Isolated Calf Deep Venous Thrombosis: Prevalence, Clinical Characteristics and Implications for Ultrasound Evaluation

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Abstract

Objectives It remains controversial whether to include calf veins in the initial ultrasound evaluation of suspected deep venous thrombosis (DVT). We sought to investigate the prevalence and clinical characteristics of isolated calf DVT.

Materials and Methods We retrospectively analyzed a cohort of 596 patients (median age 69 years, 52.3% women) evaluated with complete duplex ultrasound of the leg veins for suspected acute DVT within one year. Radiology reports were analyzed for the presence and localization of DVT. Electronic chart review was performed to collect clinical information.

Results DVT was found in 157 patients (26.3%), of which 74 patients (47.1%) had isolated calf DVT. Isolated calf DVTs were most commonly located in the posterior tibial veins (22 patients, 29.7%), fibular veins (41 patients, 55.4%) and muscle veins (19 patients, 25.7%). There were no differences in age or gender between patients with isolated calf DVT and patients with more proximal DVT. Isolated calf DVT was more commonly associated with leg pain (52.7% vs. 33.7%, $p = 0.0234$) and less commonly associated with subjective leg swelling (35.1% vs. 55.4%, $p = 0.0158$) and objectively measured difference in leg circumference (23% vs. 39.8%, $p = 0.0268$). D-Dimers were significantly lower in patients with isolated lower leg DVT (median 2.3 vs. 6.8 mg/L, $p < 0.0001$) compared to patients with more proximal DVT.

Conclusions Isolated calf DVT is almost as common as more proximal DVT. Our data supports performing complete duplex ultrasound including the calf veins in suspected DVT.

Introduction

Venous ultrasound is the standard imaging test for patients with suspected deep venous thrombosis (DVT). There is, however, great variability in the ultrasound technique performed for suspected DVT between institutions[1, 2] and guidelines.[3–7] In particular, there is disagreement on whether to include the calf veins in the initial ultrasound evaluation of suspected DVT. Some institutions perform ultrasound examinations with a limited range from the groin to the knee - sometimes in the form of two-point or three-point compression ultrasound as the initial test.[8–14] If negative, this is typically followed by a second ultrasound examination within one week to safely exclude DVT. [15]

The clinical importance of isolated calf-vein DVT is incompletely understood with regards to the risks for propagation into the popliteal and/or femoral vein, pulmonary embolism and the development of a post-thrombotic syndrome. It is currently thought that approximately 15–20% of isolated asymptomatic distal DVTs will extend to the proximal veins if untreated.[16, 17] Nevertheless, the benefit of treating patients with isolated calf DVT remains uncertain and controversial.[17–23]

In light of this ongoing controversy, we sought to investigate the prevalence and clinical characteristics of isolated calf DVT on complete duplex ultrasound examination as the initial test in patients with

suspected DVT.

Material And Methods

Ethical approval, study design and patient selection

The study was approved by our institutional review board with waiver of informed consent. The investigation was designed as a retrospective, single-center cohort study. We included all patients who were examined with venous ultrasound of the legs at our institution between January 1 and December 31, 2014 for suspected acute DVT. The year 2014 was chosen because during this year venous ultrasound evaluations were almost exclusively performed by two senior radiologists (initials blinded) with extensive experience in vascular ultrasound. We identified eligible patients through a retrospective query of our radiology information system. We excluded patients with other indications for venous ultrasound and follow-up examinations of patients with known DVT (Fig. 1). We also excluded patients referred for duplex ultrasound because of a recent diagnosis of acute pulmonary embolism under the assumption that isolated calf DVT in patients with pulmonary embolism may not be truly isolated calf DVT but rather the remnant of a more extensive proximal DVT, much of which has embolized.

Ultrasound technique

All ultrasound examinations were performed on a Toshiba Aplio XG SSA 770A ultrasound machine. Our institutional standard in suspected DVT is to always perform a complete duplex ultrasound of the symptomatic leg(s). The ultrasound evaluation is performed by board-certified radiologists with subspecialisation in vascular and interventional radiology. Our protocol includes

- a. compression ultrasound performed at 2 cm intervals from the common femoral vein to the ankle including the peroneal and posterior tibial veins and major muscle veins in the calf.
- b. color Doppler evaluation from the common femoral vein to the ankle.
- c. spectral Doppler evaluation of the wave form in the common femoral vein. In case of abnormal wave form suggesting obstruction above the inguinal ligament, additional color Doppler evaluation of the iliac veins is performed.
- d. targeted ultrasound of symptomatic areas if symptoms are not explained by findings on standard thigh-to-ankle examination.

