

## The histological examination of vena saphena magna as a graft in coronary artery bypass surgery

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### Abstract

Coronary artery bypass surgery (CABG) is one of the most frequently performed surgical procedures worldwide, owing to the increasing incidence of coronary artery disease, which remains a leading cause of death globally. Following CABG, the development of occlusion in vein grafts is one of the significant indicators of poor prognosis, resulting in an increased risk of recurrent ischemic events and repeat revascularization. In the early and late postoperative periods, the use of healthy grafts with intact endothelium is critical to reduce mortality and morbidity rates. In this study, the histopathological findings of the vena saphena magna grafts in 12 patients who underwent CABG were evaluated to identify any preoperative degenerative changes in the grafts. The findings of the study showed that preoperative morphological degeneration was minimal in most grafts. However, in one sample, intimal fibrosis narrowed the lumen, while another sample exhibited mild medial sclerosis. In contrast, all other samples showed minimal or no degeneration. Consequently, assessing the histopathological condition of vessels before the operation is crucial to avoid using unsuitable grafts and to direct the surgeon to use different grafts if necessary. This study highlights the importance of examining the histology of vena saphena magna grafts to ensure their suitability as a bypass conduit in CABG surgery.

**Keywords:** coronary artery bypass surgery, vena saphena magna, graft, histopathology

### 1. Introduction

Today, in coronary surgery, a healthy blood vessel (graft) is taken from the chest or leg area, and this blood vessel is connected beneath the blocked heart artery. This new pathway improves blood flow to the heart muscle. The grafts used contain healthy veins or arteries harvested from a separate area; the number of grafts needed will depend on how severe the coronary heart disease is and how many coronary blood vessels are narrowed. Mostly used grafts are arterial grafts, which are biologically divergent conductance arteries used in coronary artery bypass surgery, including the internal mammary artery, vena saphena magna, radial artery, and right internal mammary artery. Due to its ease of access and because its wall contains a higher percentage of elastic and muscular fibers compared to other superficial body veins, the saphenous vein is used in coronary artery bypass surgery. The removal of the saphenous vein does not require a long incision; one or two incisions are made at the knee and a small incision in the thigh. This method minimizes scarring, allowing the patient to heal faster than conventional surgery. Despite many attempts to improve the

results of using veins in coronary artery bypass grafting, they still tend to fail in the long term. There are many studies on this subject in the literature (1-3).

Studies have shown that 7–13% of grafts from the great saphenous vein used for coronary artery bypass develop occlusion within the first month after surgery, while 5–14% of venous grafts develop >50% luminal stenosis. Complete occlusion is observed in 15–26% of grafts after 6–8 months, with 5–10% having greater than 50% luminal stenosis (4). Comorbidities are repeatedly encountered in patients undergoing coronary artery bypass surgery; specifically, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and chronic kidney diseases are common in this patient group. Studies have shown that for diseases such as aging, diabetes mellitus, and chronic renal failure, structural changes in the vena saphena magna appear, increasing the chance of failure of vein grafts after surgery. Sun et al. showed differences in saphenous vein extracellular protein expression

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in diabetic patients, claiming that these contrasts may impact the long-term patency rate of saphenous veins. In another study, the negative effects of chronic renal failure on saphenous vein histology were reported (5). Patient-specific factors, such as age, diabetes, hypertension, and hyperlipidemia, are known to influence vascular health and may contribute to the development of degenerative changes in saphenous vein grafts. While our study did not specifically investigate the impact of these factors, future research should explore the relationship between patient comorbidities, graft histology, and long-term clinical outcomes (6). It is possible that the observed medial sclerosis is more prevalent in older patients or those with a history of hypertension. Larger studies are needed to determine the relative contribution of these factors to graft degeneration.

The importance of the histological study of vein grafts prior to their use in bypass surgery is vital for performing the preoperative evaluation of graft quality, which can provide the necessary knowledge to predict graft viability. The long saphenous vein is usually used as a graft for coronary artery bypass surgery. Histological changes observed after the implantation of the arterial system are well established in the literature, but little awareness has focused on the histological features of the long saphenous vein before grafting.

