

## ORIGINAL RESEARCH

# Venous Compliance in Great Saphenous Vein Incompetence: Pre- and Post-interventional Changes

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**Objective:** Venous insufficiency is associated with histological changes and structural remodelling of the venous wall. The effects of these changes on global venous function remain uncertain. The aim was to evaluate venous compliance in patients with great saphenous vein (GSV) insufficiency before and after treatment by radiofrequency ablation (RFA) and in controls.

**Methods:** Eleven patients (14 limbs) underwent endovenous RFA treatment for GSV incompetence. Duplex ultrasound and strain gauge plethysmography (SGP) were performed before and after RFA. SGP time (seconds) to reach 50% of maximum venous volume ( $T_{50}$ ) with and without superficial occlusion was used to assess global venous reflux. Venous occlusion plethysmography was used to evaluate pre- and post-operative calf venous compliance. Venous compliance was also assessed in 12 age and sex matched controls.

**Results:** Pre-operative calf venous compliance was lower in patients than in controls ( $p < .001$ ). Post-operative calf venous compliance was reduced vs. pre-operative measurements ( $p < .002$ ). The pre-operative reflux parameter  $T_{50}$  improved from  $8.0 \pm 2.0$  seconds to  $17.3 \pm 1.9$  seconds ( $p < .001$ ) after RFA. The post-operative  $T_{50}$  without superficial occlusion was similar to pre-operative  $T_{50}$  with superficial occlusion ( $17.1 \pm 2.5$  vs.  $17.3 \pm 1.9$  seconds,  $p = .84$ ).

**Conclusions:** Calf venous compliance is reduced in patients with GSV insufficiency. Venous reflux parameters markedly improved after RFA, whereas venous compliance displayed a further reduction vs. the pre-operative state, implicating generalised changes in the lower limb venous vessel wall.

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## INTRODUCTION

Venous compliance is defined as a change in venous volume ( $\Delta V$ ) related to a change in distending pressure ( $\Delta P$ , compliance =  $\Delta V/\Delta P$ ), i.e., a higher compliance is associated with a greater change in volume for a given change in pressure.<sup>1</sup> One important factor affecting compliance is venous wall properties.<sup>2</sup> Studies of isolated veins in patients with varicose veins have shown increased great saphenous vein (GSV) thickness,<sup>3</sup> larger amounts of collagen,<sup>4,5</sup> lower elastin content, and a subsequently increased collagen to elastin ratio,<sup>6,7</sup> changes that would be expected to reduce venous compliance. Few studies have evaluated the global effects and interestingly, whole limb venous function evaluated by strain gauge plethysmography (SGP) has shown

increased venous compliance in patients with venous insufficiency.<sup>8,9</sup> These findings appear to be at odds with the aforementioned histological results. The reason for these discrepancies is not clear, although it is possible that methodological difficulties concerning SGP measurements could explain the conflicting results to some extent.<sup>10,11</sup> However, to overcome the inherent problems with previous methods a new venous wall model for calculating venous compliance has been constructed.<sup>10,11</sup> Further, a SGP protocol with standardised superficial venous occlusion was recently developed for evaluation of global venous reflux and pre-operative prediction of radiofrequency ablation (RFA) outcome.<sup>12</sup> The aim of the study was to add global measurement of calf venous compliance to the SGP protocol. Thus, venous compliance was evaluated before and after RFA in patients with GSV insufficiency and in controls. The hypothesis was that venous compliance would be decreased in patients with GSV insufficiency.

## MATERIALS AND METHODS

Eleven patients (14 limbs) underwent RFA for GSV incompetence. Duplex ultrasound (DUS) and SGP were performed

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**Table 1.** Demographic and clinical data.

