Non-invasive pressure measurement of the great saphenous vein in healthy controls and patients with venous insufficiency

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Abstract: OBJECTIVES: Venous pressure measurement using an intravenous catheter is the sole method for the diagnosis of venous hypertension in patients with chronic venous insufficiency. A noninvasive tool to quantify increased venous pressure is essential for studying venous pathophysiology. Aim of the study was to investigate the value of controlled compression ultrasound (CCU) for noninvasive assessment of venous pressure (VP) of the great saphenous vein (GSV) in healthy persons and patients with venous insufficiency to quantify venous hypertension. METHODS: An optimal visible part of the GSV directly above the ankle was marked on the skin and compressed under ultrasound control and pressure needed for complete compression of the vein was recorded using a pressure manometer with a translucent silicone membrane. Complete insufficiency of the GSV (Hach IV) was documented by duplex ultrasound by an independent investigator before start of the study. VP measurement was performed while normal breathing, deep inspiration and expiration and during a standardized Valsalva maneuver. RESULTS: Twenty controls and 19 patients with complete insufficiency of the GSV were included. Valsalva maneuver induced a slight increase in VP in controls (20.1 ± 4.5 vs 25.1 ± 6.6 mbar) but a significant higher increase in patients from 26 to 37 mbar (IQR 18.5-28.0 vs 31.5-43.0; $p < 0.001$). CONCLUSION: Noninvasive venous pressure measurement of the great saphenous vein using CCU is feasible and documents an increased pressure during Valsalva maneuver in Hach IV patients compared to healthy controls.

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Non-invasive pressure measurement of the great saphenous vein in healthy controls and patients with venous insufficiency

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Abstract

Objectives. Venous pressure measurement using an intravenous catheter is the sole method for the diagnosis of venous hypertension in patients with chronic venous insufficiency. A noninvasive tool to quantify increased venous pressure is essential for studying venous pathophysiology. Aim of the study was to investigate the value of controlled compression ultrasound (CCU) for noninvasive assessment of venous pressure (VP) of the great saphenous vein (GSV) in healthy persons and patients with venous insufficiency to quantify venous hypertension.

Methods. An optimal visible part of the GSV directly above the ankle was marked on the skin and compressed under ultrasound control and pressure needed for complete compression of the vein was recorded using a pressure manometer with a translucent silicone membrane. Complete insufficiency of the GSV (Hach IV) was documented by duplex ultrasound by an independent investigator before start of the study. VP measurement was performed while normal breathing, deep inspiration and expiration and during a standardized Valsalva maneuver.

Results. Twenty controls and 19 patients with complete insufficiency of the GSV were included. Valsalva maneuver induced a slight increase in VP in controls (20.1 ± 4.5 vs 25.1 ± 6.6 mbar) but a significant higher increase in patients from 26 to 37 mbar (IQR 18.5-28.0 vs 31.5-43.0; $p < 0.001$).

Conclusion. Noninvasive venous pressure measurement of the great saphenous vein using CCU is feasible and documents an increased pressure during Valsalva maneuver in Hach IV patients compared to healthy controls.

Keywords

Chronic venous insufficiency, venous hypertension, noninvasive pressure measurement, compression ultrasound

Introduction

Venous hypertension is the major pathophysiologic cause of symptoms in chronic venous insufficiency and responsible for microangiopathy and tissue alterations finally resulting in ulcerations.[1-4] The evaluation of the microcirculatory status is challenging and time consuming.[5,6] The sole method for the quantification of venous pressure is intravasal acquisition with placing a needle in the dorsal vein of the foot.[7] However, this ambulatory venous pressure measurement (AVPM), which is a widely accepted gold standard for the diagnosis of venous hypertension, is an invasive and sometimes painful technique. A non-invasive and reliable tool to measure peripheral venous pressure under different conditions would be of great interest for further evaluation of pathophysiological mechanisms in venous disease and for studying new therapeutic options.

