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Preoperative Venous Ultrasound Characteristics Identify Patients at High Risk for Venous-Lymphatic Reflux to Guide Vein Selection in Lymphaticovenous Anastomosis

Short title: Ultrasound Characteristics Guide Vein Selection in Lymphaticovenous Anastomosis

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Abstract

Background: Lymphaticovenous anastomosis (LVA) is an effective treatment for secondary lymphedema, but its success is limited by the risk of postoperative venous-lymphatic reflux (VLR). Preoperative identification of optimal recipient veins is crucial, yet a systematic approach leveraging venous ultrasound features to predict VLR risk remains undefined.

Methods: In this retrospective cohort study, we analyzed data from 43 patients with secondary lymphedema who underwent LVA, encompassing 423 anastomotic sites. We evaluated five preoperative venous ultrasound characteristics (venous diameter, compression reflux, orthostatic reflux, layer localization, bifurcation pattern) alongside clinical and laboratory parameters. A generalized linear mixed model (GLMM) was employed to identify significant predictors of VLR while accounting for within-patient clustering of multiple LVA sites. Model performance was assessed using the area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and predictive values.

Results: VLR occurred at 82 sites (19.39%). GLMM analysis identified orthostatic reflux (OR = 57.913, 95% CI: 15.383-218.033, $p < 0.001$) and compression reflux (OR = 13.402, 95% CI: 4.006-44.838, $p < 0.001$) as the strongest risk factors for VLR. Protective factors included the presence of bifurcation (OR = 0.100, 95% CI: 0.038-0.264, $p < 0.001$), subcutaneous tissue localization (OR = 0.190, 95% CI: 0.072-0.505, $p = 0.001$), and larger venous diameter (OR = 0.002, 95% CI: 0.000-0.021, $p < 0.001$). Advanced ISL stage and longer edema duration were also

significant clinical risk factors. The GLMM demonstrated excellent discriminative performance with an AUC of 0.935, high accuracy (0.939), and robust generalizability upon internal validation (mean cross-validation AUC = 0.909).

Conclusion: Preoperative venous ultrasound characteristics are potent, independent predictors of VLR risk following LVA. A model incorporating these features, particularly reflux status and venous diameter, can accurately stratify risk. Integrating this evidence into preoperative planning offers a novel strategy to optimize vein selection, potentially improving LVA outcomes by mitigating VLR.

Keywords: Lymphaticovenous anastomosis; venous-lymphatic reflux; venous ultrasound features; generalized linear mixed model; cross-validation

Introduction

Lymphedema is a chronic, progressive condition affecting approximately 130 million individuals globally. It imposes a significant burden on patients' quality of life and substantially increases the strain on healthcare systems [1]. Secondary lymphedema frequently arises as a complication of cancer treatment, particularly in breast or gynecological malignancies, with limb lymphedema representing the predominant manifestation [2, 3]. It occurs in approximately 20% of patients following lymph node dissection for breast, prostate, uterine, or skin cancers [4]. Lymphaticovenous anastomosis (LVA), a minimally invasive surgical technique involving the anastomosis of lymphatic vessels to adjacent veins to improve lymphatic drainage, has been shown to effectively reduce edema volume and mitigate the risk of associated complications, such as cellulitis [3, 5]. However, the efficacy of LVA is highly dependent on the precise preoperative identification of functional lymphatic vessels and suitable recipient veins, coupled with optimal anastomosis site selection [6, 7].

Preoperative planning is critical for successful LVA outcomes. It necessitates the accurate localization of functional lymphatics and appropriately sized recipient veins with favorable hemodynamics to minimize the risk of postoperative venous-lymphatic reflux (VLR) [6, 8]. Ultrasound imaging offers distinct advantages in venous mapping, including real-time visualization, lack of ionizing radiation, and dynamic assessment of venous hemodynamics. While traditional imaging modalities like indocyanine green (ICG) fluorescence lymphography remain the gold standard for

lymphatic mapping, they are limited by inadequate tissue penetration depth and the inability to reliably differentiate adjacent lymphatic channels from small superficial veins [9]. Recent advancements, such as magnetic resonance lymphangiography (MRL) and contrast-enhanced ultrasound (CEUS), have improved the capacity to distinguish lymphatics from veins. CEUS, in particular, enables dynamic blood flow visualization, aiding in the intraoperative identification of potential anastomotic veins [6, 10] Recent studies demonstrate that using portable devices (e.g., Vscan Air) enhances venous selection precision, reduces incision length, and improves surgical planning [11]. Preoperative venous ultrasound is integral to LVA planning, as it allows for the assessment of venous anatomy, measurement of venous diameter, and evaluation of venous reflux – all crucial factors determining surgical strategy [12-14]. Nevertheless, a systematic methodology for leveraging venous ultrasound features specifically to prevent VLR in preoperative planning remains undefined.

This study aims to evaluate the role of preoperative venous ultrasound characteristics in predicting the risk of VLR following LVA surgery. We retrospectively analyzed data from 43 patients with secondary lymphedema who underwent LVA at our institution. Clinical, laboratory, and five predefined venous ultrasonographic parameters (venous diameter, compression reflux, orthostatic reflux, layer localization, and bifurcation pattern) were collected from electronic medical records. To address the hierarchical data structure involving multiple LVA sites nested within individual patients, we employed generalized linear mixed models (GLMM) to identify significant risk factors for VLR while accounting for within-patient variability. Model

performance was rigorously evaluated using area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and predictive values. This retrospective analysis represents the first systematic effort to develop and validate a predictive model specifically incorporating detailed preoperative venous ultrasound features alongside clinical parameters for VLR risk assessment in LVA. While acknowledging the inherent limitations of the retrospective design, our findings provide valuable insights that may enhance preoperative vein selection and inform future prospective studies.

Materials and methods

Study design and patients

This retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Zhejiang Provincial People's Hospital (Approval No. 201700705B0), with all medical records collected retrospectively. Between January 2024 and January 2025, 43 consecutive patients with secondary lymphedema undergoing LVA were enrolled at our institution. Existing clinical data were extracted and aggregated from the electronic medical record system, including baseline demographics, intraoperative characteristics, and postoperative outcomes.

Venous ultrasound characteristics

Venous ultrasonographic characteristics were evaluated using a Siemens Sequoia ultrasound system (Siemens Healthineers AG, Erlangen, Germany) equipped with an

18H6L high-definition hockey-stick transducer operating at 18-22 MHz for precise visualization of micro-veins. Patients were initially placed in the supine position, with preoperative lymphatic mapping performed via contrast-enhanced lymphosonography to identify limb lymphatic vessels. Subsequently, veins within a 1 cm radius of the mapped lymphatics were systematically scanned. Five venous ultrasonographic characteristics were assessed (Figure 1): (1) Venous luminal diameter; (2) Reflux on compression (defined as positive if reverse flow was detected upon proximal limb compression, otherwise negative); (3) Orthostatic reflux (evaluated in the standing position, with reversal of flow direction compared to supine posture considered positive); (4) Layer localization categorized as either subcutaneous adipose tissue (SAT) or the layer above SAT (LASAT) based on sonographic stratification; and (5) Bifurcation pattern (classified as bifurcated or non-bifurcated according to branching morphology in the cross-sectional view).

LVA surgery

All procedures were performed by an experienced high-volume microsurgeon (Y.F.L.) under general anesthesia. Preoperative imaging with MRI, CEUS, and ICG fluorescence lymphography identified superficial lymphatic vessels and determined LVA incision sites. Microsurgical anastomoses were conducted under a ZEISS TIVATO 700 operating microscope at magnifications ranging from 30× to 42×. Lymphatic vessel patency was confirmed by intradermal ICG injection distal to the surgical field. Anastomotic sites were meticulously sutured using 11-0 nylon sutures. All patients had received no prior therapy before surgery and were administered no

anticoagulation postoperatively.

Outcomes

The primary outcome measure was anastomotic flow direction, intraoperatively assessed under a surgical microscope using ICG fluorescence imaging. Flow direction—determined by the net pressure gradient between the lymphatic vessel and recipient vein—was categorized as: (1) antegrade (lymph-to-vein flow), confirmed by ICG-enhanced lymphatic fluid entering the venous lumen; (2) retrograde (vein-to-lymph flow); or (3) stagnant, defined as stabilization of the lymph-blood interface at the anastomotic site without net flow. Retrograde and stagnant flows were classified as VLR-positive (venous-lymphatic reflux), while antegrade flow was designated VLR-negative for prognostic modeling and outcome assessment.

