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Physiological Reflux and Venous Diameter Change in the Proximal Lower Limb Veins During a Standardised Valsalva Manoeuvre

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Objectives: *the aim of this study was to provide normal values for venous diameter at rest, and venous diameter and physiologic venous reflux during a standardised Valsalva manoeuvre. The impact of the patient's sex, body mass index (BMI), and family history was investigated.*
Material and methods: *eighty legs of 40 healthy volunteers were investigated in a supine position. The median age was 28 years (range 20–66 years). The common femoral vein (CFV), the proximal superficial femoral vein (SFV) and the proximal long saphenous vein (LSV) were investigated by duplex sonography. The following parameters were assessed: resting diameter (VD_{rest}) and maximum diameter (VD_{max}) as well as reflux time (t_r) during the Valsalva manoeuvre. The Valsalva manoeuvre was elicited by a forceful expiration into a tube system. The standard values used were a pressure of 30 mmHg, established within 0.5 seconds (s) and maintained over a time period of at least 3 s.*
Results: *mean VD_{rest} and VD_{max} were 8.3 ± 2.2 and 11.1 ± 2.8 mm in the CFV, 5.9 ± 1.3 and 7.2 ± 1.6 mm in the SFV and 3.5 ± 0.9 and 4.3 ± 1.4 mm in the LSV. Mean values for t_r were 0.61 ± 0.63 s in the CFV, 0.25 ± 0.26 s in the SFV and 0.28 ± 0.40 s in the LSV. A BMI >22.5 kg/m^2 was associated with statistically significant larger values for VD_{rest} and t_r. If adjusted for BMI, t_r in the SFV and the LSV did not differ by sex. For healthy subjects with first-degree relatives suffering from varicose veins ($n = 19$), mean VD_{rest} in the SFV as well as VD in the LSV was significantly larger ($p = 0.02$, 0.05, respectively).*
Coefficients of variation for repeated measurements (VD_{rest}, VD_{max}, t_r) in the same segment varied between 3.3% and 16.4% for the three investigated sites.
Conclusions: *normal values for VD_{rest} and VD_{max} as well as reflux time during a standardised Valsalva manouevre were assessed in the proximal lower limb veins. The influences of BMI, sex and family history were investigated. The described standardised Valsalva manoeuvre led to highly reproducible results and can be recommended for further research projects or as a routine procedure for the assessment of venous reflux.*

Key Words: Venous diameter; Venous diameter change; Valsalva manoeuvre; Venous reflux; Duplex sonography; Body mass index; Sex; Family history; Normal values.

Introduction

The most common feature of chronic venous insufficiency is valvular incompetence,[1] possibly related to abnormal distensibility of the venous wall.[2–4] The most appropriate procedure to test venous valvular function is the Valsalva manoeuvre. It leads to a short and limited reflux with competent valves,[5,6] but to a pronounced and long-lasting reflux with valvular incompetence. The Valsalva manoeuvre has been used in many research projects. However, it was often not standardised and, as a result, there is a large variation in measured Valsalva effects, making this test unreliable for quantitative research on venous diameter and physiological or pathological venous reflux. The aim of this study was to establish normal values for venous reflux and venous diameter changes with a modified standardised Valsalva manoeuvre, but also to describe the influence of BMI, gender and a positive family history for varicose veins.

Material and Methods

Subjects

Eighty legs of 40 healthy volunteers with a median age of 28 years (range: 20–66 years) were investigated.

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Eighteen female and 22 male subjects were included. None had obvious varicose veins or a history of venous disease. Volunteers with a history of asthma, obstructive and restrictive lung disease or symptomatic arterial occlusive disease were excluded.

The men had a higher body mass index (BMI) than the women (22.5 vs. 21 kg/m^2, $p=0.004$), but the women had a higher mean age (36.8 vs. 28.3 years, $p=0.006$). Both groups had the same number of subjects with family members suffering from varicose veins.

