

Saphenous vein wall thickness in age and venous reflux-associated remodeling in adults



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ABSTRACT

Objective: This prospective study was designed to determine the great saphenous vein (GSV) wall thickness in age-related and venous reflux-associated remodeling.

Methods: GSV wall thickness was measured in the thigh and calf using a duplex ultrasound 17-MHz transducer. Interobserver and intraobserver variability studies were performed. Two healthy control groups, each with 10 individuals (20 limbs), were selected on the basis of age. Group 1 had a mean age of 21 years, and group 2 had a mean age of 64 years. Forty patients with chronic venous disease signs and symptoms and GSV reflux of >2 seconds were enrolled. The vein wall thickness was assessed in vein segments with reflux and adjacent segments without reflux in the patient group.

Results: The measurements were valid as the variability for each rater was far below the difference in vein wall thickness measurements in all comparisons. In controls and patients, respectively, rater one had a range of 0.11 mm and 0.16 mm, and rater two had a range of 0.09 mm and 0.15 mm. The vein wall thickness significantly increased ($P < .05$) between each group in the following order: control group 1 (0.30 ± 0.03 mm), control group 2 (0.40 ± 0.05 mm), patients' vein segments without reflux (0.45 ± 0.07 mm), and patients' vein segments with reflux (0.58 ± 0.1 mm). These measurements were from the thigh and were comparable to those in the calf. The thickened, nonrefluxing segments were seen both proximal and distal to segments with reflux.

Conclusions: This human in vivo study demonstrated that GSV wall thickness significantly increases with age and in patients with venous reflux. The increased vein wall thickness in nonrefluxing segments of chronic venous disease patients suggests that the venous wall can be affected before reflux is present in a particular segment. (J Vasc Surg: Venous and Lym Dis 2017;5:216-23.)

The most common manifestation of chronic venous disease (CVD) is varicose veins (VVs), with a prevalence of 25% to 32% in female and 7% to 40% in male adults.¹ In diseased states, veins undergo remodeling. Wall remodeling in VVs includes intimal thickening with increased collagen content, increased connective tissue content in the media, hypertrophy of longitudinal and circular muscle layers, and, occasionally, formation of a third longitudinal muscle.²⁻⁵ This remodeling results in

an increased diameter of the lumen and an increased wall thickness in the VV, which in turn perpetuates the pathophysiologic process of venous stasis, relative hypoxia, endothelial activation, adhesion molecule expression, inflammatory cell adherence, accumulation of connective tissue, and proliferation of smooth muscle cells in the media of the VV.^{2,6,7}

Many studies use vein diameter to evaluate and to monitor venous insufficiency and its related vein remodeling as well as vein diameter and correlation to severity of CVD⁸⁻¹⁰; however, few studies have evaluated vein wall thickness. Vein wall thickness is an unaddressed scale in diagnosing, monitoring, and better understanding the pathophysiologic mechanism underlying CVD. Most studies evaluating vein wall thickness have used an ex vivo, histologic approach.¹¹⁻¹³ There are limited in vivo studies that use vein wall thickness to assess pathologic changes. Deatrick et al found that vein wall thickness increases during post-thrombotic vein wall remodeling and correlates with DVT resolution.¹⁴ Other studies analyzed vein wall thickness to better understand the remodeling observed in saphenous vein grafts after implantation and as a possible predictor of venous graft failure.^{15,16} There are no studies that have examined the wall thickness of veins in healthy controls and in patients with CVD in vivo. Our study was designed to determine

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vein wall thickness of the great saphenous vein (GSV) in various segments of venous reflux in the lower extremities and to compare it with younger venous controls and much older venous controls without CVD.

METHODS

Patient enrollment. Patients 18 years of age and older presenting with signs and symptoms of CVD and diagnosed as having venous reflux in the GSV with duplex ultrasound (DU) were enrolled. All patients had primary VVs with visible venous dilation on physical examination and belonged to Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) classes 2 and 3. For the patient group, the mean age was 49 years, with a standard deviation (SD) of 8 years and a range of 23 to 79 years. To decrease the chance of vein wall thickening from other factors, the following exclusion criteria were used for the patients and healthy controls: younger than 18 years; previous vein thrombosis, either superficial or deep; trauma; inflammatory conditions unrelated to venous disease; diabetes; unable to stand; morbid obesity; previous surgery (venous or nonvenous) in the lower extremities; and conditions in patients that could affect the venous system, such as right-sided heart failure.