Statistical Analysis

Statistical analyses were performed using R software (version 4.3.1), with continuous variables compared using Mann-Whitney U tests and categorical variables assessed via Chi-squared tests. To address the hierarchical data structure involving multiple LVA sites nested within individual patients, generalized linear mixed models (GLMM) with binomial family and logit link function were implemented, incorporating patient-level random intercepts (1 | Patients) and 15 fixed effects encompassing clinical, laboratory, and venous ultrasound characteristics. Model convergence was ensured using the bobyqa optimizer with a maximum of 200,000 function evaluations, reverting to a simplified model based on preliminary significant predictors if convergence issues arose. Performance was evaluated using area under the receiver

operating characteristic curve (AUC), sensitivity, specificity, positive and negative predictive values, F1-score, and accuracy, with adjusted odds ratios and 95% confidence intervals calculated for all features and statistical significance defined as $p < 0.05$ (trends at $p < 0.1$). Comprehensive visualization included forest plots for feature effect sizes, ROC curves with AUC values, partial dependence plots for continuous variables, and proportion bar plots for categorical variables using Fisher's exact test for 2×2 tables or Chi-square tests with simulation for sparse data. Sensitivity analyses involved five-fold cross-validation for robustness assessment, utilizing R packages including lme4, ggplot2, pROC, forestplot, ggeffects, dplyr, sjPlot, caret, broom, and ggpubr.

Results

Study Cohort

A total of 43 patients with secondary lymphedema who underwent LVA surgery were ultimately included in this retrospective analysis, involving 423 anastomotic sites. The flow of participants through the study, including screening and exclusion criteria, is detailed in Figure 2. Preoperative clinical and laboratory characteristics, intraoperative LVA site data, and postoperative VLR outcomes for the entire cohort are summarized in Table 1. The median age was 60 (53, 70) years, and the median duration of edema was 3 (1, 5) months. According to the International Society of Lymphology (ISL) staging system, stage II was the most prevalent category (n = 20, 46.51%), followed by stage III (n = 14, 32.56%), stage I (n = 7, 16.28%), and stage IV (n = 2, 4.65%). Postoperative VLR was observed at 82 anastomotic sites (19.39%).

Fifteen features were incorporated into the model development: ten clinical/laboratory variables (with height and weight excluded due to their collinearity with BMI) and five venous ultrasound characteristics. Typical venous ultrasound features and the evaluation of flow direction at the anastomotic site during LVA surgery were illustrated in Figure 3A–I.

VLR Risk Factors and Their Clinical Significance

The GLMM analysis identified several significant predictors of VLR risk (Table 2). The random effects component indicated minimal between-patient variability ($\tau = 0$), suggesting that most variance was explained by the site-level characteristics rather than patient-level factors. Venous ultrasound characteristics emerged as the most potent determinants, with orthostatic reflux demonstrating the strongest association (OR = 57.913, 95% CI: 15.383-218.033, $p < 0.001$), followed by compression reflux (OR = 13.402, 95% CI: 4.006-44.838, $p < 0.001$). Protective venous factors included the presence of bifurcation (OR = 0.100, 95% CI: 0.038-0.264, $p < 0.001$), subcutaneous tissue localization (OR = 0.190, 95% CI: 0.072-0.505, $p = 0.001$), and larger venous diameter (OR = 0.002, 95% CI: 0.000-0.021, $p < 0.001$). Clinical factors significantly associated with increased VLR risk included advanced ISL stages (stage III: OR = 8.295, $p = 0.007$; stage II: OR = 7.124, $p = 0.011$) and longer edema duration (OR = 1.222, $p = 0.049$). Platelet count showed a borderline significant protective effect (OR = 0.994, $p = 0.066$). Visualization of these relationships revealed compelling clinical patterns. The association between preoperative predictors and VLR risk is visualized in Figure 4. Veins localized in the layer above the

subcutaneous adipose tissue (LASAT) were associated with a significantly higher incidence of VLR compared to those within the subcutaneous adipose tissue (SAT) (22.8% vs. 12.7%; Figure 4A). The presence of compression reflux markedly increased VLR risk, with a 51.9% incidence in reflux-positive veins versus 4.2% in negative veins (Figure 4B). Bifurcated veins demonstrated a protective effect, showing a lower VLR incidence than non-bifurcated veins (12.0% vs. 26.5%; Figure 4C). Orthostatic reflux was the strongest risk factor, with a 56% VLR incidence in reflux-positive veins compared to only 4% in negative veins (Figure 4D). Advanced ISL stage was also associated with increased VLR risk (Figure 4E). Furthermore, partial dependence plots illustrated a strong inverse relationship between venous diameter and VLR probability, where the risk decreased substantially as the diameter increased (Figure 4F). In contrast, the partial dependence plots for clinical and laboratory variables generally demonstrated weaker associations with VLR risk, as detailed in Figure S1.

GLMM Model Performance and Validation

The forest plot in Figure 5A comprehensively displays the effect sizes and precision of all predictors, highlighting the dominant role of venous ultrasound characteristics in VLR risk stratification. The GLMM demonstrated excellent discriminative ability for VLR prediction, achieving an AUC of 0.935 (Figure 5B). The model maintained high accuracy (0.939) with balanced sensitivity (0.793) and specificity (0.974), yielding strong positive and negative predictive values of 0.878 and 0.951, respectively. The F1-score of 0.833 indicated robust performance across classification

metrics. Five-fold cross-validation confirmed model stability and generalizability, with a mean AUC of 0.909 (SD = 0.054) across validation folds, ranging from 0.820 to 0.968 (Figure 5C).

Discussion

This retrospective study demonstrates that preoperative venous ultrasound characteristics are potent predictors of VLR following LVA surgery. By employing a GLMM to account for the hierarchical structure of multiple LVA sites nested within patients, we identified several venous sonographic features independently associated with VLR risk. Orthostatic reflux emerged as the strongest predictor, followed by compression reflux, while the presence of bifurcation, subcutaneous tissue localization, and larger venous diameter served as protective factors. The GLMM demonstrated excellent discriminative performance (AUC = 0.935) and maintained robust generalizability upon internal validation. These findings establish a critical foundation for leveraging routine preoperative venous ultrasound in refining LVA surgical planning.

The utilization of recipient veins exhibiting reflux during LVA carries a potential risk for VLR, where venous blood regurgitates into the lymphatic lumen, potentially compromising long-term patency [15]. Although our protocol excluded veins with detectable reflux on preoperative ultrasound, the higher incidence of VLR observed in sites associated with compression-induced reflux or reflux in the standing position indirectly supports this concern. Reflux elicited by standing or compression maneuvers is a fundamental assessment of venous valve competence. Preoperative

venous ultrasound enables the detection of reflux in the deep, superficial, or perforating systems (e.g., great saphenous vein reflux suggesting possible iliac vein obstruction) [16-18]. The standing position, leveraging gravitational effects, may be particularly effective in unmasking subtle or occult reflux. Reflux patterns within superficial networks (e.g., the inguinal lymph node venous network) are linked to chronic venous disease, and their morphological, dimensional, and hemodynamic variations are highly relevant to LVA planning [19, 20]. Our SHAP findings align with this, indicating that veins located within the subcutaneous fat layer and exhibiting reflux are associated with increased VLR risk [15].

Our analysis revealed a significant protective effect of larger venous diameter against VLR risk, with an adjusted odds ratio of 0.002 (95% CI: 0.000-0.021, $p < 0.001$). Partial dependence plots illustrated a strong inverse relationship, showing a substantial decrease in VLR risk as venous diameter increased. This finding aligns with the established understanding that diameter mismatch between the lymphatic vessel and recipient vein is a critical factor in LVA hemodynamics. Prior research has demonstrated that significant discrepancies, particularly where the lymphatic vessel is substantially larger than the vein, substantially increase reflux risk [21, 22]. Larger recipient veins likely provide better capacitance and flow accommodation, reducing the probability of flow reversal at the anastomotic site. However, it is noteworthy that while larger diameters were protective in our cohort, diameters exceeding certain thresholds in other vascular contexts have been associated with valvular incompetence due to increased inter-valvular distance [23]. The optimal diameter range observed in

our study population suggests that veins of adequate size (generally >0.5mm in our measurements) provide the best balance between sufficient lumen for anastomosis and maintained valvular function. Future studies should explicitly investigate the interaction effect between specific lymphatic and venous diameter measurements on VLR occurrence to establish more precise matching criteria.

