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Direct oral anticoagulants in deep vein thrombosis associated with inferior vena cava agenesis: A report of three cases and a systematic review

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ABSTRACT

Background: Inferior vena cava agenesis (IVCA) is a rare vascular abnormality characterised by the absence of one or more segments of the inferior vena cava and represents an underestimated cause of deep vein thrombosis (DVT). Given the very low prevalence of this condition and the lack of clinical trials, there is no consensus about the optimal anticoagulation strategy in IVCA-associated DVT.
Objectives: To investigate efficacy and safety of direct oral anticoagulants (DOACs) in IVCA-associated DVT.
Methods: We described three patients with IVCA-associated DVT followed at our Institution and treated with DOACs. Then, we performed a systematic review of the literature for ICVA-associated DVT treated with DOACs.
Results: In addition to our 3 cases, we found data from 19 publications for a total of 30 patients with IVCA-associated DVT treated with DOACs (24 subjects treated with rivaroxaban, 8 with apixaban, and one with dabigatran). Most patients were males (72.7 %) with a median age at DVT onset of 26.0 years (min–max range 13–64 years). The majority of DVT events were unprovoked (76.0 %). The standard thrombophilia tests were mainly negative. The median follow-up period during DOAC therapy was 1.0 years (min–max range 0–10 years), with one recurrent splanchnic vein thrombosis reported and no haemorrhagic events.
Conclusions: IVCA is a rare cause of DVT, which should be suspected in young adults with unprovoked DVT. Although future studies are needed, available data may support the use of DOACs in IVCA-associated DVT, with a reassuring profile of both efficacy and safety.

1. Introduction

Embryogenesis of the inferior vena cava (IVC) occurs during weeks 4–8 of gestation, when three sets of paired veins (i.e. the supracardinal, the posterior cardinal, and the subcardinal veins) form and regress until the final mature IVC is shaped. Based on embryological development, IVC is divided into four segments: hepatic, suprarenal, renal and infrarenal [1].

Inferior vena cava agenesis (IVCA) is the absence of one or more segments of the IVC, and can be clinically distinghuished into intra-hepatic (hepatic segment), extrahepatic (suprarenal, renal and/or infrarenal segments) or complete, according to the segment(s) involved [2].

Although hystorically considered resulting from embryological dysgenesis, many data suggest that IVCA might be secondary to prenatal or perinatal thrombosis, with inherited thrombophilia representing a predisposing factor. For example, a penetrance up to 70 % for IVCA is reported in the presence of homozygous antithrombin Budapest 3 variant (p.Leu131Phe) [3].

IVCA is generally an isolated malformation, but associations with other organ abnormalities have also been described, in particular bowel (13 %), cardiac (10 %) and hepatobiliary (8.5 %) [4]. Even more rarely, IVCA may constitute part of the KILT syndrome (Kidney and IVC abnormalities with Leg Thrombosis) [5].

In the absence of IVC, venous blood from the lower limbs and the abdomen needs to find alternative vessels to return to the heart's right

Abbreviations: IVC, inferior vena cava; IVCA, inferior vena cava agenesis; DVT, deep vein thrombosis; PE, pulmonary embolism; DOAC, direct oral anticoagulant; CT, computed tomography; APC, activated protein C; COCP, combined oral contraceptive pill; VKAs, vitamin K, antagonists; IQR, interquartile range.

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atrium, which are typically represented by the azygos venous system, arising from the lumbar region and directly draining into the superior vena cava [6,7].