Venous hypertension results in capillary hypertension, which is responsible for capillary leakage leading to edema and inflammation. The marked microangiopathy in patients with chronic venous insufficiency plays a crucial role in the development of trophic skin lesions (e.g. white atrophy, hyperpigmentation).[8] Also in skin grafts of patients with venous ulcers, severe microcirculatory changes were described and were characterized by hypoxia and abnormal regeneration.[9] Novel ultrasound techniques as contrast-enhanced ultrasound are on the way to characterize microcirculatory damage in different applications.[10]

Recently, a novel ultrasound based technique for measuring venous pressure non-invasively was introduced.[11] A combination of a pressure manometer with a translucent silicone membrane was used to measure the pressure needed to compress the vein completely, which was controlled by ultrasound.[12] This method was validated at the cephalic vein at the forearm with excellent correlation compared to invasive intravenous pressure measurement (r = 0.95) within a range up to 70 cmH_2O.[12] Further studies using compression controlled ultrasound

(CCU) for central venous pressure measurement confirmed feasibility and reliability of this noninvasive technique.[13,14]

We performed a prospective study to investigate the value of CCU for noninvasive assessment of venous pressure (VP) of the great saphenous vein (GSV) in healthy persons and patients with chronic venous insufficiency to quantify venous hypertension.

Materials and Methods

Study design

This prospective study was performed at the two vascular centers of the university hospitals in Zurich and Bruderholz. Healthy volunteers without clinical signs or symptoms of chronic venous disease and without history of deep vein thrombosis were recruited for the control group in study center Zurich. Patients with known complete incompetence of the great saphenous vein (Hach IV) were recruited in both study centers. Exclusion criteria were history of deep vein thrombosis or past sclerotherapy or phlebectomy. Complete insufficiency of the GSV (Hach IV) was documented by duplex ultrasound by an independent investigator before start of the study.

The study was approved by the local ethical committees of both study centers (KEK Zurich, EK-1721 and EK beider Basel, EK 316/09). All participants gave their written informed consent. The study protocol was published at the Protocol Registration System ClinicalTrials.gov NCT01000909.

Controlled compression ultrasound and venous pressure measurement

Ultrasound imaging was performed with a high-end duplex ultrasound machine (iU22, Philips, Best, Netherlands) using a linear 17-5 MHz transducer. SonoCT Real-time Compound Imaging (Philips) was used to optimize the B-Mode images and to suppress artifacts and focus position was adapted to the depth of the visible vein. Controls and patients were investigated in supine position after a five minute rest in a temperature controlled vascular laboratory. The great saphenous vein was studied in a cross section B-mode image just above the medial ankle ***(Figure 1)***. After documentation of a satisfying image the point of measurement was marked on the skin with a waterproof marker. Cross section vein diameter and venous pressure measurement was performed under four conditions: normal breathing, deep inspiration, deep expiration and Valsalva maneuver. The Valsalva maneuver was standardized by using a tube connected to a separate manometer.[15] During Valsalva maneuver a constant pressure of 30 mmHg had to be established by the subjects. Venous pressure measurement was performed as described elsewhere.[12] The GSV was compressed under ultrasound control and the pressure needed for complete compression of the vein was recorded by a pressure manometer with a translucent silicone membrane. VP was measured three times for each maneuver and the mean value was used for further analysis.

Statistics

Statistical analysis was made by using SPSS software version 20.0 (Statistical Package for the Social Science, IBM Corporation, Armonk, New York, USA) and was carried out in cooperation with the Division of Biostatistics at the Institute for Social and Preventive Medicine of the University of Zurich. Vein diameters showed to be normally distributed. Comparison of vein diameter within healthy controls and within Hach IV patients was done by paired sample test. Using the Bonferroni-correction a significance (2-tailed) of $p < 0.01666$ was considered as significant. To compare vein diameters of healthy controls with Hach IV patients independent sample tests including Bonferroni-correction were used by which significance (2-tailed) was accepted if $p < 0.0125$.

