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● *Original Contribution*

VECTOR AND DOPPLER ULTRASOUND VELOCITIES EVALUATED IN A FLOW PHANTOM AND THE FEMOROPOPLITEAL VEIN

Thor Bechsgaard,* Kristoffer Lindskov Hansen,* Andreas Hjelm Brandt,* Simon Holbek,† Julie Lyng Forman,‡ Charlotte Strandberg,§ Lars Lönn,* Niels Bækgaard,¶ Jørgen Arendt Jensen,† and Michael Bachmann Nielsen*

*Department of Radiology, University Hospital of Copenhagen, Rigshospitalet, Copenhagen, Denmark; †Center for Fast Ultrasound Imaging, Department of Electrical Engineering, Technical University of Denmark, Lyngby, Denmark; ‡Section of Biostatistics, Department of Public Health, Copenhagen University, Copenhagen, Denmark; §Department of Radiology, University Hospital of Copenhagen, Herlev & Gentofte Hospital, Hellerup, Denmark; and ¶Department of Vascular Surgery, University Hospital of Copenhagen, Rigshospitalet & Gentofte Hospital, Hellerup, Denmark

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Abstract—Ultrasound is used for evaluating the veins of the lower extremities. Operator and angle dependency limit spectral Doppler ultrasound (SDUS). The aim of the study was to compare peak velocity measurements in a flow phantom and the femoropopliteal vein of 20 volunteers with the angle-independent vector velocity technique vector flow imaging (VFI) and SDUS. In the flow phantom, VFI underestimated velocity ($p = 0.01$), with a lower accuracy of 5.5% ($p = 0.01$) and with no difference in precision, that is, error factor, compared with SDUS (VFI: 1.02 vs. SDUS: 1.02, $p = 0.58$). *In vivo*, VFI estimated lower velocities (femoral: $p = 0.001$; popliteal: $p = 0.001$) with no difference in precision compared with SDUS (femoral: VFI 1.09 vs. SDUS 1.14, $p = 0.37$; popliteal: VFI 1.13 vs. SDUS 1.06, $p = 0.09$). In conclusion, the precise VFI technique can be used to characterize venous hemodynamics of the lower extremities despite its underestimation of velocities. (E-mail: thorbechsgaard@gmail.com) © **2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Ultrasound, Spectral Doppler, Peak velocity, Flow phantom, Popliteal vein, Femoral vein, Vector flow imaging.**

INTRODUCTION

A quarter of the world's population suffers from venous disease (Michaels et al. 2006), and ultrasound (US) is the backbone in diagnosing acute as well as chronic venous disorders of the lower extremities (Needleman 2014; Wittens et al. 2015). Doppler US—that is, color Doppler US and spectral Doppler US (SDUS)—is used to characterize hemodynamic changes in patients before further imaging and treatment. With color Doppler US, blood flow is evaluated qualitatively, whereas SDUS is used for pulse wave analyses and peak blood flow velocity measurements (Wood et al. 2010). US does not expose patients to radiation, and it is inexpensive and non-invasive unlike other medical imaging techniques, for example, computed tomography, magnetic resonance imaging, intravenous phlebography and intravascular US (Arnoldussen et al. 2013). However, color Doppler US and SDUS are limited by angle dependency and high observer variability, which affect velocity estimates and complicate evaluation of vein segments running parallel to the surface of the skin, for example, the femoral vein (Labropoulos et al. 2007; Lui et al. 2005; Ricci et al. 2015; Tortoli et al. 2015). Despite the limitations, color Doppler US and SDUS are used in combination with a clinical examination to decide the need for further imaging investigations and potential treatment (Metzger et al. 2016; Wittens et al. 2015).

The angle dependency of conventional velocity estimation with SDUS has been addressed previously, and efforts have been made to create an angle-independent vector velocity US system capable of

Address correspondence to: Thor Bechsgaard, Department of Radiology, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark. E-mail: thorbechsgaard@gmail.com

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measuring vector flow (Fox 1978; Newhouse et al. 1987; Overbeck et al. 1992, Trahey et al. 1987). The transverse oscillation vector flow imaging (VFI) method estimates the vector velocity angle independently (Jensen and Munk 1998), and several studies have been published on the subject (Brandt et al. 2016; Hansen et al. 2013, 2014, 2015a; Pedersen et al. 2012). However, there is only one preliminary study with VFI on venous flow in the popliteal vein, which reported that compared with SDUS, VFI measured a lower peak velocity, but with improved precision (Bechsgaard et al. 2016).

The objective of this study was to compare the precision of peak velocity magnitude estimation in the femoropopliteal vein in a young, healthy study population obtained with VFI and SDUS. Furthermore, in a flow phantom, the accuracy and precision of VFI estimations at flow angles between 60° and 90° were compared with those of corresponding SDUS estimations.

METHODS

Vector flow imaging

The transverse oscillation VFI method was introduced in 1998 and is an angle-independent method for estimation of blood flow (Jensen and Munk 1998). The velocity components of the blood are estimated in the axial as well as the transverse direction. The axial velocity component is found as in conventional velocity estimation, whereas the transverse velocity component is found by changing the apodization of the receiving elements and using a special estimator (Jensen 2001). VFI visualizes blood flow in a color box as in color Doppler US, with arrows superimposed on the vector map to indicate flow direction and magnitude (Fig. 1).

US equipment and data processing

Spectral Doppler US and VFI measurements were obtained on a commercial US scanner (BK3000, BK Ultrasound, Herlev, Denmark) with a linear transducer (10 L2 w Wide Linear, BK Ultrasound) for both the phantom and the *in vivo* study. VFI peak velocities were recorded with AVI files consisting of 110 vector velocity maps corresponding to 5 s of data acquisition. The corresponding SDUS peak velocities were recorded with screenshots that visualized spectrograms of 5-s duration and evaluated offline using a professional quality vector graphics editor (Inkscape, C/O Software Freedom Conservancy, Brooklyn, NY, USA).

The AVI files for VFI estimations and screenshots for SDUS estimations captured approximately 5 s of constant flow for the phantom measurements and a single venous pulse wave for the *in vivo* measurements. The VFI estimates were displayed in real time on the scanner, but the quantification of the peak velocities required offline processing with an in-house developed script for MATLAB (The MathWorks, Natick, MA, USA), as previously described (Hansen et al. 2014; Pedersen et al. 2012). In the images, that is, AVI files extracted from the US scanner, each pixel was color encoded according to the axial and transverse vector velocity magnitudes. These images were used as input to the estimator. A region of interest of 1 × 1 cm was manually chosen from within the vessel boundaries, and the peak velocity magnitude was found from a 2-D vector field within this region.