Five female and 14 male subjects had a BMI >22.5 kg/m^2 (which is a mean value for the U.S. population taken from the midpoint of the medium frame of the 1983 Metropolitan tables),[7] and 21 had a BMI $\leq$22.5 kg/m^2 (13 female, 8 male). The distribution of age and a family history of varicose vein disease did not differ significantly between the group with BMI >22.5 kg/m^2 and those with $\leq$22.5 kg/m^2 ($p=0.3$, $p=0.2$).

Nineteen subjects had first-degree relatives with varicose veins. Median BMI, age and gender did not differ significantly in the groups with and without family members with varicose veins ($p=0.24$, $p=0.22$, $p=0.78$).

Clinical investigation

Family history, personal history, clinical examination, weight and height were assessed. Volunteers with evidence of a pathological deep-venous reflux shown as a venous cw-Doppler study performed by an independent investigator at the groin above and beneath the inguinal ligament with the patient in a supine position were excluded from the study. For reflux provocation a non-standardised Valsalva manoeuvre was used. Cw-Doppler findings were graded as follows: grade 0: no reflux; 1: short self-limiting reflux of 0.5–3 s duration; grade 2: reflux of >3 s duration. None of the healthy subjects had grade 2 reflux.

Duplex examination

All investigations were performed by the same investigator in the afternoon between 1 and 5 pm with the volunteer in a supine position after a resting period of $\geq$10 minutes. The duplex device used was an ATL Ultramark 9 HDI (Advanced Technology Laboratories, Bothell, WA, U.S.A.) with a linear broad-band scanhead of 5–10 MHz (B-mode) and a fixed Doppler centre frequency of 6 MHz. All Doppler measurements were performed using a Doppler angle of 60° and a sample volume size adjusted to the vessel's cross-sectional area. Measurement sites included the common femoral vein (CFV), the superficial femoral vein (SFV) and the long saphenous vein (LSV), directly distally to an identified valve or, in cases where no valve was detectable, 1 cm distal to the next proximal venous confluence. All measurements were recorded on S-VHS video tape and analysed off-line by an independent investigator.

The following parameters were assessed from longitudinal scanning planes:

resting venous diameter (VD_{rest});
maximum venous diameter during Valsalva manoeuvre (VD_{max});
reflux time (t_r).

All measurements were taken three times, results are reported as mean values $\pm$ standard deviation (s.d.).

Valsalva manoeuvre

A standardised Valsalva manoeuvre was elicited by a forceful expiration into a tube system. The airway pressure was measured by means of a manometer attached to the tube and displayed on the duplex screen by means of a pressure transducer (Trantel Model 60-800, American Edward's Laboratories, U.S.A.). To avoid a false-positive prolonged reflux resulting from a lack of transvalvular pressure gradients, an expiratory pressure of 30 mmHg had to be established within 0.5 s and held for at least 3 s. An expiratory pressure of 30 mmHg was chosen because a pilot study had shown that all subjects were able to elicit this pressure. In our pilot study an expiratory pressure of 40 mmHg, which was used by Masuda,[6] could neither be established nor held by all subjects. A similar procedure has been described by Aschberg *et al*. in 1973 to induce reflux in venographic investigations.[8]

Statistics

Results are given as the mean $\pm$ s.d. For two-group comparisons, the paired and the unpaired *t*-test were used. The correlation Z test was used to assess a correlation between two unrelated parameters. A probability level of 0.05 or less was considered significant. Variances for repeated measurements were analysed using coefficients of variation. All computations were done using the Statview 4.5 software package.[9]

Table 1. Mean ± S.D. of venous diameter at rest (VD_{rest}), maximal venous diameter during Valsalva manoeuvre (VD_{max}), venous diameter change (VD_{diff}) in mm and reflux time (t_r) in seconds in the common femoral vein (CFV), the superficial femoral vein (SFV) and the long saphenous vein (LSV). $n = 80$ limbs in 40 subjects: paired *t*-test.