Consequently, specific venous ultrasound features—namely reflux status (particularly under orthostatic stress and compression), diameter, anatomical layer, and bifurcation pattern—constitute key, readily assessable indicators for predicting post-LVA VLR. Preoperative venous mapping guided by a standardized ultrasound protocol can significantly mitigate this risk. Prioritizing veins without reflux, situated under low pressure, and exhibiting good diameter matching with target lymphatics is paramount [24]. Patients with suspected iliac vein obstruction or pelvic reflux patterns warrant comprehensive preoperative ultrasound assessment of venous reserve and competency [25, 26]. High-frequency ultrasound facilitates the preoperative identification of functional veins while systematically avoiding those with reflux [27, 28]. If utilizing a refluxing vein is unavoidable, techniques like interposing a venous valve graft to increase distance and prevent retrograde flow could be considered [29]. Moreover, meticulous anastomotic design is essential to minimize significant diameter discrepancies [22]. Integrating the predictive factors identified by our model into preoperative planning offers a novel, evidence-based strategy to identify sites at high risk for VLR and optimize vein selection. Postoperatively, regular ultrasound surveillance of anastomotic patency and reflux detection, particularly in high-risk

patients, is recommended [16, 30].

This study has several limitations. First, as a single-center retrospective cohort study, it is inherently susceptible to selection bias and limited generalizability. Second, the granularity of postoperative follow-up data restricted our analysis primarily to the immediate VLR outcome, providing only a partial view of LVA efficacy. Future work should investigate the mechanistic link between these venous ultrasound characteristics and long-term LVA patency and clinical outcomes. Third, the retrospective nature of our dataset precluded the inclusion of detailed lymphatic vessel features (e.g., sclerosis grade, contractility, diameter), which are known critical determinants of LVA success and VLR risk [21, 31]; their absence likely impacted model performance and the comprehensiveness of our pathophysiological understanding. Finally, validation of our findings in larger, prospective, and multi-center cohorts encompassing diverse patient populations and incorporating detailed lymphatic characteristics is essential to confirm their clinical utility and robustness.

Conclusion

This study identifies specific preoperative venous ultrasound features—orthostatic/compression reflux, smaller diameter, non-bifurcated morphology, and extra-subcutaneous localization—as powerful predictors of venous-lymphatic reflux (VLR) after LVA. We developed a GLMM-based predictive model with excellent discrimination (AUC=0.935), providing an evidence-based framework for preoperative risk assessment. Integrating these readily available

ultrasound features into surgical planning allows for identifying high-risk sites and selecting optimal veins to reduce VLR risk. Our findings advocate for the standardized inclusion of venous reflux and morphological evaluation in the preoperative LVA workflow to refine decision-making and improve outcomes.

Abbreviations

CEUS: Contrast-Enhanced Ultrasound

GLMM: Generalized Linear Mixed Model

ICG: Indocyanine Green

ISL: International Society of Lymphology

LASAT: Layer Above Subcutaneous Adipose Tissue

LVA: Lymphaticovenous Anastomosis

MRL: Magnetic Resonance Lymphangiography

ROC: Receiver Operating Characteristic

SAT: Subcutaneous Adipose Tissue

VLR: Venous-Lymphatic Reflux

Ethics approval and consent to participate

This retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Zhejiang Provincial People's Hospital (201700705B0). The requirement for informed consent was waived by the IRB due to the retrospective nature of the study and the use of anonymized data.

Consent for Publication

Not Applicable

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Clinical trial number: not applicable

Authors' contributions

Yongfeng Li: Conceptualization, Methodology, Software Chunjie Hou: Data curation, Writing- Original draft preparation. Zilong Qian: Visualization, Investigation. Ying Li: Supervision.: Kewang Sun: Software, Validation.: Zhenye Lv: Visualization, Xiaozhen Liu: Software. Xuli Meng: Supervision. Kefeng Lu: Writing- Reviewing and Editing

Conflicts of interest disclosure

All authors have no conflicts of interest to declare.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Figure captions

Figure 1. Schematic diagram of the five venous ultrasound features. In the figure, ① indicates venous luminal diameter, ② indicates bifurcation, ③ indicates layer localization, ④ indicates compression reflux, and ⑤ indicates orthostatic reflux.

Figure 2. The flow diagram illustrating the initial number of participants and those excluded for any reason

Figure 3. Typical venous ultrasound features and flow direction evaluation at the anastomotic site. (A) Typical ultrasound image of a vein without bifurcation. (B) Typical ultrasound image of a vein with bifurcation structure. (C) Blood flow appears blue in the proximal vein before compression and (D) the vessel dilates and blood flow appears red after compression in a supine patient. (E) Vein in the layer above subcutaneous adipose tissue (LASAT) and (F) vein within SAT. (G-I) ICG fluorescence imaging of a successfully anastomosed site, with fluorescent signals detected flowing from the lymphatic vessel to the vein.

Figure 4. Association between preoperative predictors and venous-lymphatic reflux (VLR) risk. (A-E) Proportion bar plots demonstrating VLR incidence across categorical variables: (A) tissue layer localization (LASAT: layer above subcutaneous adipose tissue; SAT: subcutaneous adipose tissue), (B) compression reflux status, (C) bifurcation pattern, (D) orthostatic reflux status, and (E) International Society of Lymphology (ISL) stage. P-values from Fisher's exact tests or Chi-square tests are indicated. (F) Partial dependence plot illustrating the inverse relationship between venous inner diameter and predicted VLR probability. (G) Partial dependence plot

showing the relationship between edema duration and predicted VLR probability.

Figure 5. Performance of the generalized linear mixed model (GLMM) for VLR prediction. (A) Forest plot displaying odds ratios (OR) with 95% confidence intervals for all predictors in the GLMM. Venous ultrasound characteristics (bottom four factors) demonstrate the strongest effects on VLR risk. (B) Receiver operating characteristic (ROC) curve of the GLMM, showing excellent discriminative ability (AUC = 0.935) for predicting VLR. (C) Five-fold cross-validation results confirming model stability and generalizability, with a mean AUC of 0.909 across folds.

Figure S1. Partial dependence plots for clinical and laboratory variables. Relationships between predicted VLR probability and continuous clinical/laboratory parameters: body mass index (BMI), age, platelet count, hemoglobin, albumin, systolic pressure, prothrombin time, and diastolic pressure. These variables generally showed weaker associations with VLR risk compared to venous ultrasound characteristics featured in Figure 4.

