Gravity force is not a sole explanation of reflux flow in incompetent great saphenous vein

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ABSTRACT

Objective: This study aimed to evaluate the impact of gravity, reservoir size, and competence of the ostial valve on venous reflux in different body positions.

Methods: Our study included 61 lower limbs with primary incompetence of the great saphenous vein (GSV). The diameter of the GSV and its cross-sectional area, time-averaged mean velocity (TAMEAN), and reflux time (RT) were measured with duplex ultrasound with pulsed wave Doppler. Reflux volume (RV) and reflux volume flow rate (Q) were calculated. The measurements were carried out in three body positions: horizontal, A; seated upright with stretched legs, B; and vertical, C. Distal automatic cuff compression-decompression (120 mm Hg) was used as a provocation maneuver.

Results: There was 100% occurrence of reflux in the patient positions B and C. Reflux was observed in 91.8% of cases in position A. All reflux parameters (TAMEAN, RT, Q, RV) and the size of the vein were significantly different in the three studied positions. The patient's height did not influence the magnitude of change in reflux parameters. All reflux parameters increased more significantly when the position changed from A to B than from B to C (TAMEAN, +103% and +37%; GSV diameter, +33% and +5%; RV, +408% and +65%, respectively).

Conclusions: Observed positional changes in reflux parameters suggest that gravitational forces are not a sole explanation for reflux flow in incompetent GSV. It is likely that the gravitational effect on venous flow is mediated by the changes in vein diameter and the total volume of the venous reservoir of the leg. (J Vasc Surg: Venous and Lym Dis 2019;7:693-8.)

Keywords: Venous reflux; Gravity force; Duplex ultrasound; Varicose veins

Chronic venous disease (CVD) is an important public health problem. It affects up to 60% of the general population[1] and consumes 1% to 2% of the total expenditure of the health care system in European countries. The most severe form of CVD, venous leg ulcers, affects about 1% of the general population[2] and is associated with an even more significant socioeconomic impact.[2,3] CVD of primary etiology is the most common form of CVD[3] and progresses to chronic venous insufficiency at a rate of 4% per year.[4]

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Development of new diagnostic and treatment options for patients with primary CVD requires understanding of underlying pathologic mechanisms. Because the key pathologic feature of primary CVD is venous reflux, the focus of research has traditionally been the altered hemodynamics. Assessment of venous reflux conventionally relies on the use of duplex ultrasound and reflux-provoking maneuvers. Although it has been shown that nongravitational mechanisms play an essential role in venous hemodynamics,[5-7] the current concept of venous hemodynamics and its pathology assigns a dominant role to gravitational forces.[8-10] This focus on gravitational force is one of the reasons for discrepant findings between reflux parameters, such as reflux time (RT), reflux velocity, and reflux volume flow rate (Q), and the clinical severity of the disease. Several alternative approaches have been suggested to resolve this discrepancy. The concept of a venous reservoir[11] highlights the influence of residual volume and distal resistance on reflux parameters. It is reasonable to hypothesize that when the ostial valve is competent and the main source of blood flow during reflux is the great saphenous vein (GSV) tributaries, the reflux parameters should be different from cases in which reflux flow is coming from the common femoral vein. Such differentiation between combinations of competent and incompetent valves at the level of the saphenous junction was proposed as a more precise

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center prospective experimental study
- **Key Findings:** In 61 lower limbs with primary incompetence of the great saphenous vein, reflux was observed in 91.8% of cases in the horizontal position. All reflux parameters increased more significantly when the position changed from horizontal to sitting with stretched legs than from sitting to standing (time-averaged mean velocity, +103% and +37%; diameter of the great saphenous vein, +33% and +5%; reflux volume, +408% and +65% respectively).
- **Take Home Message:** The gravitational effect on venous reflux is mediated by changes in vein diameter and the total volume of the venous reservoir of the leg.

approach to clinical management,[12] but the hemodynamic aspects of this approach were not independently investigated with ultrasound.