VP in the group of the healthy subjects showed to be normally distributed. To analyze the values between the right and the left leg and between the maneuvers an ANOVA was calculated. After proving that there is no significant difference between the right and the left leg in healthy subjects only pressure values of the right side were taken to compare with Hach IV patients. As pressure values of Hach IV subjects were not normally distributed data are expressed as median with interquartile ranges (IQR). Because VP in patients with Hach IV in both legs tend to be higher compared to patients with only one diseased leg, pressure values for comparison with healthy subjects were only taken from one leg per subject.

To compare the increase of VP from normal breathing to Valsalva maneuver a quotient was calculated as follows: Quotient = $(VP_{Valsalva} / VP_{normal\ breathing}) \times 100\ \%$. Comparison of VP between the groups was done by non-parametric, unpaired Mann-Whitney test. An asymptotic significance (2-tailed) $p<0.05$ was considered significant for all pressure analysis.

Results

Healthy subjects

Twenty healthy volunteers (12 men) with a mean age of 31.0 years (range 18 - 64) were included. Mean body mass index (BMI) was 23.2 kg/m^2 (range 19.5 - 29.0). Mean systolic/diastolic blood pressure was 115 / 67 mmHg (range 95 - 138 / 55 - 84) and mean heart rate was 67 beats per minute (range 48 - 115).

Hach IV patients

Nineteen patients (13 men, 25 legs) with a mean age of 53.0 years (range 24-75) and mean BMI 29.1 kg/m^2 (19.4 - 44.6) and with complete incompetence of the GSV (Hach IV) were included in the analysis. Mean systolic/diastolic blood pressure in this group was 137.8 / 83.9 mmHg (range 117 - 176 / 70 - 105) and mean heart rate was 79 beats per minute (range 51-119).

GSV diameter in healthy subjects

Mean diameter of the GSV was 2.6 mm (right leg) and 2.6 mm (left leg) in healthy controls at rest with a slight increase during deep inspiration (right leg: $p = 0.185$, left leg: $p = 0.017$; both n.s. with Bonferroni-correction) and expiration (right leg: $p = 0.285$, left leg: $p = 0.034$; both n.s. with Bonferroni-correction) and a significant increase (right and left leg: $p < 0.001$) during Valsalva maneuver to 2.9 mm (right) and 2.9 mm (left) respectively (Table 1).

GSV diameter in Hach IV patients

Mean diameter of the GSV in Hach IV legs was 3.8 mm with no significant increase during deep expiration and a significant increase during deep inspiration ($p = 0.002$) to 4.0 mm and Valsalva maneuver ($p < 0.001$) to 4.2 mm (Table 2).

Comparison between GSV Diameter in healthy subjects and Hach IV patients

GSV diameter in Hach IV patients showed to be significantly higher in each maneuver (normal breathing, maximum inspiration, maximum expiration or Valsalva maneuver) compared to vein diameters in healthy subjects ($p < 0.001$ for each comparison).

Venous pressure in healthy subjects

As shown in Table 1, in healthy controls there is no change of VP during normal breathing, maximum inspiration and maximum expiration. However, a significant difference ($p < 0.001$) was found between normal breathing and Valsalva, but no difference ($p = 0.674$) between the two legs was registered (Figure 2).

Venous pressure in Hach IV patients

The median and IQR of VP are displayed in Table 2. Similar to the healthy controls VP changed neither during normal breathing, nor after maximum inspiration and maximum expiration. VP during normal breathing showed a significant lower value ($p < 0.001$) compared to Valsalva maneuver.

Comparison between venous pressure in healthy subjects and Hach IV patients

As mentioned above in patients with Hach IV in both legs only pressure values of the right leg were included to calculate potential differences to healthy controls. Statistical analysis showed no difference between the affected legs for normal breathing ($p = 0.974$) or Valsalva ($p = 0.202$). The diagram of the quotient between PVP during normal breathing and Valsalva is displayed in Figure 3. The median pressure augmentation in Hach IV patients is 61.6 % with an IQR of 30.9 – 94.7 % while healthy controls showed a median pressure augmentation of 23.7 % with an IQR of 7.3 – 36.3 %. Mann-Whitney test showed a highly significant increase ($p < 0.001$) of PVP values in Hach IV compared to healthy controls (Figure 2).

