Current Medical Imaging, 2021, *17*, 897-903

RESEARCH ARTICLE

Diminished Sphenous Compartment Connective Tissue Elasticity has Little Impact on Low Grade Venous Insufficiency: An Ultrasound Shear-wave Elastography Study

Nurten A. Baltacioglu[1] and Derya Tureli[2,*]

[1]*Radiology Clinic, VKV Amerikan Hospital, Istanbul, Turkey;* [2]*Department of Radiology, Marmara University School of Medicine, Istanbul, Turkey*

Abstract: ***Background*:** Greater Saphenous Vein (GSV) courses within saphenous compartment, an adipose-filled space bound by fasciae provides structural support. Ultrasound Shear-Wave Elastography (SWE) provides objective and quantitative data on tissue shear elasticity modulus.

***Objective*:** This study aims to analyze possible associations between early stage GSV insufficiency and saphenous intracompartmental SWE measurements.

***Methods*:** Two-hundred consecutive patients, ages 22 to 81 (mean=44.3) years, with venous insufficiency symptoms underwent Doppler and SWE examinations. Patients had no visible or palpable sign of venous disease or had telangiectasia and reticular veins only. Analyses regarding patient age, gender, presence of venous insufficiency of GSV proper and intracompartmental connective tissue elasticity were performed.

***Results*:** Ninety-six patients had Doppler evidence for either bilateral or unilateral insufficiency of GSV proper at mid-thigh level. Intracompartmental elasticity of patients with venous insufficiency (mean=4.36±2.24 kilopascals; range 1.55 to 10.44 kPa) did not differ significantly from those with normal veins (mean=4.82±2.61 kPa; range 2.20 to 12.65 kPa) (p=0.231). No threshold for predicting the presence of venous insufficiency could be determined. Neither were there any correlations between age, gender and intracompartmental elasticity. In patients with unilateral insufficiency, however, elastography values around insufficient veins were significantly lower compared to contralateral normal GSV (p<0.001).

***Conclusion*:** Many intrinsic and patient factors affect intracompartmental connective tissue elastography measurements; thus, cut-off values obtained from specific populations have limited generalizability. Nevertheless, statistically significant intrapatient differences of intracompartmental elasticity among diseased and normal saphenous veins indicate that lack of elastic support from surrounding connective tissues contributes to venous insufficiency in early stages.

ARTICLE HISTORY

Received: September 17, 2020
Revised: February 27, 2021
Accepted: March 26, 2021

DOI:
10.2174/1573405617666210507122819

Keywords: Chronic venous disease, shear wave elastography, saphenous compartment, saphenous vein, venous insufficiency, ultrasound.

1. INTRODUCTION

Chronic Venous Disorder (CVD) is a frequent vascular disease of adulthood and is particularly prevalent in aging populations. It preferentially affects superficial veins of lower limbs, especially Greater Saphenous Vein (GSV). Deep venous system is less frequently affected because it courses through musculofascial structures providing mechanical stabilization. On the other hand, GSV lacks such strong muscular reinforcement, and is surrounded by and courses within the saphenous compartment. This adipose-filled potential space, bound superficially by saphenous fascia and deeply by muscular aponeurosis, extends from the inguinal ligament to dorsomedial aspect of the foot and provides structural support for the vein [1, 2].

Shear-Wave Elastography (SWE) is a non-invasive ultrasonographic technique providing objective and quantitative data on tissue shear elasticity modulus. SWE involves the generation of controlled shear-waves using an ultrasound push pulse. Shear-waves propagate slowly in softer tissues and their velocity increases while traversing through firmer structures. Ultrafast ultrasound acquisition is synchronized with shear-wave generation and tracks axial shear wave propagation through tissues as a function of time. This enables

*Address correspondence to this author at the Department of Radiology, Marmara University School of Medicine, Istanbul, Turkey;
E-mail: nurtenandac@yahoo.com

1875-6603/21

quantitative measurement of shear elasticity modulus of different tissues in terms of meters per second (m/s) or kilopascals (kPa) based on their firmness [3-5]. SWE has been used extensively in research regarding skin, subcutaneous soft tissues and musculoskeletal system in general [6-9]. Regarding venous pathophysiology research, SWE has been previously shown to accurately quantify and predict venous thrombus maturity both *in vivo* and ex vivo in animal models [10, 11].