The aim of this study was to evaluate the relative impact of gravitational force, reservoir size, and competence of the ostial valve on the hemodynamic parameters of reflux in the GSV.

METHODS

Study design. This is a prospective, single-center experimental study. The local ethics committee approved the research. Patients gave their voluntary consent. The inclusion criterion was primary incompetence of the GSV and its varicose tributaries (Clinical, Etiology, Anatomy, and Pathophysiology classification C_{2-6}, E_p, A_s, $P_{r,2,3}$). Exclusion criteria were incompetence of the small saphenous vein or nonsaphenous veins, deep venous incompetence or obstruction, iliac and pelvic vein reflux or obstruction, previous venous surgery or injection sclerotherapy, and patients with arterial insufficiency ankle-brachial index <1.0.

Study protocol. All patients underwent a complete physical examination and duplex ultrasound to determine their eligibility for inclusion in the study. Duplex ultrasound served as the main investigational tool. All ultrasound examinations were performed by a trained ultrasonographer experienced in venous disease. The GSV site for subsequent repeated measurements was marked by a permanent marker. This place was 10 to 15 cm distal to the saphenofemoral junction. In patients with bilateral disease, one leg was randomly selected for study.

The diameter of the GSV and its cross-sectional area were measured in a cross-sectional B-mode image. After a provocation maneuver, time-averaged mean velocity (TAMEAN) and RT were measured by the pulsed wave Doppler in a longitudinal plane with sample volume adjusted to insonate the entire lumen of the vessel. The Doppler insonation angle was set to 60 degrees. Q rate was calculated as the product of TAMEAN and cross-sectional area. Reflux volume (RV) was calculated as the product of Q and RT.

The temperature in the research room was maintained at 22°C. An automatic cuff compression-decompression maneuver was used (Hokanson Inc, Issaquah, Wash). The cuff was positioned at the widest part of the calf, and its position was maintained unchanged through the entire study.

The measurements were performed in three body positions: horizontal, A; seated upright with stretched legs, B; and vertical, C (Fig 1). Patients were initially placed in position A. Rectangular support rollers were put under the head, shoulders, buttocks, and feet to keep the entire lower extremity at a distance from the examination table. Patients were at rest for 10 minutes to stabilize venous flow in the legs before ultrasound measurements.

After completion of all measurements in position A, patients were transferred to position B. Support rollers were put under buttocks and feet. After a 5-minute rest, the same measurements were repeated.

The same procedure was followed for position C. In this position, patients were holding onto a frame and putting all the weight on the contralateral extremity.

Stepwise positional change from A to C gradually increases gravitational hydrostatic force in each of the patients (Fig 1). Because patient height defines the magnitude of this increase, the relationships between reflux parameters and patient height were used to define the influence of gravitational forces.

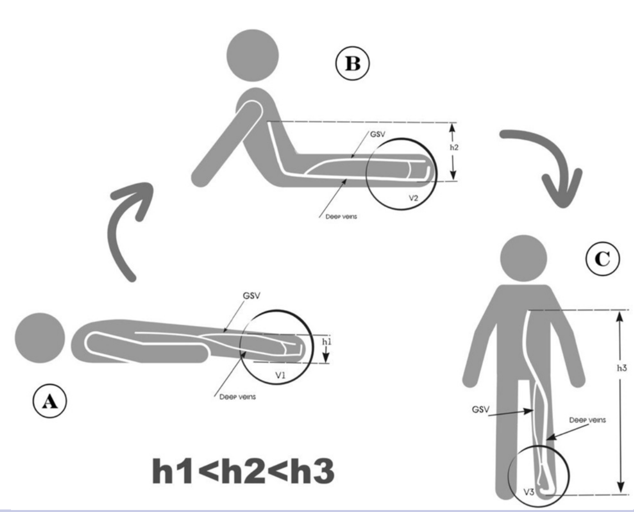

Fig 1. The change of body position (A, horizontal; B, sitting upright with stretched legs; C, vertical) and size of the veins. *h*, Height of blood column; *GSV*, great saphenous vein; *V*, venous reservoir.

