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Journal

Journal of Vascular Surgery Venous and Lymphatic Disorders, 10(6)

ISSN

2213-333X

Authors

Patel, Rhusheet
Woo, Karen
Wakefield, Thomas W
et al.

Publication Date

2022-11-01

DOI

10.1016/j.jvsv.2022.06.011

Peer reviewed

Published in final edited form as:

J Vasc Surg Venous Lymphat Disord. 2022 November ; 10(6): 1352–1358. doi:10.1016/j.jvsv.2022.06.011.

Contemporary management and outcomes of peripheral venous aneurysms: A multi-institutional study

Rhusheet Patel, MD[a], **Karen Woo, MD, PhD**[a], **Thomas W. Wakefield, MD**[b], **Robert J Beaulieu, MD, MSE**[c], **Manar Khashram, MBChB, PhD, FRACS**[d], **Giovanni De Caridi, MD, PhD**[e], **Filippo Benedetto, MD, PhD**[e], **Sherene Shalhub, MD, MPH**[f], **Asmaa El-Ghazali, BS**[f], **Jeffrey E. Silpe, MD, MS-HPEd**[g], **Mihai Rosca, MD**[g], **Tina U. Cohnert, MD**[h], **Gregor K. Siegl, MD**[h], **Christopher Abularrage, MD**[i], **Rebecca Sorber, MD**[i], **Catherine M. Wittgen, MD**[j], **Paul G. Bove, MD, FACS, FSVM**[k], **Graham W. Long, MD, FACS**[k], **Kristofer M. Charlton-Ouw, MD**[l], **Hunter M. Ray, MD**[l], **Peter Lawrence, MD**[a], **Donald Baril, MD**[m]

[a]Division of Vascular and Endovascular Surgery, Department of Surgery, University of California, Los Angeles, David Geffen School of Medicine, Los Angeles

[b]Division of Vascular Surgery, Department of Surgery, University of Michigan, Ann Arbor

[c]Division of Vascular Surgery and Disease, Department of Surgery, Ohio State University, Columbus

[d]Department of Vascular Surgery, University of Auckland Waikato Hospital, Hamilton

[e]Division of Vascular Surgery, University of Messina, Messina

[f]Division of Vascular Surgery, Department of Surgery, University of Washington School of Medicine, Seattle

[g]Division of Vascular Surgery, Department of Surgery, Northwell Health at Hofstra, Zucker School of Medicine, New Hyde Park

[h]Department of Vascular Surgery, Graz Medical University, Graz

[i]Division of Vascular Surgery and Endovascular Therapy, Department of Surgery, the Johns Hopkins Medical Institutions, Baltimore

Correspondence: Rhusheet Patel, MD, Division of Vascular and Endovascular Surgery, Department of Surgery, University of California, Los Angeles, David Geffen School of Medicine, 200 UCLA Medical Plaza, Ste 526, Los Angeles, CA 90095 (rhusheetpatel@mednet.ucla.edu).

AUTHOR CONTRIBUTIONS

Conception and design: RP, KW, PL, DB
Analysis and interpretation: RP, KW, DB
Data collection: RP, TW, RB, MK, GD, FB, SS, AE, JS, MR, TC, GS, CA, RS, CW, PB, GL, KC, HR
Writing the article: RP
Critical revision of the article: RP, KW, TW, RB, MK, GD, FB, SS, AE, JS, MR, TC, GS, CA, RS, CW, PB, GL, KC, HR, PL, DB
Final approval of the article: RP, KW, TW, RB, MK, GD, FB, SS, AE, JS, MR, TC, GS, CA, RS, CW, PB, GL, KC, HR, PL, DB
Statistical analysis: RP, KW, PL, DB
Obtained funding: Not applicable
Overall responsibility: RP

Author conflict of interest: none.

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

Presented at the plenary session of the 2021 Vascular Annual Meeting of the Society for Vascular Surgery, San Diego, CA, August 18–21, 2021.

