

Novel no touch technique of saphenous vein harvesting: Is great graft patency rate provided?

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ABSTRACT

Coronary artery bypass grafting surgery effectively relieves signs and symptoms of myocardial ischemia. The left internal thoracic artery (LITA) graft is the gold standard having 90–95% patency rate at 10 years, whereas only 50% of saphenous vein (SV) grafts are patent at 10 years. However, there is a novel "no touch" technique in order to harvest an SV complete with its cushion of surrounding tissue, thus maintaining its endothelium-intact. Significantly superior short- and long-term graft patency rates comparable to LITA grafts can be achieved. Consequently, the SV may be revived as an important conduit in coronary artery bypass surgery.

Key words: Coronary artery bypass grafting; Graft patency; Myocardial revascularization; Saphenous vein; Venous grafts

Received: 02-03-16
Accepted: 25-05-16

INTRODUCTION

Coronary artery bypass grafting effectively relieves signs and symptoms of myocardial ischemia.^[1] However, the patency of grafts used is a *sine qua non* for its long-term success.^[2] The left internal mammary artery (LIMA) is the gold standard among the conduits used for coronary artery bypass surgery (CABG).^[3,4] However, the most commonly used vessel is the saphenous vein (SV).^[5] There is an obvious superiority of LIMAs as 90–95% of LIMA grafts are patent at 10 years, whereas only 50% of SV grafts are patent at 10 years.^[6,7] More surprisingly, up to 15% of vein grafts are early occluded, just in the 1st month,^[8,9] and another 15–30% of them are occluded in the first post-CABG year.^[8,10] But why does such high early occlusion rates happen? Technical surgical factors and damage to the endothelium during SV harvesting can be the reasons why this happens.^[11] The adventitial layer of the vein is commonly extracted, so vascular spasm takes place. Consequently, high-pressure distention is required to dilate the vessel leading to extensive damage to the endothelium of the vein wall.^[12]

On the other hand, Souza^[13] proposed an innovative "no touch (NT)" technique for the harvesting of SV in 1996. No touch technique is an atraumatic approach to remove the SV complete with its cushion of surrounding tissue without touching the vessel at all.^[13] This novel method contributes to better preservation of endothelial integrity and luminal nitric oxide synthase (NOS).^[14,15] Fat, elastic fibers, nerves, and vasa vasorum supplying nutrients and oxygen to the SV wall are the components of this tissue surrounding

Access this article online

Website: www.annals.in

DOI:
10.4103/0971-9784.185537

Quick Response Code:



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Cite this article as: Papakonstantinou NA, Baikoussis NG, Goudevenos J, Papadopoulos G, Apostolakis E. Novel no touch technique of saphenous vein harvesting: Is great graft patency rate provided?. *Ann Card Anaesth* 2016;19:481-8.

the SV.^[16] Moreover, the surrounding fat tissue of the vein is a source of several vasoactive factors.^[17] When the SV is harvested using the “NT” technique, surgical instruments do not touch at all the vessel itself, so no spasm occurs making the distension of the vein graft unnecessary,^[18] thus further minimizing the endothelial damage caused.^[14,19] Therefore, “NT” technique is related to superior early and long-term graft patency when compared to the conventional technique.^[2,18] In this study, we will make a review of the literature in terms of the advantages of NT SV harvesting technique and its impact on long-term SV patency.

NO TOUCH TECHNIQUE PROCEDURE

A classic incision is made longitudinally on the skin of the leg. The incision can be either continuous^[2,18,20] or on the calf and on the thigh separately in order to avoid the multibranching SV segment of the poor quality of the knee.^[21] A plane is created around the vein using scissors. The SV is covered by a thin layer of adherent tissue anteriorly and posteriorly. Perivascular fat of 0.5-cm on either side is included in the plane.^[21] The SV is extracted from its bed with its perivascular fat pedicle and all its side branches are ligated.^[2,18,20,21] No venous spasm occurs as it is the perivascular tissue and not the vessel itself that is handled by surgical instruments.^[21] As a result, neither flushing nor manual dilation is required.^[2,18] Sponges soaked in pure saline solution are then used to cover the vessel and when it is totally extracted, blood from the aortic cannula serves as the storage solution.^[2,18,20,21] Finally, interrupted or continuous sutures are used to close the leg wounds^[21] [Figure 1].