Analysis of radiology reports

Radiology reports of all evaluations were retrospectively reviewed by a medical student (initials blinded) for the presence and location of DVT. If the localization could not be precisely determined from the radiology report alone, the images of the ultrasound examination stored in our PACS were also viewed by a board-certified radiologist. Patients were classified as having proximal DVT if any portion of the DVT was in the popliteal vein, femoral and/or iliac veins. In contrast, patients were classified as having isolated calf DVT, if DVT was exclusively in one or more veins below the knee (posterior tibial veins,

fibular veins or muscle veins of the calf). Patients with bilateral DVT were classified according to the leg with the more proximally located DVT.

Analysis of Clinical Data

Review of electronic patient charts was performed to record age, gender, presenting symptoms, risk factors, Wells scores and D-Dimer levels.

Statistical analysis

Statistical analysis was performed with GraphPad Prism (version 8.4.2, GraphPad Software Inc). Continuous were presented as median and interquartile range and compared using the nonparametric Mann-Whitney test. Categorical data were displayed as frequencies and proportions and their distribution between groups was compared using Fisher's exact test. P-Values of < .05 were regarded as statistically significant.

Results

Patient characteristics

Our final study cohort consisted of 596 patients, of which 312 (52.3%) were women. Patient characteristics are summarized in Table 1. Median age was 69 years. The most common local symptoms across all 596 patients were leg pain (40.9%) and leg swelling (40.6%). 12.9% of patients had active malignancy and 16.4% of patients had a past medical history of DVT (Table 1).

Table 1
Characteristics of Study Population

		All patients (n = 596)		No DVT (n = 439)		DVT (n = 157)		p- Value
		N	%	n	%	N	%	
Females		312	52.3%	223	50.8%	89	56.7%	0.2264
Age in years, median (interquartile range)		69 (55–78)		69 (55–77)		70 (55–79)		0.2393
Presentation	Leg pain	244	40.9%	177	40.3%	67	42.7%	0.6368
	Leg swelling	242	40.6%	170	38.7%	72	45.9%	0.1300
	Circumference difference	161	27%	111	25.3%	50	31.8%	0.1172
	Redness	40	6.7%	30	6.8%	10	6.4%	0.9999
Risk factors	Known coagulopathy	9	1.5%	6	1.4%	3	1.9%	0.7043
	Active cancer	77	12.9%	53	12.1%	24	15.3%	0.3320
	Previous DVT	98	16.4%	52	11.8%	46	29.3%	0.0004
	Wells score, median (interquartile range)	1 (0–2) [n = 188]		1 (0–2) [n = 135]		2 (1–4) [n = 53]		< 0.0001
Lab	D-dimers in mg/L, median (interquartile range)	1.7 (0.8–4.1) [n = 347]		1.4 (0.6–2.8) [n = 252]		4.2 (1.9–9.5) [n = 95]		< 0.0001
P-values < 0.05 appear bold.								

Comparison of patients with DVT vs. patients without DVT on ultrasound

DVT was found in 157 of 596 patients (26.3%, Table 1 and Fig. 1). 15 patients had bilateral DVT (9.6% of all patients with DVT). Patients with DVT were significantly more likely to have a prior history of DVT (29.3% vs. 11.8%, $p = 0.0004$) than patients without DVT on ultrasound. Patients with DVT had higher Wells scores (median 2 vs. 1, $p < 0.0001$) and higher D-Dimer levels (median 4.2 vs. 1.4 mg/L, $p < 0.0001$)

than patients without DVT. There were no differences in age, gender or leg symptoms between patients with and without DVT on ultrasound.

Prevalence of isolated lower leg DVT

Among the 157 patients with DVT, 74 patients (47.1%) had isolated lower leg DVT. These were bilateral in 2 cases. Isolated lower leg DVTs were located in the posterior tibial veins in 22 patients (29.7%), fibular veins in 41 patients (55.4%) and muscle veins (gastrocnemius or soleus) in 19 patients (25.7%). Eight of these patients had DVT in multiple calf veins.