The healthy controls were volunteers without signs or symptoms of venous disease on evaluation by physical examination and with DU. They also did not have any history of venous reflux. The healthy controls were divided into two groups; group 1 contained younger individuals (mean age, 21 years; SD, 2; range, 18-25), and group 2 contained older individuals (mean age, 64 years; SD, 7; range, 54-76). The controls in group 2 were purposefully older than the patients with reflux to evaluate any difference between aging and reflux disease. The study was approved by the Institutional Review Board, and all subjects provided informed consent.

Ultrasound examination for reflux. The examination was performed in the standing position. The superficial and deep veins of the lower extremities were imaged on B mode and color flow. The reflux and its duration were documented by using the pulse wave Doppler waveforms (Fig 1) with a DU 3- to 9-MHz, multifrequency, linear array transducer. The examination technique has been previously described in detail.¹⁷ Reflux in the superficial veins was defined as a retrograde flow lasting >0.5 second.¹⁸ In this study, only patients with >2 -second reflux were selected to ensure that there was a clear pathologic change. The distribution and extent of reflux were reported in detail, and the vein segments with and without reflux were grouped separately.

Ultrasound examination for the vein wall thickness. The iU-22 Philips (Bothell, Wash), a high-resolution DU with a 17-MHz linear array transducer, was used to measure the vein wall thickness. The transducer's axial resolution of 0.1 mm was high enough to detect wall

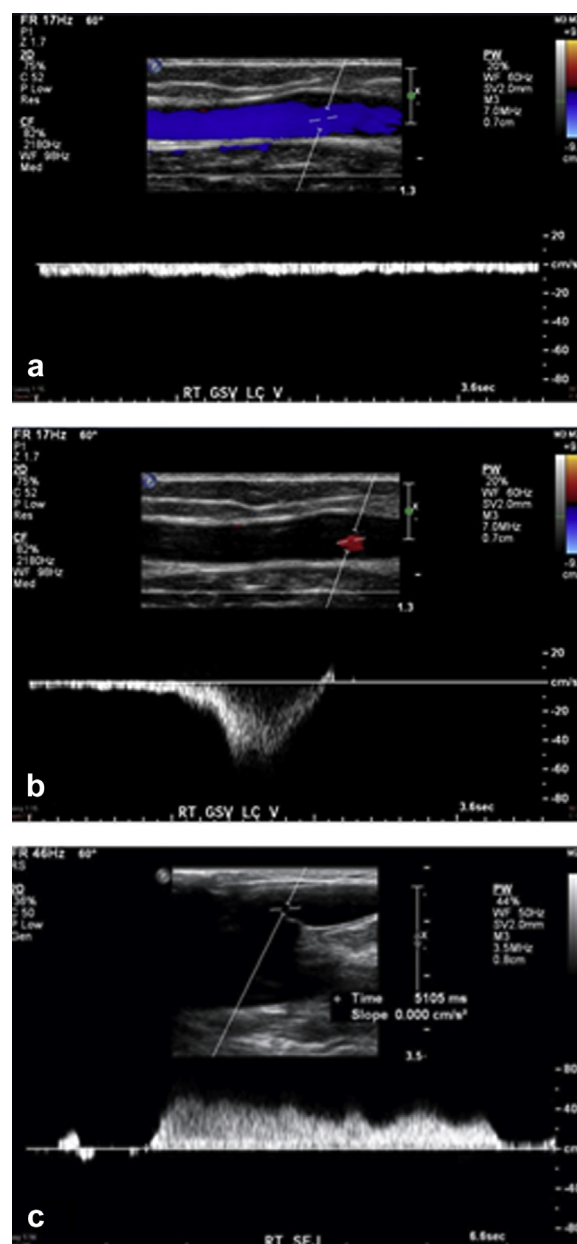


Fig 1. Images of normal and refluxing great saphenous vein (GSV). **a**, Imaging of the GSV at the lower calf from a male control volunteer. **b**, The GSV was normal throughout its length. No reflux is seen after release of distal compression. **c**, Prolonged GSV high-velocity reflux from a female patient who presented with thigh varicose veins (VVs) extending to the calf. Volunteers were selected by ultrasound not to have reflux, whereas the patients had reflux of >2 seconds as shown in this patient.

thickness changes in the study. The measurements were performed in the standing position to fully distend the veins and to eliminate variations.

The thickest area of the venous wall was measured using the far (posterior) wall because the interface between the blood and the intima allows optimal

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