IVCA is a rare condition, and its prevalence in the general population is unknown, with some authors suggesting a very low prevalence of about 0.0005–1 % [6]. IVCA is recognized as a rare cause of lower limb deep venous thrombosis (DVT) and, consistently, in young patients (< 30 years) with idiopathic venous thromboembolism its prevalence has been reported to be up to 5 % [8]. It is worthy to note that the magnitude of such association is probably underestimated because an abdominal CT scan is rarely part of the diagnostic routine for DVT, and B-mode compression ultrasound is generally limited to femoral and iliac veins [8]. In the large RIETE registry, 31 out of 50,744 patients with lower-limb DVT had IVCA (0.06 %) and the presence of IVCA was associated with either premature DVT at age < 30 with an odds ratio (OR) of 17.9 (95 % CI 7.1–45.3) or bilateral DVT with an OR of 11.5 (95 % CI 4.8–27.8) [9]. In a recent retrospective, multicenter, observational study by the IVCA Study Group, an estimated annual risk of venous thrombosis of 1.15 % (95 % CI 0.89–1.46) is reported [2]. IVCA-associated DVT is more likely to be unprovoked, more often bilateral, and presents higher rates of recurrence [2,4]. Due to anatomical factors, extrahepatic IVCA is associated with a significantly higher risk of lower limbs DVT than intrahepatic IVCA, but lower incidence of pulmonary embolism and splanchnic vein thrombosis. Indeed, in extrahepatic IVCA blood is mainly collateralised by small vertebral veins, which represent a more efficient filter but also imply a major peripheral stasis [2].

Remarkably, risk of DVT recurrence is reported to be extremely high in patients with IVCA (up to 40 %), especially in male patients and whom with extrahepatic involvement [2].

According with this profile of increased thrombotic risk, patients with IVCA-associated DVT are generally considered for indefinite anticoagulation.

Direct oral anticoagulants (DOACs) are widely used to treat venous thromboembolism (VTE) in adult subjects, both in the acute phase of the disease and in the long-term prophylaxis [10,11], but very little is known about efficacy and safety of DOACs in patients with IVCA-associated DVT.

Here, we report a case series of three patients treated with DOACs for IVCA-associated DVT who were managed at our Institute. Moreover, we systematically reviewed the medical literature on similar cases to deepen our understanding of the clinical characteristics and therapeutic use of DOACs in the peculiar clinical setting of IVCA-associated DVT.

2. Methods

2.1. Patients

Subjects with a diagnosis of IVCA-associated DVT treated at our Institute from 2016 to 2024 were included in this series. To be included, patients should fulfil the following criteria: diagnosis of IVCA made by CT scan or MRI, confirmed diagnosis of DVT made by Doppler-ultrasonography or CT scan, prior or active treatment with DOAC. All the three patients have given informed and written consent for case report publication.

2.2. Literature search and study selection

We used a systematic approach to identify studies that reported cases of IVCA-associated DVT. We included only cases treated with one of the available DOACs for the treatment of venous thromboembolism (dabigatran, apixaban, edoxaban, rivaroxaban). We searched for all publications reporting cases of IVCA-associated DVT up to February 2024. A systematic literature search was performed in MEDLINE, Science Direct, and Cochrane Library databases from 2012 (the year of rivaroxaban FDA approval for the treatment of DVT and PE) to 2024. Search terms consisted of "*inferior vena cava agenesis*" OR "*inferior vena cava atresia*", OR *"inferior vena cava hypoplasia"* OR *"absence of the inferior vena cava"*, and every single paper was read to find the mention of a DVT treated with DOACs. These concepts were extensively searched either by the use of subject headings or free text words.

Publications were included when they reported original data of clinical cases of DVT related to IVCA treated with one of the available DOACs, either in the acute phase or in the secondary prophylaxis, as well as if at least age of first thromboembolic event, sex, and type of DOAC were conveyed. Only publications written in English have been included in this review. Conference abstracts were excluded.

Review articles or previous systematic reviews were excluded but used to check for relevant publications not identified by the literature search. The selected publications were then used to identify unique case reports or case series of DVT-related IVCA patients. The study selection was performed by two independent and blinded authors (N.O. and A. M.).

Information about age, sex, site of venous thrombosis, IVCA location, thrombophilia status, presence of precipitating factors, type and dose of DOAC, years of active follow-up and complications during follow-up were extracted from each selected case description (when available).