In a study by Hess et al., 1,828 patients who had undergone coronary bypass surgery were examined, and significant vascular insufficiency requiring re-intervention was detected in vein grafts in 42.8% of the patients 12–18 months after the operation (7). Harskamp et al. determined that disease (development of occlusion) in vein grafts after the coronary bypass is one of the indicators of poor postoperative prognosis (8).

This study aims to explore the histopathological characteristics of saphenous veins in patients who have undergone coronary artery bypass surgery. In particular, this investigation seeks to identify any preoperative degenerative changes in the grafts of saphenous veins and assess their potential implications for the patient's prognosis. The research aims to elucidate the relationship between the degenerative findings of saphenous veins and the overall health outcomes of patients following CABG. By investigating these relationships, this study will contribute to the broader understanding of the significance of saphenous vein histology in the context of CABG surgery. Additionally, this study intends to inform the development of evidence-based clinical practices related to saphenous vein grafting and potentially improve patient outcomes in the long term.

## 2. Materials and methods

This research employs a qualitative flexible experimental research design that aims to conduct a histological examination of vena saphena magna as a graft in coronary artery bypass surgery. This study includes 12 patients who underwent coronary artery bypass surgery due to coronary artery disease

at Marmara University Faculty of Medicine, Department of Cardiovascular Surgery.

**Inclusion criteria:** Participants must have applied to the Marmara University Faculty of Medicine, Department of Cardiovascular Surgery due to coronary artery disease. Adult patients undergoing elective first-time CABG should be able to give informed consent and be aged >18 years.

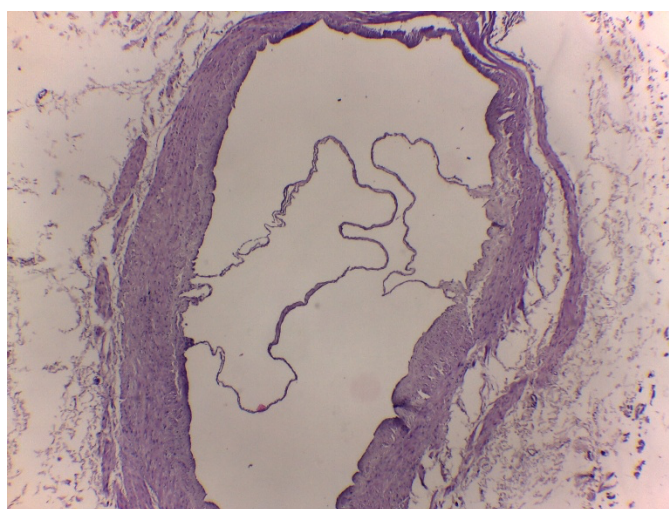
**Exclusion criteria:** Patients from whom veins cannot be removed will be excluded from the study, as well as individuals who had prior CABG surgery within one month, pregnant or lactating women, those with a myocardial infarction <48 hours prior to surgery, and patients experiencing cardiac shock within 48 hours of surgery.