Clinical severity of CVD is divided into 7 categories by the international Clinical-Etiology-Anatomy-Pathophysiology (CEAP) classification system in order to standardize diagnosis and treatment. In the earliest stages of CVD, *i.e*. C0 and C1, patients have no physical visible-palpable sign of venous disease, or telangiectasia and reticular veins only. Later stages of CVD are characterized by visible-palpable varicose veins (C2), edema (C3), pigmentation-eczema or lipodermatosclerosis (C4), occurrence of healed (C5) or active (C6) venous ulcers [5, 12]. Clinical symptoms of late CVD, however severe they may be, are indeed independent from initial etiology. These later stages CVD are characterized by extensive fluid transudation into perivenous soft tissues, vein walls and dermis resulting in increased tissue stiffness which, in turn, can be demonstrated as increased SWE values in affected structures [3-5]. Loss of elasticity of GSV wall and weakened perivenous connective tissue support resulting in diminished venous pumping function against gravity, on the other hand, is a relatively understated pathophysiologic mechanism of early stage of CVD, and has not yet been assessed using ultrasound SWE [13]. This study aims to analyze potential associations between early stage CVD, *i.e*. C0 and C1, of GSV and shear elasticity modulus of saphenous intracompartmental connective tissues.

2. MATERIALS AND METHODS

Study was carried out by the interventional radiology clinic of a teaching hospital and diagnostic radiology laboratory of an outpatient vascular interventions clinic on patients referred for planning of endovascular or surgical treatment for chronic venous disease. Institutional review board approval was obtained for the use of data collected during a period of January 2017 to December 2018; and treatment-naïve adult patients presenting with symptoms of lower extremity venous insufficiency were included after giving written informed consent. All patients were C0 and C1 by CEAP classification; *i.e*. with no visible or palpable sign of venous disease, or with telangiectasia and reticular veins only [12]. Exclusion criteria comprised the history of major trauma or limb operation, including any prior endovascular or surgical venous interventions, deep or superficial venous thrombosis, additional reflux in deep venous system or perforating veins, patients with more advanced CEAP class, and case files with missing medical history or inadequate ultrasound mapping. Each patient underwent Doppler and SWE examinations only once.

All examinations were performed by a single radiologist with more than 15 years of experience in venous Doppler imaging. A dedicated ultrasound device (Logiq S8, General Electrics, Fairfield, CT) with a 12 – 16 MHz linear transducer was used; a wide field of view (FOV) and a frame rate of 30 frames/s was employed. Venous insufficiency was defined as the presence of flow reversal lasting more than 0.5 seconds during provocation maneuvers. As standard practice, whole thigh and leg regions were mapped while patients were standing upright; this also helped prevent the inadvertent application of pressure by the operator during SWE measurements. Elasticity of saphenous intracompartmental connective tissue was measured using SWE at the mid-thigh level. Unlike more proximal and distal locations, mid-thigh level is where patency of saphenous fascia is least interrupted; thus, it is preferred as the measurement point in order to reduce confounding anatomic variations. Measurements were performed on the transverse plane, without applying manual pressure and using a standard circular Region Of Interest (ROI) of 2 mm diameter (Fig. **1**). Correct transverse orientation of the saphenous compartment was confirmed visually by seeing a circular saphenous vein outline and not an ellipsoid one which would indicate a rather slanted imaging plane. Multiple measurements were made, saturating cross-section of saphenous compartment with ROIs, and then averaged out.

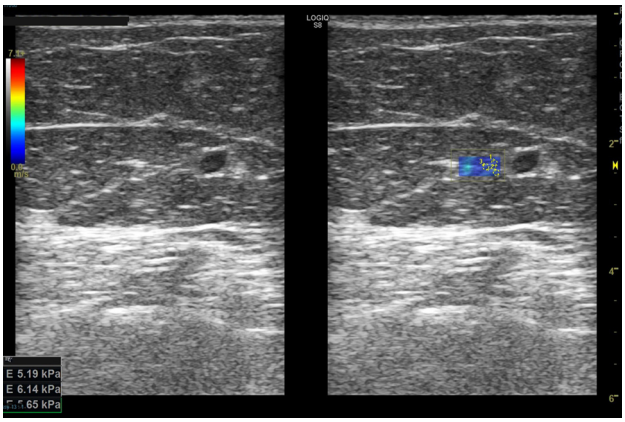

Fig. (1). Transverse scan of medial mid-thigh level visualizes GSV within saphenous compartment. Real-time B mode scan (left) and SWE measurement (right) side by side on the screen. Circular ROI of 2 millimeters diameter is used. Elasticity values, in kilopascals, are denoted on left lower corner of screen. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

Possible associations between the presence of venous insufficiency of GSV proper at mid-thigh level and intracompartmental connective tissue elasticity, measured in kPa units, was analyzed evaluated using SPSS Statistics software version 23.0 (IBM Corp. 2015. Armonk, NY). Independent samples t-test was used for comparing SWE means of refluxing and non-refluxing veins; and of female and male patients. Paired samples t-test was utilized for comparing SWE measurements of refluxing and normal veins within patients who have unilateral insufficient GSVs. Spearman's correlation analysis was done for assessing effect of patient age on SWE measurements.