2.3. Statistical analysis

Median values with minimum–maximum range were used to describe quantitative variables, while qualitative variables were expressed as count and percentage. Qualitative data were analysed using Fisher's exact test when indicated. Statistical analysis was performed using the IBM SPSS 23.0 statistical package (IBM Inc., Armonk, NY, USA).

3. Case series

From 2016 to 2023, three patients with IVCA-associated DVT were reported at our Institution. All patients presented their first thrombotic event at the age of 19. Two patients have infrarenal IVCA and one suprarenal IVCA. The location of DVT was the right lower limb in the first case, collateral renal venous circuli in the second case, and bilateral lower limbs and IVC in the third case.

At present, all three patients are taking anticoagulant therapy with DOACs. More precisely, two patients are treated with rivaroxaban (one with full dose and the other with prophylactic dose), and the third one with apixaban at prophylactic dose. Two patients are taking DOACs for a long time (4 and 7 years, respectively), while the third takes DOAC for less than one year. No complications in terms of DVT recurrences or bleeding episodes have been observed in all three patients during treatment with DOACs.

3.1. Case 1

A 42-year-old man came to our attention for the first time in June 2022. He reported a first DVT involving the right popliteal, femoral and iliac vein back in 1999 when he was 19 years old. He was treated with a one-year course of warfarin with a complete recanalisation and, afterwards, the drug was discontinued.

In 2010, when he was 30 years old, a second episode of DVT at the same site occurred, and anticoagulation with warfarin was resumed, with the indication of a life-long duration. Anticoagulation therapy with warfarin was substituted by rivaroxaban 20 mg once daily in 2019. Afterwards, in 2021, the dose was reduced to a prophylactic dose of rivaroxaban 10 mg once daily, which the patient is currently taking. Pulmonary embolism never occurred in the patient's history.

The patient had no family history of venous thromboembolism and a thrombophilia panel for traditional acquired and hereditary disorders (activated protein C resistance, factor II G20210A mutation, protein C, protein S and antithrombin levels, lupus anticoagulant, anti-cardiolipin IgG/IgM and anti-beta-2-glycoprotein I IgG/IgM antibodies) was

negative.

The possibility of IVCA was suspected after more than 20 years from the first DVT event, and a CT scan of the abdomen was obtained in 2023, which revealed a complete agenesis of the IVC infra-renal tract with the two common iliac veins draining into dilated lumbar plexuses, finally draining into a markedly dilated azygos vein. The left renal vein was also markedly dilated and curvy, emptying into the left lumbar plexus, while the right renal vein ended at the beginning of the existing IVC. Kidney dimensions were within normal ranges bilaterally, as well as laboratory biomarkers of renal function.

3.2. Case 2

In 2023, a 19-year-old man went to the emergency department reporting intense right hip pain and fever. Point of care ultrasonography showed right hydronephrosis with an absent jet of the homolateral ureter in the bladder. Therefore, kidney stones were suspected, and a CT scan of the abdomen was obtained.

The CT scan showed agenesis of the IVC infra-renal tract with acute thrombosis of multiple enlarged venous collateral circuli draining the blood from the right kidney into a dilatated azygos vein (Fig. 1). The right ureter was dilated until the crossing with the iliac thrombotic vessels.

MRI-angiography of the abdomen confirmed the presence of a complex vascular venous malformation, with agenesis of the IVC infra-renal tract. The common iliac veins drained directly into dilated lumbar plexuses and then into dilated azygos and hemiazygos veins. Renal function was within normal ranges.

After one week of full-dose subcutaneous enoxaparin, a full dose of rivaroxaban (15 mg bid for three weeks followed by 20 mg od) was started and is still ongoing.