Table I. Patients' demographics

Parameters	No.	Minimum	Lower quartile (Q25%)	Median	Upper quartile (Q75%)	Maximum
Age, years	61	19.0	39.0	45.0	57.0	75.0
Height, cm	61	150.0	161.0	165.0	175.0	186.0
Weight, kg	61	45.2	70.9	80.3	86.4	122.9
BMI, kg/m2	61	18.7	24.7	28.2	31.4	38.0
VCSS	61	1.0	3.0	4.0	5.0	11.0

BMI, Body mass index; *VCSS,* Venous Clinical Severity Score.

Statistical analysis. Median and interquartile range were used for describing quantity parameters. Nonparametric analyses were performed for statistical evaluation of the data. The Mann-Whitney *U* test was used to compare two groups, and the Kruskal-Wallis test was used to compare more than two groups. The differences in the proportion of the groups were analyzed using χ^2 test. The quantitative parameters in different body positions were compared using the Friedman test. Correlation analysis of quantitative parameters uses the Spearman rank correlation coefficient (*r*). The $|r| > 0.7$ was used as a strong correlation criterion. Statistical significance was defined as $P < .05$. The analysis was performed with Statistica 10 (StatSoft Inc, Tulsa, Okla) and JMP 11 (SAS Institute, Cary, NC).

The sample size was calculated on the basis of data published regarding the variability of reflux parameters.[13] Accepting an α error of .05 (two sided) and β error of .2 of detecting a true difference, the total number of patients needed to be studied to detect a 10% difference in RT is 60.

RESULTS

There were 61 patients (20 men, 41 women) included in this study. Distribution of patients according to clinical class was as follows: C2, 47 (77%); C3, 8 (13.1%); C4 to C6, 6 (9.9%). The patients' demographics are shown in Table I. Seventeen patients (28%) had normal body mass index (BMI; 18.5-24.9 kg/m^2), 23 patients (38%) were overweight (BMI 25-29.9 kg/m^2), and 21 patients (34%) were obese (BMI >30.0 kg/m^2). The ostial valve was incompetent in 53 patients (86.9%) and competent in 8 (13.1%) patients. GSV reflux was present in 56 (91.8%) cases in position A and in all cases in positions B and C.

All reflux parameters (TAMEAN, RT, Q, RV) and the size of the vein were significantly different in the three studied positions (Table II). After the patient's transition from position A to position B, TAMEAN increased on average by 103%; and after the transition from position B to position C, it increased an additional 37%. Similarly, the vein diameter increased by 33% after the transition from position A to position B and by an additional 5% after the transition to position C. The corresponding increases in RV were 408% and 65%.

In all three positions, GSV diameter was associated with body weight (Spearman ρ = 0.43, 0.42, and 0.41, corresponding to positions A, B, and C) but less so with height (Spearman ρ = 0.3, 0.35, and 0.31).

The patient height did not influence the magnitude of change in reflux parameters (RT, TAMEAN, Q, and RV). The positional changes in RT (from position A to B [Fig 2] and from position B to C [Fig 3]) and TAMEAN (Figs 4 and 5) were not related to the change in vein diameter. However, the increase of RV after transition from position A to position B was relatively more influenced by the increase in diameter (Pratt $r^2 = 0.785$; $P < .0001$) than by the change in TAMEAN (Pratt

Table II. Reflux parameters and size of the great saphenous vein (GSV) in the studied positions