### 2.1. Histological examination (Light microscopy).

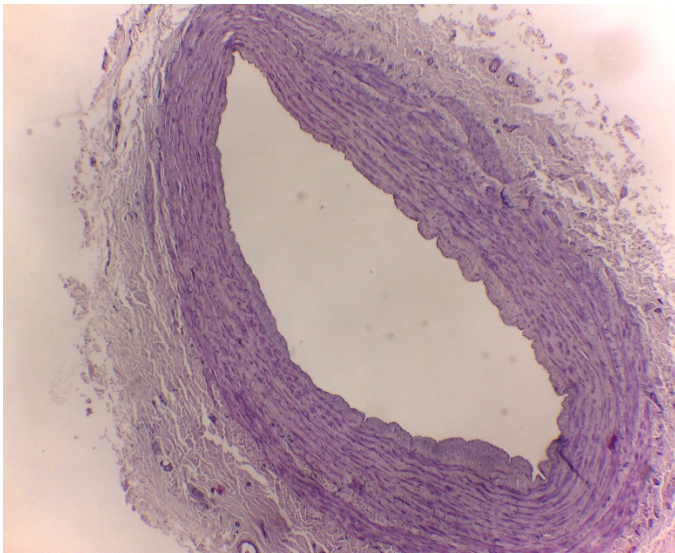
Vena saphena magna samples taken from three different regions (femoral, popliteal, and medial malleolus) were placed in 10% neutral buffered formaldehyde and sent to the pathology laboratory. Histological evaluation was performed by a pathologist blinded to patient data. Intimal fibrosis was scored according to the following criteria: 0 = normal intima, 1 = focal proliferation and minimal contraction, 2 = concentric proliferation and slight contraction, 3 = concentric proliferation and moderate narrowing (<50% narrowing of the lumen), 4 = significant narrowing (>50% narrowing of the lumen). Medial sclerosis was scored as follows: 0 = negative, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe (9).

## 3. Results

As a result of the examination, it was observed that the preoperative morphological degeneration was minimal in almost all grafts. Intimal fibrosis was observed in six of the 12 (50%) samples at varying degrees (Table 1, Fig. 1 and 2). In one sample (8.5% of all samples), intimal fibrosis was found to narrow the lumen (Fig. 3). Medial sclerosis was mild in three (25% of all samples) at varying degrees and negative in all other samples (Table 2, Fig. 4).



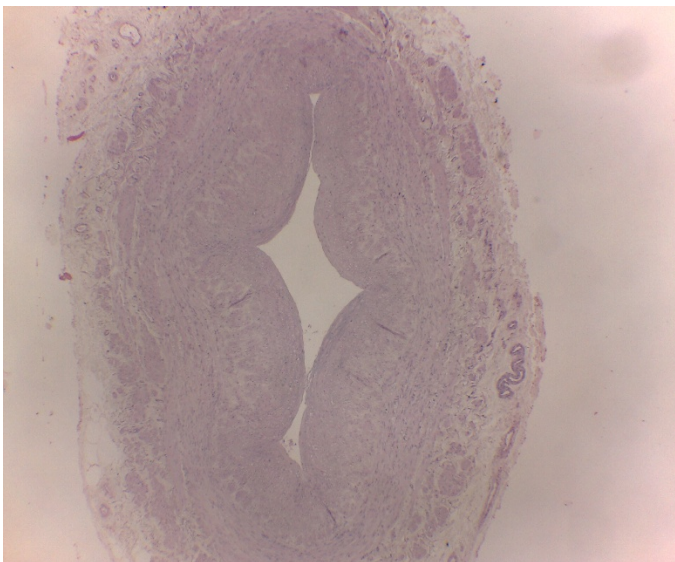
**Fig. 1.** A vessel with normal wall thickness with valves in the lumen (Hematoxylin and Eosin x40)



**Fig. 2.** The intima and media of the vein with a normal appearance (Hematoxylin and Eosin x40)

**Table 1.** The intimal fibrous thickening score by the number of patients

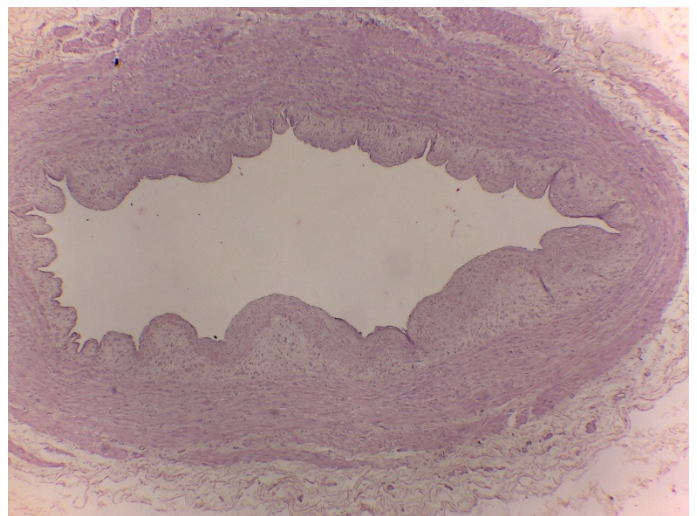
Patients no	Proximal	Medial	Distal
1	0	0	0
2	0	0	0
3	1	1	1
4	2	0	1
5	4	3	1
6	0	0	0
7	0	0	0
8	0	0	0
9	2	2	2
10	2	2	2
11	2	2	2
12	0	0	0