	Patients ( <i>n</i> = 11)	Controls ( <i>n</i> = 12)
No. of limbs	14	12
Mean (range) age, years	56 (25–83)	58 (27–79)
Sex, <i>n</i>		
Female	7	8
Male	4	4
Mean $\pm$ SD thigh level		
GSV diameter, mm	7.3 $\pm$ 1.3	
CEAP		
C2	1	
C3	10	
C4	3	

SD = standard deviation; GSV = great saphenous vein; CEAP = Clinical Etiology Anatomy Pathophysiology classification.

before and approximately one month after RFA. Disease severity was C2 – C4, according to the “C” in the CEAP (Clinical Etiology Anatomy Pathophysiology) classification.<sup>13</sup> Twelve age and sex matched healthy controls were included. None of the controls suffered from venous disease; information was assessed by history and clinical inspection. DUS was not performed in controls to exclude reflux. Demographic data are shown in Table 1. The study was approved by the regional ethical review board in Linköping, Sweden, and all participants provided written informed consent in accordance with the declaration of Helsinki.

### DUS

DUS examinations were performed with an ACUSON S2000 ultrasound system (Siemens Medical Solutions, Malvern, PA, USA), using an 18 and 9 MHz transducer. Assessment of reflux in superficial, perforator, and deep veins was conducted in accordance with the previously described standardised protocol.<sup>12,14</sup> Presence of normal phasic flow during breathing in the common femoral vein was mandatory, in order to exclude significant central obstruction.

### SGP

**Venous occlusion plethysmography.** Recordings were performed in a temperature stable room (25°C). Patients were placed in the supine position with the right leg slightly elevated and supported at the ankle. A strain gauge was applied at the point of maximum calf circumference and calibrated manually. A cone shaped thigh cuff was rapidly inflated to 60 mmHg using a cuff inflator (Bergenheim; Elektromedicin, Göteborg, Sweden) and after eight minutes of venous stasis, cuff pressure was reduced at a rate of 1 mmHg/second. The calf venous capacitance response (mL/100 mL) was separated from net fluid filtration (mL/100 mL/min) in accordance with previously used techniques.<sup>10,15</sup> Calf venous compliance (mL/100 mL/mmHg) was calculated as the derivative of the pressure–volume curve during the deflation phase for pressures between 10 and 60 mmHg as described,<sup>10</sup> and a correction model was used to subtract the confounding effect of net

fluid filtration on venous compliance.<sup>11</sup> A schematic illustration of the method is shown in Fig. 1A.

**Venous reflux measurements.** The SGP protocol and pressure calculation for superficial occlusion was described previously in detail.<sup>12</sup> In short, a strain gauge was placed around the forefoot and compression cuffs were applied just over the malleoli and below the tibial condyles. Individual calculated pressures for superficial occlusion were inflated by a cuff inflator. Patients performed 20 knee bends at one second intervals and after completion, the time taken in seconds for 50% ( $T_{50}$ ) of the venous volume to be refilled was evaluated. The procedure was repeated with individualised cuff pressure to achieve superficial occlusion. A schematic illustration of the method is shown in Fig. 1B. All SGP data were recorded, stored, and analysed using PeriVasc Software (Ekman Biomedical Data AB, Göteborg, Sweden).

### RFA

RFA was performed using the segmental heating Closure FAST radiofrequency catheter (VNUS Medical Technologies, San Jose, CA, USA) during ultrasound guidance and local (tumescence) anaesthesia. Treatment was performed from 1 – 2 cm below the tibial condyle to 1–2 cm from the saphenofemoral junction. Two cycles were used near the saphenofemoral junction and phlebectomies were performed at the physician’s discretion.