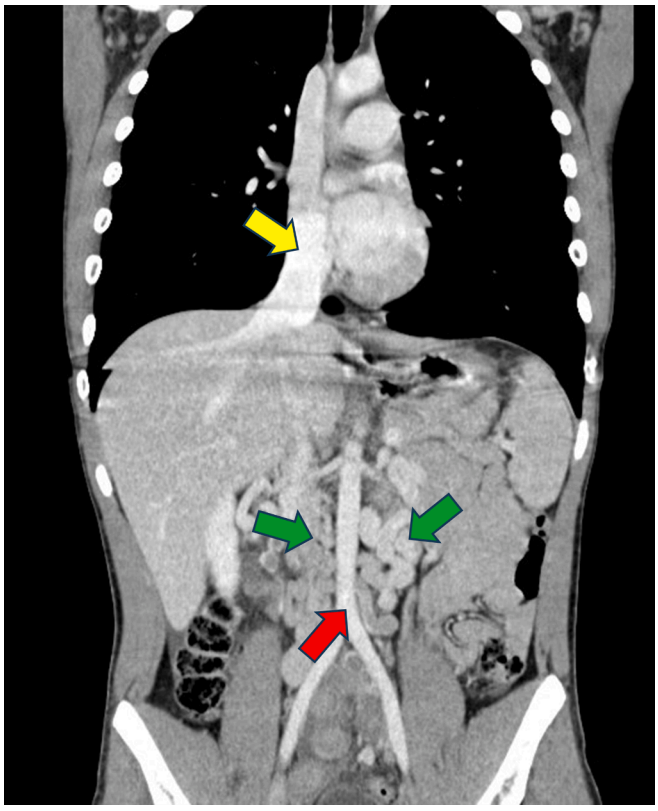

Fig. 1. Coronal reconstruction of abdominal and thoracic CT scan of patient #2. Red arrow: abdominal aorta; green arrows: dilated and tortuous azygos veins with the absence of inferior vena cava; yellow arrow: dilated superior vena cava with drainage of hepatic flow.

3.3. Case 3

A 34-year-old woman with a previous diagnosis of DVT secondary to IVC agenesis was referred to our outpatient clinic for her willingness to start a pregnancy.

Back in 2008, when she was 19 years old, she had DVT involving both popliteal-femoral-iliac axes, the infra-renal tract of the IVC and the left renal vein, with a CT scan of the abdomen showing agenesis of IVC supra-renal tract. Anticoagulation with warfarin was started, which she continued until 2016, when treatment with with rivaroxaban 20 mg daily was introduced, then switched to apixaban 2.5 mg twice daily in 2018.

MRI-angiography of the abdomen showed a fibrotic remodelling of the previous thrombosis, with severely narrowed lumen of both the iliac veins and the infra-renal-tract of the IVC, with blood draining through paravertebral and intramedullary veins into the azygos and hemiazygos veins.

Before getting pregnant, apixaban was stopped, and subcutaneous enoxaparin 100 U/kg once daily was started, which she maintained throughout the entire duration of pregnancy and breastfeeding. Finally, apixaban 2.5 mg twice daily was restarted.

4. Results of the systematic review

As shown in Fig. 2, the search strategy finally yielded 19 papers (17 case reports and 2 case series), allowing the identification of a total of 30 patients who both had a diagnosis of IVCA-associated DVT and have been treated with DOACs. Including our case series, Table 1 summarises the main clinical characteristics of the 33 patients with IVCA-associated DVT treated with DOACs.

Patients were more frequently males (72.7 %). The median age for first thrombotic complications was 26.0 years (min–max range 13–64 years). When reported (27/33 available), the most frequent site of IVCA was infrarenal (74 %, 20/27 cases). There was no association between the site of IVCA and the site of DVT presentation – unilateral vs bilateral ($p = 0.799$ by Fisher's exact test). Pulmonary embolism via vena azygos was reported only in one patient with suprarenal IVCA (Table 1, Ramos Aranda 2018).

Although not regularly investigated (data available for 26 out of 33 subjects), standard thrombophilic screen was negative in most of reported cases, with only two patients with heterozygosity for factor V Leiden and another one with not further investigated activated protein C resistance. For 8 patients (24 %, 33/33 available), a possible precipitating factor was described (two trauma, one surgery, two hormonal contraceptive therapy, one abdominal infection, one post-partum and one anabolic steroids).

