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Varicose vein treatment reduces edema not only in the treated legs but also in the entire body

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Abstract

Objectives: We explored the connection between varicose vein and edema, by investigating extracellular water ratio (E/T) using bioelectrical impedance analysis.
Methods: In a prospective cohort study 120 patients underwent varicose vein surgery with extracellular fluid to total body water ratio (E/T) and E/T postop divided by E/Tpreop (E/T ratio) measured using a body composition analyzer. Edema was defined as E/T ≥0.390. Seventy-nine patients received unilateral treatment, while 41 underwent bilateral. $p < .05$ is statistically significant.
Results: Preoperatively, patients exhibited edema (E/T) in the treated leg (0.394 ± 0.009), untreated leg (0.392 ± 0.009), trunk (0.390 ± 0.007), and whole body (0.391 ± 0.007). Postoperatively, E/T decreased across body ($p < .05$). The lowest E/T ratio was observed in the treated leg (0.991 ± 0.012), followed by the untreated leg (0.994 ± 0.012), the trunk (0.995 ± 0.009), and the whole body (0.994 ± 0.009). E/T ratio of bilateral group were lower than unilateral group ($p < .05$).
Conclusion: Varicose vein contributes to generalized edema, and treatment alleviates edema in the treated leg and the entire body.

Keywords

Varicose vein, generalized edema, extracellular water to total body water ratio

Introduction

The association between varicose veins and localized leg edema, as well as its subsequent reduction following surgical intervention, is well established.[1,2] An intriguing phenomenon often observed is the alleviation of knee pain in patients with knee osteoarthritis subsequent to varicose vein surgery, suggesting a potential link to edema reduction.[3]

Moreover, clinical anecdotes occasionally highlight instances where patients experience relief from ailments such as headaches and stiff necks following varicose vein surgery, albeit in an unanticipated manner.

Drawing upon these intriguing observations, we formulated a hypothesis positing that varicose veins might cause generalized edema, and surgical treatment of varicose veins might not only decrease edema in the treated leg but also the other parts of the body.

In the realm of cardiology, the assessment of water balance has been facilitated through bioelectrical impedance analysis, with the extracellular water/total body water ratio (E/T) serving as a recognized edema index.[4] The present study endeavors to scrutinize this hypothesis by investigating E/T.

Remarkably, our comprehensive review of existing literature yielded no precedent for the exploration of this novel hypothesis. Therefore, our investigation has the potential to instigate a burgeoning research domain, offering fertile ground for further inquiry and discovery.

Patients and methods

This original article is the prospective cohort study received ethical approval from the Institutional Review Board of Gifu Heart Center (IRB2022020). Informed consent was obtained to use data from medical chart from all patients.

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Between August and December 2022, a total of 120 cases underwent varicose vein surgery at Gifu Heart Center, Gifu, Japan. We identified venous insufficiency using echography. When patients had compression stockings prior to the surgical intervention, they had postoperatively, too. The stockings were used for 1 month postoperatively. The stockings were applied to the legs treated by radiofrequency ablation (RFA), sclerotherapy, high ligation, and additional varicose vein resection. We did not use the stockings for cyanoacrylate closure without performing any vein resection. Routinely on the day of operation we prescribed NSAID to be taken when they have postoperative pain. They usually had once or twice postoperatively.

Preoperatively, blood tests were conducted to assess N-terminal pro-brain natriuretic peptide (proBNP), albumin (Alb), and creatinine (Cr) levels. Patient background information was obtained from medical records. Using a body composition analyzer (InBody 770, InBody Japan Inc., Tokyo, Japan), various parameters—including body weight and extracellular fluid to total body water ratios (E/T) for right and left legs, trunk, and the whole body—were measured both before surgery and on postoperative day 7 (POD 7). The elastic stockings were removed when measuring body weight with a body composition analyzer, if they had been worn either before or after the operation.

Leg edema was defined as an E/T of ≥0.390.[4] The postoperative extracellular water to total body water ratio was divided by the preoperative extracellular water to total body water ratio to calculate the E/T ratio. The cases were stratified into two groups: unilateral group consisted of 79 patients who underwent surgery on the ipsilateral leg, while bilateral group comprised 41 patients who underwent bilateral leg surgery. For group 2, the E/T for each section were averaged from both legs.