Comparison of patients with isolated lower leg DVT vs. patients with more proximal DVT

There were no differences in age, gender or risk factors between patients with isolated lower leg DVT and patients with a more proximal DVT (Table 2). Isolated lower leg DVT was more commonly associated with leg pain (52.7% vs. 33.7%, $p = 0.0234$) and less commonly associated with subjective leg swelling (35.1% vs. 55.4%, $p = 0.0158$) and objectively measured difference in leg circumference (23% vs. 39.8%, $p = 0.0268$). There was a trend for Wells score to be lower in patients with isolated lower leg DVT (median 2 vs. 3, $p = 0.0915$). D-Dimers were significantly lower in patients with isolated lower leg DVT (median 2.3 vs. 6.8 mg/L, $p < 0.0001$) compared to patients with more proximal DVT. Three of 74 patients (4.1%) with isolated calf DVT had normal D-dimers (< 0.5 mg/L) compared to 1 of 83 patients (1.2%) with more proximal DVT.

Table 2
Characteristics of patients with isolated lower leg DVT vs. proximal DVT

		All patients with DVT (n = 157)		Proximal DVT (n = 83)		Isolated lower leg DVT (n = 74)		p- Value
		N	%	n	%	n	%	
Females		89	56.7%	45	54.2%	44	59.5%	0.5233
Age in years, median (interquartile range)		70 (55–79)		70 (55-79.5)		69.5 (55-78.75)		0.7689
Presentation	Leg pain	67	42.7%	28	33.7%	39	52.7%	0.0234
	Leg swelling	72	45.9%	46	55.4%	26	35.1%	0.0158
	Circumference difference	50	31.8%	33	39.8%	17	23%	0.0268
	Redness	10	6.4%	7	8.4%	3	4.1%	0.3361
Risk factors	Known coagulopathy	3	1.9%	2	2.4%	1	1.4%	0.9999
	Active cancer	24	15.3%	15	18.1%	9	12.2%	0.3765
	Previous DVT	46	29.3%	25	30.1%	21	28.4%	0.8616
Wells score, median (interquartile range)		2 (1–4) [n = 53]		3 (1–4) [n = 25]		2 (1–3) [n = 28]		0.0915
Lab	D-Dimer in mg/L, median (interquartile range)	4.2 (1.9–9.5) [n = 95]		6.8 (4.2–12) [n = 51]		2.3 (1.1-5.0) [n = 44]		< 0.0001
P-values < 0.05 appear bold.								

Discussion

Several previous studies have demonstrated that isolated calf vein DVT, that is, infra-popliteal DVT without extension to proximal veins (popliteal vein or above), is frequent and represents 30–70% of all lower-limb DVTs diagnosed on ultrasound series.[14, 24–28] Our results are in line with these earlier reports since we found that in our series 47% of DVTs diagnosed on complete duplex ultrasound as the

initial tests were isolated calf vein DVTs. This suggests that an initial ultrasound evaluation performed with a limited range (from the groin to the popliteal vein) will miss almost half of DVT cases.

Our study goes beyond previously published data, as we analyzed the clinical characteristics of patients with isolated calf DVT compared to more proximal DVT. Interestingly, we observed that isolated calf DVT was more commonly associated with leg pain than more proximal DVT. It is generally thought that acute DVT triggers an inflammatory response[29] and that pain from DVT predominantly results from inflammation of the venous wall around the clot. A possible interpretation of our results would be that the local inflammatory response to DVT may be more pronounced in the smaller calf veins than in larger proximal veins.

Less surprisingly, we found that isolated calf DVT was less commonly associated with subjective leg swelling and objectively measured circumference difference. The most straightforward explanation for this finding is that in most patients, there is a single iliac, femoral and popliteal vein for each leg. DVT in these veins will thus occlude the entire deep venous system at this level. In contrast, there are multiple deep veins in the calf (typically paired peroneal veins, anterior and posterior tibial veins as well as muscle veins). Most cases of isolated calf DVT will occlude one or few of these veins and leave other deep calf veins patent.