[j]Division of Vascular Surgery, Department of Surgery, Saint Louis University, St Louis

[k]Division of Vascular Surgery, Department of Surgery, Oakland University William Beaumont School of Medicine, Gross Pointe Farms

[l]Department of Clinical Sciences, University of Houston, College of Medicine, Houston

[m]Division of Vascular Surgery, Department of Surgery, Cedars-Sinai Medical Center, Los Angeles.

Abstract

Objective: Extremity venous aneurysms result in the risk of pulmonary embolism (PE) and chronic venous insufficiency. At present, owing to the rarity of these aneurysms, no consensus for their treatment has been established. The purpose of the present study was to review the presentation, natural history, and contemporary management of extremity venous aneurysms.

Methods: We performed a retrospective, multi-institutional review of all patients with extremity venous aneurysms treated from 2008 to 2018. A venous aneurysm was defined as saccular or fusiform with an aneurysm/vein ratio of >1.5.

Results: A total of 66 extremity aneurysms from 11 institutions were analyzed, 40 of which were in a popliteal location, 14 iliofemoral, and 12 in an upper extremity or a jugular location. The median follow-up was 27 months (range, 0–120 months). Of the 40 popliteal venous aneurysms, 8 (20%) had presented with deep vein thrombosis (DVT) or PE, 13 (33%) had presented with pain, and 19 had been discovered incidentally. The mean size of the popliteal venous aneurysms presenting with DVT or PE was larger than that of those presenting without thromboembolism (3.8 cm vs 2.5 cm; $P = .003$). Saccular aneurysm morphology in the lower extremity was associated with thromboembolism (30% vs 9%; $P = .046$) and fusiform aneurysm morphology with a thrombus burden >25% (45% vs 3%). Patients presenting with thromboembolism were more likely to have had a thrombus burden >25% in their lower extremity venous aneurysm compared with those who had presented without thromboembolism (70% vs 9%). Approximately half of all the patients underwent immediate intervention, and half were managed with observation or antithrombotic regimen. In the nonoperative cohort, three patients subsequently developed a DVT. Eight patients in the medically managed cohort went on to require surgical intervention. Of the 12 upper extremity venous aneurysms, none had presented with DVT or PE, and only 2 (17%) had presented with pain. Of the 66 patients in the entire cohort, 41 underwent surgical intervention. The most common indication was the absolute aneurysm size. Nine patients had undergone surgery because of a DVT or PE, and 11 for pain or extremity swelling. The most common surgery was aneurysmorrhaphy in 21 patients (53%), followed by excision and ligation in 14 patients (35%). Five patients (12%) had undergone interposition bypass grafting. A postoperative hematoma requiring reintervention was the most common complication, occurring in three popliteal vein repairs and one iliofemoral vein repair. None of the patients, treated either surgically or medically, had reported post-thrombotic complications during the follow-up period.

Conclusions: Large lower extremity venous aneurysms and saccular aneurysms with thrombus >25% of the lumen are more likely to present with thromboembolic complications. Surgical intervention for lower extremity venous aneurysms is indicated to reduce the risk of venous thromboembolism (VTE) and the need for continued anticoagulation. Popliteal aneurysms >2.5

cm and all iliofemoral aneurysms should be considered for repair. Upper extremity aneurysms do not have a significant risk of VTE and warrant treatment primarily for symptoms other than VTE. (J Vasc Surg Venous Lymphat Disord 2022;10:1352–8.)