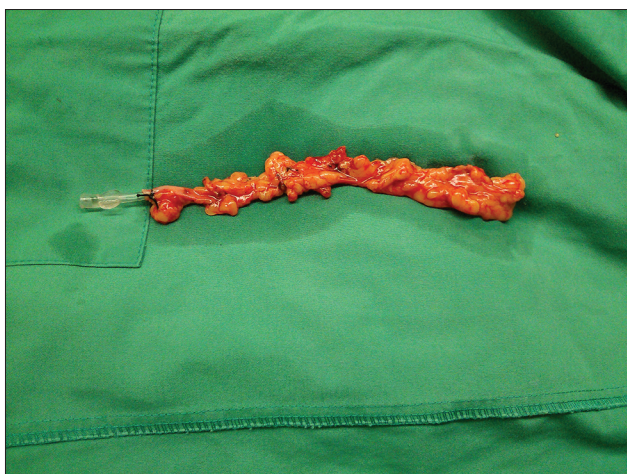


Figure 1: Saphenous vein graft harvested complete with its surrounding fat by no touch technique

PATHOGENESIS OF GRAFT OCCLUSION: WHY IS THE VEIN DAMAGED?

Vein graft failure is the result of three main causes depending on the time after surgery: Acute thrombosis, intimal hyperplasia, and atherosclerosis.^[1] During the 1st postoperative month, acute thrombosis is the main cause of graft failure.^[1,19] Acute thrombosis can occur due to technical factors such as small size of the target vessel leading to poor distal runoff and size mismatch between the graft and the target vessel resulting in turbulent flow. Graft ischemia and endothelial layer removal because of mechanical trauma and manual distention can also cause acute thrombosis. Platelet adhesion and thrombosis are induced by the removal of the endothelial layer. Furthermore, nitric oxide (NO) levels are decreased leading to vasospasm.^[1] Distension with normal saline to overcome spasm causes more damage to the media and intima layers of the graft.^[21]

From 1 to 12 months after surgery (the subacute period), intimal hyperplasia is responsible for graft failure.^[1,19] Both hemodynamic and nonhemodynamic factors, such as mechanical stretch and vascular injury, provoke the activation of vascular smooth muscle cells (VSMCs) which contribute to neointimal hyperplasia.^[22,23] Higher arterial pressures make smooth muscle cells proliferate and then migrate into the intima, where proliferation goes on.^[1] This proliferation does not significantly differ between the uninjured vein and the ITA,^[24] but the damaged vein endothelium results in more intense proliferation.^[20] Vein wall ischemia due to loss of vasa vasorum blood supply is another contributing factor leading to intimal hyperplasia.^[25]

Atheroma development following intimal hyperplasia is responsible for graft failure after the 1st postoperative year.^[19] Vein atheromas can rupture and cause thrombotic occlusion of the graft just like coronary artery atheromas.^[26] However, vein atheromas characteristics make them more prone to rupture. They are more diffuse and concentric, less calcified and have poorly developed or no fibrous caps.^[27]

The deleterious effects of endothelial damage of SV during its preparation^[28] appeared immediately after its introduction in CABG in the 1960s.^[29] Injuries happening during surgery lead to intimal loss and consequently to biochemical and functional changes of the graft.^[30] During the removal of the perivascular SV tissue when the conventional method is used, the adventitia of the

vein is damaged and vasospasm of the vessel takes place.^[31] Subsequent distention is responsible for the reduction of endothelial NOS (eNOS) concentration in the endothelium and in the medial layer, and stripping is associated with the removal of eNOS from the adventitia.^[20] All vessel layers and their cells are affected by the harvesting approach.^[28] For example, deformed, flattened, and polymorphic endothelial cells containing an abundance of cytoplasmic vesicles^[32] and VSMC with altered medial morphology and signs of nuclear division indicating VSMC proliferation^[33] are observed when conventional SV harvesting is adopted.