Statistical analyses involved paired t-tests for intragroup comparisons and unpaired t-tests for intergroup comparisons. Patient background factors were assessed using chi-squared tests. A significance level of $p < .05$ was considered statistically meaningful. I disclose the use of AI and AI-assisted technologies to improve readability and language of the work. Data were described as mean ± SD.

Results

Patient characteristics

Patient characteristics were presented in Table 1 (Table 1). There was no exclusion case. Hyperlipidemia was observed in 54.2% of the patients, followed by hypertension at 35.8%, overweighted at 24.1%, diabetes at 23.3%, and slightly elevated proBNP levels at 118 ± 164 pg/mL.

We did not have any patients with venous obstruction or deep venous disease. CEAP classification distributed as follows: C0 (0), C1 (1), C2 (25), C3 (58), C4 (34), C5 (2), C6 (0). We have eight redo cases. Forty-three patients (35.8%) had compression stockings prior to the surgical intervention and postoperative compression rate was at 78.3%.

Table 1. General patient characteristics.

Number of patients	120
Gender	
Male	48 (40%)
Female	72 (60%)
Age (years)	67 (12)
Heart disease	12 (10%)
Hypertension	43 (35.8%)
Hyperlipidemia	65 (54.2%)
Diabetes	28 (23.3%)
Overweighted (>BMI 25)	29 (24.1%)
Diuretics	7 (5.8%)
proBNP (pg/ml)	118 (164)
Albumin (g/ml)	4.4 (0.3)
Creatinine (mg/ml)	0.8 (0.2)

Data are *n* (%), or mean (SD).
proBNP = N-terminal pro-brain natriuretic peptide.

A total of 161 legs in 120 patients were treated using various interventions: cyanoacrylate closure (CAC) (82), radiofrequency ablation (RFA) (17), high ligation (34), and sclerotherapy (28) for 108 great saphenous veins, 25 small saphenous veins, and 28 other veins (Table 2).

There were no significant difference between unilateral group and bilateral group in age (66.3 ± 13.1, 69.9 ± 9.5), female (47(59.5%), 25(61.0%)), hypertension (26(32.9%), 17(41.5%)), hyperlipidemia (42(53.2%), 23(56.1%)), diabetes (16(20.3%), 12(29.3%)) proBNP (115 ± 167pg/mL, 125 ± 159pg/mL) creatinine (0.8 ± 0.2 mg/mL, 0.8 ± 0.3 mg/mL)) except for obesity (13(16.5%), 16(39.0%) (p = .006) in the preoperative data. More than C3 in CEAP classification in unilateral group was at 74.7%, while that in bilateral group was at 85.4%.

preOP E/T

Preoperative extracellular fluid to total body water ratio (E/T) values were ≥0.390 for the treated leg, untreated leg, trunk, and whole body, indicating systemic edema (Table 3). Among these, the highest E/T value was observed in the treated leg, followed by the untreated leg (p = .096), the trunk (p = .0003), and the whole body (p = .0004).

The trend of preoperative E/T of unilateral and bilateral groups were similar to that of total cases in Table 3. In unilateral group preoperative E/T values were≥0.390 for the treated leg (0.394 ± 0.009), untreated leg (0.392 ± 0.009), trunk (0.390 ± 0.007), and whole body (0.390 ± 0.008), indicating systemic edema. Among these, the highest E/T

Table 2. Treatment modality and sites.

CAC	82 (50.9%)
RFA	17 (10.6%)
High ligation	34 (21.1%)
Sclerotherapy	28 (17.4%)
Total	161
GSV	108 (67.1%)
SSV	25 (15.5%)
Other	28 (17.4%)
Total	161

CAC = cyanoacrylate closure.
RFA = radiofrequency ablation.
GSV = great saphenous vein.
SSV = small saphenous vein.

Table 3. Preoperative value using InBody 770.

