH (95\% CI, OR 1.34 [1.14-1.59], p<0.001). Overall graft occlusion was 24.2\% for EVH and 19.4\% for OVH (95\% CI, OR 1.39 [1.17-1.66], p<0.001), see Table III. Lopes et al\textsuperscript{1} used logistic-regression analysis to assess graft-failure outcomes per patient. They report that their analysis adjusted for quality of the worst graft, the use of a composite or noncomposite graft, patient weight, duration of surgery, and quality of target artery. Lopes et al\textsuperscript{1} report a propensity score for endoscopic harvesting that included baseline variables other than the enrolling center, and still found the odds ratio
of vein graft failure to be 1.35 (95% CI, 1.15-1.60; p<0.001). Lastly, they concluded that there was no interaction between treatment with edifoligide and endoscopic harvesting for any of these outcomes.

DISCUSSION:

The nature of examining saphenous graft patency necessitates that confounding variables or prognostic factors be taken into account. Grafts do not exist in a vacuum, a myriad of factors influence the longevity of graft patency. To isolate specifically endoscopic technique versus open technique as an independent risk factor for graft failure requires a cleanly run, large number, randomized study, with meticulous documentation of technique and confounding variables. These confounding variables can be categorized as preoperative, intraoperative and postoperative. Each study included in this systematic review had specific limitations in addressing these critical confounding factors. Therefore, the conclusion of each study regarding graft patency must be carefully evaluated based upon specific study limitations.

Overview of variables: Preoperative, Intraoperative, Postoperative

Preoperative

Patient characteristics innately influence grafts. However, ensuring statically similar patient populations through preoperative randomization should adjust for patient variation.

Intraoperative

Intraoperatively, there is a learning curve associated with EVH.\textsuperscript{4} Therefore, technician experience with EVH, including specific device, should be considered in evaluating graft patency. Additionally, data presented at the 2008 Annual Scientific Meeting of the International Society of Minimally Invasive Cardiothoracic Surgery, purported that administering heparin before vein harvest may improve graft patency, this data is not yet published. It has also been reported by Lamm\textsuperscript{11} that harvested grafts undergoing continuous perfusion with autologous blood, as compared to storage in a crystalloid solution, have significantly better endothelial integrity.\textsuperscript{11} To address these variables, a detailed clinical
trial should record the storage solution used for the conduit and should also document the time and
dose of heparin administration. Additionally, the quality of vein conduit and target vessel should be
recorded intraoperatively, so that poor quality conduits or target vessels effecting graft patency are not
later attributed to harvesting technique.

Postoperative

Postoperatively, for patients undergoing CABG by either EVH or OVH, administering an antiplatelet
drug has become standard therapy. The treatment effect of using aspirin versus clopidogrel is currently
being studied, however Gao et al\textsuperscript{12} concluded that either clopidogrel plus aspirin or clopidogrel alone
maintains high graft patency in the early postoperative phase after CABG. Documentation of post
operative concomitant medications would be helpful in viewing graft patency data.

\textbf{Perrault et al}\textsuperscript{9}

The randomized clinical trial done by Perrault et al\textsuperscript{9} in 2004, used a relatively small sample size
of 40 patients. The patient characteristics prior to randomization were similar between the groups,
however the overall sample did demonstrate a younger and more male dominated population, (64 +/-
7.9 years, with 1/15 women for OVH and 2/17 women for EVH), than the other two studies. Therefore,
the applicability of this study to older women with potential more friable veins is uncertain.

Perrault et al\textsuperscript{9} failed to collect documentation of technician experience with a harvesting device
in cases in which EVH was performed. Additionally, the quality of target vessel, vein conduit size, and
vein quality were not assessed intraoperatively. Perrault et al\textsuperscript{9} reported that “all native vessels had a
high-grade stenosis of more than 70% (except one patient in each group) and [that] the majority were
good target vessels for bypass grafting.” However, there were no clear methods reported for a
standardized evaluation of these statements, so it is difficult to assess the validity of the study
outcomes. Also intraoperatively, there was no documentation as to whether heparin was administered
prior to vein harvest, and there was no documentation of which solution the harvested vessel was placed in prior to use for anastomosis.

Postoperatively, there was no documentation of whether clopidogrel was administered. Additionally, the coronary angiographic follow up time period was not standardized. And although 40 patients were randomized into the clinical trial, 8 patients refused postoperative angiography. These patients were not included in an intent to treat analysis.