However, the NT SV harvesting approach prevents endothelial damage and subsequent intimal hyperplasia which result in graft failure.^[1] The major advantages of NT method are as follows:

- Vein trauma is limited during vein harvesting.^[13] Electron microscopy proves that NT technique preserves the endothelium to the maximum extent.^[14,34] A continuous endothelium attached to the basal membrane in veins received with the NT technique is recognized by the electron microscopy, whereas veins prepared with the conventional technique have not a continuous endothelium and the endothelial cells are separated from the basal membrane.^[13,14,33] As a result, an intact adventitial layer with microvessels is recognized by immunohistochemistry after the NT technique, whereas the conventional technique is not associated with such an observation.^[20] An intact vasa vasorum channel contributes to the improved vein graft patency rate.^[16] Dreifaldt *et al.*^[16] observed a significant reduction of vasa vasorum in the media ($P = 0.007$) and adventitia ($P = 0.014$) of SVs harvested by the conventional technique in comparison with those prepared with the NT technique. A continuous endothelium and an intact adventitial collagen layer after NT technique are also confirmed by an ultrastructural analysis.^[35] Hence, intact structure, preserved endothelial function, preserved levels of eNOS, and reduced neutrophil adhesion are typical of the NT SV harvesting technique.^[22,23,32] Slower progression of atherosclerosis is also observed resulting in improved graft patency rate^[36]
- The vein wall is maintained intact, so no spasm occurs.^[36] As a result, there is no need for high-pressure distension to overcome venous spasm^[13,37]
- The perivascular adipose vein pedicle is preserved.^[13] This perivascular fat serves as an

“external biological stent”^[28,37] which is consisted of numerous collagen fibers that prevent from the deleterious effects of aortic pressure to the vein wall.^[20] This external stent has been shown effective in reducing early thrombotic occlusions, intimal, and medial hyperplasia.^[38-40] In addition, the surrounding tissue of the vein is a source of NO and vasodilatory adipokines such as leptin,^[41] and eNOS activity is recognized in all three layers of the vein wall after NT technique, whereas stripping and distention used during the conventional technique lead to the reduction of eNOS.^[20,35] eNOS activity preservation offers increased thromboresistance of the vein, improves its vasorelaxation and prevents venospasm.^[13-15,19]

GRAFT PATENCY

Harvesting the SV graft by the conventional technique leads to graft occlusion within the 1st month in up to 15% of SV grafts.^[8,9] Another 15–30% of SV grafts occlude during the 1st year.^[8,10] When the conventional technique is used, handling the vein with surgical instruments, stripping and dilation in order to overcome spasm injure the vein wall.^[42] According to Souza *et al.*,^[2] the harvesting technique of the SV for CABG, which is directly related to the preoperative quality of the vein,^[2,43] constitutes the most significant factor for graft patency.^[2] According to this study by Souza *et al.*, the NT technique not only provides a significantly better SV patency rate in comparison with the conventional technique ($P = 0.007$) but also SV patency is similar to that of the left internal thoracic artery (LITA).^[2] According to an angiography assessment by Souza *et al.*^[44] comparing 52 patients whose veins were harvested by the NT technique with 52 patients submitted to the conventional technique, graft patency of veins harvested with the conventional technique was 89% versus 95% for the NT technique at 18 months postoperatively.^[44] Same results were reported by Rueda *et al.*^[20] who compared NT technique with the conventional one and with an intermediate harvesting technique. The angiography assessment at a mean of 18 months showed that 118 out of the 124 veins were patent in the NT Group (95.4%) which was significantly higher than the 88.9% (113/127) patency rate of the conventional group and the 86.2% (100/116) patency rate of the intermediate group ($P = 0.025$). Even ITA patency rate (91.5%) was lower than the NT SV patency rate in both studies.^[20,44] At 8.5 years postoperatively, there was a clear difference between the two groups. NT Group presented a 90% SV graft patency whereas the