Keywords

Deep vein thrombosis; DVT; Multi-Institutional; Venous aneurysm

Peripheral venous aneurysms are rare, and the true prevalence of extremity venous aneurysmal disease is unknown. Since venous aneurysms were first described in 1968,[1] only case reports and small series have been reported. Thus, the natural history and optimal management of venous aneurysms has remained poorly defined. The prior largest single series of extremity aneurysms, collected >22 years ago, with limited imaging capabilities available early in the study, had included 30 upper and lower extremity aneurysms, and 20% of the patients had presented with deep vein thrombosis (DVT) or pulmonary embolism (PE).[2] All the patients had been treated surgically.[2]

The low prevalence and variable clinical presentation of venous aneurysms has resulted in variability in management. Other investigators have recommended screening for popliteal venous aneurysmal disease in all patients undergoing leg duplex ultrasound and those with unprovoked DVT or PE and surgery as the best treatment option for saccular lower extremity venous aneurysms and fusiform aneurysms containing thrombus >2 cm in diameter.[3,4] However, the treatment of asymptomatic patients with venous aneurysms has remained controversial because multiple case reports have not described thromboembolic events in asymptomatic patients with smaller aneurysms.[5,6] Furthermore, the surgical approaches and perioperative care have varied and have been largely determined by individual institution and surgeon experience.

The objective of the present study was to report on the natural history of extremity venous aneurysms in a multi-institutional cohort and to describe the modern outcomes of medical and surgical management.

METHODS

The present study was performed using the Vascular Low Frequency Disease Consortium (VLFDC).[7] The VLFDC is a multi-institutional collaboration developed to improve patient care for those with uncommon vascular diseases, for whom limited data are available for clinical decision-making or when discrepant management recommendations have been reported. The VLFDC uses standardized definitions and a standardized database to minimize variations in data collection.

All extremity venous aneurysms diagnosed and treated between 2008 and 2018 at each participating institution were included. The aneurysms were identified using duplex ultrasound, cross-sectional magnetic resonance imaging (MRI), and/or computed tomography (CT). Consistent with prior reports, venous aneurysms were defined as an aneurysm/vein ratio of >1.5.[8] Patients with pseudoaneurysms, arteriovenous fistulas, and varicose veins were excluded.

Each contributing institution was responsible for obtaining institutional review board approval. Because of the retrospective nature of the present study and the minimal risk posed to the patients, all institutional review boards had waived the requirement for patient written informed consent. The principal investigators from each institution were responsible for the completeness of the submitted data. The study data were collected and managed using the Research Electronic Data Capture (REDCap) electronic data capture tools hosted by the VLFDC at the University of California, Los Angeles.[9] REDCap is a secure, web-based software platform designed to support data capture for research studies. The data acquisition template and definitions were developed by the team at the University of California, Los Angeles, with the intent of capturing all relevant data in an easy-to-input format. Data from REDCap were de-identified and exported to an Excel, version 15, database (Microsoft Corp, Redmond, WA). The patient demographics, aneurysm features, and presentation were compared using the χ^2, *t* test, and analysis of variance, as appropriate.

RESULTS

Presentation

A total of 66 extremity venous aneurysms were identified at 11 international institutions during the study period. The cohort included 40 popliteal aneurysms, 14 iliofemoral, and 12 upper extremity or jugular vein aneurysms (Table I). Slightly more than one half of the patients were men, with a mean age of 54 years, and a normal mean body mass index. Of the 66 patients, 15 (23%) had had a history of trauma to the site of their venous aneurysm, 17 had had ipsilateral venous insufficiency, and only 1 patient had had a known family history of venous aneurysmal disease.

Duplex ultrasound was the primary diagnostic imaging modality, used for 57 aneurysms (86%). The remaining aneurysms were diagnosed using MRI or CT. Of the aneurysms diagnosed using duplex ultrasound alone, additional axial imaging, CT or MRI, was obtained for 26 patients. Of the 41 patients who had undergone surgical intervention, 34 had undergone preprocedure axial imaging.