Body weight (kg)	59.9 (14.0)
BMI(kg/m²)	23.0 (4.2)
Body fat (%)	26.5 (8.5)
E/T	
Treat leg	0.394 (0.009)
Untread leg	0.392 (0.009)
Trunk	0.390 (0.007)
Whole body	0.391 (0.007)

Preoperative E/T of treated leg, untreated leg, trunk, and whole body ≥0.390.
Data are mean (SD).
E/T = extracellular water/total body water.

value was observed in the treated leg, followed by the untreated leg (p = .2791), the trunk at (p = .005), and the whole body (p = .005). Even untreated legs without venous insufficiency exhibited edema preoperatively. In the bilateral group, the averaged E/T value derived from both treated legs (0.395 ± 0.007) was found to be larger than that of the trunk (0.392 ± 0.007) (p = .019) and the whole body (0.392 ± 0.006) (p = .028).

Both the trunk and the whole body showed edema preoperatively in both groups. Although it did not reach significant difference, the E/T of the treated leg, trunk, and whole body in bilateral group was slightly higher than that in unilateral group.

postOP E/T

Post-surgery, a significant reduction in E/T was observed not only in the treated leg but also in the untreated leg, trunk, and whole body (p < .05) (Figure 1). Specifically, E/T values decreased from 0.394 ± 0.009 to 0.391 ± 0.009 in the treated leg, from 0.392 ± 0.009 to 0.390 ± 0.009 in the untreated leg, from 0.390 ± 0.007 to 0.389 ± 0.007 in the trunk, and from 0.391 ± 0.007 to 0.389 ± 0.007 in the whole body.

The extent of E/T changes was assessed using the E/T ratio (Figure 2). The lowest E/T ratio was observed in the treated leg (0.991 ± 0.012), followed by the untreated leg (0.994 ± 0.012), the trunk (0.995 ± 0.009), and the whole body (0.994 ± 0.009). The surgery most effectively reduced edema in the treated leg, followed by the untreated leg and the trunk.

The postoperative changes of E/T of unilateral and bilateral groups were similar to that of total cases in Figure 1. In unilateral group a significant decrease in E/T was observed not only in the treated leg but also in the untreated leg, trunk, and whole body after the surgery (p < .05). Specifically, E/T values decreased from 0.394 ± 0.009 to 0.391 ± 0.009 in the treated leg, from 0.392 ± 0.009 to 0.390 ± 0.009 in the untreated leg, from 0.390 ± 0.008 to 0.388 ± 0.008 in the trunk, and from 0.390 ± 0.008 to 0.388 ± 0.008 in the whole body. In bilateral group, There was same trend of decrease of ET as in unilateral group (p < .05). Specifically, E/T values decreased from 0.395 ± 0.007 to 0.391 ± 0.008 in the treated leg, from 0.392 ± 0.007 to 0.389 ± 0.007 in the trunk, and from 0.392 ± 0.006 to 0.388 ± 0.007 in the whole body.

The E/T ratios of the treated leg, trunk, and whole body in bilateral group were significantly lower than those in unilateral group (Figure 3). The extent of reduction of edema was much observed in the treated leg, trunk, and whole body in bilateral group compared to unilateral group.

The treated legs of preoperative E/T and E/T ratio in CEAP were comparable between more than C3 (95 cases) and less than C2 (25 cases), with no significant differences observed: (0.394 ± 0.009 vs 0.395 ± 0.008) and (0.991 ± 0.012 vs 0.991 ± 0.01), respectively (NS).

In examining the impact of compression stockings, Dr. S.T. analyzed data from patients who underwent CAC for GSV of a unilateral leg (47 individuals). The preoperative E/T in the treated leg showed slightly higher values between stockings (0.395 ± 0.01) compared to those without compression (0.392 ± 0.09, NS). The patients were categorized into three subgroups: compression both preoperatively and postoperatively (14), compression only postoperatively (13), and no compression (20). The E/T ratio for patients with compression only postoperatively was the lowest (0.987 ± 0.008), followed by 0.996 for those without stockings (p = .01), and 0.996 for those with stockings both preoperatively and postoperatively (NS).