Perrault et al\textsuperscript{9} failed to document many important intraoperative confounding variables in their trial. The validity of the coronary angiographic measurement data is therefore difficult to assess. For instance, utilization of a lower quality vein conduit will likely later result in decreased graft patency. That patency may be a reflection of the lower quality vein, or it may be a reflection of the method of vein harvest. Without meticulous documentation the data is less meaningful.

Perrault et al\textsuperscript{9} recognized that their relatively early (1-9 months post surgery) angiographic assessment was of limited use in evaluating late graft intimal hyperplasia and subsequent stenosis. However, they concluded that their data demonstrated a lack of vein trauma and subsequent early conduit stenosis that was previously associated with EVH. Vein graft occlusion rates 1-9 months after surgery in this study were 14.8\% for OVH and 15.6\% for EVH, p=.973, a statistically insignificant value. The limitations of this study are many and are highlighted above. However, as the first study comparing EVH to OVH in regard to graft patency via angiographic evaluation, this study served as a basis for further research to build upon in establishing more applicable validity criteria for further research.

\textbf{Yun et al}\textsuperscript{5}

Yun et al\textsuperscript{5} conducted a relatively meticulous trial that is frequently referenced in the EVH versus OVH debate. Many shortcomings present in the Perrault et al\textsuperscript{9} trial were absent here. For example, a larger original sample size of 200 patients was utilized in a randomized trial of EVH versus
OVH. Patient characteristics preoperatively were similar between the two groups. The interoperative documentation was remarkable in that many important operative variables were recorded for each patient. These included; vein conduit quality, atherosclerotic disease of the target vessel, technician experience, and specific EVH device. Yun et al\textsuperscript{5} additionally recorded that the patients were heparinized prior to saphenous vein harvest, and that the harvested vein was kept in a solution of heparinized blood with papavarine prior to anastomosis.

One of the few flaws of the trial was the relatively small sample size of the study, which limited its statistical power. Although 200 patients were randomized into this study, 56 refused angiographic follow-up. Therefore, 166 EVH grafts and 170 OVH grafts were analyzed. The angiographic evaluation was completed at six months post surgery, this was a rather short timeframe for angiographic patency evaluation. Also postoperatively, it was not noted if patients received clopidogrel or another anti-platelet drug. Despite these flaws, the study design was well thought out and executed.

Yun et al\textsuperscript{5} concluded that there was no statistically significant difference in graft occlusion and disease rates in EVH as compared to OVH six months after surgery. Vein graft occlusion rates were 21.7\% for EVH and 17.6\% for OVH, \( p=.584 \). This trial remains one of the more often cited studies demonstrating comparable saphenous graft patency rates regardless of harvest technique. The inclusion of so many confounding variables allowed for a more detailed examination of the correlation between method of harvest and graft patency.

\textbf{Lopes et al\textsuperscript{1}}

Lopes et al\textsuperscript{1} concluded that patients who underwent EVH had higher rates of vein-graft failure than patients who underwent OVH, this was 27.2\% for EVH and 22.6\% for OVH ,\( p<0.001 \). Additionally, they found 24.2\% of EVH and 19.4\% of OVH grafts to be fully occluded \( p<0.001 \). However, the conclusions of Lopes et al\textsuperscript{1} were based upon a retrospective cohort study in which the
primary randomization was for edifoligide versus placebo, harvest method was not a predefined subanalysis for this study.

In the evaluation of graft patency, the methods of the Lopes et al\textsuperscript{1} study were flawed. First, the operating surgeon determined the method of saphenous vein harvest on a case by case basis, without randomization. Also, this study was multi-centered, institution case experience as well as operator experience with EVH varied. However, neither of these variables was documented. A so-called “center affect” is mentioned in the article by Lopes et al\textsuperscript{1}, the authors report that the association between vein graft failure and EVH was no longer significant when statistically adjusted for enrolling centers that utilized both EVH and OVH.\textsuperscript{1} This suggests that vein graft failure may more closely correlate to the center in which the harvesting procedure and surgery is done.

