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Endoscopic Versus Conventional Vein Harvest Technique: Histological and Immunohistochemical Evaluation of Venous Wall Integrity

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ABSTRACT

Background: The introduction of endoscopic saphenous vein graft harvesting has been known for two decades. It offers benefits related to decreased rate of donner site complications. Debates related to its safety in terms of trauma to the wall of the venous graft and long-term graft patency have been raised, but few studies had investigated this point. Our aim is to compare the endoscopic saphenous vein harvest and conventional harvest techniques, in terms of the integrity of the wall of the vein graft.

Methods: A prospective study in which we examined 80 samples of saphenous vein from 80 patients to whom coronary artery bypass grafting was done. Patients randomly were assigned to either technique. Vein samples were taken from patients having the conventional technique (group 1, 40 patients) and from patients having endoscopic vein harvest (group 2, 40 patients). Vein samples were stained with Hematoxylin & Eosin, Masson's trichrome, and immunohistochemical stain for CD 31 and then examined by light microscopy. The degree of intimal staining was graded from 0% to 100%, which is directly related to the degree of intimal preservation (the least injury, the more the staining score) and vein media changes were reported.

Results: Patient characteristics were comparable in the groups. Group 1 (conventional group) was better than group 2 (endoscopic group), regarding endothelial integrity and medial changes although it was statistically not significant.

Conclusion: Both the conventional and endoscopic techniques are comparable, regarding the intimal preservation of the venous graft.

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INTRODUCTION

Saphenous vein graft as a conduit for revascularization in coronary artery bypass graft surgery (CABG) remains the most used conduit. Endoscopic vein-graft harvesting is a minimally invasive technique designed to reduce the rate of donner-site complications after open saphenous vein (SV) harvest for CABG. Endoscopic saphenous vein harvesting (ESVH) technology first was clinically introduced in the mid-1990s and currently is being used in more than 90% of CABG cases in the United States [Jacobs 2017]. The introduction of endoscopic saphenous vein harvesting has been found to decrease saphenectomy wound-associated complications like infection, pain, and disfigurement, compared with the traditional open conventional saphenous vein harvesting (OCSVH) technique. Despite these advantages, the rate of adoption among cardiac surgeons has been variable [Hashmi 2015].

Obesity, diabetes, hyperlipidemia, female gender, peripheral vascular disease, and advanced age are known risk factors for wound healing complications after OCSVH [Olsen 2003]. However, research has shown that these particularly high-risk patients benefit from ESVH techniques. For example, in patients with diabetes and obesity, no additional risk of wound healing disturbances can be found anymore if ESVH is used [Nasso 2007].

Criticism of this technique focuses on the risk of vein injury at the time of harvest with its potential deleterious effect on structural integrity and long-term patency [Hashmi 2015].

The integrity of the endothelial lining is affected by many factors, mainly the technique of harvesting and preservation solution used. Due to the potentially harmful effects of the solution constituents on the vein endothelium, the proper components of the solution used for saphenous vein preparation in coronary bypass surgery may affect the ultimate graft patency [Rubens 1998].

Other concerns exist with regards to thermal spread due to diathermic control of side branches, hazardous effects of CO_2

insufflation, and formation of microscopic clots in the collapsed vein due to the high-pressure endoscopic field that can be overcome by early systemic heparinization [Brown 2007]. The use of diathermy in the vein vicinity may cause thermal injury to the vessel wall, which may impair graft quality by compromising the viability of endothelial cells, resulting in platelet aggregation and thrombus formation. Chronic endothelial damage and dysfunction stimulate the migration and proliferation of smooth muscle cells into the intima, a key cause in the development of atherosclerosis and graft failure [Allen 1998].

Our aim is to investigate the extent of endothelial injury by histological examination, using light microscopy of the saphenous vein graft to rule out endothelial damage as a direct result of manipulation or instrumentation by endoscopic technique compared to the standard open conventional harvesting technique.

METHODS

In this prospective observational study, we analyzed the histological changes of saphenous vein samples from 80 patients, who underwent elective CABG between April 2019 and August 2021, in King Fahad Hospital of the University, Khobar, Saudi Arabia. Patients randomly were allocated to either open or endoscopic vein harvest without selection bias, irrespective of age, sex, number of planned grafts, or associated risk factors such as obesity, diabetes, or peripheral vascular disease. Exclusion criteria were cases that underwent conversion from ESVH to OCSVH and cases of combined harvest techniques.

Two groups of vein samples were defined: group 1 (N = 40), which included vein samples from open conventional saphenous vein harvesting (OCSVH) patients and group 2 (N = 40), which included vein samples from endoscopic vein harvest (ESVH) patients. The protocol of the study was approved by our local ethical committee (IRB-2019-01-375), before we started allocation of patients in the study and informed consent was taken from all patients.