We used several procedure types to treat varicose veins. We examined the disparity in preoperative E/T and E/T ratio of the treated leg in the unilateral group, depending on the procedure type, including CAC (51), RFA (8), high ligation (10), and sclerotherapy (10). No statistically significant differences were observed among these procedures.

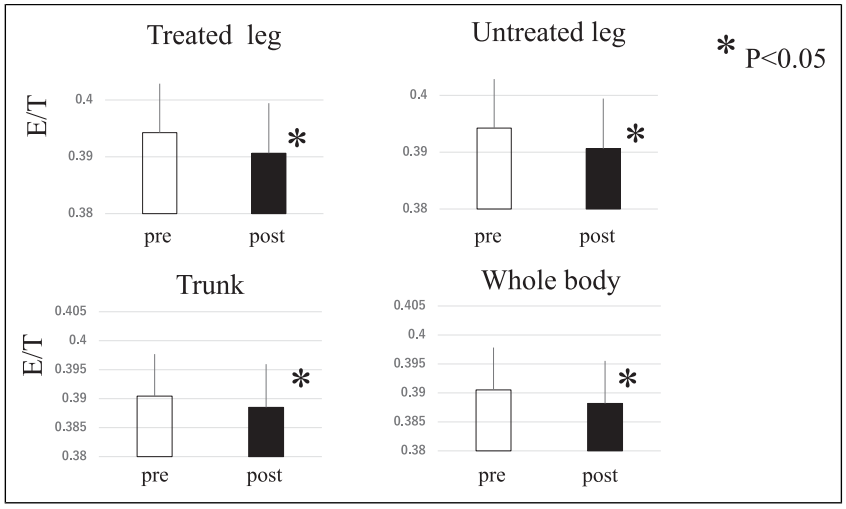

Figure 1. Postoperative changes of E/T. The E/T decreased not only in the treated leg but also in the untreated leg, trunk, and the whole body. (n = 120), E/T = extracellular water/total body water ratio, pre: preoperatively, post: on POD 7.

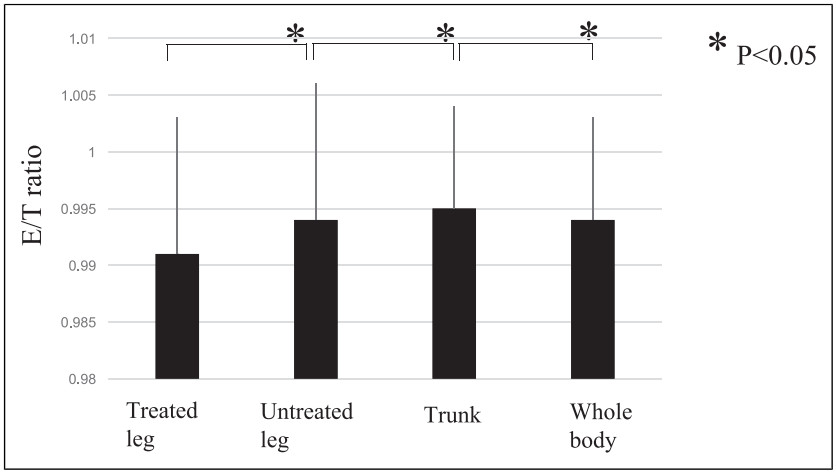

Figure 2. E/T ratio. The E/T ratio of the treated leg was the lowest, followed by the untreated leg, the whole body, and the trunk. (n = 120), The postoperative extracellular water to total body water ratio was divided by the preoperative extracellular water to total body water ratio to calculate the E/T ratio.

Discussion

In summary, patients with varicose veins frequently exhibit an extracellular water ratio exceeding 0.390, indicative of edema. After varicose vein treatment, the E/T ratio decreases not only in treated legs but also in the trunk and the entire body. Bilateral treatments yielded a more pronounced decrease in the E/T ratio compared to unilateral treatment.

Edema can be categorized as generalized edema related to heart or renal diseases and localized edema due to varicose veins.[5,6] Local edema attributed to varicose veins has traditionally been linked primarily to leg swelling within this context. It's important to acknowledge that generalized edema can affect various body parts, including the face, hands, and legs.