Vein segments	VD_{rest}*	VD_{max}*	VD_{diff}**	t_r***
CFV	8.3 ± 2.2	11.1 ± 2.8	2.8 ± 1.7	0.61 ± 0.63
SFV	5.9 ± 1.3	7.2 ± 1.6	1.3 ± 0.67	0.25 ± 0.26
LSV	3.5 ± 0.9	4.3 ± 1.4	0.75 ± 0.19	0.28 ± 0.4

* $p<0.0001$ for comparison VD_{rest} and VD_{max} in all three vein segments.
** $p<0.0001$ for comparison CFV and SFV, CFV and LSV, SFV and LSV, respectively.
*** $p<0.0001$ for comparison CFV and SFV, CFV and LSV, respectively, $p = 0.7$ for comparison SFV and LSV.

Table 2. Mean ± S.D. venous diameter in mm at rest (VD_{rest}) and during Valsalva (VD_{max}) as well as reflux time (t_r) in seconds, in the CFV, the SFV and the LSV in subjects with BMI ≤22.5 kg/m^2 and BMI >22.5 kg/m^2: unpaired *t*-test.

Parameter	BMI ≤22.5	BMI >22.5	*p*
CFV: VD_{rest}	7.8 ± 2.1	8.9 ± 2.1	0.02
SFV: VD_{rest}	5.6 ± 1.3	6.0 ± 1.2	0.2
LSV: VD_{rest}	3.2 ± 0.7	3.9 ± 1.0	0.02
CFV: VD_{max}	10.4 ± 2.4	11.9 ± 3.1	0.02
SFV: VD_{max}	6.8 ± 1.4	7.6 ± 1.7	0.02
LSV: VD_{max}	3.9 ± 0.7	4.6 ± 1.7	0.01
CFV: t_r	0.45 ± 0.38	0.81 ± 0.79	0.01
SFV: t_r	0.19 ± 0.10	0.33 ± 0.38	0.04
LSV: t_r	0.18 ± 0.10	0.31 ± 0.35	0.02

Table 3. Mean ± S.D. venous diameter in mm at rest (VD_{rest}) and during Valsalva (VD_{max}) as well as reflux time (t_r) in seconds in the CFV, the SFV and the LSV in males and female subjects: unpaired *t*-test.

Parameter	Female	Male	*p*
CFV: VD_{rest}	7.4 ± 2.2	9.6 ± 2.1	0.003/0.09*
SFV: VD_{rest}	5.3 ± 1.1	5.8 ± 1.6	0.3
LSV: VD_{rest}	3.2 ± 0.6	3.4 ± 0.8	0.3
CFV: VD_{max}	10.3 ± 2.9	12.3 ± 2.9	0.03/0.5*
SFV: VD_{max}	6.4 ± 1.3	7.3 ± 2.1	0.1
LSV: VD_{max}	3.7 ± 0.71	4.2 ± 1.1	0.1
CFV: t_r	0.30 ± 0.20	0.72 ± 0.78	0.03/0.05*
SFV: t_r	0.19 ± 0.07	0.31 ± 0.29	0.1
LSV: t_r	0.16 ± 0.06	0.32 ± 0.41	0.1

* After adjustment for BMI.

Results

Valves

In the CFV valves were visualised by B-mode proximal to the saphenofemoral junction in nine legs (11%) of four male and five female subjects and distal to the saphenofemoral junction in 52 legs (65%) of 36 female and 16 male subjects. In the LSV and the SFV at least one valve was seen in 100% of the limbs investigated.

Venous diameter

Resting and maximal diameters during the Valsalva manoeuvre are given in Table 1. The Valsalva-dependent change in diameter was statistically significant for all vein segments investigated. The difference between VD_{rest} and VD_{max} in the CFV was significantly larger than the difference regarding these values for the SFV and the LSV, as listed in Table 1.

Reflux parameters

Valve closure was achieved in all investigated vein segments. Reflux times for all subjects are summarised in Table 1. CFV reflux time exceeded 0.5 s in six limbs (range: 0.5–2.6 s), in the LSV in three limbs (range: 0.5–2.4 s) and in the SFV in four limbs (range: 0.5–1.9 s).

Impact of body mass index

In subjects with BMI >22.5 kg/m^2 venous diameters were significantly larger and reflux times were significantly longer than in subjects with BMI ≤22.5 kg/m^2. Results are listed in Table 2.