Phantom setup

A flow phantom (Cole-Parmer centrifugal pump, Vernon Hills, IL, USA) recirculated a blood-mimicking fluid (BMF-US, Shelley Medical Imaging Technologies, Toronto, ON, Canada) with a controlled velocity of 60.3 cm/s (MAG1100, Danfoss, Nordborg, Denmark). The transducer was fixated at 5 cm from a 12-mm-diameter vessel and examined with VFI at beam-to-flow angles of 90°, 80°, 70° and 60°. With SDUS, the transducer was in the same position as the corresponding VFI measurements, but electronic angle correction of 30° changed the beam-to-flow angles to 60°, 50°, 40° and 30°. With both techniques, 10 repeated measurements were recorded at each of the four different angle positions. VFI pulse repetition frequency was set at 7 kHz, and SDUS pulse repetition frequency at 4 kHz. The smoothing filter, persistence, wall filter and c-gain were set identically with the two techniques. The size and location of the color box and the depth of the B-mode image were kept constant through all measurements. The SDUS and VFI recordings were blinded during the data acquisition.

Volunteers

Twenty healthy volunteers (Table 1), 10 men and 10 women, participated and were evaluated with SDUS and VFI (Fig. 1). The study was approved by the Danish National Committee on Biomedical Research Ethics and the local ethics committee (H-1-2014-FSP-072), as well as by the Danish Data Protection Agency (2012-58-0004). All volunteers were included in the study after submitting informed consent.

Controlled scan setup

The set-up previously described by Bechsgaard et al. (2016) was used. A cuff compression–decompression system was applied to the lower leg of a standing volunteer according to a setup described by van Bemmelen et al. (1989) and replicated by others to ensure a standardized pulse wave in the veins (Konoeda et al. 2014) (Fig. 2). For each volunteer, the right popliteal vein and the right femoral vein in the midthigh region were scanned longitudinally. To avoid manual compression, the transducer was not tilted during examination, as

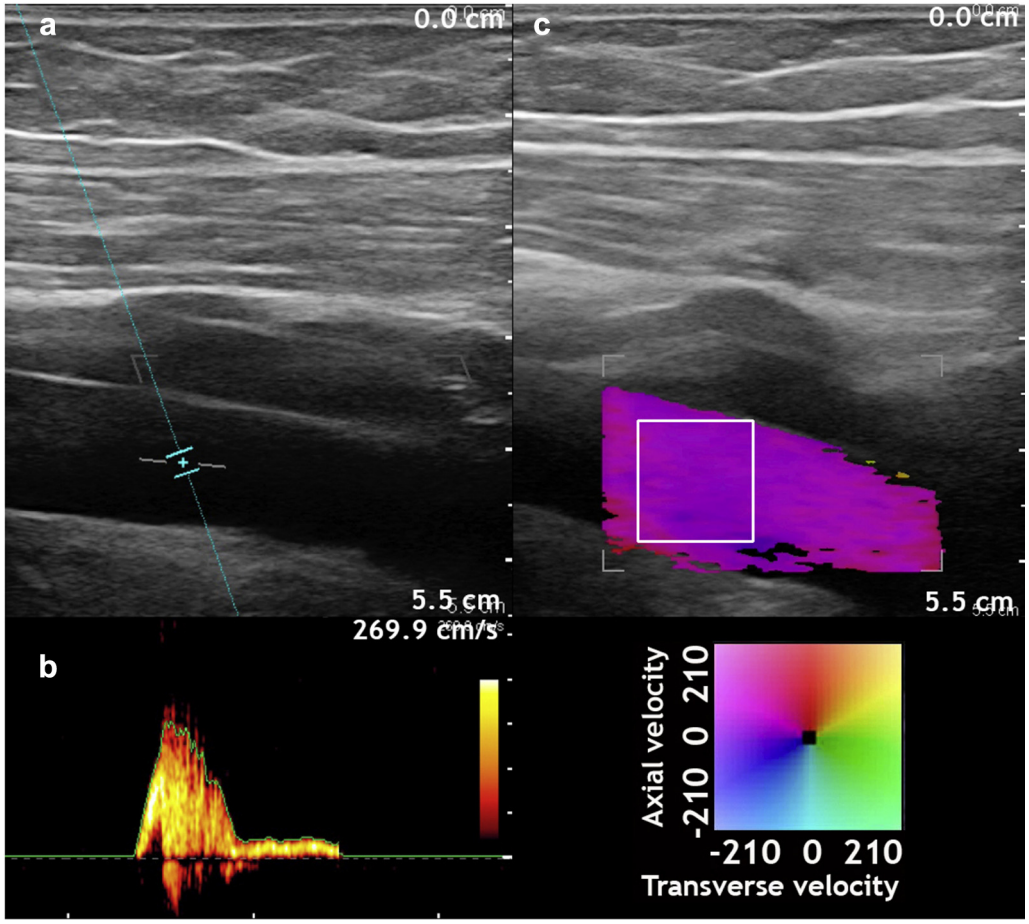

Fig. 1. (a) Longitudinal scan of the femoral vein with conventional spectral Doppler ultrasound (SDUS). A range gate is placed centrally in the vessel and the angle correction is applied. The SDUS spectrogram (b) visualizes spectral data over time. Peak velocity is calculated by reading the highest point of the flow pulse spectral curve and comparing it with the velocity axis of the spectrogram in a professional quality vector graphics editor. (c) Longitudinal scan of the same femoral vein with vector flow imaging (VFI) estimation of the venous flow pulse. The videos were extracted from the scanner and analyzed in the editor in MATLAB. The *white box* outlines the region of interest. The color map in the lower right corner indicates flow direction and magnitude. The superimposed arrows are optional with VFI. In this study, no arrows were shown on the vector maps of the videos extracted for velocity estimation.

manual compression may influence flow velocity estimates (Metzger et al. 2016; Spinedi et al. 2016). Electronic angle correction for SDUS was performed by the examiner to achieve a beam-to-flow angle $<70^\circ$ and preferably $<60^\circ$ with respect to the course of the vein (Park et al. 2012; Pozniak and Allan 2013; Rumack et al. 2011). Angle correction was made automatically by the estimator for VFI. The popliteal vein was easily accessible because of its superficial and oblique course in contrast to the femoral vein, which was located deeper and with a perpendicular course relative to the surface of the skin.