Regarding DOAC treatment, rivaroxaban was the most frequently used, reported in 24 cases (73 %), while apixaban and dabigatran were reported in 8 (24 %) cases and one case (3 %), respectively. Only in 23 out of 33 cases was the DOAC dose reported (17/24 for rivaroxaban, 5/8 for apixaban, 1/1 for dabigatran). DOACs reduced prophylactic dose was administered in 7 out of 17 patients treated with rivaroxaban (41 %) and 4 out of 5 patients treated with apixaban (80 %).

During the follow-up with a calculated median period of 1.0 years (min–max range 0–10 years), only one thrombotic recurrence involving superior and inferior mesenteric veins has been reported in a patient treated with rivaroxaban and for which the dose of the drug was not stated (see Table 1, Tufano 2017). No bleeding complications have been reported in all 33 cases. In 8 out of 33 patients, an endovascular treatment before anticoagulant therapy has been reported.

When considering separately the 23 patients in which the DOAC dose was reported, patients treated with a full vs a prophylactic dose of DOACs had a median follow-up of 1.5 years (min–max range 0–10 years, 12 patients) and 2.0 years (min–max range 0–7 years, 11 patients), respectively. Table 2 summarises the clinical characteristics and outcomes of the cases included in the systematic review by the dose of

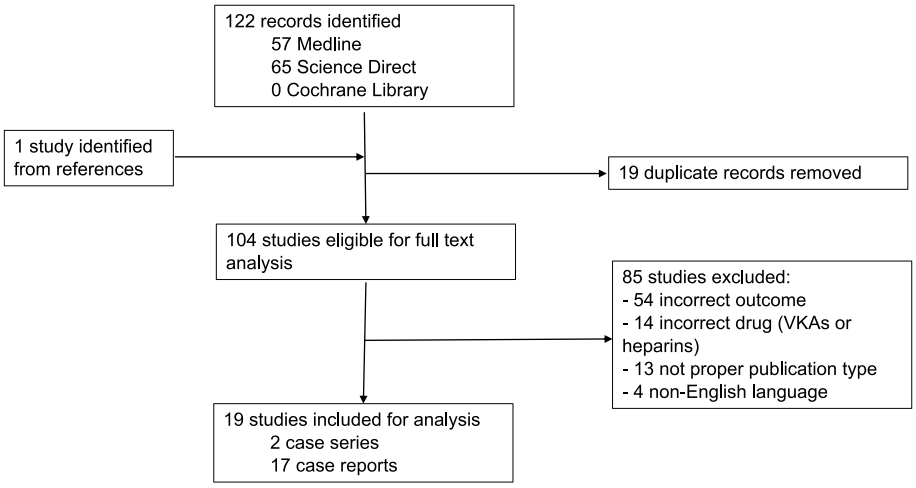

Fig. 2. Flowchart of literature search and study selection.

DOAC administered.

5. Discussion

To the best of our knowledge, in this systematic review we collected data from the largest cohort of patients with IVCA-associated DVT treated with DOACs reported so far.

Even in a recent report from the IVCA study group, DOACs were used as frontline therapy only in 7 out of 210 patients, and sequentially to vitamin K antagonists in only 16 patients. In the same cohort, after a mean follow-up of 73 months (IQR 31–169), a DVT recurrence rate of 35 % was reported, despite secondary prophylaxis, mainly with VKAs [2].

In our review, during secondary prophylaxis with DOACs only one splanchnic vein thrombosis recurrence (1/33, 3 %) and no bleeding complication have been reported, thereby reassuring regarding efficacy and safety of DOACs, at least rivaroxaban and apixaban, in this peculiar clinical setting. Moreover, it is worthy to note that the prophylactic doses of DOACs, either rivaroxaban or apixaban, appeared to show similar efficacy profiles.

The clinical characteristics of our case series match those of previous ones of IVCA-associated DVT not treated with DOACs, regarding age at first DVT event, IVCA localisation, absence of precipitating factors, and absence of thrombophilia abnormalities [2,4].