Differences according to sex

After adjustment for BMI the resting diameter, maximum diameter during the Valsalva manoeuvre, and reflux time were not statistically significantly different between sexes, except that reflux time in the CFV was significantly longer in males than in females. The results are summarised in Table 3.

Impact of family history

In subjects with first-degree relatives suffering from varicose veins ($n = 19$) the mean resting venous diameter in the SFV as well as the maximal venous diameter in the LSV were significantly larger than in family history negative cases, as shown in Table 4. Regarding all other variables assessed, there were no further significant differences.

Table 4. Mean ± s.d. venous diameter in mm at rest (VD_{rest}), maximal venous diameter during Valsalva manoeuvre (VD_{max}) and reflux time (t_r) in seconds in the CFV, SFV and the LSV in 19 subjects with (FH pos) and 21 without (FH neg) family members suffering from varicose veins: unpaired *t*-test.

	FH neg $n=21$	FH pos $n=19$	p
CFV: VD_{rest}	8.6 (±2.4)	7.9 (±1.8)	0.1
SFV: VD_{rest}	5.6 (±1.4)	6.2 (±1.0)	0.02
LSV: VD_{rest}	3.3 (±0.7)	3.6 (±0.7)	0.09
CFV: VD_{max}	11.4 (±3.0)	10.8 (±2.6)	0.3
SFV: VD_{max}	6.9 (±1.8)	7.4 (±1.3)	0.2
LSV: VD_{max}	3.9 (±0.9)	4.4 (±0.9)	0.05
CFV: t_r	0.53 (±0.63)	0.71 (±0.63)	0.2
SFV: t_r	0.26 (±0.23)	0.25 (±0.29)	0.8
LSV: t_r	0.25 (±0.32)	0.31 (±0.46)	0.5

Table 5. Mean coefficient of variation (± s.d.) of venous diameters at rest (VD_{rest}), maximal venous diameter during Valsalva manoeuvre (VD_{max}) and reflux times (t_r) in the CFV, the SFV and the LSV.

Vein segment	VD_{rest} (%)	VD_{max} (%)	t_r (%)
CFV	3.8 (±1.4)	3.3 (±0.9)	13.0 (±3.1)
SFV	4.8 (±2)	3.7 (±1)	10.4 (±3.7)
LSV	5.0 (±1.9)	3.6 (±1.6)	10.9 (±4.5)

Reproducibility of the measurements

The reproducibility of the measurements was tested by studying five legs in five healthy subjects five times. The mean coefficients of variation are listed in Table 5.

Discussion

Increase of venous diameters

Normal values for venous diameters reported in this trial were in good agreement with reference values obtained from B-mode or M-mode measurements.[5] The diameters in all three vein segments investigated increased during the Valsalva manoeuvre. The most pronounced effects, up to 30%, were seen in the CFV. The less-marked Valsalva effects seen in the SFV and the LSV are probably due to the higher frequency of valves in these segments. This may have two effects: firstly, a competent valve will "dampen" the Valsalva effect measured distally to the valve; secondly, valve-tissue contains a high amount of collagen fibres[1] and it may be postulated that the distensibility of the venous wall directly adjacent to the valve area may be lower. The hypothesis that the number of valves and the differing composition of the vascular wall in the valve area are the explanation for differing Valsalva effects in different segments is supported by the literature,[10,11] as well as by the distribution of valves seen in this study. Gender had no influence on resting diameters and maximum diameters during Valsalva manoeuvre, as long as diameters were adjusted by BMI.

Venous diameters and the family history

Griton and Schadeck investigated 237 children of mothers suffering from varicose veins.[12] In 96% of the children enlarged palpable saphenous veins were found; in 54% all four saphenous veins were affected. This is in agreement with our finding that subjects with a positive family history had an increased maximal venous diameter in the LSV during the Valsalva manoeuvre, and larger resting diameters in the deep vein (SFV). However, the significance of an increased deep venous resting diameter as a prognostic factor for varicose vein disease must be evaluated in long-term prospective studies.