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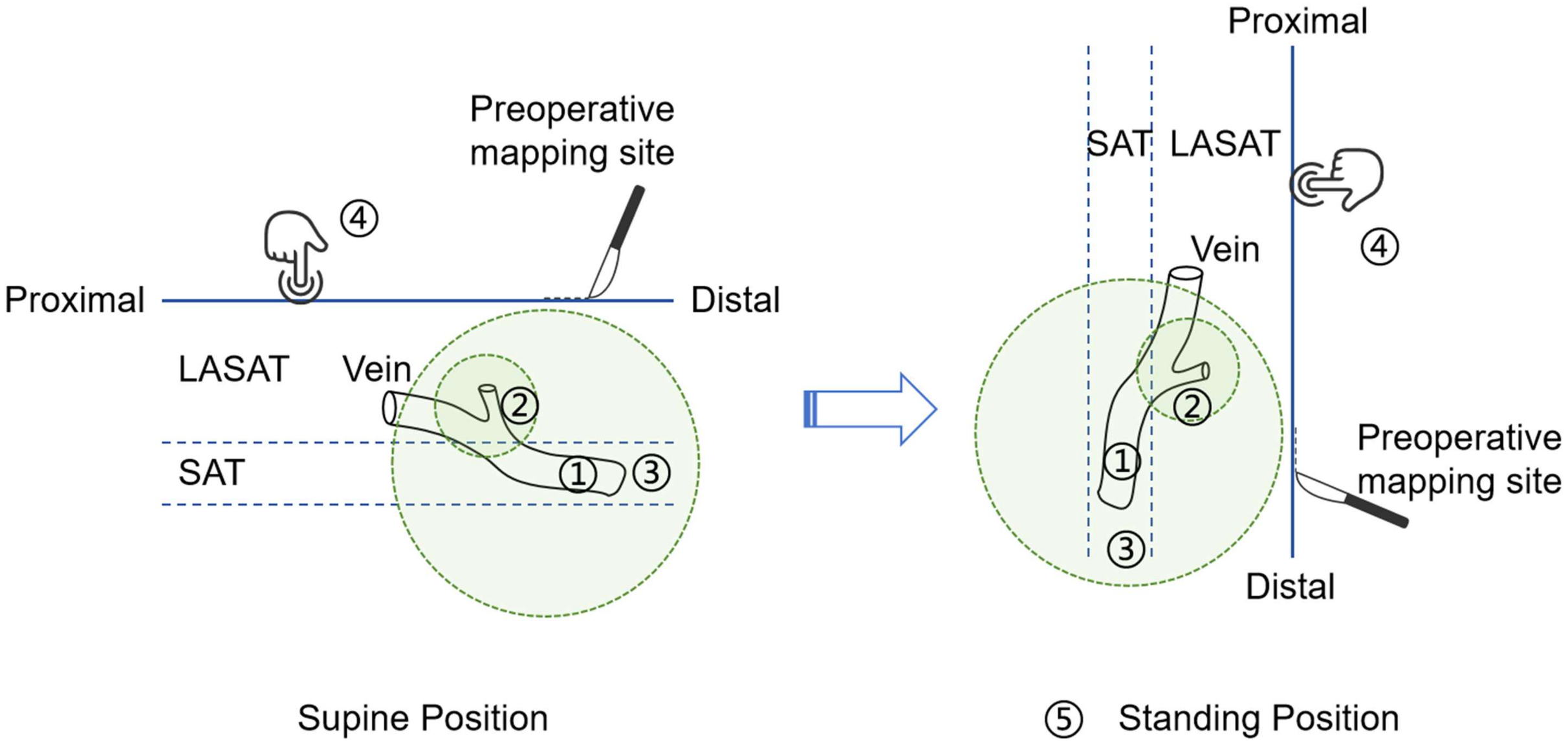
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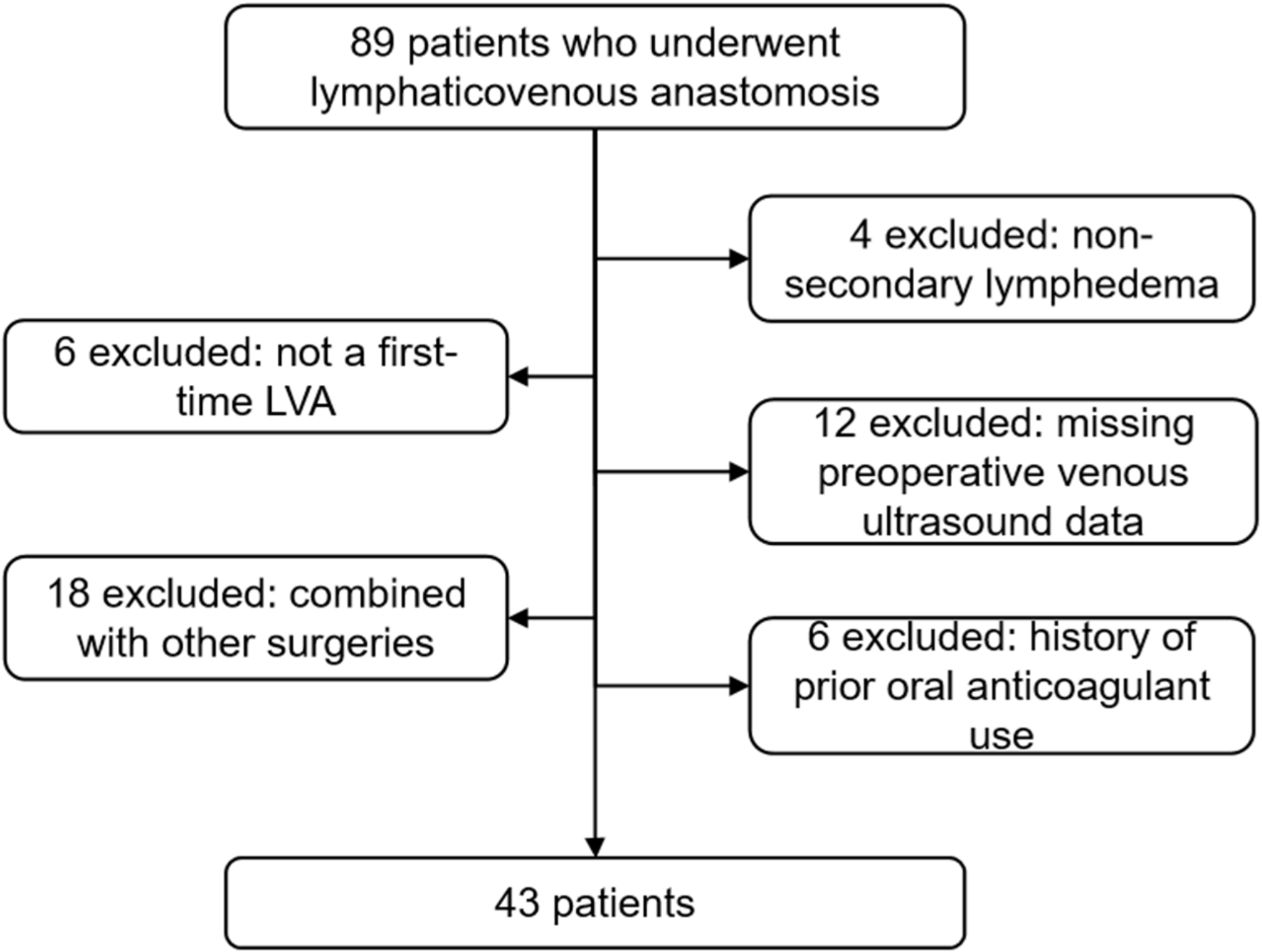
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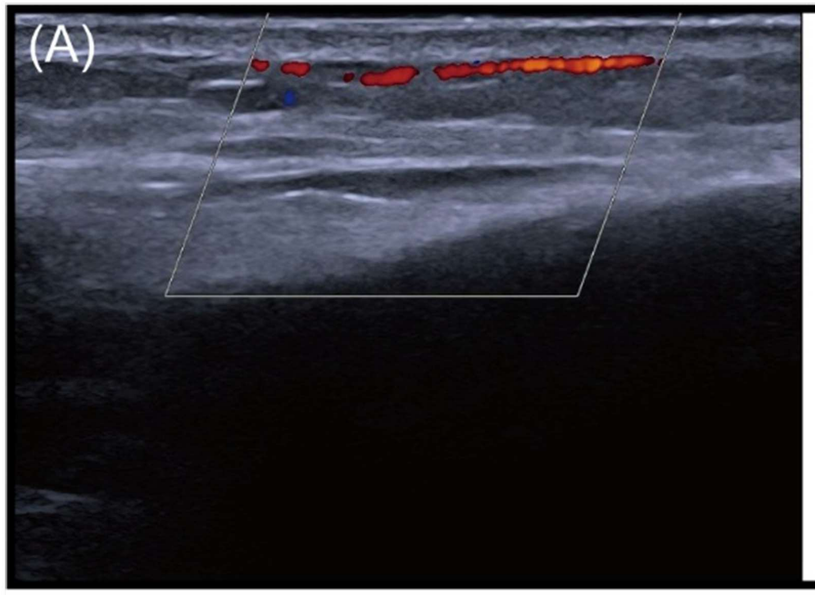
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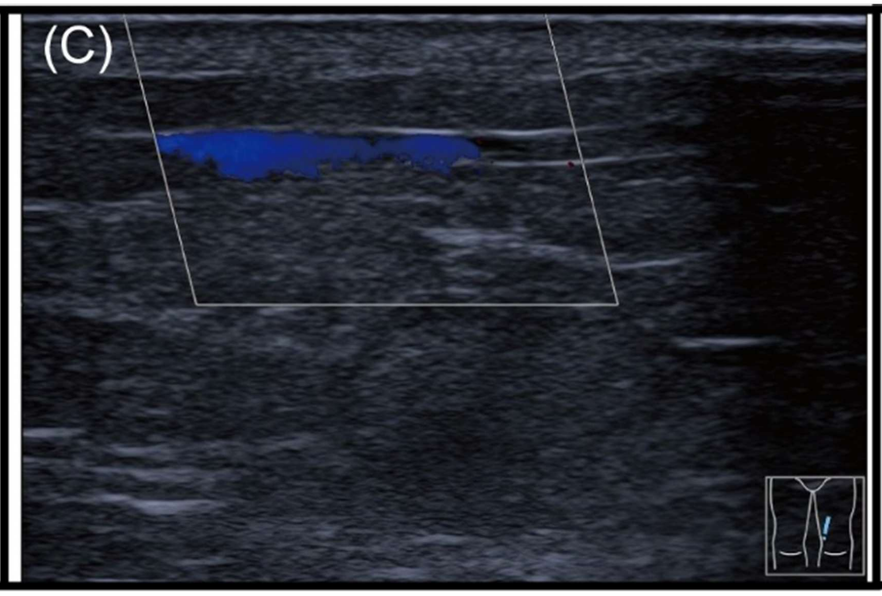
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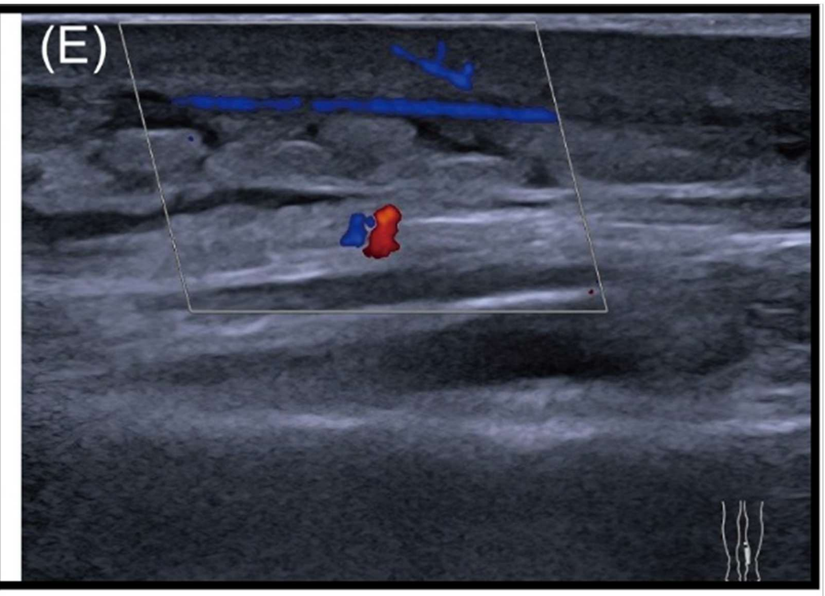
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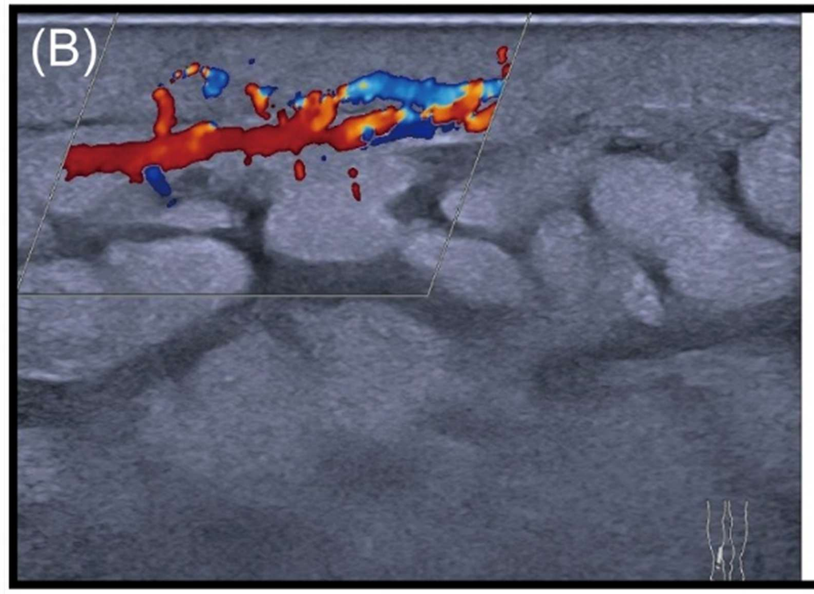