Discussion

In this study a novel non-invasive method for measuring venous pressure of the great saphenous vein was evaluated in healthy controls and patients with venous insufficiency. In contrast to AVPM in CCU there is no need for inserting an intravenous line into a dorsal foot vein. Venous pressure was investigated in different physiologic provocation maneuvers with reproducible and plausible pressure values. Valsalva maneuver induced only a slight increase in VP in healthy persons but a pronounced venous hypertension in insufficient veins. CCU is easy to learn and can be performed repeatedly under different conditions. It is therefore an ideal method to further study pathophysiology of venous hypertension without an invasive tool. Additional to the measurement of an elevated venous pressure, a parallel characterization of microcirculatory changes with contrast enhanced ultrasound may be very useful and is planned in ongoing studies. Venous hypertension, measured non-invasively, is a crucial but not the sole factor in microcirculatory damage in chronic venous insufficiency. Hemorheological parameters are known to be a marker of venous hypertension in patients with venous disease and independent predictors of venous thromboembolism.[16,17] Elevated vein pressures may also have an influence on transplanted flap microcirculation.[18]

However, the study has some limitations. First, we did not compare venous pressure measurements with the gold standard AVPM to avoid patients' discomfort by inserting a catheter in the dorsal foot vein. Our method has been validated at the cephalic vein with an excellent correlation compared to invasive intravenous pressure measurement.[12] Second, blinding of the study was not possible due to the fact, that on ultrasound enlarged veins of Hach IV patients are easily visible to the investigator. The selection criterion of a complete valve insufficiency of the GSV was implemented to achieve a homogenous patient collective with comparable vascular pathology. The relatively small number of patients and controls do not legitimate to establish normal or cut-off values with this method. Further investigations in our vascular laboratory may lead to reliable standards.

Conclusion

Noninvasive venous pressure measurement of the great saphenous vein using controlled compression ultrasound is feasible and documents an increased pressure during Valsalva maneuver in Hach IV patients compared to healthy controls. This study is the basis to further evaluate therapeutic measures for chronic venous insufficiency regarding their effect on venous pressure.

Acknowledgments

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Figure legends

Figure 1: Non-invasive venous pressure measurement of the great saphenous vein at the ankle using a using a pressure manometer with a translucent silicone membrane.

Figure 2: Venous pressure of the great saphenous vein in healthy controls and patients in supine position at rest and during Valsalva maneuver.

Figure 3: Increase in venous pressure of the great saphenous vein during Valsalva maneuver in healthy controls and patients

Table 1

Vein diameter (VD) and venous pressure (VP) of 20 healthy controls

	Healthy controls	
	Right legs n = 20	Left legs n = 20
VD [mm]		
Maneuver	Mean (SD)	Mean (SD)
Normal breathing	2.6 (0.9)	2.6 (0.9)
Maximum inspiration	2.7 (0.9)	2.7 (0.9)
Maximum expiration	2.7 (0.9)	2.7 (1.0)
Valsalva	2.9 (0.9) *	2.9 (1.1) *
VP [mbar]		
Maneuver	Mean (SD)	Mean (SD)
Normal breathing	20.1 (4.5)	21.2 (6.0)
Maximum inspiration	21.9 (5.8)	22.8 (7.2)
Maximum expiration	19.8 (5.1)	21.4 (6.3)
Valsalva	25.1 (6.6) *	23.3 (6.1) *