Popliteal venous aneurysms

The most common anatomic location of the venous aneurysms was popliteal. A total of 40 popliteal venous aneurysms were reported, with a mean diameter of 2.7 cm. The aneurysms had been most often discovered as an incidental imaging finding. However, 16 popliteal aneurysms (40%) had presented with pain, 3 with DVT, and 4 with PE (Fig 1). Fusiform morphology was more common for the popliteal aneurysms and was present in 25 patients (63%). Most popliteal aneurysms (87%) had had a thrombus burden of <25% of the lumen; only five patients (13%) had had thrombus occupying >25% of the vessel lumen (Fig 2).

Iliofemoral venous aneurysms

A total of 14 iliofemoral aneurysms were reported, with a mean diameter of 4.1 cm. Of these 14 patients, 6 (43%) had presented with pain, 3 (21%) with DVT, and 5 (36%) had been found incidentally. No patient with an iliofemoral venous aneurysm had presented with PE (Fig 1). Of the 14 aneurysms in the iliofemoral location, 6 were fusiform and 8

were saccular. Of these 14 patients, 8 (57%) had had thrombus that occupied <25% of the aneurysm lumen and 6 (43%) had had thrombus occupying >25% (Fig 2).

Upper extremity and jugular venous aneurysms

Five upper extremity and seven jugular vein aneurysms were reported, with an average size of 2.7 cm. All aneurysms in this cohort had presented with pain or localized swelling; however, none had presented with either DVT or PE (Fig 1). Of these 12 upper extremity aneurysms, 8 had had saccular morphology and 4 were fusiform. Of these 12 patients, 4 (33%) had had a thrombus burden >25% of the lumen (Fig 2).

Thromboembolic risk

Among the popliteal venous aneurysms, a statistically significant difference was found in the size between those presenting with and without thromboembolic complications. The mean size of the venous aneurysms presenting with DVT or PE was 3.8 cm, and the mean size of those presenting without thromboembolism was 2.5 cm ($P = .003$). No association was found between a larger aneurysm size and presentation with DVT or PE for the iliofemoral and upper extremity aneurysms.

Saccular morphology in the lower extremity venous aneurysms was also significantly associated with a thromboembolic presentation and was related to the thrombus burden. Of the saccular aneurysms in the lower extremity, 30% had presented with thromboembolism vs only 9% of fusiform aneurysms presenting with DVT or PE ($P = .046$). Of the saccular aneurysms, 45% had had a thrombus burden >25% of the aneurysm lumen vs only 3% of fusiform aneurysms. Thrombus that was >25% of the lumen in lower extremity venous aneurysms was independently associated with DVT or PE. Of 10 patients who had presented with DVT or PE, 7 had had a thrombus burden >25% of their lower extremity venous aneurysm. In contrast, of those with a nonthromboembolic presentation, only 4 of 44 patients with lower extremity aneurysms had had thrombus >25% of the lumen (Fig 3).

Management

Nonoperative management.—Of the 66 patients, 33 (50%) had initially been managed nonoperatively and 33 (50%) had undergone a primary operative intervention (Fig 4). The patients managed nonoperatively had had a mean aneurysm size of 2.2 cm and 3.4 cm in the popliteal and iliofemoral locations, respectively.

Nonoperative management consisted of observation alone for 19 patients, observation and anticoagulation therapy for 6 patients, and observation and antiplatelet therapy for 8 patients. All 33 patients had undergone imaging studies during observation follow-up. One patient with a popliteal venous aneurysm had developed a new DVT during observation without anticoagulation therapy, and two patients with an iliofemoral aneurysm had developed a new DVT during observation. Both of the latter patients had been receiving therapeutic anticoagulation at the development of the new DVT.

Aneurysm growth occurred in three patients in the observation group without surgical intervention. Two iliofemoral aneurysms had grown for an average period of 39 months, and

one upper extremity aneurysm had grown for a period of 25 months. No popliteal venous aneurysms had exhibited growth during a mean follow-up of 22 months.