3. RESULTS

Two-hundred consecutive eligible subjects, 108 women and 92 men, underwent Doppler and SWE. Ninety-six patients had Doppler evidence for either bilateral or unilateral insufficiency of GSV proper at thigh level reflux. Patients' ages ranged from 22 to 81 years with a mean age of 44.3 ± 18.7 years.

For those with GSV venous insufficiency, ultrasound SWE values of intracompartmental connective tissue ranged between 1.55 and 10.44 kilopascals (mean= 4.36±2.24 kPa); and for those without GVS insufficiency, elastography ranged from 2.20 to 12.65 kPa (mean= 4.82±2.61 kPa) (Fig. **2**). Difference among groups was statistically insignificant (p=0.231) (Table **1**). In addition, both groups had a wide range and overlap of elasticity values; this precluded calculation of an elasticity threshold for predicting presence of venous insufficiency.

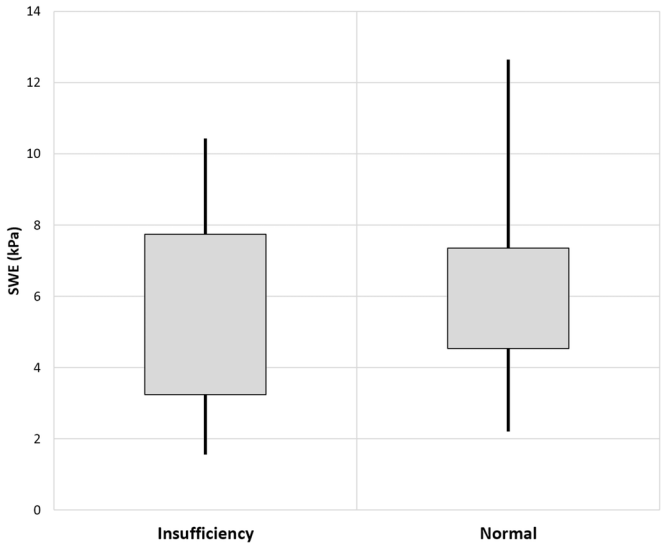

Fig. (2). Box-plot chart of compartment elasticity versus GSV insufficiency. Both groups have wide ranges with large overlap of elasticity values, precluding calculation of an elasticity threshold for venous insufficiency.

Table 1. Mean elasticity values of intracompartmental connective tissue surrounding refluxing and competent greater saphenous veins at mid-thigh level. Pearson *Chi*-square test did not reveal a statistically significant difference (p > 0.05).

-	Mean Elasticity±SD (kPa)	p
Insufficiency	4.36±2.24	0.231
Normal	4.82±2.61	

There was no statistically significant association between intracompartmental elasticity and gender (Fig. **3**). Mean elasticity values of intracompartmental connective tissue in female and male patients were 5.22±2.85 kPa and 4.93±2.47 kPa, respectively (p=0.453) (Table **2**). There was also no correlation between patient age and intracompartmental tissue elasticity (Spearman's rho=0.044 and p>0.05) (Fig. **4**).

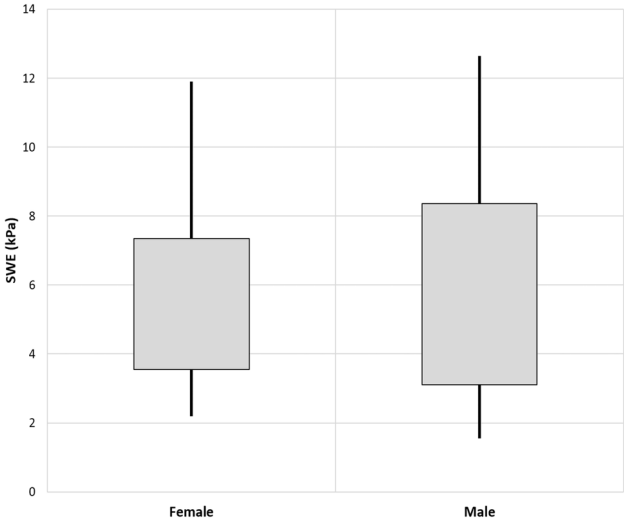

Fig. (3). Box-plot chart of compartment elasticity versus gender. Both groups have wide ranges of elasticity values and considerable overlap in between.