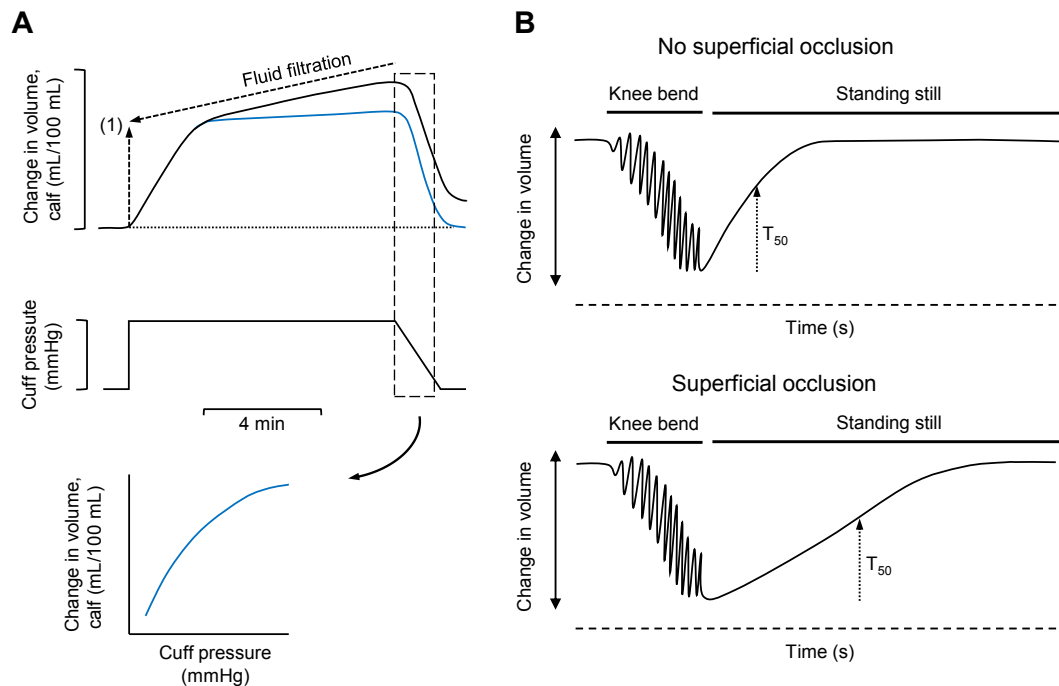
### Statistics

Data are expressed as mean  $\pm$  standard error unless otherwise indicated. Between group data were analysed using the Student’s *t* test or paired Student’s *t* test when appropriate. Two way analysis of variance with repeated measures was applied to compare the pressure–volume relationship and venous compliance using cuff pressure and condition (controls vs. patients or pre-operative vs. post-operative) as independent variables. If main effects or pressure  $\times$  condition interactions were detected, post hoc analysis with Bonferroni correction was performed. Statistical significance was defined as a *p* value  $<$ .05. Statistical analyses were carried out using SPSS 23.0 for Windows (IBM, Armonk, NY, USA).

## RESULTS

### Venous reflux

Pre-operative  $T_{50}$  increased from 8.0  $\pm$  2.0 to 17.1  $\pm$  2.5 seconds ( $p <$  .001) when superficial veins were occluded. Comparison between pre- and post-operative  $T_{50}$  without occlusion displayed an increase from 8.0  $\pm$  2.0 to 17.3  $\pm$  1.9 seconds ( $p <$  .001). Pre-operative  $T_{50}$  with superficial occlusion was comparable to post-operative  $T_{50}$  without occlusion (17.1  $\pm$  2.5 vs. 17.3  $\pm$  1.9 seconds;  $p =$  .84).



**Figure 1.** Schematic illustrations of venous occlusion plethysmography (VOP) measurements of venous compliance and strain gauge plethysmography (SGP) reflux measurements. (A) The black curve shows changes in calf volume without correction for fluid filtration. The initial rapid volume increase represents the capacitance response (1) and the following slower increase represents fluid filtration. The blue curve shows changes in calf volume with subtraction of fluid filtration. Calf venous compliance was derived from the pressure volume relationship. (B) SGP measurement without superficial venous occlusion in a patient with superficial venous insufficiency. The illustration below shows a typical improvement in  $T_{50}$  during SGP with superficial venous occlusion. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