Operative management.—A total of 41 patients had undergone surgical intervention, of whom 8 had initially been managed nonoperatively. The primary indication for surgery was absolute size for 20 patients, pain or swelling for 11, DVT for 7, and PE for 3 (Table II). Of the eight patients who had crossed from nonoperative to surgical management, the indication for surgery was pain for three, a new DVT for two, and an absolute size increase for three. The average size of the aneurysms treated for the indication of size was 3 cm for the popliteal location, 5.5 cm for the iliofemoral location, and 2.5 cm for the upper extremity and jugular vein location.

Surgical repair was performed via aneurysmorrhaphy for 24 patients, excision and ligation for 13 patients, and bypass for 4 patients. Aneurysmorrhaphy was performed using closed plication in nine cases, all for popliteal aneurysms. For those patients who had undergone interposition or bypass, the small saphenous vein had been used the most often for popliteal aneurysms and the contralateral femoral vein for iliofemoral aneurysms.

Four postoperative hematomas had occurred and required surgical reintervention, and one surgical site infection had developed that was treated nonoperatively. None of the surgically treated patients had experienced recurrent thromboembolic events. No patient, treated either surgically or medically, had reported symptoms of chronic venous insufficiency or persistent swelling during a mean follow-up of 27 months.

Postoperative imaging was performed using duplex ultrasound, MRI, or CT venography for all but seven patients. Of the 41 patients, 31 (76%) had been followed up with duplex ultrasound, 1 had undergone follow-up MRI, and 2 had been followed up with CT. Of the seven patients without postoperative imaging studies, two had had a popliteal venous aneurysm, two had had an iliofemoral aneurysm, and three had had an upper extremity aneurysm. Two patients who had undergone aneurysmorrhaphy had not been followed up with imaging studies; the remainder of patients without follow-up imaging studies had undergone ligation.

Postoperative antithrombotic therapy

Six patients (15%) had received antiplatelet therapy alone postoperatively, and 20 patients (49%) had received anticoagulation therapy for a mean duration of 7.4 months. All 20 of the latter patients had eventually transitioned from anticoagulation to antiplatelet therapy or observation alone. The anticoagulation agent was warfarin for 10 patients, enoxaparin for 5 patients, rivaroxaban for 4 patients, and apixaban for 1 patient. No bleeding complications due to anticoagulation therapy were reported.

DISCUSSION

Historically, the concern for VTE has largely guided the management of venous aneurysms. The risk of VTE with lower extremity venous aneurysms has previously been reported to be 25% to 50%, and PE can be the presenting symptom in ≤80% of patients.[10–12] In addition

to symptoms resulting from VTE, patients can also develop chronic venous disease.[10,12] In contrast, in our multi-institutional series, <10% of patients with lower extremity aneurysms had had PE as their presenting symptom. Also, even when patients who had presented with DVT were included, the prevalence had increased to only 19%. In addition, only patients with a popliteal venous aneurysm had presented with PE; surprisingly, no patient with an iliofemoral vein aneurysm had presented with PE. Consistent with historical reports, upper extremity and neck venous aneurysms in our series were not associated with a significant risk of VTE.[13]

Most investigators have recommended that all symptomatic venous aneurysms should be repaired. However, the factors associated with a high risk of VTE and the management of asymptomatic patients has remained undefined. An increased size has traditionally been thought to be a marker of increased risk, and even with the absence of established size criteria for repair, the absolute aneurysm size was the most common indication for repair in our cohort.[3,4] However, a large aneurysm size was only associated with VTE on presentation for venous aneurysms in the popliteal location. The average size of popliteal aneurysms presenting with VTE was 3.8 cm, with a minimum diameter of 2.7 cm. Thus, for popliteal venous aneurysms, 2.5 cm might represent a size threshold above which repair should be offered for surgically fit patients to decrease risk of VTE.

In our series, saccular morphology and an increased thrombus burden >25% in the popliteal and iliofemoral aneurysms were also associated with VTE in the lower extremity aneurysms. These features can be readily identified via ultrasound imaging and should be considered risk factors for VTE. Based on our findings, these features could serve as an indication for repair of venous aneurysms.