Table 1. Characteristics of study population (volunteers)

No. (sex) of volunteers	20 (10 female, 10 male)
Age	
All	27.1 (20–39)
Females	26.0 (20–39)
Males	28.1 (22–33)
Mean body mass index	
All	22.1 (17–30)
Females	21.0 (17–25)
Males	23.3 (21–30)

Data are presented as mean (range).

For SDUS estimation, the range gate was placed centrally in the vessel and covered a third of the diameter, while the entire lumen of the vessel was covered by the color box during VFI estimation. Optimal gain, pulse repetition frequency, wall filter and smoothing filter were set with both techniques. Special care was taken to avoid aliasing for both techniques by adjusting the pulse repetition frequency. All scans with VFI and SDUS were performed by a medical doctor (T.B.).

Fig. 2. (Left) Ultrasound recordings were acquired with the patient standing on the leg opposite the leg being examined. (Right) The cuff, connected to the cuff compression–decompression system, was inflated to 100 mm Hg over 3 s.

Cuff compression of the leg

The cuff compression–decompression system (Rapid Cuff Inflation System, Hokanson, Bellevue, WA, USA) consisted of an air source (AG101), a rapid cuff inflator (E20) including output tubing, a 3-s timer and a foot switch. A 13 × 85-cm cuff (SC12-D) was applied to the lower leg and connected to the output tubing. A 3-s timer was customized to enable activation of the system by a foot switch (Fig. 2). This modification was necessary for a single person to operate the equipment.

The examination

The volunteer was standing on the leg opposite that being examined for 1 min before the recording to compensate for the venous refill time in the examined leg in accordance with studies done with plethysmography (Eberhardt and Raffetto 2014). Each volunteer underwent three measurements of flow pulses in the popliteal and femoral vein with each technique. Between measurements, the settings of the US scanner were optimized and the transducer was lifted from the skin of the volunteer.

Statistics

In the phantom setup, the mean peak velocity of three replicated measurements was compared between VFI and SDUS at different angles using Welch's *t*-test. Similarly, standard deviations were compared using *F*-tests, and velocity errors (mean absolute deviations), using Wilcoxon's rank sum test. To investigate whether accuracy decreased with increasing beam-to-flow angle for VFI and SDUS, the Jonckheera–Terpstra test for trend was applied to the velocity errors. Additionally, coefficients of variation (standard deviation as percentage of mean) and relative errors (mean absolute deviation as percentage of true velocity) were calculated for each method at each of the four angle positions: 90°/60°, 80°/50°, 70°/40° and 60°/30°. Standard deviations were compared between different angles using Bartlett's test.

In the *in vivo* setup, mean individual peak velocities by method, that is, VFI and SDUS, and position, that is, popliteal and femoral vein, were calculated by averaging the three replicate measurements. Standard deviations and error factors for the replicated measurements were likewise calculated. The error factor was supplied as a measure of relative precision, because there was increased variability at increased velocities. The interval from median/error factor to median × error factor delimits the central range in the log-normal distribution and parallels the interval mean ± SD in the normal distribution. For instance, an error factor of 1.10 describes a central range of approximately median ± 10%. Averages were summarized with means and standard deviations and compared between the methods and positions with the paired *t*-test. Standard deviations and error factors were summarized with median and interquartile range and compared with Wilcoxon's signed rank test. Average coefficients of variation were calculated for the femoral and popliteal vein with VFI and SDUS.

A linear mixed model was used to quantify the bias between SDUS and VFI under varying conditions given by position, that is, popliteal and femoral veins, and beam-to-flow angle. Correlation between repeated measurements was accounted for by including random effects in the model. It was expected that the correlation between the repeated measurements on the same subject would be stronger when made under more similar conditions. Therefore, random effects were included, corresponding to a multilevel model with four levels: (i) variation between patients; (ii) variation between positions within subject; (iii) variations between methods within position and subject; and (iv) residual

variation or measurement error. Likelihood ratio tests were used to compare measurement error between methods and positions. Finally, it we investigated whether measurement accuracy was further influenced by beam-to-flow angle. Because the linear mixed model does not allow residual variances to depend on continuous covariates, the standard deviations were computed for replicates made at identical angles and used as outcomes in a robust regression analysis. Mutual adjustment was made for the covariates method, position and angle. Because of a highly skewed distribution, the standard deviations were log-transformed before analysis. A 0.05 level of significance was chosen. SPSS Version 22 (IBM, Armonk, NY, USA) was used for the descriptive statistics, and statistical analyses were performed with SAS enterprise guide Version 6.1 (SAS Institute, Cary, NC, USA).

RESULTS

In the phantom, no difference in precision was found between the two techniques overall (error factor VFI: 1.02 vs. error factor SDUS: 1.02, $p = 0.58$). The two techniques measured different mean peak velocities at all four angle positions ($p < 0.001$), and standard deviations did not differ significantly. Table 2 lists the mean velocities, standard deviations, coefficients of variation, velocity errors, relative errors, error factors, biases and relative biases at beam-to-flow angles of 60–90° for VFI and at electronically angle corrected beam-to-flow angles of 30–60° for SDUS. VFI underestimated peak velocity at all but one angle position, and the mean absolute deviation across beam-to-flow angles, that is, a measure of accuracy, indicated that VFI was less accurate overall compared with SDUS ($p < 0.0001$ at all four angle positions). The average SDUS accuracy was 1.7% versus 5.5% for VFI, whereas the coefficient of variation, a measure of precision, did not differ significantly between VFI and SDUS at any of the angle positions. A significantly decreasing trend in accuracy with increasing beam-to-flow angle was found for both techniques (VFI: $p < 0.001$ and SDUS: $p < 0.001$). The coefficient of variation tended to decrease with increasing beam-to-flow angle for SDUS, whereas no systematic trend in precision was found for VFI except from the largest coefficient of variation appearing at the beam-to-flow angle of 90°.