In the standard open conventional technique for vein harvesting, the great saphenous vein was exposed and harvested under direct vision through a long continuous skin incision starting lateral to the medial malleolus and extending toward the thigh. The vein was dissected from its perivascular fat minimizing manipulation and instrumentation of the vein. Side branches were identified, clipped, and divided.

While in the endoscopic vein harvesting technique, a 2-cm incision was made at the medial aspect of the knee, and the saphenous vein was identified, dissected, and surrounded by a vessel loop. Then, the vein was dissected both proximally and distally under endoscopic visualization through the incision using the closed-tunnel technique with a CO_2 pressure of around 10 mmHg and flow rate of 3-5 L/min. The vein circumferentially was dissected, and side branches were cauterized using a C-ring dissector and bipolar cautery. The procedure's standard instrumentation is known commercially as VASOVEIW HEMOPRO 2, Endoscopic Vessel Harvesting System (MAQET Cardiovascular LLC, Barbour Pond Drive Wayne, NJ, USA). It is made up of a subcutaneous C-distributor, bipolar arm, and 5-mm port. Also included is standard endoscopic equipment, such as a fiberoptic camera with a 5-mm lens, light source, and monitor. (Figure 1) (Figure 2)

Both techniques were done by experienced harvesters. Overdistension of the vein was avoided to prevent endothelial stretch. At least 1 cm of the vein harvested was taken for biopsy. In patients with only one venous graft, the vein sample was taken from the remaining part away from both ends as possible, while in patients with more than one venous graft the vein sample was taken from the middle part of the vein, usually after completion of the first venous graft. We voided the proximal part that is usually manipulated by instruments and cannulae.

All samples immediately were immersed in saline solution at 4°C after harvesting, tagged, and transported to the research lab for storage in liquid nitrogen until further use at the end of surgery. After thawing for 10 minutes at 37°C, sectioned vein specimens in labelled tissue processing cassettes were fixed in freshly made neutral buffered formalin 10%, which is buffered with sodium dihydrogen phosphate and disodium hydrogen phosphate to pH 7.0.

A 1 cm length of vein sample was taken from each patient, and it was processed to take at least 10 sections from it, three from each stain, each one was 5 mm in thickness. All samples were embedded in paraffin. Examination of the vein sample by light microscope was done after staining with Hematoxylin-eosin (H&E), Masson's trichrome, and immunohistochemical stain with CD31.

Statistical analysis: For data analysis, the Statistical Package for the Social Sciences (SPSS) version 20.0 was used. The data were presented in the form of mean, standard deviation, median, and ranges. Comparisons between the groups were made using the chi-square test for categorical variables and the student t-test for continuous variables. For all analyses, a P-value of ≤0.05 was considered statistically significant.

RESULTS

The study enrolled 40 patients in each group. Group 1 (OCSVH) included 34 males (85%) and six females (15%), with a mean age of 63 ±3.5 years. Group 2 (ESVH) included 32 males (80%) and eight females (20%), with a mean age of 61.1 ±4.3 years. Patient characteristics and risk criteria are tabulated in Table 1. (Table 1)

Harvesting time was comparable in both techniques, 42±2.1 minutes in OCSVH versus 45±3.5 minutes in ESVH (P = .013). Regarding the length of vein harvested in both techniques, it was 32±2.7 cm in the OCSVH and 30±2.4 cm in ESVH. This was statistically insignificant (P = .0.265). (Table 2)

In the Hematoxylin-Eosin-stained samples, the degree of endothelial preservation was graded, according to the percentage of luminal endothelium staining integrity, so the higher the percentage of endothelial staining integrity the better the endothelial preservation.

In group 1, we found the mean percentage of endothelial staining was 91±3.1 (range 100-87%), while in group 2 it was 88±4.3 (range 100-81%). Hematoxylin-Eosin stain revealed a statistically insignificant higher percentage of well-preserved endothelial cells in group 1 than in group 2 (P = 0.213). (Figure 3)

Regarding the Masson's trichrome and immunohistochemical stain with CD31, there were small areas of hemorrhage within the vein wall media, which was comparable in both groups. (Table 3)

DISCUSSION

Despite its inferior patency rates compared to arterial grafts, the saphenous vein graft (SVG) is widely used for CABG due to its ease of manipulation and generous length available and consequently, the long-term patency of SVG has been thoroughly investigated [Samano 2018; Saito 2020]. Studies examining the role of harvest techniques, vein preparation, or storage media have suggested that endothelial cell injury directly affects graft patency [Lawrie 1990; Cable 1990]. The standard conventional preparation of SVG, consisting of dissection from its surrounding fat and dilatation, has been used for decades but is reported to be associated with earlier atherosclerosis and poor long-term patency rates [Khaleel 2012].

