



Commentary



Human Great Saphenous Vein: Uncertainty in Interpretation of Intimal Openings

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The potential role of the vasa vasorum in the human great saphenous vein (GSV) harvested for coronary artery bypass grafting (CABG) is particularly relevant to the phenomenon of the blood re-entry into the vein graft wall after surgery [1]. A recent article [2] described small openings (5–20 μm) in the luminal intima of the GSV harvested for CABG. However, it remains unclear whether these openings are related to the vein's vasa vasorum system or whether they are involved in blood reflow to the vein graft wall after CABG surgery, or whether they instead act as “communication channels” of yet unknown function. These observations and conclusions were based on studies of GSV graft material harvested without stripping the pedicle and without distension (the “no-touch” technique) [3]. Examination of these GSV preparations at the scanning (SEM) and transmission (TEM) electron microscopy levels revealed variety of morphological and/or ultrastructural features of the GSV [4,5].

The luminal intima of the human GSV stem is a complex three-dimensional structure composed of morphologically heterogeneous endothelial cells, which display varying positional orientations and cover the uneven subintima as part of the vein's characteristic folds [2,4]. These intimal features may become distorted during conventional vein harvesting for CABG. The heterogeneity of endothelial cells can be attributed, for example, to natural processes such as aging, degeneration, and renewal [6]. It is also noteworthy that a GSV used for CABG, regardless of whether it is harvested using conventional, no-touch, or endoscopic techniques, may be affected by subtle pathological changes that are difficult to detect during pre-surgical assessment [7].

Given the complex structural features of the intima of the human GSV, the nature and role of at least some of the small intimal openings remain uncertain. Importantly, the mere presence of such openings in the luminal intima does not necessarily indicate that they represent terminal connections of the vasa vasorum system. To date, no direct evidence of continuity between the GSV vasa vasorum and these intimal openings has been demonstrated, except under pathological conditions in failed GSV as coronary grafts [8].

In contrast, detailed studies using corrosion casts of the GSV obtained during CABG have not identified luminal terminations of the vasa vasorum [9]. Similarly, such openings were not observed in GSV graft material examined intraoperatively or post-mortem using combined histological, corrosion casting, and injection techniques [10]. Notably, that study demonstrated that the venae vasorum typically drain into terminal segments of the largest tributaries of the GSV, while the closest vasa vasorum capillaries were located approximately 250–660 μm from the GSV lumen. Our own SEM studies showed that the nearest vasa vasorum profiles were located 60–70 μm from the GSV lumen [4], while the TEM and laser confocal microscopy showed no immediate subendothelial profiles of vasa vasorum microvessels [2].

Taken together, these observations suggest that extension of the vasa vasorum toward the vein lumen is more likely a feature of pathological remodelling, as reported in explanted failed GSV coronary grafts [8]. Furthermore, the spread of India ink into the vasa vasorum following its injection into the GSV lumen [11] may be better explained by connectivity between the vasa vasorum and venous tributaries [8], rather than diffusion through putative intimal openings.

Although various fine structural aspects of the vasa vasorum and luminal openings in GSV grafts have been reviewed in detail elsewhere [2,12], some degree of structural uncertainty remains. Figure 1 illustrates how uncertainty in the interpretation of morphological findings can lead to misinterpretation and may require resolution through a combination of complementary technical approaches, including electron microscopy.