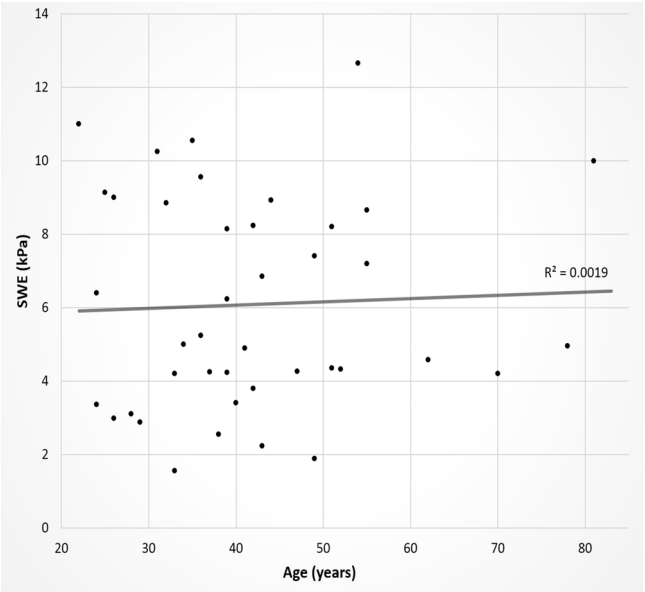

Fig. (4). Linear plot of compartment elasticity versus patient age. There is no statistically significant correlation between two parameters (Spearman's rho=0.044; p=0.154).

Table 2. Mean elasticity values of intracompartmental connective tissue in female and male patients. Pearson *Chi*-square test did not reveal a statistically significant difference (p > 0.05).

-	Mean Elasticity±SD (kPa)	p
Female	5.22±2.85	0.453
Male	4.93±2.47	

Forty-two patients had unilateral insufficiency of GSV at mid-thigh level. Intracompartmental elasticity around insufficient saphenous veins was lower than those around normal contralateral GSV (paired samples t-test p=0.001) (Table **3**; Figs. **5** and **6**).

Table 3. Mean elasticity values of intracompartmental connective tissue in patients with unilateral GSV insufficiency. Paired samples t-test revealed significantly lower values for tissues surrounding refluxing GSV when compared to those around contralateral normal GSV.

-	Mean Elasticity±SD (kPa)	p
Refluxing (Unilateral)	4.32±2.12	0.001
Normal (Contralateral)	6.14±3.04	

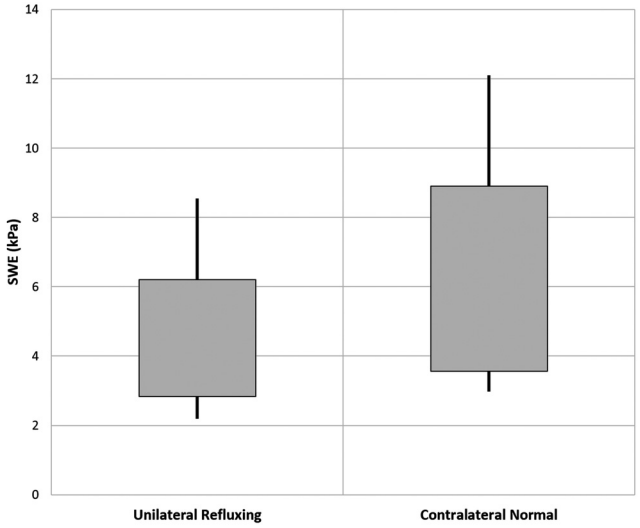

Fig. (5). Box-plot chart of intracompartmental elasticity comparing refluxing with non-refluxing contralateral saphenous veins. Though there is overlap of elasticity values, a significant difference is present when refluxing and normal veins are compared within each patient.

4. DISCUSSION

This study revealed statistically significant intrapatient differences among intracompartmental SWE measurements of refluxing and non-refluxing GSV. There were no correlations between elasticity modulus and age or gender. SWE measurements of both healthy and refluxing venous compartments showed a wide range of distribution with statistically insignificant mean and median differences. This ruled out any potential utility of a threshold value in predicting venous insufficiency solely by looking at elasticity values.