The Lopes et al\textsuperscript{1} study included emergent, urgent, and routine CABG surgeries in the data analysis. The effect of emergent or urgent surgery on graft quality has not been studied. Of further concern is that no adjustment was made for off-pump or left internal thoracic artery grafts. In a separate analysis of the PREVENT IV data, off-pump bypass with the use of internal thoracic artery grafts was shown to increase graft failure.\textsuperscript{13} Also, although vein quality was mentioned, methods used to quantify vein quality were not documented. Target vessel quality was also not documented. It was not noted which solution the harvested vessel was stored in prior to anastomosis. Finally, this study also included the use of edifoligide. It is unclear how this pharmacologic variable may effect the outcome of angiographic graft patency.

The largest factor affecting the validity of the Lopes et al\textsuperscript{1} trial is the lack of prospective randomization for the intervention studied. Despite the author’s efforts to statistically adjust for this, the trial was not designed to assess method of harvest related to graft patency. The lack of a predetermined subanalysis in this study, combined with the lack of documentation of almost all of the essential confounding variables are insurmountable problems effecting the validity of this study’s conclusion. In correspondence with the NEJM, Dr. Connolly, a cardiothoracic surgeon at Boston
University Medical Center, notes “limitations of the post hoc, retrospective analysis of PREVENT IV data by Lopes et al\textsuperscript{1} preclude a definitive attribution of negative outcomes to endoscopic vein-graft harvesting, rather than to confounding factors.”\textsuperscript{14}

CONCLUSION:

The question remains, does overall graft patency depend on confounding variables such as target related variables and patient related characteristics or can it be independently linked to harvest method? In studies with long-term angiographic follow-up utilizing conventional OVH, the incidence of vein graft occlusion is 15\% to 20\% at one year.\textsuperscript{15} This number is not precise, as actual occlusion rates are difficult to collect. However, using these numbers as a general range, the Lopes et al\textsuperscript{1} trial was the only trial with EVH occlusion rates significantly higher than is typical for OVH occlusion rates.

Further research is needed to adequately address confounding variables contributing to graft failure, and therefore permit a more accurate assessment of the impact of harvest technique on graft patency. Ideally, a prospective randomized controlled trial examining EVH versus OVH in patients undergoing CABG would be performed. The study should include a population of at least 400 patients, with prospective randomization to EVH or OVH, in patients undergoing routine CABG on or off pump. The study should follow the technique of Yun et al\textsuperscript{5} in recording operative procedure including; type of harvesting device used, operator experience with the device, documentation of heparin administration prior to vein harvest, storage solution of conduit prior to anastomoses, quality of conduit as assessed by a standardized method, and quality of target vessel as assessed by the operating surgeon. Post operative documentation should include a list of concomitant medications maintained through the conclusion of the trial. Angiographic follow-up should be performed at six months post surgery and again at 18 months post surgery. The radiologist interpreting the angiogram should be
blinded to harvest method. A trial with adequate power including these confounding variables would more accurately assess the link between graft patency and harvesting technique.

The limited state of current research has failed to demonstrate significant harm that may otherwise persuade the Society for Thoracic Surgery and the Association of Physician Assistants in Cardiovascular Surgery (APACVS) to negate the important proven benefits of EVH over OVH. These benefits are landmark in their own right. As mentioned previously they include; decreased wound morbidity, decreased infection rates, and decreased length of hospital stay. The APACVS, in a meeting held in January of 2010, noted a need for more randomized clinical trials utilizing so-called “best practices” that address the confounding variables noted in this systematic review. It was noted that in general “best practices” would include: an experienced vein harvester, utilization of veins in the lower leg, preheparinization prior to vein harvest, non-thermal side branch ligation, prevention of over-distension of the conduit through use of a pressure pop-off syringe, minimization of traction on the harvested vein, and demonstrated patience by the operating cardiothoracic surgeon.

Widespread adaptation of best practices may more easily allow for an angiographic patency comparison between EVH and OVH to be completed across multiple surgical centers. More importantly, the adaptation of best practices will ultimately contribute to better patient outcomes. Until further research is completed, EVH remains the preferred method of saphenous vein harvest.
REFERENCES