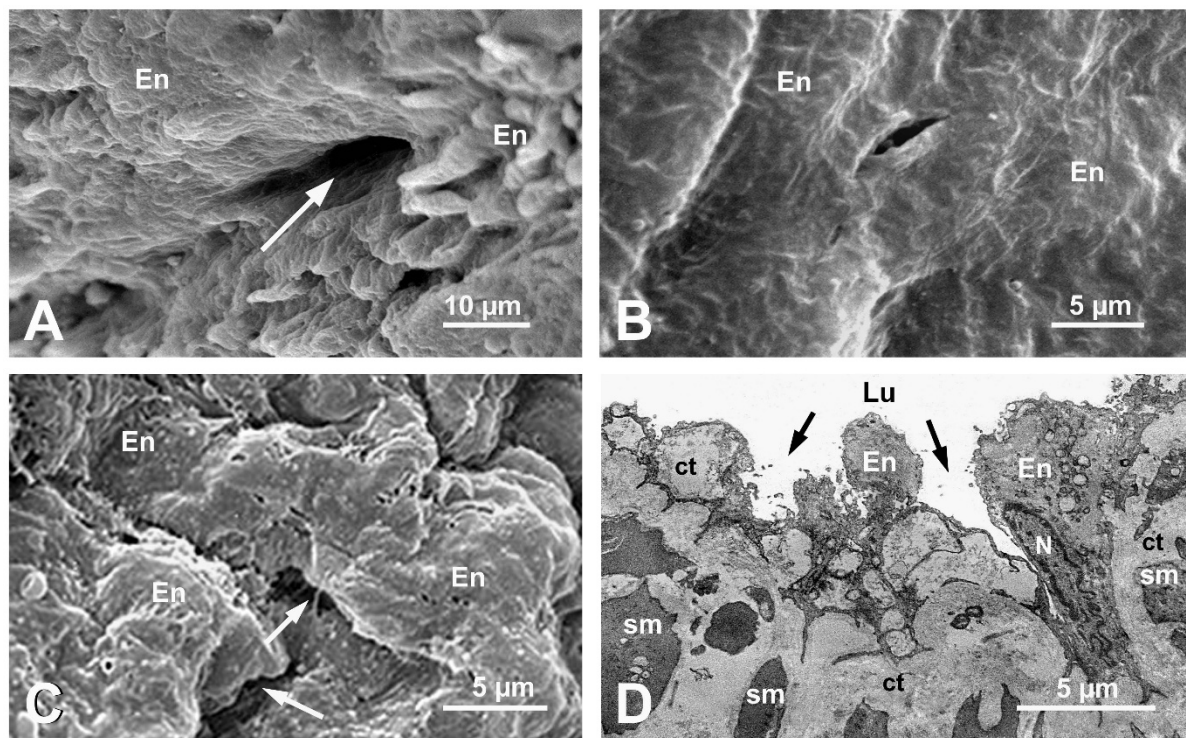


Figure 1. Scanning electron microscopy (SEM; (A)–(C)) and transmission electron microscopy (TEM; (D)) of the luminal intima of a human GSV harvested as a coronary graft using the no-touch method, displaying true and false (imitative) intimal openings. (A) SEM image shows a vessel opening (arrow) within the luminal endothelium (En) of the vein; due to its size ($>10\ \mu\text{m}$), it is more likely to represent a tributary branch rather than a vasa vasorum vessel terminating at the vein lumen. (B) SEM image shows a small ($<5\ \mu\text{m}$) intimal opening ("channel") with a morphology resembling a plant open stoma apparatus. (C) SEM image shows a surface view of the vein intima with false (imitative) openings (arrows) formed by the shape of endothelium. (D) TEM image shows a cross-section of the intima-subintima region of the vein with visible 'gaps'—putative openings (arrows) between soma of neighbouring endothelial cells. Notably, although the endothelium remains continuous, there is no continuity across the gaps with the subendothelial structures, and no vasa vasorum microvessels are present at this site. The vein lumen (Lu), vascular smooth muscle (sm), endothelial cells nucleus (N), and the abundance of subendothelial connective tissue (ct) are visible. It is acknowledged that images have been modified from: (A) Loesch and Dashwood [13], (B) Loesch [2], (C) Vasilakis et al. [4], with permission, and (D) is from an unpublished study by A. Loesch.

As an example of the misinterpretation of morphological details, Figure 3-NTSVG in [14] can be cited. In this figure, the original description of the "wavy alignment of endothelial cells" (Figure 3b in [4]) was replaced with the description of "the termination of the vasa vasorum in the lumen of a NTSVG" [14].

It is reasonable to state that the uncertain nature of the small luminal openings in the human GSV warrants further investigation, particularly in the context of blood re-entry into the newly implanted GSV graft during CABG surgery. However, the possibility cannot be excluded that these small intimal openings (or at least some of those measuring $<10\ \mu\text{m}$) represent an intrinsic structural feature of the endothelium, especially since no connectivity has been identified between the endothelial openings and the vasa vasorum. Nevertheless, the presence of small openings in the intima of the GSV may also be considered a contributor to the complexity of vascular endothelial function [15,16], particularly when structural changes occur in the GSV during CABG surgery [3–5,17,18].

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Conflicts of Interest

The author declares no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

Abbreviations

CABG	Coronary artery bypass grafting
Ct	Connective tissue
En	Endothelium (Endothelial cell)
GSV	Great saphenous vein
Lu	Lumen
N	Nucleus
SEM	Scanning electron microscopy
Sm	Smooth muscle cell
TEM	Transmission electron microscopy

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