Preoperative
mapping site
④
Proximal
Distal
LASAT
Vein
②
SAT
①
③
Supine Position
Proximal
SAT
LASAT
Vein
④
②
①
③
Preoperative
mapping site
Distal
⑤ Standing Position

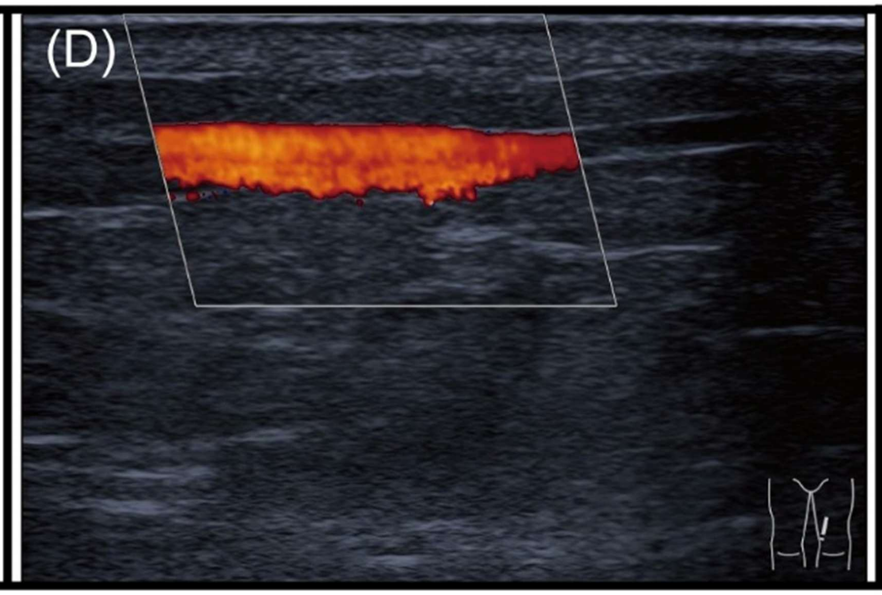

89 patients who underwent lymphaticovenous anastomosis
4 excluded: non-secondary lymphedema
6 excluded: not a first-time LVA
12 excluded: missing preoperative venous ultrasound data
18 excluded: combined with other surgeries
6 excluded: history of prior oral anticoagulant use
43 patients

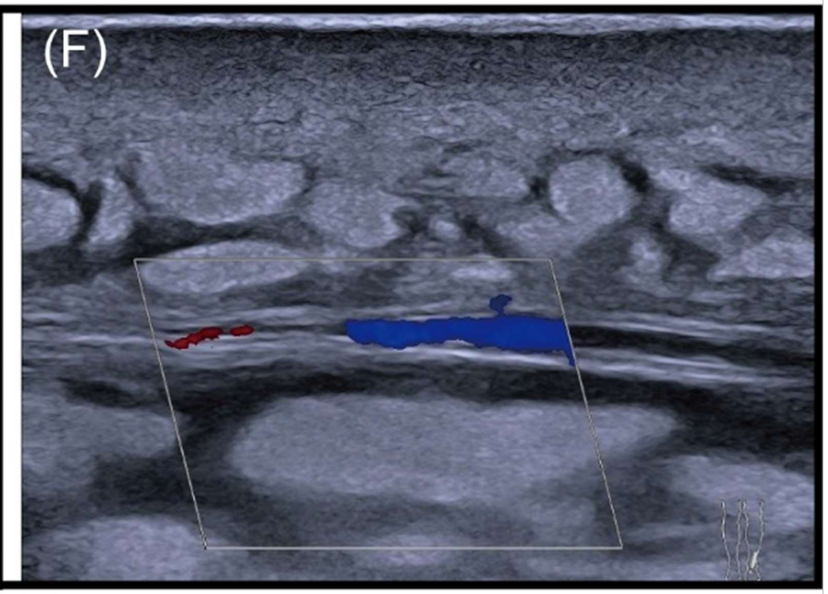

(A)

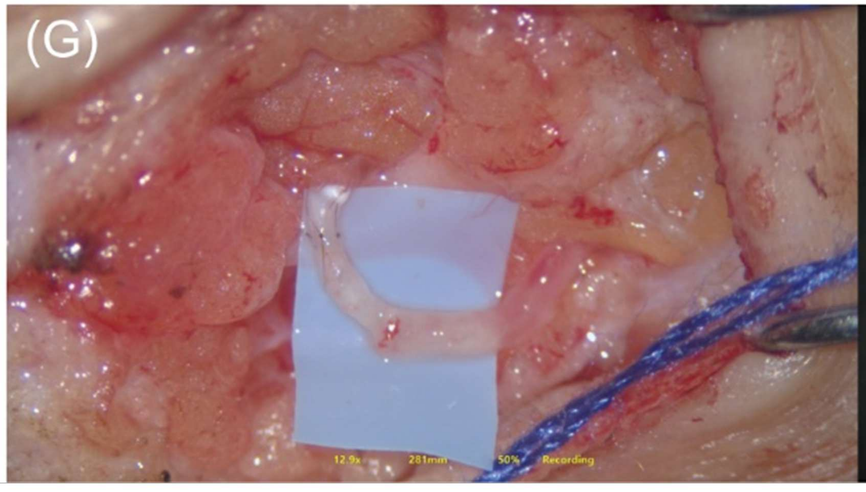

(C)


(E)

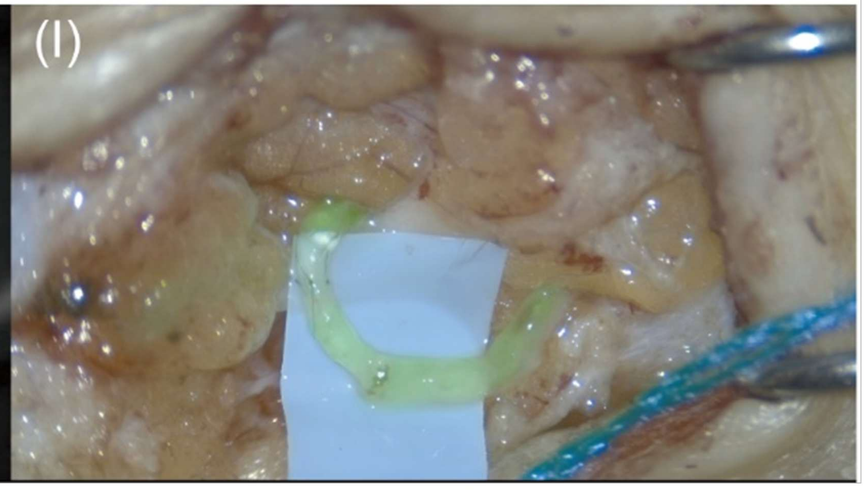

(B)