* $P < 0.001$ compared to normal breathing

Table 2

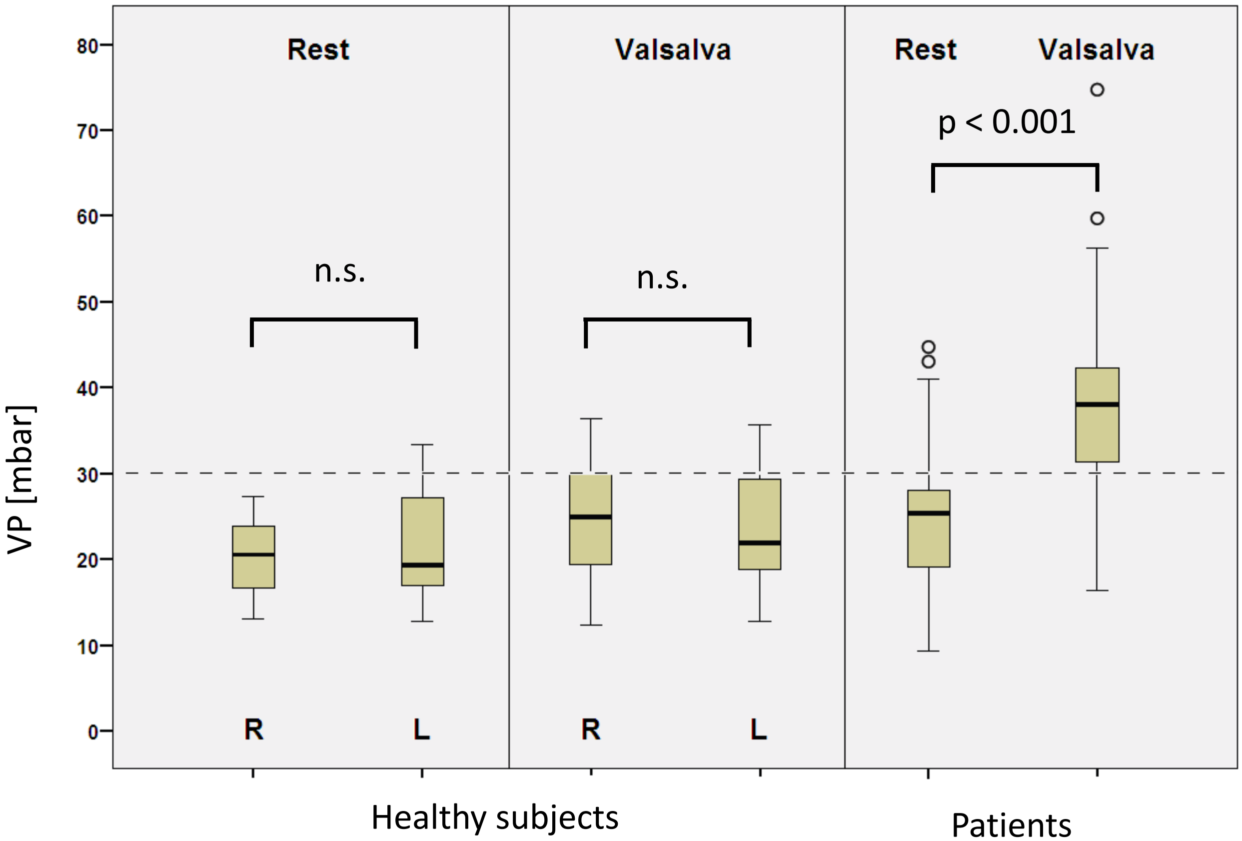
Vein diameter (VD) and venous pressure (VP) of 19 patients

	Patients
	Hach IV legs
VD [mm]	n = 19
Maneuver	Mean (SD)
Normal breathing	3.8 (0.9)
Maximum inspiration	4.0 (0.9) *
Maximum expiration	3.9 (0.8)
Valsalva	4.2 (0.9) **
VP [mbar]	n = 25
Maneuver	Median (IQR)
Normal breathing	26 (18.5-28.0)
Maximum inspiration	30 (23.5-34.5)
Maximum expiration	24 (20.5-27.5)
Valsalva	37 (31.5-43.0) **