In vivo, the two techniques estimated different peak velocities in the popliteal vein ($p < 0.0001$) and the femoral vein ($p < 0.0001$) (Figs. 3 and 4; Table 3). SDUS measured a higher mean peak velocity in both positions, and the bias between the methods appeared more pronounced in the femoral vein, where measurements were made at higher beam-to-flow angles (Fig. 3; Table 3). The VFI mean peak velocity declined from the popliteal to the femoral vein ($p < 0.01$); this change was not observed with SDUS ($p = 0.43$) (Table 3). When absolute numbers were compared, VFI estimated peak velocity with a significantly lower standard deviation compared with SDUS in the femoral vein ($p < 0.01$), whereas there was no significant difference in the popliteal vein ($p = 0.87$), as outlined in Table 3 and illustrated in Figure 4. However, the relative precision as measured by the error factor did not differ systematically between the two methods in the popliteal vein ($p = 0.09$) or in the femoral vein ($p = 0.37$) (Table 3). With SDUS, the beam-to-flow angles were between 22° and 55° with a mean of 43.6° in the popliteal vein and between 47° and 74° with a mean of 57.6° in the femoral vein. With VFI, the beam-to-flow angles were between 52° and 85° with a mean of 73.6° in the popliteal vein and between 77° and 104° with a mean of 87.6° in the femoral vein.

Average coefficients of variation for peak velocity for SDUS were 6.5% in the popliteal vein and 10.5% in the femoral vein. For VFI, the average coefficients of variation were 9.4% in the popliteal vein and 7.4% in the femoral vein.

Table 2. Phantom validation of vector flow imaging at different angles

Beam-to-flow angle	Mean ± SD over 10 repeated measurements (coefficient of variation) [error factor]	Velocity error over 10 repeated measurements (relative error)	Bias [relative bias]
Spectral Doppler US with electronic angle correction of 30°			
60°	60.5 ± 2.2 cm/s (3.6%) [1.01]	1.7 cm/s (2.8%)	0.2 [0.3%]
50°	57.1 ± 1.3 cm/s (2.2%) [1.02]	3.2 cm/s (5.3%)	−3.2 [–5.3%]
40°	58.9 ± 1.0 cm/s (1.7%) [1.02]	1.4 cm/s (2.3%)	−1.4 [–2.3%]
30°	60.7 ± 0.3 cm/s (0.6%) [1.04]	0.5 cm/s (0.8%)	0.4 [0.7%]
Vector flow imaging			
90°	55.3 ± 1.8 cm/s (3.2%) [1.01]	5.0 cm/s (8.3%)	−5.0 [–8.3%]
80°	54.6 ± 0.8 cm/s (1.4%) [1.01]	5.7 cm/s (9.5%)	−5.7 [–9.5%]
70°	60.4 ± 0.5 cm/s (0.9%) [1.01]	0.3 cm/s (0.5%)	0.1 [0.2%]
60°	58.2 ± 0.8 cm/s (1.3%) [1.04]	2.1 cm/s (3.5%)	−2.1 [–3.5%]

SD = standard deviation; US = ultrasound.
Constant flow in phantom with velocity of 60.3 cm/s.

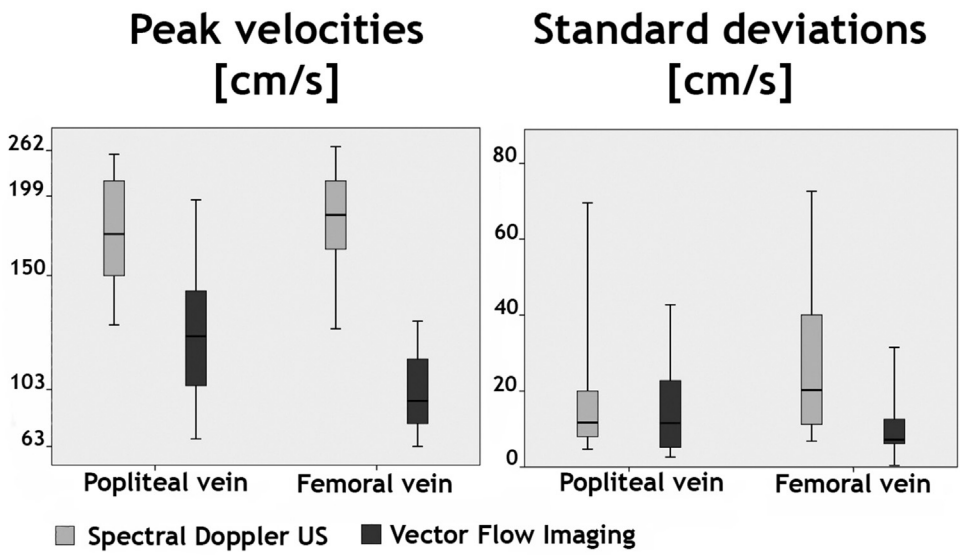

Fig. 3. (Left) Boxplot of the peak velocities of the provoked antegrade flow pulses. The *light gray boxes* represent the velocities measured with spectral Doppler ultrasound (US), and the *dark gray boxes*, the velocities measured with vector flow imaging. (Right) Boxplot of the standard deviations of the three peak velocity measurements of each volunteer. The *light gray boxes* represent the standard deviations of the US measurements, and the *dark gray boxes*, the standard deviations of the vector flow imaging measurements.

Biases and repeatability calculated with mixed model results

The mixed model estimated that the bias between SDUS and VFI was +47% in the popliteal vein and +55% in the femoral vein at a fixed angle of 50° (Table 4). The effect of angle on bias was found to differ between positions ($p = 0.01$). In the femoral vein, the relative bias between the methods was estimated to increase by 3.1% per degree increase in angle (95% confidence interval [CI]: 1.5%–4.6%, $p < 0.01$), whereas at the popliteal vein, there was no significant effect of angle on the bias (estimate: −0.2% per degree, 95% CI: −1.7% to 1.3%, $p = 0.78$).

The relative precision of the replicate measurements did not vary between positions with SDUS ($p = 0.08$), between positions with VFI ($p = 0.66$), between techniques at the popliteal vein ($p = 0.40$) nor between techniques at the femoral vein ($p = 0.53$) (Table 4). The relative precision of the measurements did not vary significantly between the positions or techniques (Table 3). The star plot indicates the maximum number of pairs between the repeated measurements of the two techniques in each position of each volunteer (Fig. 4). Each star represents the replicate measurements on one subject. The center of the star corresponds to the average measurements, and the spikes, to pairs of replicates. In the femoral vein, the stars have a greater width on the x-axis compared with the y-axis, which indicates the higher standard deviation of SDUS measurements compared with VFI measurements in these patients. In some cases, not all three repeated measurements were performed at the exact same beam-to-flow angle. In these situations, the stars consist of fewer spikes, because of the fewer pairs of measurements contributing to the star. The star of such a patient consisted of nine spikes if all measurements were done at the same beam-to-flow angle, whereas it consisted only of four spikes if two measurements were done at the same beam-to-flow angle for each technique.