Regarding laboratory values, we observed that levels of D-dimers were significantly lower in patients with isolated lower leg DVT compared to patients with more proximal DVT. This likely reflects the greater thrombus burden in patients with DVT in larger, more proximal veins compared to isolated calf DVT. In our analysis, 4.1% of patients with isolated calf DVT had “negative” D-dimers (reference value of our hospital laboratory < 0,5 mg/L) compared to 1 of 83 patients (1.2%) with more proximal DVT, suggesting that D-dimer testing is somewhat less sensitive for isolated calf DVT.

Our results should be interpreted in light of the controversies surrounding isolated calf DVT. It is known that venous ultrasonography is less accurate for isolated distal deep venous thrombosis than for proximal deep venous thrombosis.[30] Additionally, the clinical utility of including the calf veins in venous ultrasound is under debate because there is limited data about the natural course of isolated calf DVT and the benefit of anticoagulation.[21, 22] Unlike for proximal DVT and PE, which have been extensively studied and for which management is well standardized, much less is known about the optimal management of isolated distal DVT. The rate of extension to the proximal veins and the rate of PE associated with distal DVT are highly variable from one study to another and significant variation exists in diagnostic and therapeutic practices.[16, 19, 22, 31] In some centers, both the proximal veins and the calf veins are imaged in all patients with suspected DVT, and patients diagnosed with isolated calf DVT are treated with anticoagulant therapy.[32] There appears to be a positive effect of anticoagulation treatment on the proximal progression of the thrombus, PE and development of a postthrombotic syndrome [16–20, 33–35].

According to the consensus guideline of the German, Swiss and Austrian Societies for Vascular Medicine [3] an additional advantage of whole-leg ultrasound is to identify differential diagnoses for example

Baker's cyst, muscle fiber tear, aneurysm, hematoma, tumor as the reason for the patient's symptoms if negative for acute DVT.

Several limitations of our investigation should be mentioned. This single-center study was performed at a university hospital. This may be a more selected cohort of patients than patients with suspected DVT seen by primary care physicians. No external reference standard is available to confirm findings at ultrasound. Due to the retrospective nature of our investigation, Wells scores and D-Dimer levels were not available for all patients. Also, the precise time from symptom onset was not available in all cases. This may affect the findings on D-Dimer levels, which typically change over the course of acute DVT.

In summary, we found that isolated calf DVT is almost as common as more proximal DVT. Venous ultrasound with a limited range from the groin to the knee will therefore miss almost half of DVT cases. We conclude that it is prudent to perform complete duplex ultrasound including the calf veins in suspected DVT.

Declarations

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Disclosure of Potential Conflicts of Interest

The authors declare that there are no conflicts of interest related to this investigation.

Availability of data and materials

All supporting data is available from the corresponding author upon reasonable request.

References

1. Needleman L, Cronan JJ, Lilly MP, Merli GJ, Adhikari S, Hertzberg BS, et al. Ultrasound for Lower Extremity Deep Venous Thrombosis: Multidisciplinary Recommendations From the Society of Radiologists in Ultrasound Consensus Conference. *Circulation*. 2018;137:1505–15. doi:10.1161/CIRCULATIONAHA.117.030687.
2. Pomero F, Dentali F, Borretta V, Bonzini M, Melchio R, Douketis JD, Fenoglio LM. Accuracy of emergency physician-performed ultrasonography in the diagnosis of deep-vein thrombosis: a systematic review and meta-analysis. *Thromb Haemost*. 2013;109:137–45. doi:10.1160/TH12-07-0473.
3. Bein- und Beckenvenenthrombose (TVT). *VASA*. 2016;45 Suppl 90:8–26. doi:10.1024/0301-1526/a000485.