patency rate of the veins prepared with the conventional technique was only 76% ($P = 0.01$).^[2] Furthermore, the NT technique was associated with an impressively higher SV graft patency rate than the conventional technique in veins of poor quality having either varicose or fibrotic changes during surgery. The patency rate of veins of poor quality before harvesting at 8.5 years was 88.9% versus 36.4%, respectively ($P = 0.002$).^[2] It is important to mention that the overall long-term LITA patency was 90% at 8.5 years.^[2] In a subsequent study, the same group compared long-term graft patency rates of an SV harvested by the NT technique with a radial artery graft.^[45] If harvested by the conventional technique, an SV graft has a lower long-term patency rate compared to a radial artery.^[46] However, the patency rate of the NT SV graft at 3 years was 94% which was significantly higher than the 82% patency rate of the radial artery graft ($P = 0.01$).^[45] In another randomized study, 49 patients in NT Group were compared with 44 patients in the conventional group with regard to graft occlusion rates at 8.5 years on average. NT Group was superior to conventional group (24.3% vs. 43.2%) ($P = 0.14$)^[47] [Table 1].

Similarly, Johansson *et al.*^[36] compared graft patency rates with a focus on early atherosclerotic changes between veins harvested by the NT technique and by the conventional technique in a short term at 18 months and in a long term at 8.5 years study. In the short-term study, graft patency was 89% for the NT Group, whereas it was 75% for the conventional group ($P = 0.006$). A bolus of 12,500 IU of heparin intravenous and 0.2 mg nitroglycerin was administered and then intravascular ultrasonography was performed. If the diameter of the target coronary artery was over 2 mm forming a favorable angle with the SV graft, the ultrasound catheter was advanced into the coronary artery, or else it was advanced close to the junction of the graft with

the coronary vessel.^[36] Intravascular ultrasonography showed less intimal thickness ($P = 0.03$), less grafts with considerable intimal hyperplasia ($P = 0.011$), and larger graft lumen volumes ($P = 0.07$) in the NT Group. In the long-term study (8.5 years), the NT technique was associated with a 92.3% patency rate which was superior to the 84.4% patency rate of the conventional technique ($P = 0.14$).^[36] Intravascular ultrasonography also revealed much more intense atherosclerotic changes in the conventional group at 8.5 years. In overall, fewer patients in the NT Group had grafts containing plaque compared to the conventional group (50% vs. 80%, $P = 0.13$). In detail, comparing the NT group to the conventional one, there were significantly fewer grafts containing multiple plaques in the former (14.8% vs. 50%, $P = 0.008$), significantly less advanced plaque with lipid (11.8% vs. 63.9%, $P = 0.0004$) and significantly less maximal plaque thickness (1.04 mm vs. 1.32 mm, $P = 0.02$). Finally, lumen volumes continued to be significantly larger in the NT Group ($P = 0.03$)^[36] [Table 1].

COMPLICATIONS

It is hypothesized that wound complications following the NT method happen more often than when using the conventional approach due to the removal of the pedicle of perivascular tissue during the former.^[48,49] Rueda *et al.*^[20] compared three groups of patients: A group of NT SV grafts (NT Group), another of veins prepared with the conventional technique (C Group), and the third one including veins prepared with the conventional technique but not distended (I Group). About 10% of patients in each group developed cellulites and superficial infection of the leg wound. In another study comparing same groups with the aforementioned, two of 46 patients (4.3%) in C Group, three of 41 patients (7.3%) in I Group, and five of 45 patients (11.1%) in NT

Table 1: Harvesting the saphenous vein with surrounding tissue provides high short- and long-term patency rates comparable to the left internal thoracic artery