DISCUSSION

Overall, VFI and SDUS performed similarly in the phantom model. Although SDUS had higher accuracy (an average accuracy of 1.7% compared with 5.5%), the two techniques had similar precision (Table 2). The precision for VFI estimations at the four different beam-to-flow angle positions used in this study did not deviate from the precision of 1.4% recently reported in another phantom study, except at the 90° position, where the precision appeared lower (Hansen et al. 2017a) (Table 2). It should be noted that the angle was known exactly in the flow phantom experiment, and it was set accordingly in the scanner for SDUS, whereas it was estimated for VFI. An angle error of only ±2° at a 60° true angle can result in a ±6% error in the velocity estimate for SDUS, which was not included in the phantom study. For increasing angles, the error is progressively worse (Evans et al. 1989). The *in vivo* peak velocities with SDUS differed in the two locations, femoral and popliteal veins, as velocities

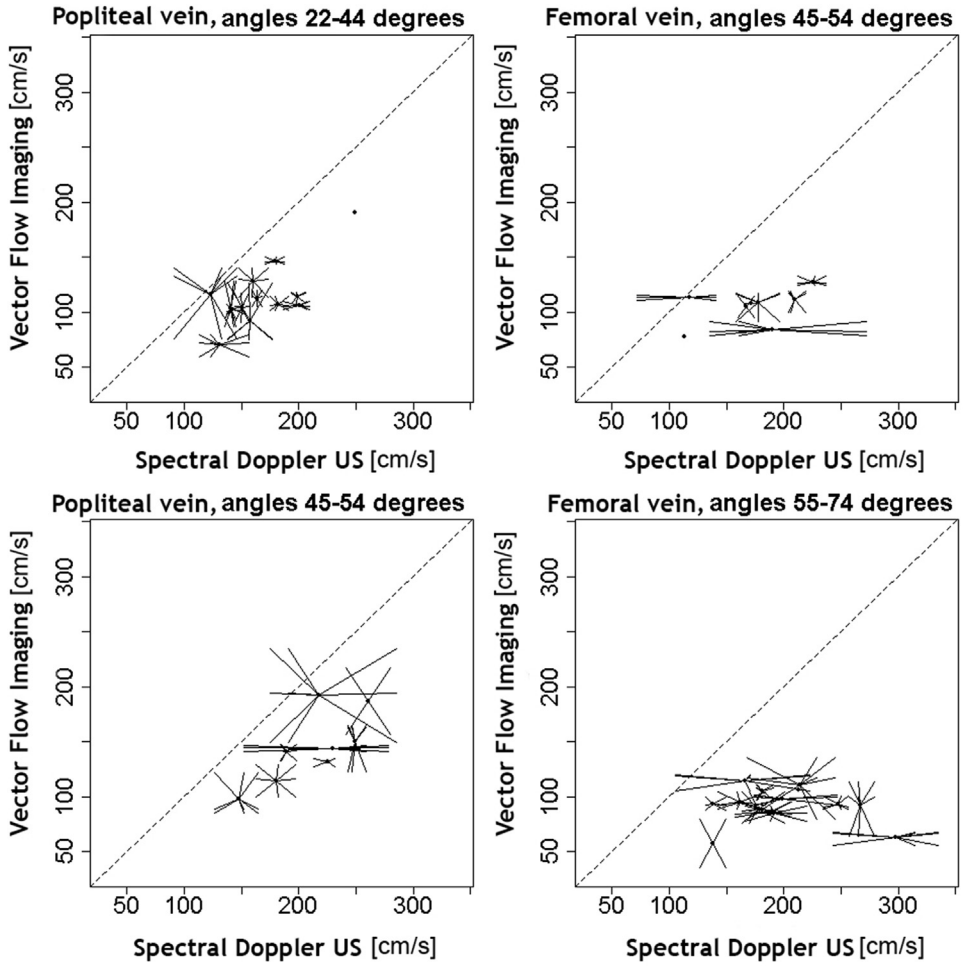

Fig. 4. Star plots showing the recordings in the popliteal vein at low beam-to-flow angles (upper left) and optimal angles (lower left) and in the femoral vein at optimal angles (upper right) and high angles (lower right). US = ultrasound.

estimated with VFI were significantly lower than the corresponding SDUS estimates (Table 3). The difference between VFI and SDUS peak velocities was most pronounced in the femoral vein, which can only partly be explained by the higher velocity error for VFI at 90°, as shown in the flow phantom study (Table 2). For SDUS, the averaged peak velocities were nearly twice those of VFI in the femoral vein (191.7–97.3 cm/s), but with a significantly higher standard deviation (43.9–16.3 cm/s, $p < 0.0001$). The angles were also higher, ranging up to 74° for SDUS and close to 90° for VFI. For such high angles, an inaccuracy in angle of 5° can lead to biases of ±25% for SDUS (Evans et al. 1989), and this in combination with the relative error of −8.3% for VFI is a possible reason for the differences in averaged peak velocities.

In a recent study by Hansen et al. (2017a), the precision of replicated velocity measurements was examined in a phantom with a beam-to-flow angle of 90° for constant and pulsatile flow, as well as *in vivo* in the ascending aorta. Here the inaccuracy in precision of flow rate measurements increased from constant to pulsatile flow in the phantom and increased even more when pulsating flow in patients was examined. Differences in precision of velocity estimation for VFI in flow phantoms and *in vivo* were also found in this study. The discrepancy in this study was caused by a greater number of variables affecting the outcome *in vivo*, for example, the performance of the cuff compression–decompression system, the cooperation capacity of the patients examined, the movement of tissue, variations in flow angles and variation in position of the transducer between repeated measurements. The phantom results from our study and the study by Hansen et al. (2017a) covered constant and pulsatile flow, at different flow angles and velocities. The phantom results validate the *in vivo* results in this study.