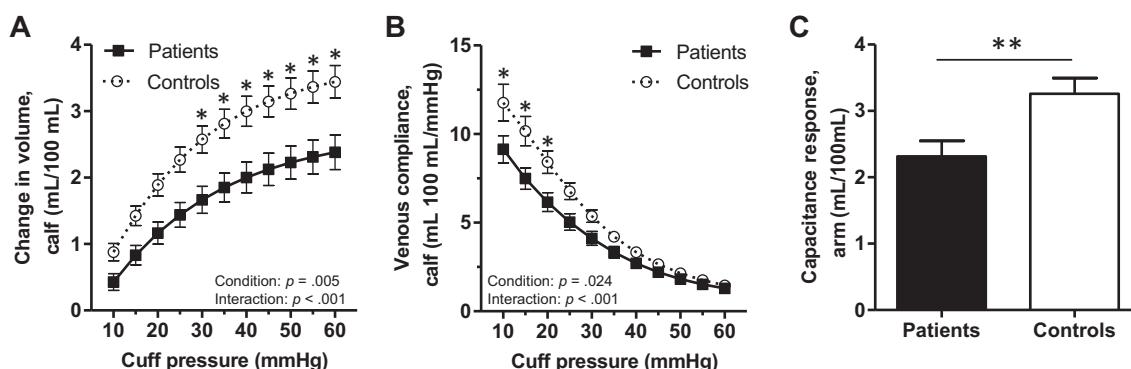
### Venous compliance

Compared with controls, the pre-operative pressure–volume curve was significantly less steep in patients (interaction  $p < .001$ , condition  $p = .005$ ; Fig. 2A). Similarly, the corresponding pressure–compliance curves displayed reduced compliance in patients (interaction  $p < .001$ , condition  $p = .024$ ; Fig. 2B). Calf venous capacitance response was decreased in patients vs. controls ( $2.31 \pm 0.23$  vs.  $3.26 \pm 0.24$  mL/100 mL;  $p = .009$ ; Fig. 2C). In patients, no significant changes were observed between the pre- and post-operative pressure–volume curves (interaction  $p = .32$ , condition  $p = .58$ ; Fig. 3A). However, the

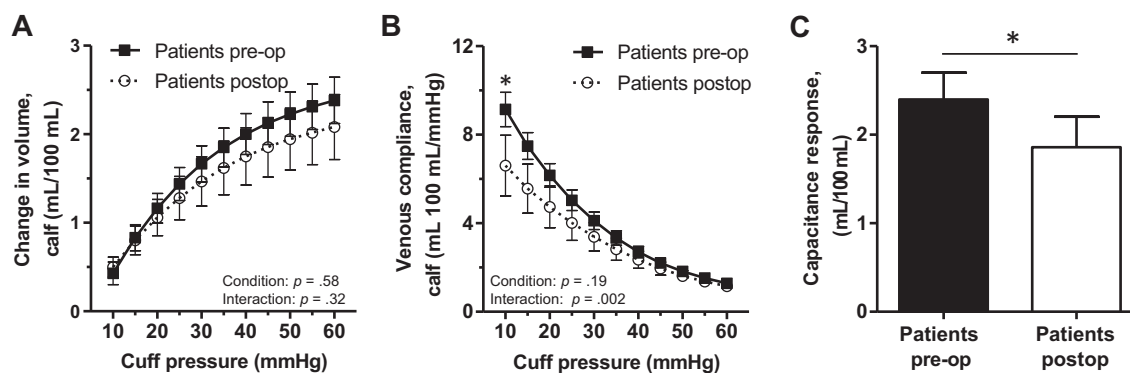
corresponding pressure–compliance curves displayed reduced compliance in the post-operative state (interaction  $p = .002$ , condition  $p = .19$ ; Fig. 3B). Calf venous capacitance response was decreased post-operatively vs. pre-operatively in patients ( $2.40 \pm 0.30$  vs.  $1.86 \pm 0.35$  mL/100 mL,  $p = .021$ ; Fig. 3C).