No data were found about DOACs use in patients < 18 years with IVCA-associated DVT, since in all case reports and case series regarding paediatric patients, DOAC was started only once patients became 18 years old [12]. As regards such issue, it should be noted that dabigatran and rivaroxaban have been only recently approved by FDA and EMA for VTE treatment in paediatric patients [13].

Pulmonary embolism is rarely reported in IVCA, which may represent a natural filter against thrombus migration from lower limb veins to pulmonary arteries. For this reason, a long-term treatment with a reduced prophylactic dose of DOACs might be a good option for patients with IVCA-associated DVT. However, it should be taken into account that pulmonary embolism may still be possible through enlarged azygos and hemiazygos systems, especially in intrahepatic IVCA. Moreover, even if pulmonary embolism could be less worrisome, many other aspects of managing anticoagulant therapy must be considered, regarding the choice between full and prophylactic doses of DOACs. For example, many patients might present a severe post-thrombotic syndrome, where the patency of the residual venous vessels must be preserved to avoid further thrombotic events that could lead to significant or even dramatic complications like limb amputation. In this case, the Villalta score might be used to identify the early signs of post-thrombotic syndrome, and elastic stocking should be associated with the anticoagulant treatment [14].

In addition, many patients may have complex and bizarre aberrations of the splanchnic venous system, especially when IVCA involves the suprarenal or hepatic segment. In the case of significant and major splanchnic vein thrombosis, full anticoagulant doses of DOACs may be preferred over prophylactic doses [15].

Data reported in this review cannot resolve the doubts about the use of different dosages of DOACs in the long-term management of ICVA-associated DVT. At present such decision should be individualized on the basis of patient's characteristics and preferences, as well as these therapeutic issues should be addressed by future clinical trials. On the other hand, our data may reassure about the safety profile of both doses, even after long-term follow-up.

In addition to anticoagulant therapy, which remains the mainstay of treatment for IVCA-associated DVT, in selected cases with extended or complicated thrombosis, endovascular intervention, such as in situ thrombolysis or thrombectomy, has been reported to minimise long-term complications [16]. In the current review, an endovascular treatment was reported in about one-quarter of the patients with an adequate safety profile and a subsequent either immediate or delayed initiation of DOAC treatment.

This study has many limitations which should be acknowledged. At first, our conclusions are based on a relatively small number of patients included in the systematic review, with clinical characteristics extracted from only English-written published data. These limitations lead to publication bias since patients with worse outcomes might not have been reported and, therefore, were underrepresented. Additional analyses were impossible due to the limited clinical data available in the extracted articles and, without randomisation, selection bias and allocation bias might have played a role in our results. Furthermore, data on follow-up were reported in less than half of retrieved publications since only a few of them were thought to give information about the effectiveness or safety of DOAC treatment in this clinical setting. The mean calculated follow-up period is relatively short, reducing the clinical validity of our data. Finally, a direct comparison between DOACs and VKAs is currently not possible given the paucity of data.

Nonetheless, our study may represent a clinically useful evidence about the use of DOACs in IVCA-associated DVT.

In summary, IVCA-associated DVT is an underdiagnosed anatomic prothrombotic condition in which treatment might be challenging. Available literature data suggest that DOACs might be effective and safe in these patients, both in the first-line therapy and the long-term secondary prophylaxis.

Table 1
Manuscripts selected for the systematic review and case description. DVT: deep vein thrombosis; IVC: inferior vena cava; IVCA: inferior vena cava agenesis; DOAC: direct oral anticoagulant; M: males; F: females; FVL: factor V Leiden; APCR: activated protein C resistance COCP: combined oral contraceptive pill; NA: not available.