* $p = 0.002$ and ** $p < 0.001$ compared to normal breathing

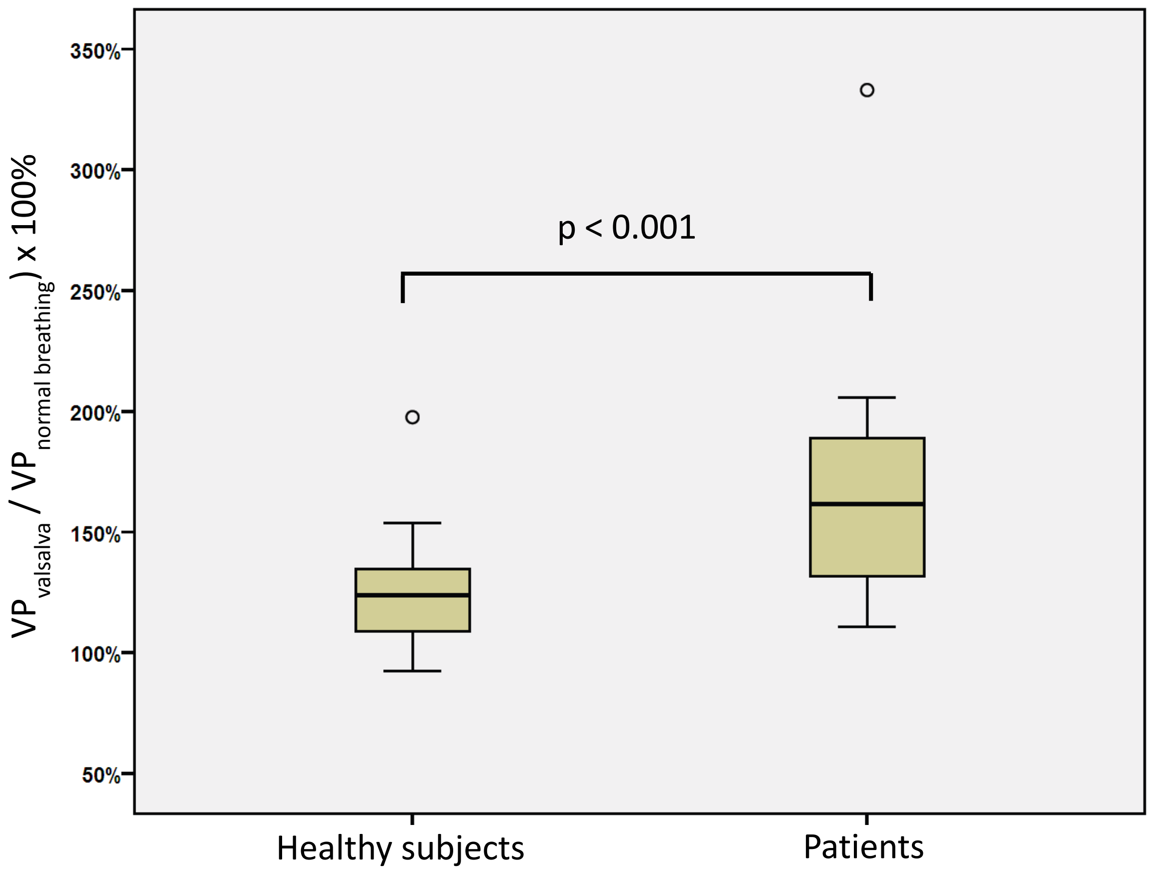
Figure 1

Figure 2



Rest
Valsalva
Rest
Valsalva
p < 0.001
n.s.
n.s.
VP [mbar]
80
70
60
50
40
30
20
10
0
R
L
R
L
Healthy subjects
Patients

Figure 3


350%
300%
250%
200%
150%
100%
50%
VP valsalva / VP normal breathing) x 100%
p < 0.001
Healthy subjects
Patients