Endoscopic harvesting of the saphenous vein although its effectiveness in minimizing the incidence of leg-wound

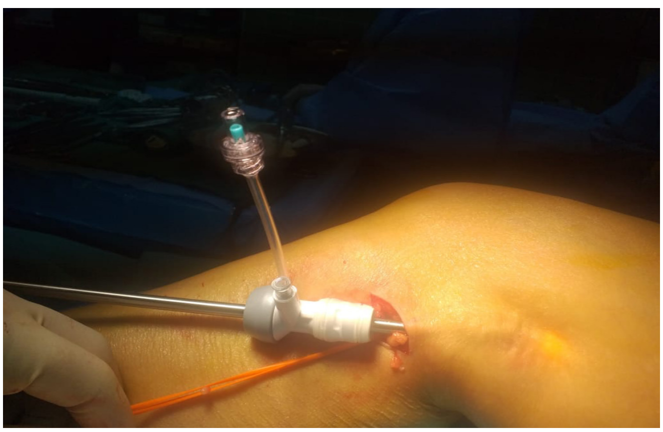

Figure 1. Identification and dissection of the vein, then the introduction of a 5 mm camera.

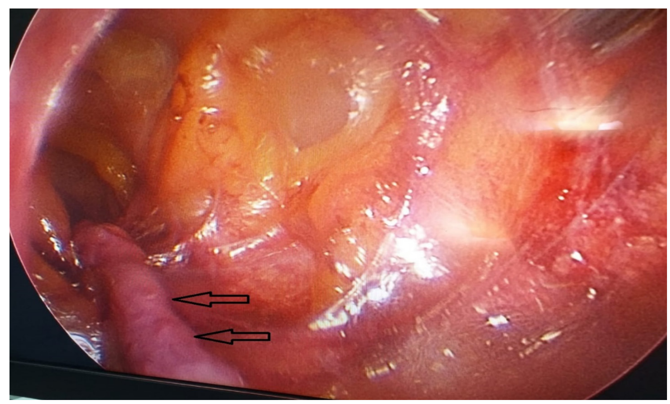

Figure 2. Saphenous vein after dissection by closed tunnel endoscopic technique.

Table 1. Patient characteristics

Variable	Group 1 OCSVH (*N* = 40)	Group 2 ESVH (*N* = 40)	*P*-value
Male	34 (85%)	32 (80%)	0.152
Female	6 (15%)	8 (20%)	0.224
Age/years (Mean±SD)	63 ± 3.5	61.1 ± 4.3	0.352
Risk factors			
Diabetes mellitus	16 (40%)	14 (35%)	0.461
Smoking	19 (47.5%)	17 (42.5%)	0.153
Dyslipidemia	30 (75%)	42 (72.4%)	0.822
Hypertension	17 (42.5%)	20 (50%)	0.221
Obesity	5 (12.5%)	10 (25%)	0.521
Renal dysfunction	4 (10%)	3 (7.5%)	0.287

Table 2. Operative data

Variable	Group 1 OCSVH (*N* = 40)	Group 2 ESVH (*N* = 40)	*P*-value
Harvest time (min)	42 ± 2.1	48 ± 3.5	0.013*
Length of vein harvested (cm)	32 ± 2.7	36 ± 2.4	0.265

healing complications is settled, data about its safety in terms of major adverse cardiac events is derived from randomized trials of limited statistical power, relatively small size, and short follow-up periods [Ferdinand 2017; Neumann 2018]. Furthermore, the patency of venous graft with endoscopic harvesting consistently has been lower than with open-wound harvesting technique, possibly because of mechanical factors related to overstretch and cautry [Kiani 2012; Kodia 2018]. A publication had raised doubts about whether the quality and durability of an endoscopically harvested vein are comparable with that harvested by the traditional open technique [Rousou 2009].

We compared the histological changes in 80 venous graft samples of 80 patients, who underwent CABG with saphenous vein harvested conventionally, open wound, in 40 patients (group 1) and in another 40 patients in whom the vein was harvested endoscopically (group 2). Vein samples from group 1 had better luminal endothelial staining rates with less venous wall medial injury than the samples of group 2, although it was statistically insignificant. Saito et. al [Saito 2020] found preserved endothelium even on the ultrastructure level between both groups, comparing the conventional and non-touch techniques.

In a randomized controlled trial of 300 patients undergoing CABG, Krishnamoorthy et al. [Krishnamoorthy 2017] reported a marginally better, although statistically insignificant, histological vein integrity in the open vein harvest technique than in the two methods of the endoscopic technique. This supports our results.

Early studies about graft histology did not find significant differences in vascular wall integrity with comparable endothelial preservation after endoscopic vein harvest compared to open harvest [Kiaii 2002; Bonde 2004]. These results coincide with ours, as we found no statistically significant difference between the OCSVH (group 1) and ESVH (group 2), although the grades of luminal staining were better in the OCSVH than in the endoscopic group.