The impact of BMI

Lapidus *et al*. found a positive correlation between a high body mass index and the occurrence of varicose veins.[13] It was hypothesised that in patients with a high BMI the baseline compliance of the venous wall may be higher, the resting diameter larger, and the diameter change following the Valsalva manoeuvre may be more pronounced.[13] Our results support this hypothesis, as we found larger venous diameters and longer reflux times in subjects with higher BMI (>22.5 kg/m^2). Long-term follow-up studies are needed to allow final conclusions to be drawn about the impact of the BMI on the evolution of varicose vein disease.

Valsalva manoeuvre and venous reflux

The provocation of deep venous reflux is performed to test for the competence of deep venous valves. Reflux can be provoked in two ways: by the rapid release of distal compression or the application of proximal pressure. Either way, valve closure results from a retrograde flow that is elicited by a reversed transvalvular gradient. In the first case, this pressure gradient is composed of the negative pressure occurring with cuff release plus gravitational forces on the blood column if the subject is in the upright position. In the latter case the closure of the valve is not simply a response to the cessation of forward flow, but requires the generation of a reverse flow exceeding a certain threshold velocity[14]; this retrograde flow velocity is the flow equivalent to a sudden reversal of the pressure gradient. Rather than applying proximal manual pressure or using a distal blood pressure cuff, the Valsalva manoeuvre will lead to the physiological effect of a reversed deep venous pressure gradient with consecutively induced reverse flow. Using the Valsalva manoeuvre, some points must be considered which potentially interfere with the interpretation of the test results:

(a) functional iliofemoral valves may interfere with the testing of deep venous valves in a more distal segment. In autopsy studies iliac valves were shown to be present in up to 24%.[11] However, as the Valsalva manoeuvre was successfully applied in a number of test series in the literature[6,14,15] as well as in this trial, the functionality of these valves may be doubted. So far, this question has never been answered beyond doubt;
(b) a suboptimal increase in intra-abdominal pressure by a non-standardised Valsalva manoeuvre can result in a reverse venous pressure gradient below threshold, leading to a low velocity leakage through still-open valves, which should not be confused with the reverse flow required to test valve competence;[14]
(c) the subject's position will influence the test results. The pressure gradient resulting from the Valsalva manoeuvre applied to a subject in supine position is the equivalent of an increase in intra-abdominal pressure. Also, as shown in this paper, the vein diameter increases significantly, increasing the capacity of the venous segment under investigation. In a standing position, the pressure gradient produced by the Valsalva manoeuvre will represent the sum of the intra-abdominal and the hydrostatic pressure. As shown in the literature, a significant Valsalva-related venous dilation does not occur in this situation,[15] resulting in much shorter reflux times in an upright as compared to a supine position;[6]
(d) even in studies using the Valsalva manoeuvre as a reflux-provocation test in a supine patient position, results on reflux times vary substantially. For the CFV, van Bemmelen describes a mean reflux time in healthy volunteers of 1.77 ± 0.96 s.[16] Masuda *et al.*, using Valsalva in a 15° reverse Trendelenburg position, found a reflux time of 1.3 ± 2.1 s.[6] In the present study the normal reflux time amounted to 0.61 ± 0.63 s. Assuming that all the studies were correctly performed, the most plausible explanation would be that the reverse pressure gradient resulting from the Valsalva manoeuvre varied widely between studies. Thus normal values for the venous reflux time provoked through a Valsalva manoeuvre are not comparable between centres and trials, as long as the Valsalva manoeuvre is not standardised.

Standardisation is needed in respect of the time to build up a reverse pressure gradient, the magnitude of the pressure gradient and the period during which the pressure gradient is effective. The situation is further complicated by the fact that no "gold standard" yet exists; in this study the Valsalva manoeuvre was standardised by predefining the pressure build-up time (0.5 s), the expiratory pressure (30 mmHg) and a minimum time period during which the pressure gradient was effective (≥ 3 s).

This procedure resulted in highly reproducible reflux times with coefficients of variation ranging between 3.3% and 16.4% for the CFV, the SFV and the LSV, and may thus be recommended for further use in the future. If a standardised test is widely used, it will be possible to compare results between studies and draw more reliable conclusions about the relationship between the test results.

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