**Fig. 3.** Intimal and medial thickening causing severe narrowing of the lumen (Hematoxylin and Eosin x40)

**Table 2.** Medial fibrous thickening score by the number of patients

Patients no	Proximal	Medial	Distal
1	0	0	0
2	0	0	0
3	0	0	0
4	1	0	0
5	2	2	2
6	0	0	0
7	0	0	0
8	0	0	0
9	0	0	0
10	0	0	0
11	1	1	1
12	0	0	0



**Fig. 4.** Intimal and medial thickening causing narrowing of the lumen (Hematoxylin and Eosin x40)

#### 4. Discussion

This study aimed to investigate the histology of vena saphena magna in the patient population who underwent coronary artery bypass surgery and select the degenerative findings of the grafts in these patients. Our study showed that although VSM grafts appear macroscopically normal, they may show some histopathological features such as intimal fibrosis and medial sclerosis. Intimal fibrosis was observed in six of the 12 (50%) samples included in our study, and medial sclerosis was identified in three samples.

The observed intimal fibrosis and medial sclerosis, even in minimal forms, may contribute to reduced graft compliance and increased resistance to blood flow. This, in turn, could accelerate the development of graft stenosis or occlusion, ultimately impacting long-term patency and increasing the risk of recurrent ischemic events.

Our findings align with previous research demonstrating that pre-existing structural abnormalities in saphenous vein grafts can negatively influence their long-term performance (10). However, our study provides a unique perspective by focusing on early histological changes in a general CABG population, allowing us to assess the baseline condition of the grafts before significant postoperative remodeling occurs.

Future studies should correlate these histological findings with angiographic follow-up data to determine the predictive value of preoperative graft histology for long-term clinical outcomes.

The research conducted by Lawrie et al. aimed to assess the morphological characteristics of grafts derived from the internal thoracic artery and the great saphenous vein before their utilization in aortocoronary bypass surgery. The primary objective was to determine the suitability and viability of these grafts for the surgical procedure. The findings of the study revealed significant necrosis of endothelial cells within the examined grafts, leading to the exposure of the underlying basement membrane, which became susceptible to interactions with blood cells. Notably, the observed chronic lesions primarily affected venous grafts and were characterized by distinct atheromatous plaques or thickening of the intima and media layers (9). These observations highlight the importance of preoperative assessment and careful consideration of the morphology of grafts in aortocoronary bypass surgery. Further research is warranted to investigate strategies to improve the quality and durability of grafts, particularly in the context of venous grafts.

In a separate investigation conducted by Perek et al., the histological characteristics of saphenous vein reconstruction were examined concerning aging and determining the optimal age limits for selecting grafts in clinical practice. Distal segments of venous grafts were collected from a cohort of 110 patients who underwent venous coronary artery bypass grafting (CABG). The results revealed a progressive and age-dependent thinning of the venous wall and tunica media, accompanied by elongation of smooth muscle cell (SMC) nuclei. These histological changes suggest potential impairment in the migration and proliferation rates of SMCs with advancing age. Interestingly, the results suggest that individuals aged 70 years and above may derive greater clinical benefits from venous CABG procedures compared to younger patients (10). The implications of these findings are significant, highlighting the need for considering chronological age when determining the most appropriate candidates for venous CABG procedures.