Regarding pathophysiology of primary venous insufficiency, the extent of the role played by perivenous structural support is still unclear. Under normal physiological conditions, saphenous fascia stretches GSV during contractions of neighboring thigh muscles thereby increasing venous flow. In addition, adipose tissue within saphenous compartment opposes venous dilation, and saphenous ligaments provide anchoring of GSV, making it less likely to become tortuous. This is thought to be the reason why GSV proper is often the last superficial vein to decompensate with CVD. In a significant number of cases, CVD initially becomes apparent not in the GSV proper, but in the suprafascial tributaries, which are surrounded only by loose adipose tissue [1, 14, 15].

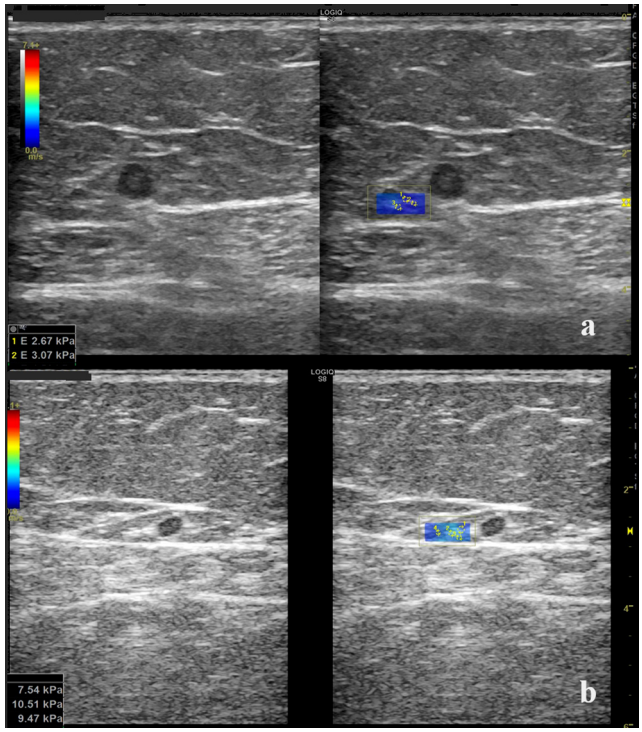

Fig. (6). Real-time B mode scan (left) and SWE measurement (right) of intracompartmental tissue surrounding **(a)** unilateral refluxing GSV and **(b)** contralateral non-refluxing GSV. As expected refluxing saphenous vein has a larger diameter compared to normal contralateral GSV. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

Recent practice guidelines recommend therapeutic leg compression, in the form of elastic stockings or bandages, in the management of chronic venous disease. Proposed mechanism of action of this treatment modality, *i.e.* compression of veins and improvement of muscle pump function leading to reduction of venous pressure and edema, perhaps hint to a possible association between mechanical supportive function of perivenous structures and venous insufficiency [16]. A previous case series of elective fasciotomies has shown an inverse association between the integrity of venous compartments and development of saphenous reflux. While venous filling index and ejection fraction mostly remained normal, there were three cases of de novo post-fasciotomy GSV reflux. Preoperatively present GSV reflux, in two cases, did not worsen, though [17].

A recent study measuring venous wall elasticity has shown that insufficient veins have more stiff walls com-

pared to those of normal veins. Shear modulus of vein wall was measured on the transverse plane by manually drawing a free-hand ROI along the outline of vessel wall. This, while being a seemingly tedious procedure with low repeatability, has provided an elasticity threshold for predicting venous insufficiency. Our study, and its results therein, are not comparable to the mentioned study for the following reasons. First, parameters investigated were different, *i.e*. venous wall stiffness was measured in that study, whereas we studied perivenous connective tissue elasticity regardless of venous wall deformability. Secondly, study populations were quite different regarding CVD severity: We focused solely on patients in the earliest stages of CVD, *i.e*. C0 and C1 patients who have no or minimal visible-palpable signs of venous insufficiency. In the mentioned study, patient group consisted mostly of advanced CVD in later stages of venous insufficiency spectrum with dilation and tortuous deformation of GSV [3]. Another recent venous SWE study has demonstrated significantly increased shear elasticity modulus of connective tissues around refluxing perforating veins, namely the largest Cockett's perforator, as they pass through fasciæ. Though seeming otherwise, this does not contradict our findings because that particular study involved patients in later stages of CVD whose perforating vein insufficiency may even be secondary to advanced stage reflux of superficial veins [4].