	Position A	Position B	Position C	*P*	*P*, A vs B	*P*, B vs C
D, mm	4.8 (3.9-6.0)	6.4 (5.2-7.4) (33%)[a]	6.7 (5.8-7.8) (4.7%)[b]	<.0001	.0041	.0120
S, cm^2	0.2 (0.1-0.3)	0.3 (0.2-0.4) (65%)[a]	0.4 (0.3-0.5) (12%)[b]	<.0001	.0048	.0104
TAMEAN, cm/s	3.4 (2.3-5.6)	6.9 (5.0-8.8) (103%)[a]	9.4 (7.4-12.5) (37%)[b]	<.0001	.0212	.0017
RT, seconds	3.0 (1.6-4.2)	4.5 (3.5-5.7) (50%)[a]	4.85 (3.7-6.0) (7%)[b]	<.0001	.0023	.9903
Q, mL/s	0.7 (0.4-1.7)	2.0 (1.1-3.6) (180%)[a]	3.89 (2.0-5.8) (90 %)[b]	<.0001	.0358	.0005
RV, mL	2.0 (0.8-5.4)	10.4 (5.9-16.1) (408%)[a]	17.0 (10.3-25.3) (65%)[b]	<.0001	.0002	.0005

D, Diameter; *Q,* reflux volume flow rate; *RT,* reflux time; *RV,* reflux volume; *S,* cross-sectional area; *TAMEAN,* time-averaged mean velocity.
The data are presented as median (interquartile range). *P* value for Friedman test. Statistical significance was defined as $P < .05$.
[a]The parameters are increasing regarding position A.
[b]The parameters are increasing regarding position B.

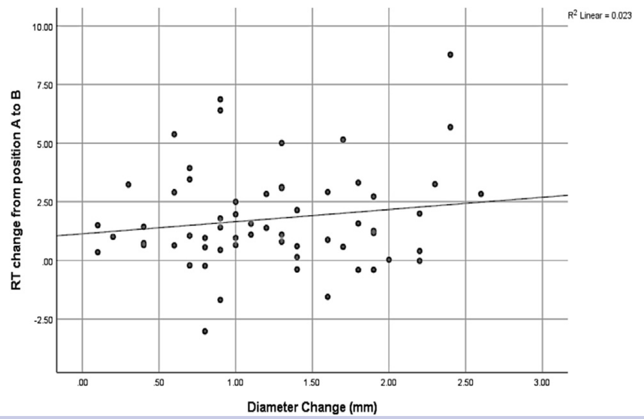

Fig 2. Positional changes (from A to B) in great saphenous vein (GSV) diameter and reflux time (*RT*).

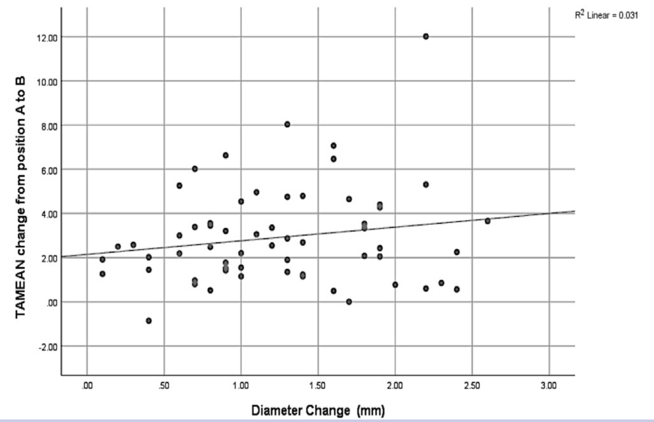

Fig 4. Positional changes (from A to B) in great saphenous vein (GSV) diameter and time-averaged mean velocity (*TAMEAN*).

r^2 = 0.215; $P < .0001$). Interestingly, these relationships reversed after transition from position B to position C, and increase of RV was relatively more influenced by the increase in TAMEAN (Pratt $r^2 = 0.636$; $P < .0001$) than by the change in diameter (Pratt $r^2 = 0.136$; $P = .003$).

The competence of the ostial valve significantly influenced positional changes in reflux parameters (Table III).