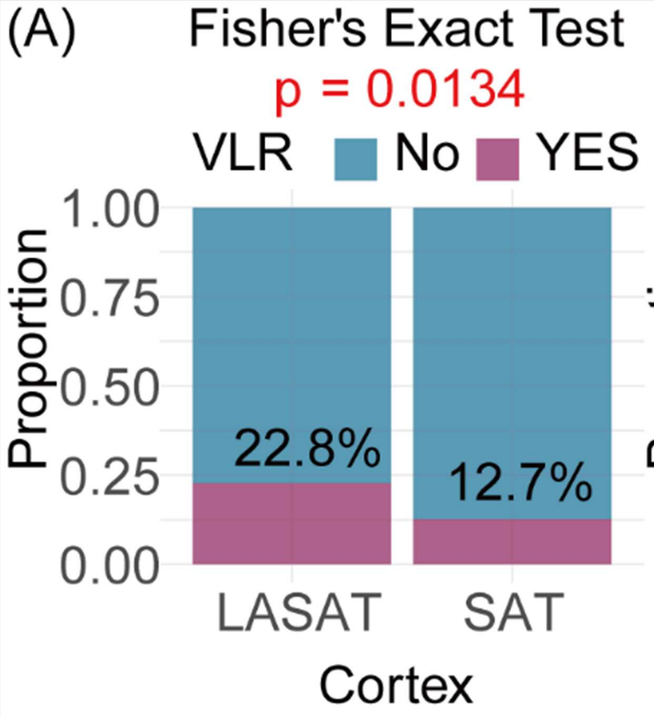

(D)

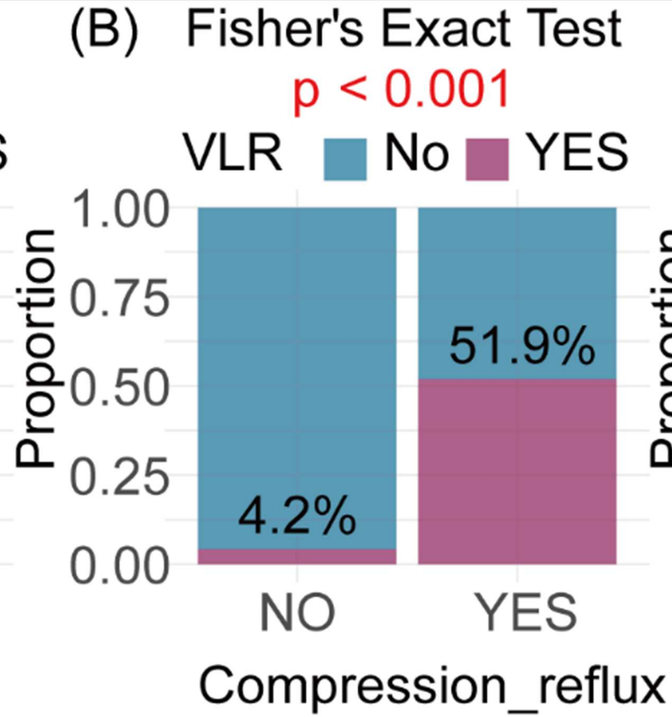

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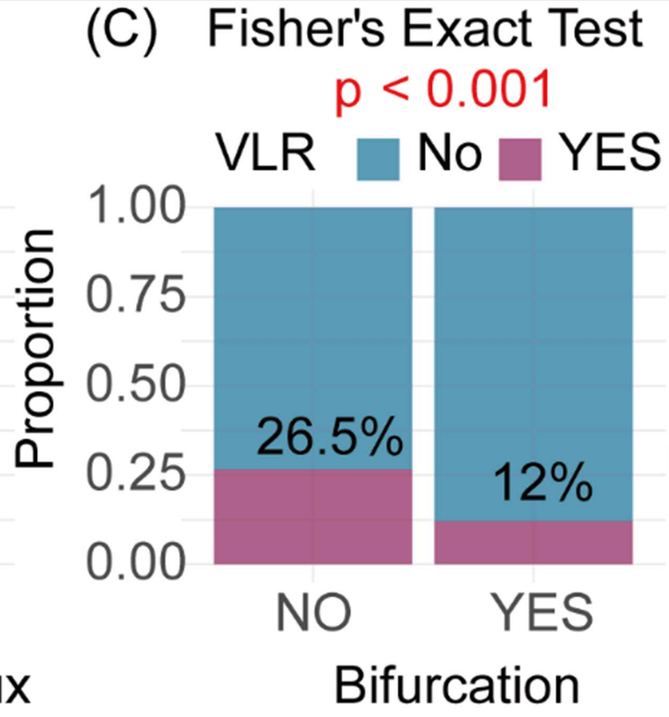

(G)
12.9x
281mm
50%
Recording

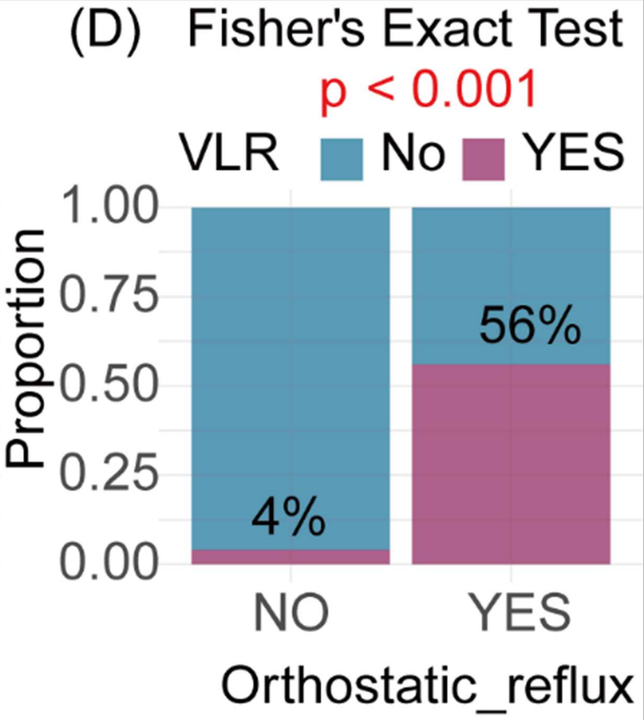

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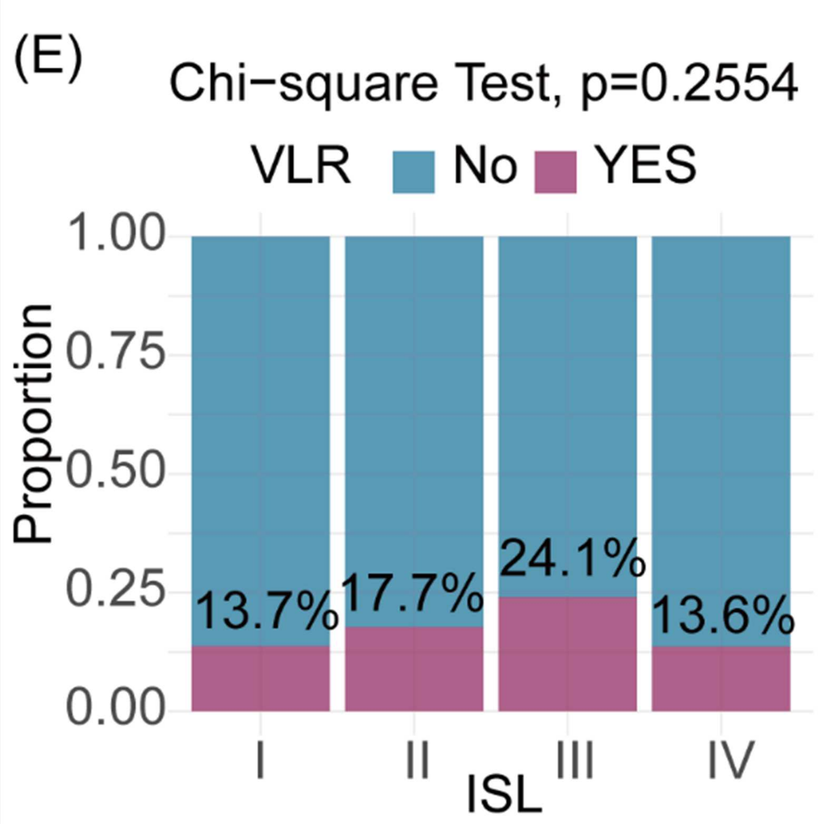