4. International Union of Angiology. International Union of Angiology (2013) guideline for PREVENTION AND TREATMENT OF VENOUS THROMBOEMBOLISM. *Int Angiol.* 2013;Volume 32:111–258.
5. National Institute for Health and Care Excellence. The National Institute for Health and Care Excellence (NICE) (2013) guideline for Venous thromboembolism in adults: diagnosis and management. <https://www.nice.org.uk/guidance/qs29>.
6. Shannon M. Bates, Roman Jaeschke, Scott M. Stevens, Steven Goodacre, Philip S. Wells, Matthew D. Stevenson, et al. Diagnosis of DVT: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. CHEST. 2012;141:e351S-e418S. doi:10.1378/chest.11-2299.
7. Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galiè N, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). *Eur Heart J.* 2008;29:2276–315. doi:10.1093/eurheartj/ehn310.
8. Zuker-Herman R, Ayalon Dangur I, Berant R, Sitt EC, Baskin L, Shaya Y, Shiber S. Comparison between two-point and three-point compression ultrasound for the diagnosis of deep vein thrombosis. *J Thromb Thrombolysis.* 2018;45:99–105. doi:10.1007/s11239-017-1595-9.
9. Adhikari S, Zeger W, Thom C, Fields JM. Isolated Deep Venous Thrombosis: Implications for 2-Point Compression Ultrasonography of the Lower Extremity. *Ann Emerg Med.* 2015;66:262–6. doi:10.1016/j.annemergmed.2014.10.032.
10. Lee JH, Lee SH, Yun SJ. Comparison of 2-point and 3-point point-of-care ultrasound techniques for deep vein thrombosis at the emergency department: A meta-analysis. *Medicine (Baltimore).* 2019;98:e15791. doi:10.1097/MD.00000000000015791.
11. Kruger PC, Eikelboom JW, Douketis JD, Hankey GJ. Deep vein thrombosis: update on diagnosis and management. *Med J Aust.* 2019;210:516–24. doi:10.5694/mja2.50201.
12. Cabrera R, Chimalakonda N, Rosario J, Ganti L. The Role of Serial Ultrasounds in Diagnosing Suspected Deep Venous Thrombosis. *Cureus.* 2019;11:e4337. doi:10.7759/cureus.4337.
13. Bernardi E, Camporese G, Büller HR, Siragusa S, Imberti D, Berchio A, et al. Serial 2-point ultrasonography plus D-dimer vs whole-leg color-coded Doppler ultrasonography for diagnosing suspected symptomatic deep vein thrombosis: a randomized controlled trial. *JAMA.* 2008;300:1653–9. doi:10.1001/jama.300.14.1653.
14. Ageno W, Camporese G, Riva N, Iotti M, Bucherini E, Righini M, et al. Analysis of an algorithm incorporating limited and whole-leg assessment of the deep venous system in symptomatic outpatients with suspected deep-vein thrombosis (PALLADIO): a prospective, multicentre, cohort study. *The Lancet Haematology.* 2015;2:e474-e480. doi:10.1016/S2352-3026(15)00190-8.
15. Cogo A, Lensing AW, Koopman MM, Piovella F, Siragusa S, Wells PS, et al. Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein thrombosis: prospective cohort study. *BMJ.* 1998;316:17–20. doi:10.1136/bmj.316.7124.17.