SWE has certain inherent limitations because elastic modulus is basically a function of the density of tissue examined and velocity of shear wave propagation in that tissue. This formula assumes that the tissue being examined is homogeneous, elastic, incompressible and isotropic, whereas *in vivo*, soft tissue elasticity is more likely to be nonlinear and dependent on varying tissue density and strain magnitude. In addition, all soft tissues are viscoelastic whereas SWE techniques ignore the viscosity component and assume that tissues are solely elastic. Understandably, this assumption biases velocity-derived elasticity measurements. Omission of tissue viscosity is in part due to the scarcity of ultrasonographic viscosity measurement techniques, in comparison to magnetic resonance imaging techniques, which is attributable to immaturity of the ultrasonic technique. For the time being, no commercially available SWE system can recompense for errors based on inherent characteristics of tissue being examined and such limitation of *in vivo* SWE applications may be unavoidable [18-21].

Shear modulus measurements are influenced by tissue anisotropy and stretch stress of musculature. In highly anisotropic tissues such as muscles, shear wave measurements obtained with the probe parallel to muscle fibers are greater than those obtained with the probe in perpendicular plane. This effect also confounds SWE measurements in structures located deeper to muscles and produces falsely elevated shear modulus. Therefore, in order to standardize shear modulus measurements, SWE of such structures should be done on the plane that is perpendicular to the plane of anisotropy [18, 20, 22]. Though shear modulus measurement errors may be significant regarding anisotropic structures such as muscles, tendons, vessel walls and nerve bundles; it may be less consequential in the case of saphenous intracompartmental soft tissues becausethe saphenous compartment is not covered by muscles and intracompartmental connective tissue inside saphenous compartment consists mostly of amorphous adipose tissue which tends to be isotropic. There are also, to a minor and microscopic extent, elastic fibers dispersing radially from GSV wall to neighboring fascia; but anisotropy of those are practically impossible to account for *in vivo* due to having differing planes of orientation and being ambiguous under ultrasound [1, 14]. Nevertheless, in this study, SWE measurements were only performed in the transverse plane, *i.e*. perpendicular to the plane of underlying anisotropic thigh musculature. SWE was not performed in the longitudinal plane due to practical reasons: In subjects with small amounts of adipose tissue in saphenous compartment, *i.e*. in thinner individuals, transverse plane imaging visualizes perivenous connective tissue only on both sides of GSV, and not below or under it; and in longitudinal plane this area of interest and GSV are in different planes. Thus, with the probe parallel to the axis of anisotropy, visual orientation is impaired and risk of misplacing the ROI is greatly increased.

A limitation is due to the fact that the anisotropy ratio of the fascia forming the roof of saphenous compartment and the effect of its anisotropy on intracompartmental SWE measurements are unknown and are unaccounted for in this study. Anisotropy of surrounding tissues might influence intracompartmental soft tissue density and shear wave velocity, however, this study is unable to evaluate such effects of anatomy on SWE assessment of saphenous compartment.

In addition to anisotropy, another confounder of SWE measurements of saphenous compartment may be the stretch stress exerted by underlying thigh muscles. Both stretch stress and anisotropy are highly dependent on anatomic and physiologic factors including, but not limited to, muscle mass and tonus, level of physical fitness and hormonal status; and thus exhibit significant intersubject differences. Such variations may partially account for the wide range of intersubject discrepancy observed in our SWE measurements. Two deductions may be made based on data: Firstly, comparison of shear modulus during early stages of CVD is only relevant within the same subject, *i.e*. with contralateral extremity. Secondly, a shear modulus threshold in predicting venous insufficiency is impractical due to the wide range of distribution with statistically insignificant mean and median differences among normal and refluxing veins. Both inferences are drawn based on high variance data. Validation of SWE in identifying CVD, on the other hand, requires a lower variance which requires identification of potential factors causing over or underestimation of pathology. A lower variance may be achieved by reducing the number of features in the model, *i.e*. by refining SWE protocol after evaluating intrasubject variability on repeated measurements, perhaps after a preliminary study.