## Table I Summary of Reviewed Articles

<table>
<thead>
<tr>
<th>Author/Title/Journal</th>
<th>Yr. enrolled</th>
<th>Study Type</th>
<th>Patients/Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome(s)</th>
<th>p Value</th>
<th>Validity Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perrault LP et al</td>
<td>2000-2002</td>
<td>Randomized</td>
<td>40 patients</td>
<td>EVH of SV by Vasoview system</td>
<td>OVH</td>
<td>1-9 months stenosis + occlusion</td>
<td>Occlusion p=.933</td>
<td>8.5/9</td>
<td>Occlusion= 100% of luminal diameter, Hemodynamically sig stenosis= 50-99%</td>
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<td></td>
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<td></td>
<td>routine CABG on or off pump requiring ≥1 SV graft</td>
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<td>27 OVH grafts</td>
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<td>32 EVH grafts</td>
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<tr>
<td>Yun KL et al</td>
<td>2000-2002</td>
<td>Randomized</td>
<td>200 patients</td>
<td>EVH of SV by Vasoview system</td>
<td>OVH</td>
<td>6 month stenosis + occlusion</td>
<td>Occlusion and Significant disease p=.584</td>
<td>8.5/9</td>
<td>Occlusion=100% of luminal diameter, Significant disease= &gt;50% stenosis</td>
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<tr>
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<td></td>
<td>Routine CABG on pump requiring ≥1 SV graft with sufficient subcutaneous tissue for EVH device insertion</td>
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<td>170 OVH grafts</td>
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<td>166 EVH grafts</td>
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<tr>
<td>Lopes R et al</td>
<td>2002-2003</td>
<td>Retrospective Cohort</td>
<td>2400 patients in angiographic cohort</td>
<td>EVH of SV, unknown system Edifoligide</td>
<td>OVH Placebo</td>
<td>12-18 months graft failure</td>
<td>Graft failure p&lt;.001</td>
<td>2/9</td>
<td>Multi-center study, No randomization</td>
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<td></td>
<td>Randomized double-blind placebo controlled-edifoligide in patients having CABG (Emergent, Urgent or Routine) on or off pump requiring ≥2 SV grafts</td>
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<td>1969 OVH grafts</td>
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## Table II- Validity Score

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<tr>
<th>Criteria</th>
<th>+1 pt</th>
<th>-1pt</th>
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<tbody>
<tr>
<td>Study Type</td>
<td>Prospective</td>
<td>Retrospective Cohort</td>
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<tr>
<td>Study personnel (Radiologist) blinded to intervention method</td>
<td>Yes</td>
<td>No or can’t tell</td>
</tr>
<tr>
<td>Sample Size</td>
<td>&gt;200</td>
<td>&lt;200</td>
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<tr>
<td>Statistically similar patient Characteristics at the start of the trial</td>
<td>Yes</td>
<td>no</td>
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<tr>
<td>Were patient analyzed in the groups to which they were randomized (intent to treat)?</td>
<td>Yes</td>
<td>no</td>
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<tr>
<td>Operative technique: (2pts, ½ point each)</td>
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<tr>
<td>• Harvesting personel experience documented</td>
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<tr>
<td>• Type of EVH device used documented</td>
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</tr>
<tr>
<td>• Type of solution for harvested vein documented</td>
<td></td>
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<tr>
<td>• Heparin prior to harvest documented</td>
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<tr>
<td>Quality (1pt, ½ point each)</td>
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<tr>
<td>• target vessel quality measured</td>
<td></td>
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<tr>
<td>• vein conduit quality measured and documented</td>
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<tr>
<td>PostOperative (1pt, ½ point each)</td>
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<tr>
<td>• groups treated the same</td>
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<tr>
<td>• documentation of clopidogrel administered</td>
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</table>

9 points possible
## Table III- Summary of Findings

<table>
<thead>
<tr>
<th>Harvest Method</th>
<th><strong>Perrault et al</strong> 2004 <em>Randomized Trial</em></th>
<th><strong>Yun et al</strong> 2005 <em>Randomized Trial</em></th>
<th><strong>Lopes et al</strong> 2009 <em>Retrospective Cohort</em></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>EVH</td>
<td>OVH</td>
<td>EVH</td>
</tr>
<tr>
<td>Total Number of grafts</td>
<td>32</td>
<td>27</td>
<td>166</td>
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<tr>
<td>Occluded Grafts</td>
<td>15.6%</td>
<td>14.8%</td>
<td>21.7%</td>
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<tr>
<td>Plus Stenosis or Significant disease</td>
<td>0%</td>
<td>3.7%</td>
<td>10.2%</td>
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<tr>
<td><strong>P value</strong></td>
<td>Occluded Grafts p=0.973</td>
<td>Occluded and Significantly Stenosed Grafts p=0.584</td>
<td>Occluded Grafts p&lt;0.001</td>
</tr>
</tbody>
</table>