The aim of the study conducted at St. Mary's Hospital Medical School was to assess the preoperative quality of the long saphenous vein (LSV) wall using ultrasound and histology. A total of 40 limbs from 38 patients were included in the evaluation, and three segments of the LSV (ankle, knee, and mid-thigh) were examined preoperatively using ultrasound imaging. The results revealed significant insights into the histological characteristics of the LSV wall. Upon histological examination, only eight specimens exhibited a normal appearance, indicating the absence of notable abnormalities. In contrast, six specimens displayed severe fibrosis, suggesting a considerable degree of pathological tissue remodeling within the LSV wall. Importantly, varying grades of fibrosis were observed in different anatomical sites of the same vein,

implying localized heterogeneity in the structural integrity of the LSV. These findings underscore the importance of comprehensive preoperative evaluation in assessing the quality and suitability of the LSV as a potential conduit in surgical interventions (11). By combining ultrasound imaging and histological analysis, a comprehensive understanding of the morphological characteristics of the LSV wall can be obtained, enabling surgeons to make informed decisions regarding its utilization in clinical practice.

The University of Copenhagen in Denmark conducted a study aiming to analyze the histopathological features of in situ vein bypass stenoses. In this study, a total of nineteen specimens of primary (n = 16) or recurrent (n = 3) vein graft stenosis were collected from seventeen patients during surgical revision. The median time interval between bypass surgery and stenosis excision was 5 months, with a range of 2 to 52 months. Upon analysis, the histopathological characteristics of the graft stenoses were identified and documented, showing moderate to severe intimal hyperplasia primarily composed of actin-positive but desmin-negative cells. The concurrent presence of fibrotic areas further contributed to the narrowing of the lumen (12). The findings emphasize the significant histological changes that occur within in situ vein bypass stenosis, showcasing the crucial role endothelial dysfunction plays in its pathogenesis.

A comprehensive investigation was conducted by the University of Padova Medical School to assess the condition of the venous wall prior to its utilization as an aortocoronary conduit. This study meticulously examined autologous saphenous veins used as bypass conduits in a consecutive series of 150 patients undergoing aortocoronary bypass procedures. To analyze potential age-related differences, the patients were stratified into four distinct groups based on their age. The histological examination yielded valuable insights into pathological features present within the venous structures. Notably, primary pathological findings encompassed a range of intimal fibrous thickening, sclerosis of the medial longitudinal muscular layer, and elastosis of the internal elastic lamina (8). These alterations underscore the necessity of assessing the pre-existing condition of the venous wall, which facilitates informed decision-making during bypass surgery and enhances our understanding of the processes underlying vein graft failure.

In a meticulous investigation by Hess et al., the primary objective was to gain a deeper understanding of the factors associated with vein graft failure (VGF) to enhance patient outcomes. The study involved an extensive examination of 1,828 participants enrolled in the Project of Ex Vivo Vein Graft Engineering via Transfection IV (PREVENT IV) trial. Angiographic assessments were performed between 12 to 18 months post-coronary artery bypass grafting (CABG) (6). Notably, the findings revealed that among the total cohort, 782 individuals exhibited VGF at the 12 to 18-month follow-up.

The detailed assessments highlighted associations between various demographic characteristics and comorbid conditions with VGF. The study underlines the complexity of VGF and the need for further investigation into its contributing factors to improve clinical outcomes.

The success of coronary artery bypass grafting (CABG) using the vena saphena magna (VSM) graft depends on the preoperative histopathological condition of the vessels. Therefore, preoperative examination is crucial in identifying suitable grafts and guiding the surgeon toward alternative options when necessary. In our study, the degree of preoperative morphological degeneration was evaluated in nearly all VSM grafts, with observations indicating that this degeneration was minimal. The presence of even mild intimal fibrosis and medial sclerosis could compromise the long-term patency of saphenous vein grafts, increasing the risk of thrombosis and accelerated atherosclerosis within the graft.