In the present study, duplex ultrasound was the primary mode of diagnosis in most institutions; however, most of the patients requiring surgical intervention had also undergone preoperative CT or magnetic resonance venography. Although some investigators have suggested the need for venography to define the venous anatomy before surgical intervention, the preoperative imaging modality used has not been shown to be associated with the outcome.[5]

For both popliteal and iliofemoral locations, smaller aneurysms were most often managed nonoperatively. Among this cohort of smaller lower extremity aneurysms that were observed, only 5% of the popliteal venous aneurysms had developed a new DVT, although 33% of the observed iliofemoral aneurysms had developed a new DVT. Some investigators, citing the low morbidity of surgical repair, have recommended a more aggressive approach toward surgical repair.[3,4,14]

Although all operative cases of upper extremity aneurysms were treated with open surgical repair, endovascular treatment of a patient with a symptomatic subclavian vein aneurysm has been previously reported.[15] Endovascular aneurysm exclusion was not performed in our patient cohort. Tangential excision and lateral venorrhaphy was the most common surgical approach, although nine patients had successfully undergone aneurysmorrhaphy via the previously described closed plication technique.[16]

Although considerable variability in the initial management and patient selection was present between the institutions and surgeons, the results from our series suggest that smaller popliteal aneurysms can be safely managed nonoperatively with a minimal risk of growth or VTE. Other investigators have also advocated for a nonoperative approach for smaller popliteal venous aneurysms without concerning features.[6] Iliofemoral aneurysms, however, appear to have a persistent risk of DVT, even at smaller sizes and when treated with anticoagulation.

A significant portion of patients with saccular and fusiform lower extremity aneurysms were treated with vein ligation, with no adverse sequela of deep vein ligation reported. Other small series of deep vein ligation for the treatment of venous aneurysms have similarly reported acceptable outcomes.[14,17] Adequate collateral venous circulation should ideally be evaluated before any deep vein ligation. Also, deep vein ligation might not be the preferred surgical option for younger patients or those with evidence of reflux at the level of venous aneurysmal disease. Surgical intervention via any of the reported methods resulted in no recurrent VTE or post-thrombotic symptoms during the follow-up period. However, our follow-up period did not extend beyond a mean of 3 years.

Surgical intervention eliminated recurrent VTE in all cases. Although postoperative medical management varied among the institutions, long-term anticoagulation therapy was not necessary after surgical intervention. No patient had continued anticoagulation therapy for >1 year postoperatively. However, the optimum length of postoperative anticoagulation therapy could not be determined from our sample. Prior reports have similarly recommended anticoagulation for 3 to 6 months.[3,18,19]

No recurrent DVT had developed in the patients who had undergone surgery in our series, although recurrent DVT has been reported ≤4 years postoperatively.[20] The optimal follow-up interval or end point could be determined from our study. Magnetic resonance venography and CT venography were not used during follow-up in our study and are likely seldom required. Duplex ultrasound will allow for visualization of the repair in most cases and represents an economic and noninvasive method of postoperative surveillance after venous aneurysm repair.

The strength of the present study was the standardized data collection from multiple institutions. However, our study was still subject to the limitations of a retrospective design with considerable variability in disease management, which was at the discretion of each clinician. Although our results have provided a better understanding of the natural history and efficacy of the management options, larger, ideally prospective, studies with long-term follow-up, are needed to better guide the management of venous aneurysms.

CONCLUSIONS

The results from our study have shown that large lower extremity venous aneurysms and saccular aneurysms with a thrombus burden >25% of the lumen are more likely to present with thromboembolic complications. Surgical intervention for lower extremity venous aneurysms is indicated to reduce the risk of VTE and the need for continued anticoagulation

therapy. Popliteal aneurysms >2.5 cm and all iliofemoral aneurysms should be considered for repair. Upper extremity aneurysms do not carry a significant risk of VTE and warrant treatment primarily for symptoms other than VTE.