DISCUSSION

The main finding of the study was the discrepancy between the predicted and measured change in reflux parameters. The magnitude of the change in the gravitational force acting on the blood in the lower extremities is much larger when the patient transitions from sitting to standing position compared with the transition from a horizontal to a sitting position (Fig 1). Contrary to this change in the gravitational force, the increase in reflux velocity was larger when position changed from horizontal to sitting (+103%) than from sitting to standing (+37%). In addition, in the majority of patients (92%), a calf compression-decompression maneuver resulted in significant reflux even when the patient was in a horizontal position, in which gravitational force is negligible. These findings indicate that gravity does not directly influence reflux occurrence and reflux hemodynamic parameters.

The presence of reflux in horizontal and in reversed Trendelenburg position was consistently reported before.[13-16] Despite these observations, the gravitational forces are frequently considered the cause of and the necessary condition for reflux occurrence.[8,9]

The indirect effect of gravity was observed in this study as the difference in RV in three body positions (Table II). Change in the patient's position was associated with statistically significant change in diameter of the GSV. In turn, diameter of the GSV correlated with RV in all positions (A, $r = 0.83$ [$P < .001$]; B, $r = 0.79$ [$P < .001$]; C, $r = 0.81$ [$P < .001$]). That GSV diameter and RV have a direct

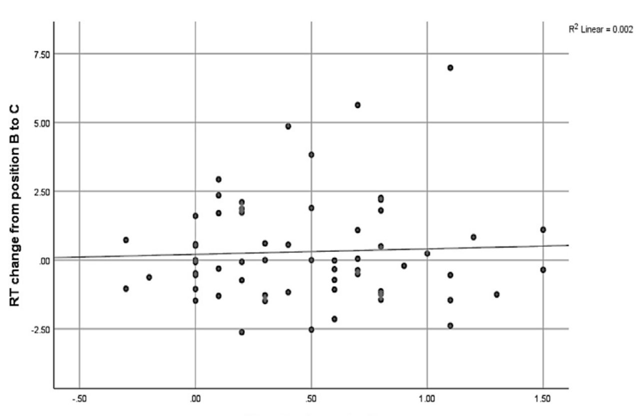

Fig 3. Positional changes (from B to C) in great saphenous vein (GSV) diameter and reflux time (*RT*).

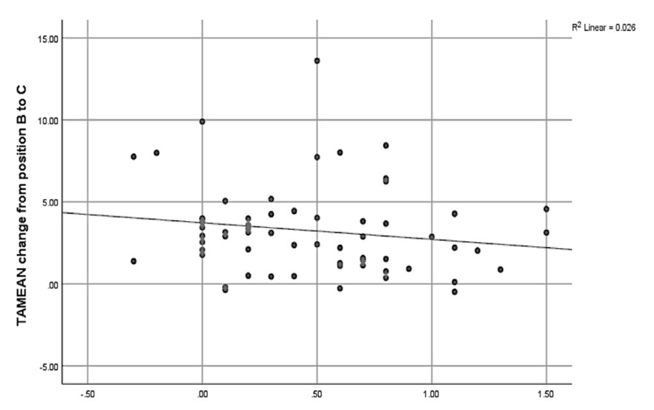

Fig 5. Positional changes (from B to C) in great saphenous vein (GSV) diameter and time-averaged mean velocity (*TAMEAN*).

Table III. Reflux volume (RV) change in different body positions in patients with competent and incompetent ostial valve

	Incompetent ostial valve (n = 53)	Competent ostial valve (n = 8)	*P*
Position A	2.7 (1.1-6.9)	0.5 (0.3-0.7)	.0018
Position B	11.3 (7.8-16.4)	3.5 (1.0-6.0)	.0004
Position C	18.2 (11.8-27.6)	6.9 (4.1-9.8)	.0007

The data are presented as median (interquartile range). *P* value for Mann-Whitney *U* test. Statistical significance was defined as $P < .05$.

correlation was established before.[17,18] Although the volume of the entire venous reservoir of the leg was not measured in this study, it is reasonable to assume that its changes were similar to changes in GSV diameter and were caused by the increase in gravitational force.[19,20] Because BMI is a good surrogate for measurement of lower leg venous reservoir capacity,[21] it was not surprising that it correlated with RV in each of the three positions (A, $r = 0.42$ [$P < .0001$]; B, $r = 0.38$ [$P < .0001$]; C, $r = 0.43$ [$P < .0001$]).