(I)

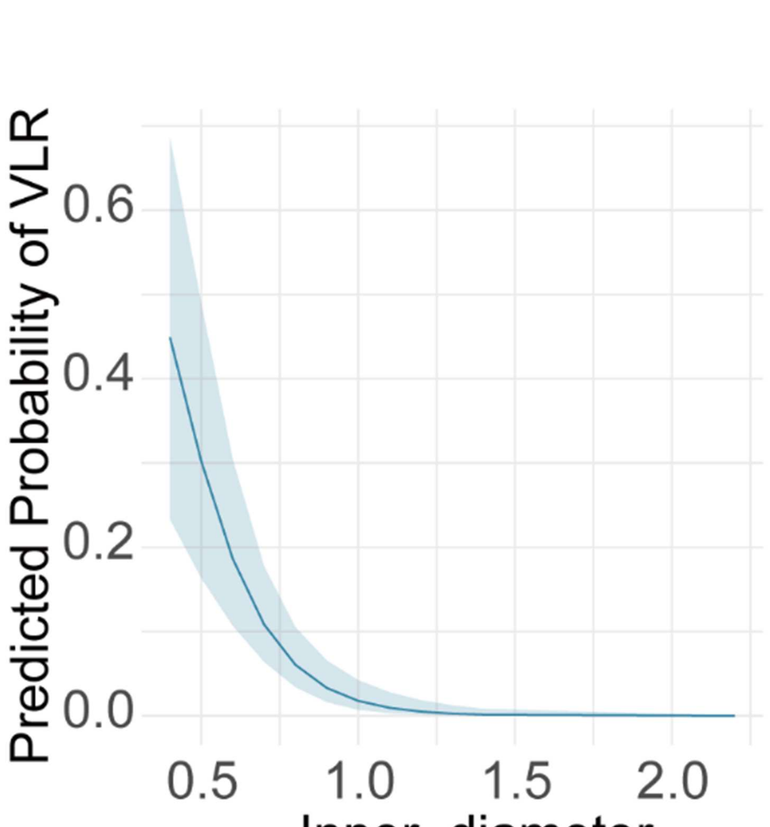
(A)

Fisher's Exact Test
p = 0.0134
VLR No YES
Proportion
1.00
0.75
0.50
0.25
0.00
22.8%
12.7%
LASAT
SAT
Cortex

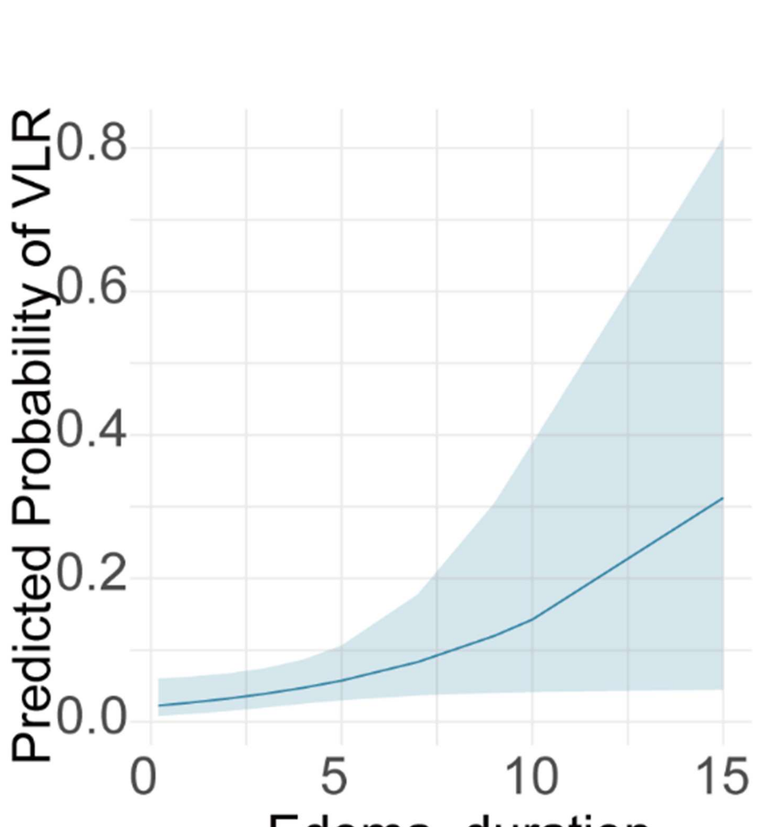
(B)

Fisher's Exact Test
p < 0.001
VLR No YES
Proportion
1.00
0.75
0.50
0.25
0.00
4.2%
51.9%
NO
YES
Compression_reflux

(C)

Fisher's Exact Test
p < 0.001
VLR No YES
Proportion
1.00
0.75
0.50
0.25
0.00
26.5%
12%
NO
YES
Bifurcation

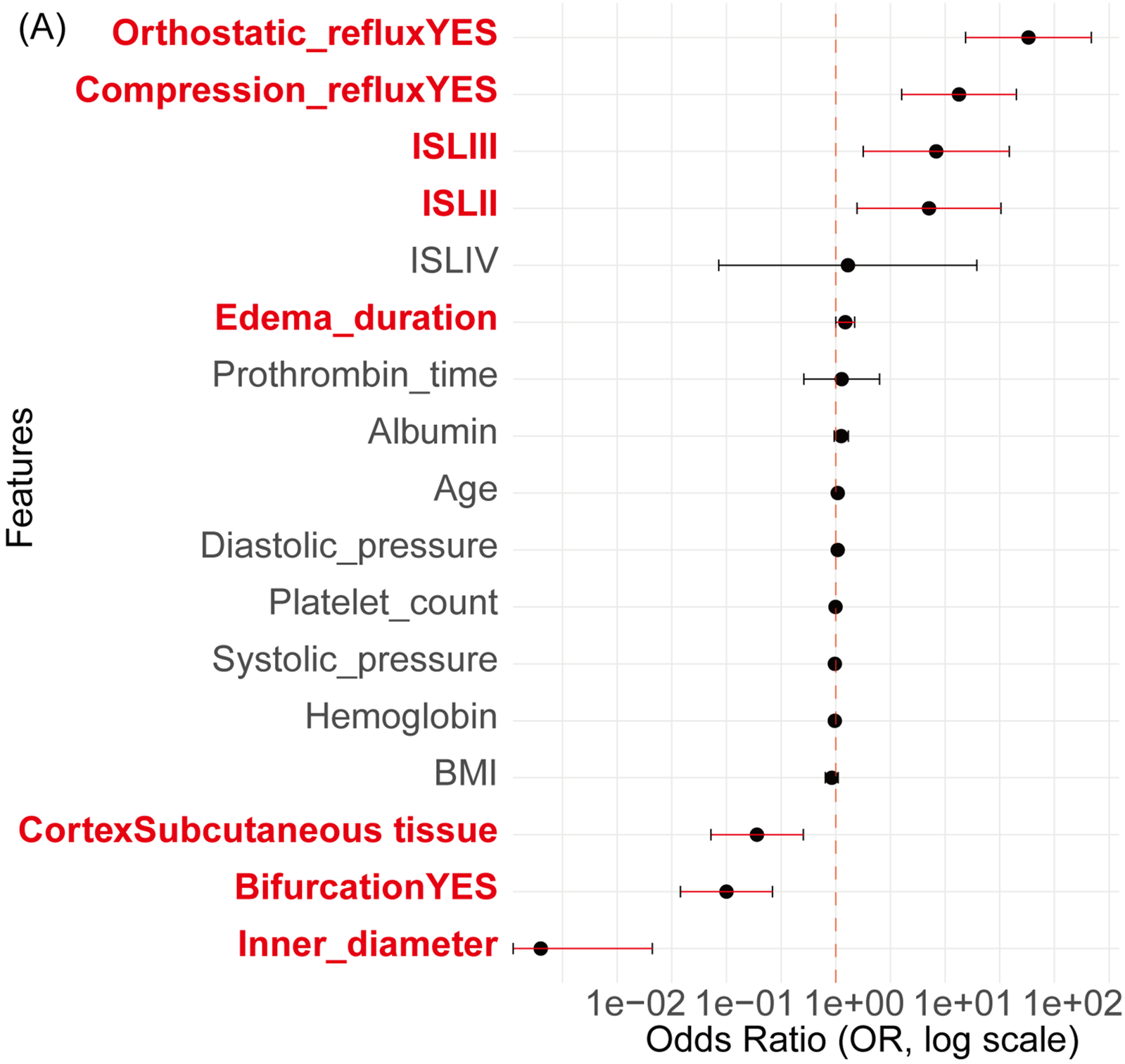
(D)