Study	Early patency rate for C SV (18 months), %	Early patency rate for NT SV (18 months), %	P_e	Late patency rate for C SV (8.5 years), %	Late patency rate for NT SV (8.5 years), %	P_l	Early patency rate for LITA (18 months), %	Late patency rate for LITA (8.5 years), %
Souza <i>et al.</i> ^[44]	88.9 (113/127)	95.4 (118/124)	0.10	-	-	-	91.5 (108/118)	-
Souza <i>et al.</i> ^[2]	-	-	-	76 (77/101)	90 (91/101)	0.01	-	90 (63/70)
Rueda <i>et al.</i> ^[20]	88.9 (113/127)	95.4 (118/124)	0.025	-	-	-	91.5 (108/118)	-
Johansson <i>et al.</i> ^[36]	75 (84/112)	89 (105/118)	0.006	84.4	92.3	0.14	-	-
Johansson <i>et al.</i> ^[47]	-	-	-	75.7	66.8	0.14	-	-

C: Conventional, SV: Saphenous vein, NT: No touch, P_e : P value for statistical significance between the two groups for early patency rate, P_l : P value for statistical significance between the two groups for late patency rate, LITA: Left internal thoracic artery

Group suffered superficial infection or cellulitis.^[21,44] Verma *et al.*^[49] observed leg wound infections only in diabetic patients submitted to NT harvesting technique. Nonetheless, there was no significant difference with regard to functional recovery of the leg between those treated by the NT method and those treated by the conventional one at the 1st postoperative year.^[49] In addition, an endoscopic method for SV harvesting has been adopted by many cardiac surgical centers as it is related to a lower rate of harvest site complications.^[50] Mannion *et al.*^[48] compared 87 patients whose SVs were harvested NT with 123 patients whose veins were prepared endoscopically during 2 years. Harvest site complications were significantly higher in the NT Group. Eighteen percent of the patients submitted to NT approach required vacuum-assisted wound closure or intravenous antibiotics, whereas only 2% of the endoscopically treated patients did ($P < 0.0001$). However, NT technique was related to a superior vein graft patency than the endoscopic approach (94% vs. 27%, $P < 0.02$).^[48] Therefore, an NT endoscopic approach would be an advantageous technique. To do so, a device which would allow one to remove the vein intact together with its perivascular tissue is required.^[2]

In another study, patients treated by the NT method complained about mild-to-severe numbness and swelling. Greater swelling seems to be reasonable as more venous and lymphatic vessels are injured. However, this effect is minor and it is resolved over time.^[49] On the other hand, numbness sensation may be explained by the fact that the saphenous nerve is inevitably extracted within the perivascular SV pedicle during NT approach, whereas it is usually preserved during conventional approach.^[49] Souza *et al.*^[18] observed that although the saphenous nerve was damaged in the NT technique, no severe neurological symptoms were observed. The sensory reduction at harvesting site was the most common neurological finding. However, in another study, similar neurological symptoms were also observed in most patients submitted to the conventional technique due to the saphenous nerve innervations.^[51]

Kinking is another possible complication after the removal of the surrounding tissue of the vein when the graft is too long. Kinking leads to later functional impairment. Consequently, when the conventional technique is used, graft size has to be carefully adjusted to avoid the risk of kinking.^[20] Nevertheless, in the NT technique, the perivascular tissue of the vein is preserved thus supporting the graft and safely

preventing from kinking no matter the length of the graft.^[2,18,20]

MORBIDITY AND MORTALITY

Neither mortality nor morbidity is increased by NT technique compared to conventional technique. No perioperative myocardial infarction or death was occurred in 52 patients who underwent coronary artery bypass grafting with NT SVs according to a Souza *et al.* study in 2001.^[18] Rueda *et al.*^[20] compared three groups of patients: A group of NT SV grafts (NT Group), another of veins prepared with the conventional technique (C Group), and the third one including veins prepared with the conventional technique but not distended (I Group). Mortality rate was 0% in all three groups. Two patients in the C Group suffered perioperative acute myocardial infarction and one patient in the NT Group was reoperated due to bleeding from the internal mammary artery. In another study, comparing same groups with the aforementioned, no major complication requiring surgery was occurred in either of the three groups. Mortality was also zero in all three groups, whereas two patients of the Group C suffered a myocardial infarction preoperatively.^[21] Similar results were also observed by Souza *et al.* in 2006. No perioperative death was observed in either group and two patients from Group C suffered a perioperative myocardial infarction.^[2] In another randomized study by Johansson *et al.*^[47] comparing 49 patients in group NT to 44 patients in Group C at 8.5 years postoperatively, no cardiac death was found in group NT, whereas three patients died in Group C. Moreover, there was a statistically significant advantage for the NT patients as 67.3% of them were asymptomatic-free from angina and in New York Heart Association Class I versus 43.2% of C patients ($P = 0.02$). Trends toward fewer cardiac deaths and myocardial infarctions (3.8 vs. 13.4%; $P = 0.16$) as well as toward more patients free from angina (75.5 vs. 63.6%; $P = 0.26$) were also observed.^[47]