This study was not designed to differentiate the role of venous reservoir capacity vs GSV diameter on the volume of reflux. The observation that RV correlated with GSV diameter independent of body position and that positional changes in RV are similar in subgroups with different initial GSV diameter suggests that RV changes reflect just the change in GSV diameter (Table IV). This, however, was not the case. Although mean TAMEAN values were higher in positions B and C, the relative positional change in TAMEAN did not follow the same pattern, and resulting RV was less dependent on positional change than on GSV diameter. Examining relative strength of associations between positional changes in RV and other parameters showed that after transition from position A to position B, RV was relatively more influenced by the increase in diameter (Pratt $r^2 = 0.785$; $P < .0001$) than by the change in TAMEAN (Pratt $r^2 = 0.215$; $P < .0001$). It is likely that the venous reservoir capacity of the leg and its positional change influenced RV at least as much as the GSV diameter. These relationships may explain the association between BMI and severity of CVD.[22-24]

It has been recognized that the flow from the tributaries contributes to reversed flow in the GSV during the time of reflux.[8,12] This was reported in cases of the competent ostial valve and incompetent more distal segments of the GSV. The hemodynamic role of the ostial valve has been studied by using air plethysmography. In this study, patients with competent ostial valve and with incompetent ostial valve had a statistically significant difference by venous filling index and did not have a difference by residual volume fraction.[25] In our study, extremities with an incompetent ostial valve had a larger magnitude of RV than extremities with a competent ostial valve. This difference was greater in position A and progressively smaller in positions B and C, suggesting again that the gravitational forces alone are not sufficient to explain observed patterns of blood flow in incompetent veins.

CONCLUSIONS

Observed positional changes in reflux parameters suggest that gravitational forces are not a sole explanation of reflux flow in incompetent GSV. It is likely that the gravitational effect on venous flow is mediated by the changes in vein diameter and the total volume of the venous reservoir for the leg. These observations warrant further investigation of the mechanisms behind the occurrence and severity of venous reflux.

AUTHOR CONTRIBUTIONS

Conception and design: RT
Analysis and interpretation: RT, FL, SS, DB, KM
Data collection: RT
Writing the article: RT, FL
Critical revision of the article: RT, FL, SS, DB, KM
Final approval of the article: RT, FL, SS, DB, KM
Statistical analysis: RT, FL
Obtained funding: Not applicable
Overall responsibility: RT
RT and FL contributed equally to this article and share co-first authorship.

Table IV. Positional reflux volume (RV) changes in limbs with different great saphenous vein (*GSV*) diameters

	GSV <5.5 mm (n = 14)	GSV = 5.5-7.5 mm (n = 25)	GSV >7.5 mm (n = 22)	P ($df = 2$)	P, D_1 vs D_2	P, D_1 vs D_3	P, D_2 vs D_3
Position A	0.3 (0.0-0.6)	1.4 (1.0-2.7)	6.9 (4.0-13.1)	<.0001	.0247	<.0001	.0006
Position B	3.0 (1.2-6.1)	9.5 (6.3-12.4)	16.2 (14.1-24.5)	<.0001	.0119	<.0001	.0054
Position C	7.6 (5.1-11.2)	16.3 (10.3-21.0)	27.5 (18.7-37.7)	<.0001	.0147	<.0001	0.0115

The data are presented as median (interquartile range). *P* value for Kruskal-Wallis test. Statistical significance was defined as $P < .05$.

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