Acknowledgments

The present study was supported by the National Center for Advancing Translational Sciences, National Institutes of Health (grant UL1TR001881).

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ARTICLE HIGHLIGHTS

- **Type of Research:**

A multicenter, retrospective, longitudinal study

- **Key Findings:**

The mean size of popliteal aneurysms presenting with deep vein thrombosis or pulmonary embolism was 3.8 cm. Of the lower extremity venous aneurysms, 30% of the saccular aneurysms and 64% of the aneurysms with >25% intraluminal thrombus had presented with thromboembolism. None of the surgically treated patients had experienced recurrent thromboembolic events.

- **Take Home Message:**

Our results have shown that surgical intervention for large lower extremity venous aneurysms is indicated to reduce the risk of venous thromboembolism and the need for continued anticoagulation.

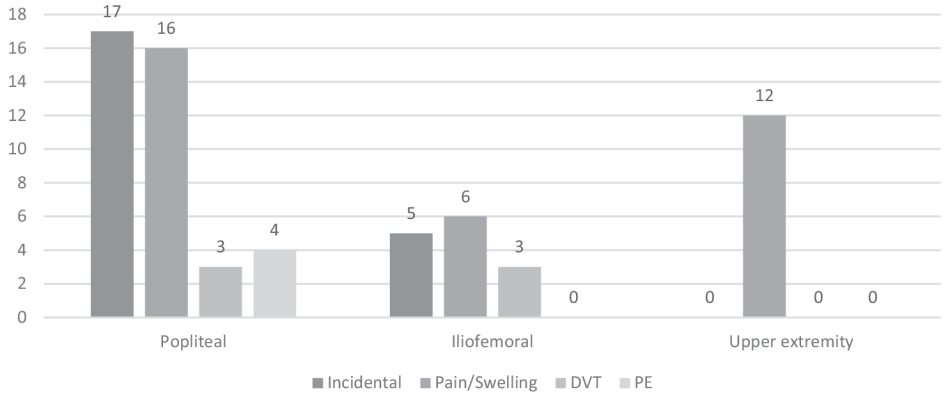

Fig 1.

Presentation stratified by aneurysm location. *DVT*, Deep vein thrombosis; *PE*, pulmonary embolism.

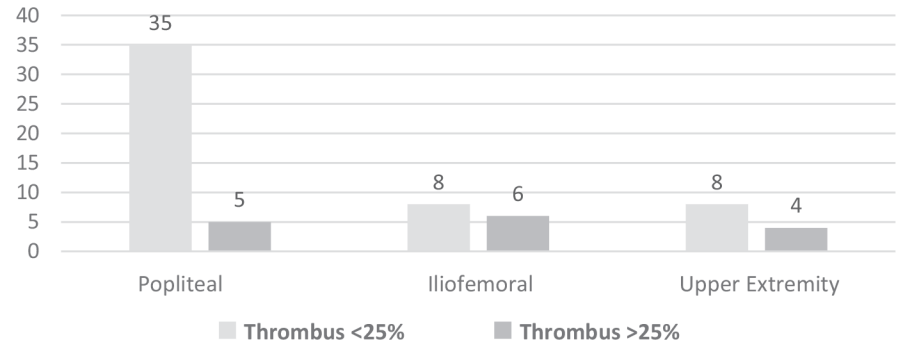

Fig 2.
Thrombus burden stratified by venous aneurysm location.