### DISCUSSION

Venous compliance is strongly affected by mechanical vessel wall properties, where collagen and elastin play an important role.<sup>2</sup> Several histopathological findings in varicose veins suggest abnormal collagen and elastin content,<sup>4,5</sup>



**Figure 2.** (A) Pressure–volume relationship (B) pressure–compliance relationship, and (C) capacitance response in patients and controls. \* $p < .05$ , \*\* $p < .01$ .



**Figure 3.** Pre- and post-operative (A) pressure–volume relationship (B) pressure–compliance relationship, and (C) capacitance response in patients. \* $p < .05$ .

with increased collagen to elastin ratio in the lower limb venous vessel wall.<sup>6,7</sup> This seems to be in agreement with animal studies showing increased collagen to elastin ratio and stiffness in venous hypertension models.<sup>16</sup> How these changes in the isolated vein segment affect global vessel wall function remains uncertain. In accordance with histopathological evidence, decreased venous compliance was found in patients with GSV insufficiency (Fig. 2A and B). Venous capacitance was also found to be reduced in patients (Fig. 2C). These findings differ from previous SGP measurements showing increased venous compliance.<sup>8,9</sup> The reason for this is unclear; however, venous compliance was calculated with a new venous wall model able to adopt the curvilinear form of the venous pressure–volume curve and thus characterise compliance correctly over the entire pressure range.<sup>10</sup> A validated correction model was used to subtract the effect of fluid filtration on venous compliance to avoid its confounding effect.<sup>11</sup> This seems especially important as microcirculatory abnormalities have been associated with venous incompetence.

Reflux parameters were assessed by SGP with and without selective superficial occlusion and DUS in accordance with the developed protocol.<sup>12</sup> Post-operative refill time,  $T_{50}$ , improved significantly and DUS revealed complete obliteration of the GSV. No differences in  $T_{50}$  were detected when pre-operative SGP with superficial occlusion was compared with post-operative SGP without superficial occlusion, strengthening the impression of a successful intervention. Nevertheless, venous compliance demonstrated a further reduction in the post-operative state (Fig. 3A and B). A decrease in venous capacitance was also seen (Fig. 3C). This study cannot specify the direct cause of the further post-operative reduction in compliance. However, a downward shift of the pressure–volume curve after RFA, owing to volume reduction, would not necessarily imply a change in compliance as compliance is only affected if the slope of the pressure–volume relationship is shifted.<sup>1</sup> As no trend toward normalisation of venous compliance after intervention was found, the results suggest that changes in venous function are not restricted to the isolated vessel with obvious incompetence. This is in agreement with findings of increased wall thickness in non-refluxing

segments.<sup>3</sup> Although it is unclear if reduced compliance is a result of reflux or the original venous state leading to the reflux, this study seems to support the theory that vein wall properties are affected before development of reflux and that these changes have global effects on lower limb venous function.<sup>3,17</sup> The study population was limited in the present study and larger studies are needed to evaluate possible alterations in compliance in relation to the “C” of the CEAP classification system, as well as the reasons for decreased compliance in the post-operative state.

Finally, measurement of venous compliance may be a future step towards functional diagnosis using the non-invasive pressure–volume curve together with the recorded volume changes during SGP reflux measurement to estimate ambulatory venous pressure. Future measurement of venous compliance may also have clinical implications in the pre-operative evaluation of vein graft material as reduced compliance has been associated with lower graft patency rates.<sup>18,19</sup>

## CONCLUSIONS

Calf venous compliance was reduced in patients with GSV insufficiency. Despite post-operative improvements in venous reflux parameters, venous compliance was further reduced compared with the pre-operative state, implicating generalised changes in the lower limb venous vessel wall.

## CONFLICT OF INTEREST

None.

## FUNDING

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