Various advantages of VFI have been reported including precise peak velocity measurements, volume flow measurements and quantification of complex blood flow (Hansen et al. 2014, 2015a, 2016;

Table 3. Summary statistics

Peak velocities, standard deviations and error factors	SDUS (cm/s)	VFI (cm/s)	*p* Value*
Popliteal vein			
Angle range		22°–55°, 52°–85°	
Average of replicate PVs, mean (SD)	181.3 (39.2)	123.1 (30.4)	<0.0001
SD of replicate PVs, median (IQR)	11.7 (8.0; 20.0)	11.6 (5.2; 22.7)	0.87
EF of replicate PVs, median (IQR)	1.06 (1.04; 1.14)	1.13 (1.05; 1.20)	0.09
Femoral vein			
Angle range		47°–74°, 77°–104°	
Average of replicate PVs, mean (SD)	191.7 (43.9) cm/s	97.3 (16.3) cm/s	<0.0001
SD of replicate PVs, median (IQR)	20.2 (11.2; 40.0) cm/s	7.2 (6.2; 12.6) cm/s	0.001
EF of replicate PVs, median (IQR)	1.14 (1.05; 1.20) cm/s	1.09 (1.07; 1.13) cm/s	0.37
p Values for comparison between popliteal and femoral veins	SDUS	VFI	
Average of replicate PVs	0.43	0.001	
SD of replicate PVs	0.10	0.37	
EF of replicate PV	0.14	0.93	

SDUS = spectral Doppler ultrasound; VFI = vector flow imaging; PV = peak velocity; SD = standard deviation; IQR = interquartile range; EF = error factor.
* Paired *t*-test or Wilcoxon's signed rank test.

Pedersen et al. 2012). However, it has been found that VFI underestimates peak velocities and volume flow compared with other techniques (Bechsgaard et al. 2016, Brandt et al. 2016, Hansen et al. 2014, 2015a). In this study, it was found that VFI underestimated peak velocity compared with venous peak velocity measurements obtained with SDUS. This is in accordance with previously published work indicating that peak systolic velocity was lower in the carotid artery (Pedersen et al. 2012) and the portal vein compared with SDUS (Brandt et al. 2015) as well as in the ascending aorta compared with SDUS using transesophageal echocardiography (Hansen et al. 2013). It is, however, also known that SDUS overestimates peak velocities because of intrinsic spectral broadening (Tortoli et al. 2015). Volume flow has been evaluated with VFI in two studies on dialysis fistulas, and in both studies, flow was underestimated compared with the values obtained with the US dilution technique (Brandt et al. 2016; Hansen et al. 2014).

Additionally, VFI performance was not superior to that of SDUS in the phantom or in the popliteal vein, where the beam-to-flow angles were optimal for SDUS. However, advantages of the VFI technique may become obvious in examination of deeply located vessels running perpendicular to the surface of the skin, for example, the femoral vein, as the US examination is performed with a steep beam-to-flow angle. The angle dependency of SDUS influenced the precision of *in vivo* velocity estimates, as the operator was bound to use a constant and arbitrary beam-to-flow angle for the blood flow, which has alternating and diverging velocity components.

In the flow phantom, operator and angle dependency is reduced as the flow is laminar and uniform, and the scan setup is standardized with a fixated probe. In this study, the precision of SDUS declined in the femoral vein compared with the popliteal vein, despite an average electronical corrected beam-to-flow angle of 57.6° in the femoral vein.

The higher precision of VFI *in vivo* compared with conventional methods was previously been reported by

Table 4. Biases and limits of agreement

Estimated biases between SDUS and VFI		
Angle (range)	Popliteal vein (22°–55°)	Femoral vein (47°–74°)
40°	50% (95% CI: 34%–67%)	NA
50°	46% (95% CI: 27%–68%)	55% (95% CI: 32%–81%)
60°	NA	109% (95% CI: 87%–133%)

Limits of agreement between two replicate measurements* and comparison of variance between techniques and positions			
Technique	Popliteal vein	Femoral vein	*p* Value
SDUS	(–31%; 45%)	(–39%; 64%)	0.08
VFI	(–34%; 52%)	(–36%; 57%)	0.66
p Value	0.40	0.53	

SDUS = spectral Doppler ultrasound; VFI = vector flow imaging; CI = confidence interval; NA = not available.
* How much above or below the previous measurement a replicate can be expected to be found.

Hansen et al. (2014) and Brandt et al. (2016). VFI can automatically detect the flow angle, as well as quantify the angle diversity of the blood flow, which may eliminate angle dependency and reduce operator dependency *in vivo*. The equal error factor of VFI compared with SDUS in the volunteers found in this study suggests that VFI can be applied to assess peak velocities in the veins of the lower extremities, which is in accordance with previously published work concerning peak velocity measurements in both arteries and veins (Bechsgaard et al. 2016; Hansen et al. 2015a; Pedersen et al. 2012). Precise velocity estimates will make VFI a reliable tool in the clinic, if the bias in accuracy is systematic. In this study, no systematic bias for VFI was found for a fixed flow velocity with changing beam-to-flow angle in a flow phantom. However, Hansen et al. (2017a), in a previous VFI study on a flow phantom, reported a strong systematic bias for increasing flow velocities at 90° for both constant and pulsatile flow, indicating that the systematic bias for VFI should be found for changing velocities at fixed beam-to-flow angles. In this study, the accuracy of VFI was found to be on the same order as the error introduced by a 2° error in angle for SDUS at a 60° beam-to-flow angle.

Vector flow imaging could play an important role in patients with venous symptoms of the lower extremities by quantifying hemodynamic changes. Symptoms are not pathognomonic for venous disorders and cannot be used to discriminate between the different disease entities. Clinicians rely on ultrasound and clinical judgment to make decisions on advanced medical imaging like CT venography, MR venography, digital subtraction angiography and intravascular ultrasound (Arnoldussen et al. 2013; Eklof et al. 2009; Metzger et al. 2016). VFI can potentially quantify hemodynamic changes in venous diseases to clarify the need for additional medical imaging and treatment.

In addition to venous disorders, VFI could also play a role in examination of the carotid and femoral arteries, in cardiology and in abdominal ultrasound, all areas recently examined with VFI (Brandt et al. 2015; Hansen et al. 2015b, 2016, 2017b; Pedersen et al. 2012). The vessels in the thorax and abdomen are deeply located and examined with phased and convex arrays respectively, which means that electronic beam-to-flow angle correction may be limited, and valid velocity estimates may be difficult to attain with SDUS. Recently published reviews have underlined the diverging recommendations of abdominal vessel stenosis assessment with peak velocity estimation (AbuRahma and Yacoub 2013; AbuRahma et al. 2012). These discrepancies may reflect different scan protocols, and operator dependency related to parameter settings used for conventional SDUS, for example, the manual angle correction (Park et al. 2012). The lack of consistency may be solved by the less operator dependent and precise VFI method.