Though our findings are promising, they have not necessarily revealed a causality relation, but a mere association. Venous insufficiency is a progressive condition becoming more severe and diffuse gradually [23, 24]. Transudation

and inflammation in later stages of chronic venous disease would probably lead to increased venous and perivenous stiffness; hence, our results showing lower perivenous elasticity may look counter-intuitive at first. However, this study elaborates on the loss of perivenous support function as a factor in the occurrence of GSV insufficiency in its early stages; thus, only C0 and C1 patients were included. Chronic hydrostatic edema or inflammatory processes may eventually lead to further disruption of structural integrity of neighboring tissues in a vicious cycle; still, it would be imprudent to extrapolate our inferences to more advanced stages of CVD. Intracompartmental connective tissue elastography measurements are affected by many intrinsic and patient factors such as tissue edema and inflammation due to prior unnoticed trauma or phlebitis, hormonal effects including menstrual cycle, continuity and patency of saphenous fasciae and other musculofascial factors. Thus, elastography cut-off values obtained from specific populations may have limited generalizability.

CONCLUSION

Statistically significant intrapatient differences of intracompartmental elasticity among refluxing and normal saphenous veins indicate that lack of elastic support from surrounding connective tissues contributes to venous insufficiency. This, compared to venous valve integrity and venous flow studies, is a mostly overlooked aspect of underlying pathophysiology in the early stages of CVD and may merit further elaboration.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of Marmara University School of Medicine (No. 09/2019/479), Turkey.

HUMAN AND ANIMAL RIGHTS

No animals were used in this study. Reported study on humans was followed in accordance with ethical standards and the Helsinki Declaration of 1975, as revised in October 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from subjects.

AVAILABILITY OF DATA AND MATERIALS

Additional data shall be provided upon request.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Findings were previously presented at EVIS 2019 – Endovascular and Interventional Symposium (April 2019, Istanbul, Turkey).

REFERENCES

[1] Cavezzi A, Labropoulos N, Partsch H, *et al.* Duplex ultrasound investigation of the veins in chronic venous disease of the lower limbs–UIP Consensus Document. Part II: Anatomy. Phlebology 2006; 21: 168-79. http://dx.doi.org/10.1258/026835506779115799

[2] Kachlik D, Pechacek V, Baca V, Musil V. The superficial venous system of the lower extremity: New nomenclature. Phlebology 2010; 25(3): 113-23. http://dx.doi.org/10.1258/phleb.2009.009046 PMID: 20483860

[3] Durmaz MS, Arslan S, Baysal AN, *et al.* Experience of using shear wave elastography imaging in superficial venous insufficiency of the lower extremity. Ultrasound Q 2018; 34(3): 176-82. http://dx.doi.org/10.1097/RUQ.0000000000000356 PMID: 29634667

[4] Durmaz MS, Kesimal U, Ünal HA, Özbakır B. Evaluation of perforating venous insufficiency with shear wave elastography: A preliminary study. J Ultrasound 2020. [published online ahead of print, 2020 Sep 9]. http://dx.doi.org/10.1007/s40477-020-00527-x PMID: 32902811

[5] Mofid Y, Faleweei G, Chartier C, *et al.* High-frequency transient elastography prototype to assess skin (Dermis) fibrosis: A diagnostic study in patients with venous insufficiency and controls. Ultraschall Med 2020. [published online ahead of print, 2020 Mar 18]. http://dx.doi.org/10.1055/a-1047-3146 PMID: 32187631

[6] Arda K, Ciledag N, Aktas E, Aribas BK, Köse K. Quantitative assessment of normal soft-tissue elasticity using shear-wave ultrasound elastography. AJR Am J Roentgenol 2011; 197(3): 532-6. http://dx.doi.org/10.2214/AJR.10.5449 PMID: 21862792

[7] Taljanovic MS, Gimber LH, Becker GW, *et al.* Shear-Wave Elastography: Basic Physics and Musculoskeletal Applications. Radiographics 2017; 37(3): 855-70. http://dx.doi.org/10.1148/rg.2017160116 PMID: 28493799

[8] Yang Y, Wang L, Yan F, *et al.* Determination of normal skin elasticity by using real-time shear wave elastography. J Ultrasound Med 2018; 37(11): 2507-16. http://dx.doi.org/10.1002/jum.14608 PMID: 29575120

[9] Drakonaki EE, Allen GM, Wilson DJ. Ultrasound elastography for musculoskeletal applications. Br J Radiol 2012; 85(1019): 1435-45. http://dx.doi.org/10.1259/bjr/93042867 PMID: 23091287

[10] Liu X, Li N, Wen C. Effect of pathological heterogeneity on shear wave elasticity imaging in the staging of deep venous thrombosis. PLoS One 2017; 12(6): e0179103. http://dx.doi.org/10.1371/journal.pone.0179103 PMID: 28614362