Limitations of the studies

In spite of the encouraging results, there is an absence of clinical outcomes in most studies.^[2,16,19,20,28,32,36] Outcomes extracted by intravascular ultrasonography were reported by Johansson *et al.*^[36] Angiography assessment results were reported by Rueda *et al.*^[20] and by Souza *et al.*^[2] Morphometric analysis of the vessel wall and ultrastructural analysis was the basis on which other studies extracted their results,^[16,19,20,28,32] In Dreifaldt *et al.*'s^[16] study, veins harvested from a

limited number of patients were examined to extract their results with regard to vasa vasorum of the veins. A relatively high variability in measurements was also existed due to the individual variations among patients, the variation of vessel wall thickness within the same vein, and the variation related to stripping the adventitia during the conventional technique.^[16] According to Verma *et al.*'s^[49] study limitations, there cannot be a secure conclusion by their protocol if the VSMC changes are secondary to the harvesting technique, no need for distension or the intact surrounding adipose tissue. They also mention that *ex vivo* time prior to fixation was not estimated and NT veins were usually harvested prior to the conventional veins leading to greater activation in NT veins. Moreover, NT veins were preserved *ex vivo* in heparinized blood solutions, whereas conventional veins were kept *ex vivo* in normal saline solutions. In addition, all measurements were not made in the same sample due to the limited amount of tissue collected. Finally, the absence of clinical outcomes and complications due to insufficient sample size was another limitation of this study.^[49]

CONCLUSIONS

In conclusion, the conventional technique of SV harvesting includes the removal of SV without its surrounding tissue and the distension of the vein at high-pressure after harvesting in order to abolish the potential spasm of the graft. In contrast to this, during the NT technique, the perivascular tissue of the vein is prepared together with the vessel in order to prevent any spasm of the graft.^[35] The preservation of the surrounding tissue of the vein keeps the endothelium of the vein intact. As a result, the endothelium maintains its structure and its functionality,^[18] sources of NO^[28] and vasa vasorum of the vein^[16] are also preserved, atherosclerosis progresses slower^[36] and therefore, a better graft patency rate is achieved.^[16,18,28,36] In contrast, when the SV is stripped off its surrounding tissue, spasm of the graft happens and mechanical distension is necessary in order to overcome it. As a result, endothelial, medial, and adventitial integrity is compromised and both short- and long-term venous graft patency are influenced.^[21] In addition, a long vein graft without the threat of kinking can be achieved when the surrounding tissue is maintained.^[21] In overall, the "NT" SV harvesting technique can produce significantly superior short- and long-term graft patency than the conventional technique can, and more importantly, the patency rates of the grafts harvested by the NT

technique are even comparable to that of the LITA graft.^[2,35] Consequently, the SV is revived as an important conduit in CABG surgery. The novel NT technique of SV harvesting provides better structural, functional, and mechanical protection of the vein wall. As a result, a nonthrombogenic graft is produced and less intimal and medial hyperplasia take place.^[2] However, more studies with clinical outcomes are required in order to confirm these encouraging observations. Perfecting the technique of this harvesting method and more reliable future studies may reveal a graft comparable to arterial grafts in terms of quality and long-term patency.

Acknowledgments

The authors had full control of the design of the study, methods used, outcome parameters and results, analysis of data, and production of the written report.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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