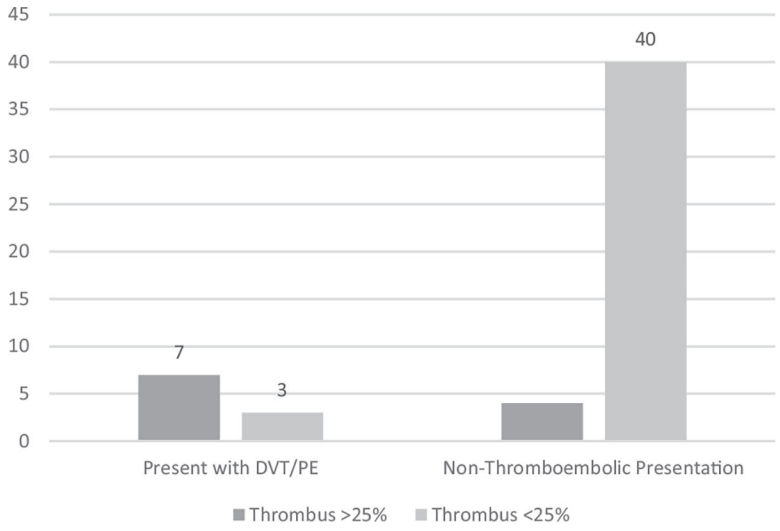

Fig 3.

Percentage of thrombus and thromboembolic presentation in popliteal vein aneurysms. *DVT*, Deep vein thrombosis; *PE*, pulmonary embolism.

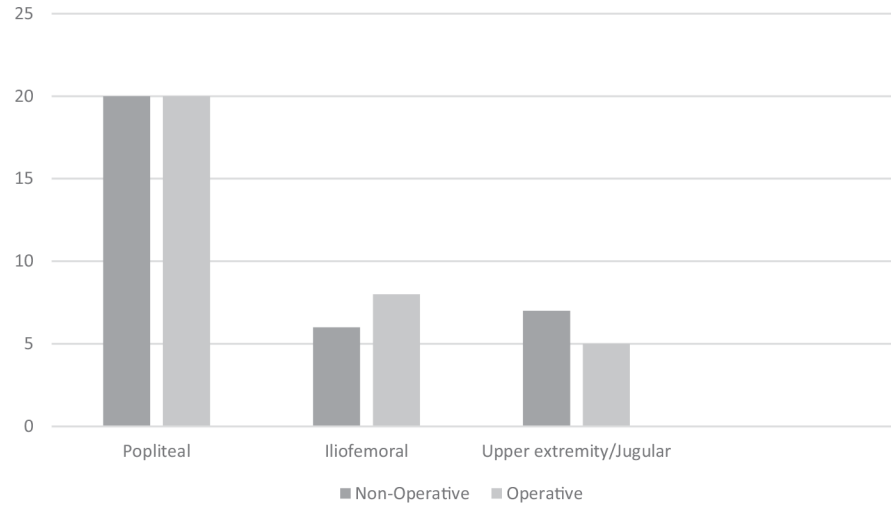

Fig 4.
Initial nonoperative vs operative management stratified by aneurysm location.

Table I.

Demographics and comorbidities

Variable	Patients, No. (%)
Male sex	34 (52)
Mean age, years	53.7
Mean BMI, kg/m^2	26.3
Smoking history	26 (39)
Trauma history	15 (23)
Family history of connective tissue disorder	0 (0)
Family history of venous aneurysm	1 (2)
Family history of arterial aneurysm	4 (6)
Known hypercoagulable disorder	3 (5)
Ipsilateral venous insufficiency	17 (26)

BMI, Body mass index.

Table II.

Surgical intervention

Variable	Aneurysm, No.
Popliteal location	24
Indication	
Size	14
Pain/swelling	3
DVT/PE	7
Repair	
Aneurysmorrhaphy	15
Excision/ligation	6
Bypass	3
Iliofemoral location	11
Indication	
Size	4
Pain/swelling	4
DVT/PE	3
Repair	
Aneurysmorrhaphy	8
Excision/ligation	2
Bypass	1
Upper extremity/jugular location	6
Indication	
Size	2
Pain/swelling	4
Repair	
Aneurysmorrhaphy	1
Excision/ligation	5

DVT, Deep vein thrombosis; *PE,* pulmonary embolism.sss