Also, Rousou et al. [Rousou 2009] showed evidence of the inferiority of endothelial lining preservation of vein graft during endoscopic harvest using three independent techniques (western blot, immunohistochemistry, and multiphoton microscopy). They found signs of the impaired structural integrity of saphenous vein endothelium. The authors stated these detrimental effects may lead to decreased graft patency and worse patient outcome.

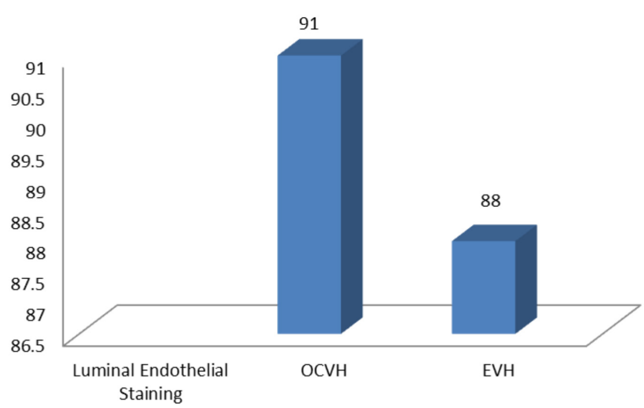

Figure 3. Percentage of luminal endothelium staining

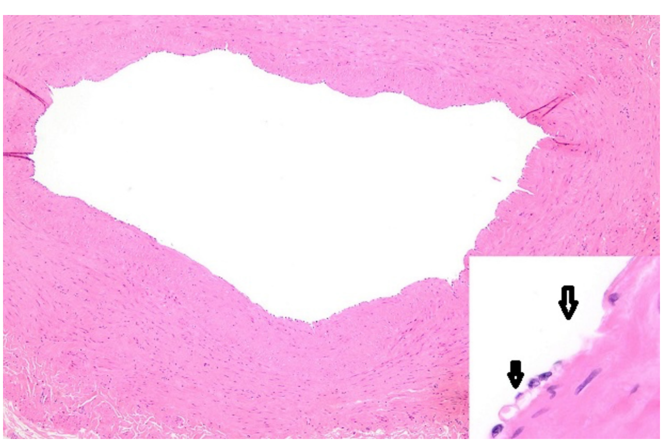

Figure 4. H&E stain show a breach in the endothelial continuity with endothelial cells swelling (arrow)

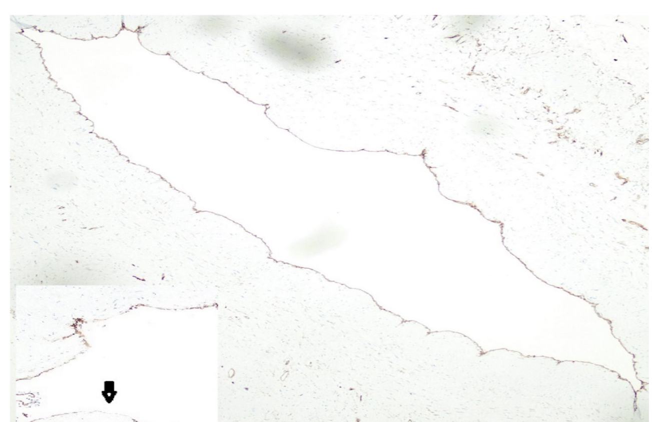

Figure 5. CD 31 immunohistochemical stain with breach in endothelial lining (arrow)

Table 3. Number of vein samples with medial hemorrhage and damage with Masson trichrome stain

Vein media	Conventional (OCVH) (*N* = 40), (%)	Endoscopic (EVH) (*N* = 40), (%)	*P*-value
Medial hemorrhage	11 (27.5%)	14 (35%)	0.334
Medial damage	4 (10%)	7 (17.5%)	0.128

Meyer et al. [Meyer 2000] studied histological changes in vein grafts in 14 patients. Nine patients had saphenous veins harvested endoscopically, and the authors found no significant difference between the two techniques, regarding the structural integrity of the vein graft.

In a multicenter study of 1150 patients undergoing CABG, Zenati et al. [Zenati 2019] randomly assigned patients for ESVH versus OCSVH and found no significant difference between the two techniques, regarding the long-term venous graft patency.

Study limitations: Our study has some limitations. First, the small number of cases may not give powerful statistical data. Second, correlation of histologic results with long-term angiographic patency may be necessary to demonstrate that the preserved graft endothelium has any effect on long-term patency rates of vein grafts.

CONCLUSION

We concluded that the safety of the endoscopic vein harvest technique in preserving luminal endothelium and wall integrity of vein graft is comparable with the already settled conventional technique. However, long-term follow up with direct assessment of graft patency may be needed to assess more the safety and efficacy of this technique.

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