The previously described hypothesis in the literature that chronic venous disease is not merely peripheral venous reflux and dilated tortuous subcutaneous veins. It is a systemic condition that impairs the entire cardiovascular system.

Based on this previous idea, Our hypothesis was formulated, positing that varicose vein treatment not only reduces edema in treated legs but also extends its impact to untreated legs and the trunk. The study was designed with this hypothesis in mind.

Our analysis based on the Extracellular-to-Total body fluid ratio (E/T) revealed that a significant number of

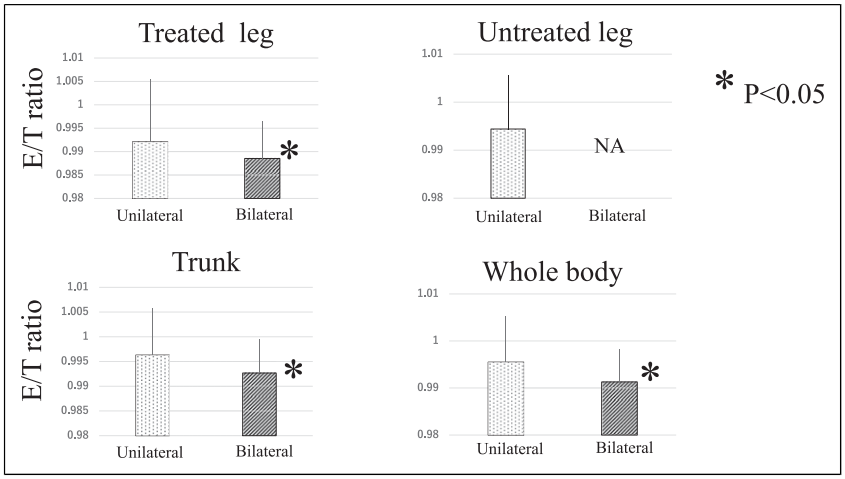

Figure 3. E/T ratio in unilateral and bilateral groups. The E/T ratio of the treated leg, the trunk, and the whole body in bilateral group was found to be lower than that of unilateral, The postoperative extracellular water to total body water ratio was divided by the preoperative extracellular water to total body water ratio to calculate the E/T ratio. Unilateral: unilateral group, bilateral: bilateral group.

patients with varicose veins experienced edema in both legs and the trunk. This observation suggests that varicose veins may contribute to trunk edema, indicating that untreated leg and the trunk were also edematous, potentially challenging the notion of their true health status.

These findings collectively suggest that varicose veins could potentially induce edema in multiple body parts beyond the affected legs. This premise is supported by the increase in E/T ratio exceeding 0.390 in the entire body.

Edema is characterized by the excessive accumulation of extracellular water due to microvascular circulation disturbances and venous insufficiency.[7] Understanding the mechanisms contributing to edema in chronic venous insufficiency is crucial for developing effective therapeutic strategies. In this paper, we explore various factors that may play a role in the observed edema in patients with venous insufficiency. Specifically, we discuss the impact of arterial stiffness, cardiac function, inferior vena cava (IVC) compliance, and circadian rhythms on edema development. By examining these factors, we aim to shed light on the complex interplay between venous insufficiency and its associated edema, providing insights that may inform clinical practice and treatment strategies.

One potential mechanism contributing to edema in venous insufficiency is arterial stiffness. The insufficiency of superficial veins can lead to increased vascular resistance in peripheral arteries. Studies conducted by E. Ozpelit et al. have suggested a link between chronic venous disease and subclinical conditions in both arterial and cardiac systems.[8] Elevated proBNP levels and increased arterial stiffness in patients with chronic venous insufficiency may be contributing factors.[9,10] The interplay between venous hypertension and arterial changes could explain the observed increase in arterial stiffness. Surgical intervention for varicose veins may reduce venous hypertension, leading to decreased arterial stiffness, which, in turn, facilitates smoother blood perfusion from the heart, ultimately reducing generalized edema and associated symptoms.