In the context of surgical coronary artery bypass procedures, the preoperative assessment of grafts is crucial in determining their viability and predicting long-term durability. Various methods have been proposed for preoperative screening of grafts, including angioscopy and intravascular ultrasound. Combining these methods allows for the detection of small lesions in the vessel wall, such as intimal hyperplasia, making the quality assessment of grafts more effective. However, it should be noted that ultrasound alone may not reliably identify these changes, which can be readily diagnosed using angioscopy or histological examination (13).

In this study, we employed light microscopy to examine biopsies of grafts taken from the great saphenous vein, which were remnants from surgical coronary artery bypass procedures. Our aim was to draw conclusions regarding the preoperative morphology of the grafts and correlate this with their future viability. Our results suggest that thorough preoperative assessment is indeed crucial, as even grafts that appeared macroscopically normal were found to carry histopathological findings of vascular abnormality such as intimal fibrosis and medial sclerosis. The use of a combination of screening methods, including light microscopic examination, angioscopy, and intravascular ultrasound, may aid in the detection of these lesions and improve the accuracy of preoperative quality assessment. Ultimately, these improvements could lead to better surgical outcomes and increased graft durability.

Preventing vein graft failure (VGF) is a critical objective in coronary artery bypass graft (CABG) surgery, and various preoperative measures have been proposed to enhance graft potency and durability. Intraoperative strategies aimed at minimizing graft trauma and optimizing handling techniques have proven effective in preventing early graft failure. These measures include avoiding graft distention, employing a no-touch technique, and minimizing graft manipulation during harvesting and implantation. However, their impact on late

graft failure remains limited.

Pharmacological interventions have also been extensively investigated as a means to prevent VGF. Hypercholesterolemia has been identified as a risk factor for graft failure, and aggressive lipid-lowering therapy utilizing statins has demonstrated promising results in reducing neointimal hyperplasia—a common contributor to graft failure in CABG surgery. Antithrombotic therapy represents another avenue for preventing VGF by reducing the occurrence of thrombotic graft occlusion and potentially preventing distal embolization and associated myocardial ischemic injury. Aspirin, for instance, has exhibited efficacy in mitigating early graft failure through its antiplatelet properties; however, its long-term effect on graft patency is limited, and it does not inhibit hyperplasia development.

While these preoperative measures and pharmacological interventions have shown promise in mitigating VGF, further research is needed to optimize their effectiveness and identify additional strategies for preventing graft failure in the long term. A comprehensive understanding of the underlying mechanisms involved in VGF, coupled with advances in surgical techniques and adjunctive therapies, may pave the way for more targeted and effective approaches to enhance graft durability and improve clinical outcomes in CABG surgery.

Saphenous vein conduit selection is established based on lumen characteristics, so our study's limitations include:

1. Patients who required coronary bypass surgery and who would use vena saphena magna as a graft in this surgery were included in our study.
2. If the entire saphenous vein is used during the operation and there is no residual vein, these patients will be excluded from the study.

Our study is also limited by a relatively small sample size, which may affect the generalizability of our findings. Future studies with larger, multi-center cohorts are needed to validate these observations and to identify potential subgroups of patients who may be at higher risk for graft failure based on preoperative histology. Since this study was not a group comparison study and the sample size was small, statistical analysis was not performed, which also limits the robustness of our conclusions.

### **Ethical Statement**

This study was approved by the Clinical Research Ethics Committee of Marmara University Faculty of Medicine (Protocol No: 09.2016.631; Date: 02.11.2016).

### **Conflict of interest**

There is no conflict of interest.

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No to declare.

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None to declare.

# Authors' contributions

Concept: A.H.M.A., K.A., A.M., Design: A.H.M.A., K.A., A.M., Data collection or Processing: A.T., C.C.U., M.E.D., S.T., Analysis or Interpretation: A.H.M.A., A.M., Literature Search: A.T., C.C.U., Writing: K.A., M.E.D., S.T.

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