Furthermore, VFI-derived measures such as velocity ratios and vector concentration could also be used to characterize venous flow patterns, and both measures are unaffected by underestimation of the actual velocity (Hansen et al. 2015b, 2016, 2017b). The vector concentration has been used to characterize aortic valve stenosis, indicating a strong association with peak systolic velocity (Hansen et al. 2016, 2017b). The velocity ratio obtained with VFI for assessment of stenosis has been tested in the superficial femoral artery, and correlated well with digital subtraction angiography (Hansen et al. 2015b).

With VFI, additional regions and vessels may be accessible in the human body, providing angle-independent velocity estimation and new hemodynamic findings with clinical relevance.

The first article describing venous blood flow imaging using vector velocity estimation achieved with plane wave emission revealed highly complex flow patterns around the cusps of the valve in the jugular vein (Hansen et al. 2009). Flow complexity, that is, vector concentration, should in future studies be applied to venous flow, for example, around venous valves, to relate venous blood flow complexity and venous disease (Hansen et al. 2016). Future research will determine if the quantitative characterization of complex alterations in the flow, as well as angle-independent peak velocity estimations, achievable with VFI, can be of value in evaluation of patients with venous disease of the lower extremities. Furthermore, a study should be designed in which the exact data—that is, with simultaneous acquisition—are used for both VFI and SDUS to test the true performance of the two estimators in comparison.

The present study was limited by the study population of normal-weight volunteers. The linear transducer used has a limited scan depth, which might be insufficient for patients with high body mass index. However, in overweight patients it should be possible to perform the examination with a curved array transducer, with which VFI recently has been implemented (Jensen et al. 2015).

Furthermore, VFI is currently limited because velocity quantification is not applicable in the real-time velocity estimator on the scanner. The implementation of real-time velocity quantification would allow multicenter studies to be performed, thereby emphasizing the relevance of the technique in clinical practice. SDUS estimates velocities from a larger number of observations (usually 128 emissions), whereas the current VFI implementation uses only 16 emissions. Using 128 emissions for VFI can increase precision, as reported by Jensen (2016) to further benefit quantification.

CONCLUSIONS

The study revealed that VFI estimates of peak velocity in the femoropopliteal veins of volunteers were lower compared with those measured with SDUS, and that the difference in peak velocity was accentuated in the femoral vein, that is, at higher beam-to-flow angles. Furthermore, the *in vivo* results indicated that VFI offers velocity estimates with no difference in precision compared with SDUS. Phantom measurements supported the *in vivo* results, but indicated that flow examination at 90° also is a challenge for VFI. In conclusion, compared with SDUS, VFI can provide precise but underestimated peak velocity measurements of the antegrade flow in the veins of the lower extremities in standing, healthy, normal-weight volunteers. Hemodynamic characterization is crucial in venous disorders. The research based on VFI vein examinations of the lower extremities may be a key to an effective diagnostic strategy in the future.

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REFERENCES

AbuRahma AF, Yacoub M. Renal imaging: Duplex ultrasound, computed tomography angiography, magnetic resonance angiography, and angiography. Semin Vasc Surg 2013;26:134–143.

AbuRahma AF, Mousa AY, Stone PA, Hass SM, Dean LS, Keiffer T. Duplex velocity criteria for native celiac/superior mesenteric artery stenosis vs in-stent stenosis. J Vasc Surg 2012;55:730–738.

Arnoldussen CW, de Graaf R, Wittens CH, de Haan MW. Value of magnetic resonance venography and computed tomographic venography in lower extremity chronic venous disease. Phlebology 2013;28(Suppl 1): 169–175.

Bechsgaard T, Hansen KL, Brandt AH, Holbek S, Lönn L, Strandberg C, Bækgaard N, Nielsen MB, Jensen JA. Blood flow velocity in the popliteal vein using transverse oscillation ultrasound. Proc SPIE Med Imaging 2016;1–8.

Brandt AH, Hansen KL, Nielsen MB, Jensen JA. Velocity estimation of the main portal vein with transverse oscillation. Proc IEEE Int Ultrason Symp 2015;1–4.

Brandt AH, Jensen J, Hansen KL, Hansen P, Lange T, Rix M, Jensen JA, Lonn L, Nielsen MB. Surveillance for hemodialysis access stenosis: Usefulness of ultrasound vector volume flow. J Vasc Access 2016; 17:483–488.

Eberhardt RT, Raffetto JD. Chronic venous insufficiency. Circulation 2014;130:333–346.

Eklof B, Perrin M, Delis KT, Rutherford RB, Gloviczki P. Updated terminology of chronic venous disorders: The VEIN-TERM transatlantic interdisciplinary consensus document. J Vasc Surg 2009;49: 498–501.

Evans DH, McDicken W, Skidmore R, Woodcock J. Doppler ultrasound: Physics, instrumentation, and clinical applications. Chichester: Wiley; 1989.

Fox MD. Multiple crossed-beam ultrasound Doppler velocimetry. IEEE Trans Sonics Ultrason 1978;25:281–286.

Hansen KL, Udesen J, Gran F, Jensen JA, Bachmann Nielsen M. In-vivo examples of flow patterns with the fast vector velocity ultrasound method. Ultraschall Med 2009;30:471–477.

Hansen KL, Pedersen MM, Moller-Sorensen H, Kjaergaard J, Nilsson JC, Lund JT, Jensen JA, Nielsen MB. Intraoperative cardiac ultrasound examination using vector flow imaging. Ultrason Imaging 2013;35:318–332.

Hansen PM, Olesen JB, Pihl MJ, Lange T, Heerwagen S, Pedersen MM, Rix M, Lonn L, Jensen JA, Nielsen MB. Volume flow in arteriovenous fistulas using vector velocity ultrasound. Ultrasound Med Biol 2014;40:2707–2714.

Hansen KL, Moller-Sorensen H, Pedersen MM, Hansen PM, Kjaergaard J, Lund JT, Nilsson JC, Jensen JA, Nielsen MB. First report on intraoperative vector flow imaging of the heart among patients with healthy and diseased aortic valves. Ultrasonics 2015a;56:243–250.