Impaired relaxation of the heart in patients with varicose veins is a result of two factors: impaired venous return and structural changes in the heart.[11] This leads to low central venous pressure and low early diastolic cardiac inflow, compensatorily increased late diastolic cardiac inflow, and increased central venous pressure (IVC diameters) and early diastolic cardiac inflow (E-waves). The study by Tamura et al. reported increased B-type natriuretic peptide (BNP) levels in patients with varicose veins, which decreased after surgical varicose vein removal.[12] In our study preoperatively slight elevation of proBNP was observed, too. This suggests that varicose veins can negatively impact cardiac function and their surgical removal can have a positive influence.

Chronic venous disease affects the function and morphology of the inferior caval system and the heart.[13] Compliance of the IVC during ventilation is compromised, reducing the suction power from the legs toward the heart. Patients with recurrent and bilateral varicose veins exhibit similar respiratory biometry of the IVC. Narrowing of the IVC with age may indicate more profound changes in systemic venous return in patients with varicose veins compared to those without chronic venous disease. [13]

While surgical intervention may improve peripheral venous return in healthier patients, it may be difficult to achieve the same level of improvement in more diseased and older patients due to structural changes in the IVC and right ventricle. Patients with good heart function show a

more rapid response to surgery, resulting in reduced edema-related symptoms.

Circadian rhythms may impact the severity of edema, with varicose legs exhibiting more swelling in the evening and reduced edema in the morning. Nocturnal polyuria shed light on a possible mechanism for whole-body edema. During the day, water intake and retention, exacerbated by venous insufficiency, contribute to leg edema. At night, the spine's position equalizes water distribution throughout the body, leading to increased urine production and reduced leg swelling upon waking. This ebb and flow pattern of water shift in the circadian rhythm by varicose veins may not only compromise heart function but also contribute to generalized body edema. Compression therapy, commonly employed for varicose veins, was found to increase right atrial pressure and transiently impair right and left ventricular function, potentially exacerbating cardiac issues.[14] This effect could be particularly significant during the circadian water shift at night.

Several potential factors can influence the E/T ratio. However, we observed no significant difference in preoperative E/T and E/T ratio concerning the type of procedure performed. Regardless of the procedure type, venous insufficiency can be mechanically treated. Patients wore compression stockings before surgical intervention due to compromised sensitivity to edema. Interestingly, their E/T remained higher even with compression compared to patients without compression preoperatively. The greatest magnitude of E/T change occurred with postoperative compression and surgical intervention, particularly when no preoperative compression was applied.

Several limitations of this study warrant consideration. The sample size is relatively small, and the establishment of robust evidence may necessitate further research through randomized controlled trials (RCTs). The subjective nature of the interviews and absence of quantification could be addressed in future investigations. Additionally, preoperative clinical complaints were not assessed in this study.

Conclusion

Our study reveals a crucial finding: individuals afflicted with varicose veins exhibit edema not only in their affected legs but also in other areas of the body. This underscores the notion that varicose veins constitute more than just a localized leg ailment; rather, they manifest as a systemic condition exerting influence on the entirety of the body.

In this paper, we present a pioneering investigation that sheds light on the potential benefits of varicose vein treatment in mitigating edema not only in the treated leg but also in the untreated leg and trunk. Through objective measurements, we have aimed to comprehensively elucidate the edema dynamics associated with varicose veins, spanning from the preoperative to the postoperative phase.

Through this study, we have inaugurated a novel avenue of research. The regulation of the extracellular fluid to total body water ratio (E/T) throughout the entire body may involve intricate hormonal pathways. Unraveling the mechanisms underlying the alleviation of discomforts in other body parts necessitates further exploration and investigation.

Author's note

We disclose the use of AI (Chat GPT) to improve readability and language of the work.

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Declaration of conflicting interests

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Ethical statement

Ethical approval

The Institutional Review Board (IRB) of Gifu Heart Center approved this study (IRB2022020).

Guarantor

ST.

Contributorship

ST researched literature and conceived the study and involved in protocol development, gaining ethical approval, and wrote the first draft of the manuscript. YK, MI, SO, and YO involved in patient recruitment and TM performed data analysis. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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