[11] Mfoumou E, Tripette J, Blostein M, Cloutier G. Time-dependent hardening of blood clots quantitatively measured *in vivo* with shear-wave ultrasound imaging in a rabbit model of venous thrombosis. Thromb Res 2014; 133(2): 265-71. http://dx.doi.org/10.1016/j.thromres.2013.11.001 PMID: 24315316

[12] Eklöf B, Rutherford RB, Bergan JJ, *et al.* American venous forum international Ad Hoc committee for revision of the CEAP classification. revision of the CEAP classification for chronic venous disorders: Consensus statement. J Vasc Surg 2004; 40(6): 1248-52. http://dx.doi.org/10.1016/j.jvs.2004.09.027 PMID: 15622385

[13] Gianesini S. Venous Reflux Patterns.Saphenous Vein-Sparing Strategies in Chronic Venous Disease. Springer International Publishing 2018; pp. 35-74. http://dx.doi.org/10.1007/978-3-319-70638-2_3

[14] Caggiati A, Bergan JJ, Gloviczki P, Jantet G, Wendell-Smith CP, Partsch H. International interdisciplinary consensus Ccommittee on venous anatomical terminology. Nomenclature of the veins of the lower limbs: An international interdisciplinary consensus statement. J Vasc Surg 2002; 36(2): 416-22. http://dx.doi.org/10.1067/mva.2002.125847 PMID: 12170230

[15] Lee BB, Nicolaides AN, Myers K, *et al.* Venous hemodynamic changes in lower limb venous disease: The UIP consensus according to scientific evidence. Int Angiol 2016; 35(3): 236-352. PMID: 27013029

[16] Wittens C, Davies AH, Bækgaard N, *et al.* Esvs guidelines committee. Editor's Choice - Management of chronic venous disease: Clinical practice guidelines of the european society for vascular surgery (ESVS). Eur J Vasc Endovasc Surg 2015; 49(6): 678-737. http://dx.doi.org/10.1016/j.ejvs.2015.02.007 PMID: 25920631

[17] Singh N, Sidawy AN, Bottoni CR, *et al.* Physiological changes in venous hemodynamics associated with elective fasciotomy. Ann Vasc Surg 2006; 20(3): 301-5. http://dx.doi.org/10.1007/s10016-006-9041-z PMID: 16612581

[18] Ryu J, Jeong WK. Current status of musculoskeletal application of shear wave elastography. Ultrasonography 2017; 36(3): 185-97. http://dx.doi.org/10.14366/usg.16053 PMID: 28292005

[19] Nenadic IZ, Qiang B, Urban MW, *et al.* Attenuation measuring ultrasound shearwave elastography and *in vivo* application in post--transplant liver patients. Phys Med Biol 2017; 62(2): 484-500. http://dx.doi.org/10.1088/1361-6560/aa4f6f PMID: 28000623

[20] Gennisson JL, Deffieux T, Macé E, Montaldo G, Fink M, Tanter M. Viscoelastic and anisotropic mechanical properties of *in vivo* muscle tissue assessed by supersonic shear imaging. Ultrasound Med Biol 2010; 36(5): 789-801. http://dx.doi.org/10.1016/j.ultrasmedbio.2010.02.013 PMID: 20420970

[21] Rus G, Faris IH, Torres J, Callejas A, Melchor J. Why are vscosity and nonlinearity bound to make an impact in clinical elastographic diagnosis? Sensors (Basel) 2020; 20(8): 2379. http://dx.doi.org/10.3390/s20082379 PMID: 32331295

[22] Lee HY, Lee JH, Shin JH, *et al.* Shear wave elastography using ultrasound: Effects of anisotropy and stretch stress on a tissue phantom and *in vivo* reactive lymph nodes in the neck. Ultrasonography 2017; 36(1): 25-32. http://dx.doi.org/10.14366/usg.16003 PMID: 27459989

[23] Lee AJ, Robertson LA, Boghossian SM, *et al.* Progression of varicose veins and chronic venous insufficiency in the general population in the Edinburgh Vein Study. J Vasc Surg Venous Lymphat Disord 2015; 3(1): 18-26. http://dx.doi.org/10.1016/j.jvsv.2014.09.008 PMID: 26993676

[24] Chastanet S, Pittaluga P. Patterns of reflux in the great saphenous vein system. Phlebology 2013; 28 (Suppl. 1): 39-46. http://dx.doi.org/10.1177/0268355513477021 PMID: 23482533