Fisher's Exact Test
p < 0.001
VLR No YES
Proportion
1.00
0.75
0.50
0.25
0.00
4%
56%
NO
YES
Orthostatic_reflux

(E)

Chi−square Test, p=0.2554
VLR No YES
Proportion
1.00
0.75
0.50
0.25
0.00
13.7%
17.7%
24.1%
13.6%
I
II
III
IV
ISL

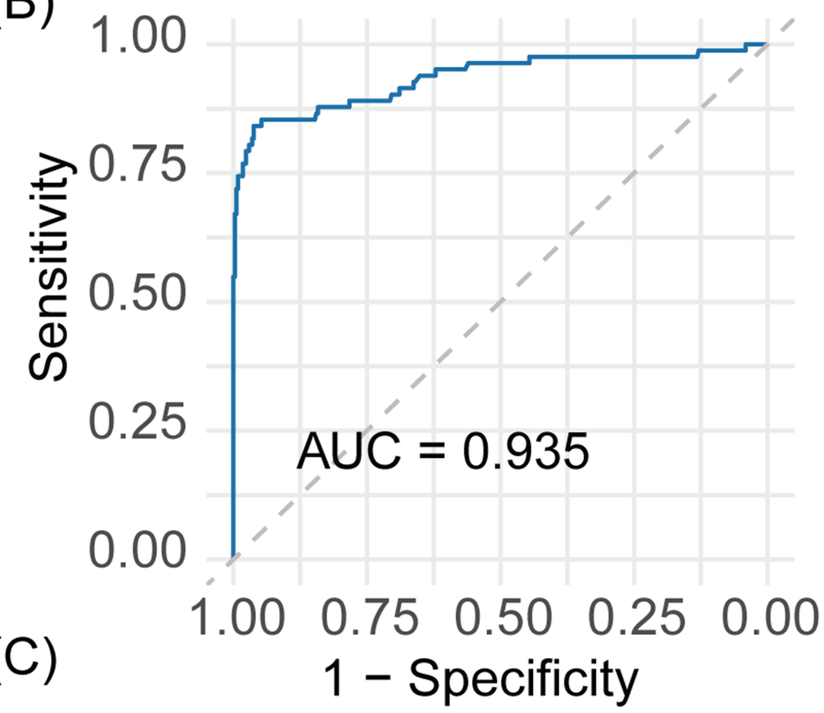
(F)

Predicted Probability of VLR
0.6
0.4
0.2
0.0
0.5
1.0
1.5
2.0
Inner_diameter

(G)

Predicted Probability of VLR
0.8
0.6
0.4
0.2
0.0
0
5
10
15
Edema_duration

(A)


Orthostatic_refluxYES
Compression_refluxYES
ISLIII
ISLII
ISLIV
Edema_duration
Prothrombin_time
Albumin
Age
Diastolic_pressure
Platelet_count
Systolic_pressure
Hemoglobin
BMI
CortexSubcutaneous tissue
BifurcationYES
Inner_diameter
Features
1e−02 1e−01 1e+00 1e+01 1e+02
Odds Ratio (OR, log scale)

(B)


Sensitivity
1.00
0.75
0.50
0.25
0.00
AUC = 0.935
1.00 0.75 0.50 0.25 0.00
1 − Specificity

(C)

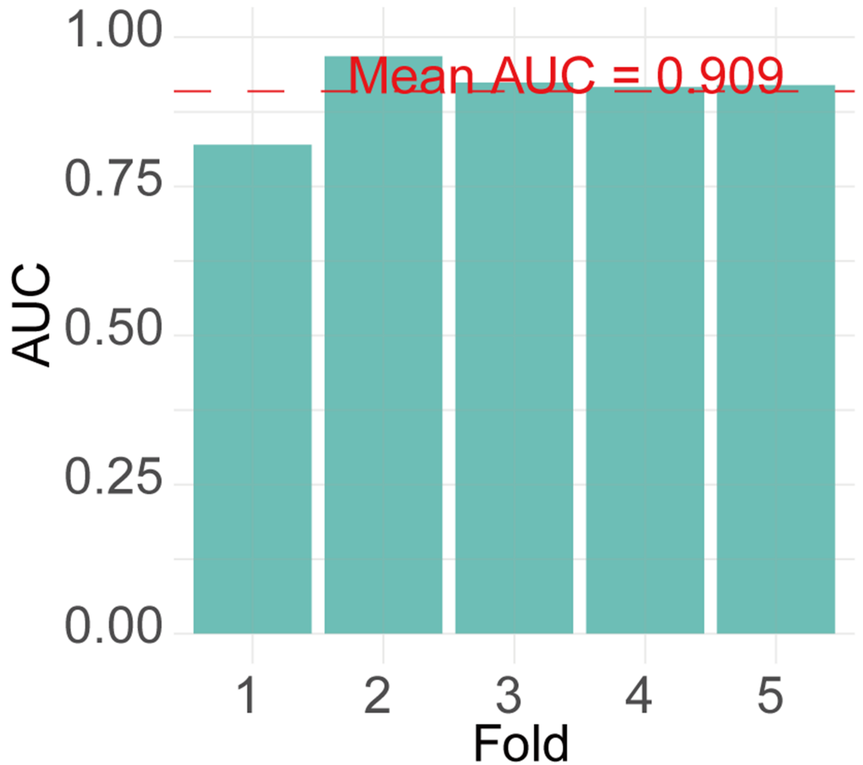

AUC
1.00
0.75
0.50
0.25
0.00
Mean AUC = 0.909
1
2
3
4
5
Fold

Table 1. Preoperative and intraoperative clinical and laboratory variables and outcomes.

Variables	**overall**
Number of patients	43
Clinical variables	
LVA sites	423
Height, cm	157 (153.5, 162.5)
Weight, kg	65 (57.9, 70.9)
BMI, kg/m^2	25.8 (23.92, 28.31)
Age, years	60 (53, 70)
Systolic pressure, mmHg	131 (121, 143)
Diastolic pressure, mmHg	76 (71.5, 84.5)
ISL stage	
I	7 (16.28)
II	20 (46.51)
III	14 (32.56)
IV	2 (4.65)
Edema duration, months	3 (1, 5)
Laboratory variables	
Platelet count, 10^9/L	216 (179.5, 247.5)
Hemoglobin, g/L	123 (115.5, 131.5)
Albumin, g/L	36.7 (34.95, 40.55)
Prothrombin_time, sec	11 (10.75, 11.3)

[a]Continuous data was showed as median (interquartile range, Q1, Q3) and categoric data as number (%). Abbreviations: LVA, Lymphaticovenous Anastomosis, ISL, International Society of Lymphology

Table 2. Multivariable generalized linear mixed model for predicting venous-lymphatic reflux risk in patients undergoing lymphaticovenous anastomosis.

Predictors	*Odds Ratios*	*CI*	*Statistic*	*p*
(Intercept)	0.062	0.000 – 20339.950	-0.429	0.668
Inner_diameter	0.002	0.000 – 0.021	-5.008	**<0.001**
Bifurcation (YES)	0.1	0.038 – 0.264	-4.64	**<0.001**
Cortex (subcutaneous adipose tissue)	0.19	0.072 – 0.505	-3.334	**0.001**
Compression_reflux (YES)	13.402	4.006 – 44.838	4.212	**<0.001**
Orthostatic_reflux (YES)	57.913	15.383 – 218.033	6.001	**<0.001**
Age	1.042	0.992 – 1.094	1.627	0.104
BMI	0.919	0.803 – 1.051	-1.236	0.217
Platelet_count	0.994	0.987 – 1.000	-1.836	0.066
Hemoglobin	0.979	0.931 – 1.029	-0.836	0.403
Albumin	1.121	0.966 – 1.301	1.5	0.134
Prothrombin_time	1.132	0.510 – 2.514	0.304	0.761
Systolic_pressure	0.98	0.951 – 1.010	-1.295	0.195
Diastolic_pressure	1.041	0.984 – 1.101	1.393	0.164
ISL (II)	7.124	1.564 – 32.459	2.538	**0.011**
ISL (III)	8.295	1.779 – 38.683	2.693	**0.007**
ISL (IV)	1.292	0.085 – 19.548	0.185	0.854
Edema_duration	1.222	1.001 – 1.492	1.97	**0.049**
Random Effects				
σ^2	3.29			
$\tau_{00\ Patients}$	0			
$N_{\ Patients}$	43			
Observations	423			

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FigureS1.tif