Hansen PM, Jensen JA, Bachmann Nielsen M. First clinical investigations of new ultrasound techniques in three patient groups: Patients with liver tumors, arteriovenous fistulas, and arteriosclerotic femoral arteries. PhD thesis. Denmark: Department of Electrical Engineering, Technical University of Denmark; 2015b.

Hansen KL, Moller-Sorensen H, Kjaergaard J, Jensen MB, Lund JT, Pedersen MM, Lange T, Jensen JA, Nielsen MB. Intra-operative vector flow imaging using ultrasound of the ascending aorta among 40 patients with normal, stenotic and replaced aortic valves. Ultrasound Med Biol 2016;42:2412–2422.

Hansen KL, Moller-Sorensen H, Kjaergaard J, Jensen MB, Lund JT, Pedersen MM, Olesen JB, Jensen JA, Nielsen MB. Vector flow imaging compared with conventional Doppler ultrasound and thermodilution for estimation of blood flow in the ascending aorta. Ultrason Imaging 2017a;39:3–18.

Hansen KL, Moller-Sorensen H, Kjaergaard J, Jensen MB, Jensen JA, Nielsen MB. Aortic valve stenosis increases helical flow and flow complexity: a study of intra-operative cardiac vector flow imaging. Ultrasound Med Biol 2017b;43:1607–1617.

Jensen JA. A new estimator for vector velocity estimation. IEEE Trans Ultrason Ferroelectr Freq Control 2001;48:886–894.

Jensen JA. Quantitative measurements using ultrasound vector flow imaging. Proc IEEE Int Ultrason Symp 2016;1–4.

Jensen JA, Munk P. A new method for estimation of velocity vectors. IEEE Trans Ultrason Ferroelectr Freq Control 1998;45: 837–851.

Jensen JA, Brandt AH, Nielsen MB. Convex array vector velocity imaging using transverse oscillation and its optimization. IEEE Trans Ultrason Ferroelectr Freq Control 2015;62:2043–2053.

Konoeda H, Yamaki T, Hamahata A, Ochi M, Sakurai H. Quantification of superficial venous reflux by duplex ultrasound-role of reflux velocity in the assessment the clinical stage of chronic venous insufficiency. Ann Vasc Dis 2014;7:376–382.

Labropoulos N, Borge M, Pierce K, Pappas PJ. Criteria for defining significant central vein stenosis with duplex ultrasound. J Vasc Surg 2007;46:101–107.

Lui EY, Steinman AH, Cobbold RS, Johnston KW. Human factors as a source of error in peak Doppler velocity measurement. J Vasc Surg 2005;42:972–979.

Metzger PB, Rossi FH, Kambara AM, Izukawa NM, Saleh MH, Pinto IM, Amorim JE, Thorpe PE. Criteria for detecting significant chronic iliac venous obstructions with duplex ultrasound. J Vasc Surg Venous Lymphat Disord 2016;4:18–27.

Michaels JA, Campbell WB, Brazier JE, Macintyre JB, Palfreyman SJ, Ratcliffe J, Rigby K. Randomised clinical trial, observational study and assessment of cost-effectiveness of the treatment of varicose veins (REACTIV trial). Health Technol Assess 2006;10:1–196.

Needleman L. Update on the lower extremity venous ultrasonography examination. Radiol Clin North Am 2014;52:1359–1374.

Newhouse VL, Censor D, Vontz T, Cisneros JA, Goldberg BB. Ultrasound Doppler probing of flows transverse with respect to beam axis. IEEE Trans Biomed Eng 1987;34:779–789.

Overbeck JR, Beach KW, Strandness DE Jr. Vector Doppler: Accurate measurement of blood velocity in two dimensions. Ultrasound Med Biol 1992;18:19–31.

Park MY, Jung SE, Byun JY, Kim JH, Joo GE. Effect of beam-flow angle on velocity measurements in modern Doppler ultrasound systems. AJR Am J Roentgenol 2012;198:1139–1143.

Pedersen MM, Pihl MJ, Haugaard P, Hansen JM, Hansen KL, Nielsen MB, Jensen JA. Comparison of real-time in vivo spectral and vector velocity estimation. Ultrasound Med Biol 2012;38:145–151.

Pozniak M, Allan P. Clinical Doppler ultrasound. London: Churchill Livingstone; 2013.

Ricci S, Vilkomerson D, Matera R, Tortoli P. Accurate blood peak velocity estimation using spectral models and vector doppler. IEEE Trans Ultrason Ferroelectr Freq Control 2015;62:686–696.

Rumack CM, Wilson SR, Charboneau JW, Levine D. Diagnostic ultrasound. Philadelphia: Elsevier Mosby; 2011.

Spinedi L, Broz P, Baldi T, Imfeld S, Staub D, Jaeger K, Aschwanden M, Uthoff H. Evaluation of varicose veins of the lower extremity: The value of the duplex ultrasound (Part 1). Ultraschall Med 2016; 37:348–365.

Tortoli P, Lenge M, Righi D, Ciuti G, Liebgott H, Ricci S. Comparison of carotid artery blood velocity measurements by vector and standard Doppler approaches. Ultrasound Med Biol 2015;41: 1354–1362.

Trahey GE, Allison JW, von Ramm OT. Angle independent ultrasonic detection of blood flow. IEEE Trans Biomed Eng 1987; 12:965–967.

van Bemmelen PS, Bedford G, Beach K, Strandness DE. Quantitative segmental evaluation of venous valvular reflux with duplex ultrasound scanning. J Vasc Surg 1989;10:425–431.

Wittens C, Davies AH, Baekgaard N, Broholm R, Cavezzi A, Chastanet S, de Wolf M, Eggen C, Giannoukas A, Gohel M, Kakkos S, Lawson J, Noppeney T, Onida S, Pittaluga P, Thomis S, Toonder I, Vuylsteke M, Esvs Guidelines C, Kolh P, de Borst GJ, Chakfe N, Debus S, Hinchliffe R, Koncar I, Lindholt J, de Ceniga MV, Vermassen F, Verzini F, Document R, De Maeseneer MG, Blomgren L, Hartung O, Kalodiki E, Korten E, Lugli M, Naylor R, Nicolini P, Rosales A. 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;49:678–737.

Wood MM, Romine LE, Lee YK, Richman KM, O'Boyle MK, Paz DA, Chu PK, Pretorius DH. Spectral Doppler signature waveforms in ultrasonography: A review of normal and abnormal waveforms. Ultrasound Q 2010;26:83–99.