16. Palareti G. How I treat isolated distal deep vein thrombosis (IDDTV). *Blood*. 2014;123:1802–9. doi:10.1182/blood-2013-10-512616.
17. Gillet J-L, Perrin MR, Allaert FA. Short-term and mid-term outcome of isolated symptomatic muscular calf vein thrombosis. *J Vasc Surg*. 2007;46:513-9; discussion 519. doi:10.1016/j.jvs.2007.04.040.
18. Schwarz T. Therapy of isolated calf muscle vein thrombosis: A randomized, controlled study. *J Vasc Surg*. November 2010;52:1246–50.
19. Masuda EM, Kistner RL, Musikasinthorn C, Liquido F, Geling O, He Q. The controversy of managing calf vein thrombosis. *J Vasc Surg*. 2012;55:550–61. doi:10.1016/j.jvs.2011.05.092.
20. Garcia R, Probeck K, Elitharp DM, Gasparis AP, Labropoulos N. Diverse management of isolated calf deep venous thrombosis in a university hospital. *J Vasc Surg Venous Lymphat Disord*. 2018;6:139–45. doi:10.1016/j.jvsv.2017.08.021.
21. Robert-Ebadi H, Righini M. Should we diagnose and treat distal deep vein thrombosis? *Hematology Am Soc Hematol Educ Program*. 2017;2017:231–6.
22. Righini M. Is it worth diagnosing and treating distal deep vein thrombosis? No. *J Thromb Haemost*. 2007;5 Suppl 1:55–9. doi:10.1111/j.1538-7836.2007.02468.x.
23. Righini M, Paris S, Le Gal G, Laroche J-P, Perrier A, Bounameaux H. Clinical relevance of distal deep vein thrombosis. *Thromb Haemost*. 2006;95:56–64. doi:10.1160/TH05-08-0588.
24. Bressollette L, Nonent M, Oger E, Garcia JF, Larroche P, Guias B, et al. Diagnostic accuracy of compression ultrasonography for the detection of asymptomatic deep venous thrombosis in medical patients—the TADEUS project. *Thromb Haemost*. 2001;86:529–33.
25. Galanaud J-P, Sevestre-Pietri M-A, Bosson J-L, Laroche J-P, Righini M, Brisot D, et al. Comparative study on risk factors and early outcome of symptomatic distal versus proximal deep vein thrombosis: results from the OPTIMEV study. *Thromb Haemost*. 2009;102:493–500. doi:10.1160/TH09-01-0053.
26. Elias A, Mallard L, Elias M, Alquier C, Guidolin F, Gauthier B, et al. A single complete ultrasound investigation of the venous network for the diagnostic management of patients with a clinically suspected first episode of deep venous thrombosis of the lower limbs. *Thromb Haemost*. 2003;89:221–7.
27. Schellong S, Schwarz T, Halbritter K, Beyer J, Siegert G, Oettler W, et al. Complete compression ultrasonography of the leg veins as a single test for the diagnosis of deep vein thrombosis. *Thromb Haemost*. 2003;89:228–34. doi:10.1055/s-0037-1613436.
28. Sevestre M-A, Labarère J, Casez P, Bressollette L, Taiar M, Pernod G, et al. Accuracy of complete compression ultrasound in ruling out suspected deep venous thrombosis in the ambulatory setting. A prospective cohort study. *Thromb Haemost*. 2009;102:166–72. doi:10.1160/TH09-01-0048.
29. Roumen-Klappe EM, den Heijer M, van Uum SHM, van der Ven-Jongekrijg J, van der Graaf F, Wollersheim H. Inflammatory response in the acute phase of deep vein thrombosis. *J Vasc Surg*. 2002;35:701–6. doi:10.1067/mva.2002.121746.

30. Kearon C, Julian JA, Newman TE, Ginsberg JS. Noninvasive diagnosis of deep venous thrombosis. McMaster Diagnostic Imaging Practice Guidelines Initiative. *Ann Intern Med.* 1998;128:663–77. doi:10.7326/0003-4819-128-8-199804150-00011.
31. Almosni J, Meusy A, Frances P, Pontal D, Quéré I, Galanaud J-P. Practice variation in the management of distal deep vein thrombosis in primary vs. secondary cares: A clinical practice survey. *Thromb Res.* 2015;136:526–30. doi:10.1016/j.thromres.2015.06.013.
32. Johnson SA, Stevens SM, Woller SC, Lake E, Donadini M, Cheng J, et al. Risk of deep vein thrombosis following a single negative whole-leg compression ultrasound: a systematic review and meta-analysis. *JAMA.* 2010;303:438–45. doi:10.1001/jama.2010.43.
33. Singh K, Yakoub D, Giangola P, DeCicca M, Patel CA, Marzouk F, Giangola G. Early follow-up and treatment recommendations for isolated calf deep venous thrombosis. *J Vasc Surg.* 2012;55:136–40. doi:10.1016/j.jvs.2011.07.088.
34. Solis MM, Ranval TJ, Nix ML, Eidt JF, Nelson CL, Ferris EJ, et al. Is anticoagulation indicated for asymptomatic postoperative calf vein thrombosis? *J Vasc Surg.* 1992;16:414-8; discussion 418-9.
35. Ageno W, Mantovani LG, Haas S, Kreutz R, Monje D, Schneider J, et al. Patient Management Strategies and Long-Term Outcomes in Isolated Distal Deep-Vein Thrombosis versus Proximal Deep-Vein Thrombosis: Findings from XALIA. *TH Open.* 2019;3:e85-e93. doi:10.1055/s-0039-1683968.

Figures

Figure 1

Flow chart of patient inclusion