Paper	Age at first DVT	Sex	DVT localization	IVCA location	Precipitating factors	DOAC	Dose	Thrombophilia	Follow-up under DOAC (years)
Our case series	19	M	unilateral ileo-femoro-popliteal	infrarenal	no	rivaroxaban	10	no	4
	19	M	right renal	infrarenal	no	rivaroxaban	mg	no	1
	19	F	bilateral iliac-femoral-popliteal + infrarenal IVC + left renal	suprarenal	no	apixaban	20 mg 2,5 mg	no	7
Iarossi 2023 [17]	19	M	unilateral iliac	infrarenal	trauma	rivaroxaban	10	no	2
	39	F	unilateral ileo-femoral	infrarenal	no	rivaroxaban	mg	FVL	2
	48	M	bilateral iliac	infrarenal	no	rivaroxaban	10	no	5
	21	M	bilateral superficial	infrarenal	no	rivaroxaban	mg	no	0
	27	M	bilateral iliac	infrarenal	no	apixaban	20	no	6
	33	F	bilateral ileo-femoral	infrarenal	surgery	rivaroxaban	mg	no	0
	18	M	unilateral ileo-femoral	infrarenal	no	rivaroxaban	10	no	0
	17	F	bilateral iliac	infrarenal	COCP	apixaban	mg	no	1
	64	M	bilateral iliac	infrarenal	no	rivaroxaban	2.5	no	3
	19	M	bilateral iliac	infrarenal	no	rivaroxaban	mg	no	10
	27	M	unilateral ileo-femoral	infrarenal	no	rivaroxaban	10 mg 20 mg 2.5 mg 10 mg 20 mg 20 mg	no	7
Williams 2022 [18]	40	M	bilateral iliac aNA femoral	hepatic	no	apixaban	NA	NA	1
Tufano 2017 [19]	32	M	bilateral ileo-femoral	NA	no	rivaroxaban	NA	no	NA
Arikan 2019 [20]	17	M	bilateral femoro-popliteal + right iliac	NA	no	rivaroxaban	20 mg	no	4
Brkić 2023 [21]	23	M	bilateral iliac + left testicular	infrarenal	no	dabigatran	150 mg	no	2
Castro 2021 [22]	26	F	femoral bilateral + unilateral iliac vein aNA artery	NA	no	rivaroxaban	20 mg	no	5
Prado 2021 [23]	35	M	unilateral ilieo-femoro-popliteal	infrarenal	no	rivaroxaban	20 mg	no	0
Cruz 2019 [24]	20	M	bilateral ileo-femoral	infrarenal	no	rivaroxaban	10 mg	no	4
Pasqui 2022 [7]	31	M	bilateral iliac	infrarenal	no	apixaban	5 mg	APCR	1
Heafner 2019 [25]	47	M	bilateral ileo-femoral + left renal + infrarenal IVC	suprarenal	no	rivaroxaban	NA	NA	1
Koppisetty 2015 [26]	36	M	bilateral femoro-popliteal + right iliac	hepatic	no	rivaroxaban	NA	NA	1
Menning 2021 [27]	35	F	NA	infrarenal	post-partum	rivaroxaban	NA	NA	1
Ramos AraNAa 2018 [28]	23	M	bilateral iliac	infrarenal	trauma	rivaroxaban	NA	NA	1
	30	M	left iliac aNA femoropopliteal + infraneral IVC + left renal + bilateral PE	suprarenal + duplicated IVC	anabolic steroids	rivaroxaban	NA	NA	1
RaymuNAo 2019 [29]	36	F	massive bilateral lower limbs + IVC + splancnic	suprarenal	COCP	rivaroxaban	20 mg	NA	1
Kalogridaki 2018 [30]	13	M	right ileo-femoral	NA	no	rivaroxaban	15 mg	no	1
Jiang 2022 [31]	20	M	left ileo-femoro-popliteal	infrarenal	no	apixaban	2.5 mg	heterozygous FVL	1
Grieff 2020 [32]	36	M	left femoral	suprarenal	no	apixaban	NA	no	1
Thein 2018 [33]	26	F	left ileo-femoral	NA	abdominal infection	rivaroxaban	NA	no	NA
Man 2016 [34]	19	F	bilateral iliac	suprarenal	no	apixaban	NA	no	NA

CRediT authorship contribution statement

Nicola Osti: Conceptualization, Data curation, Formal analysis, Writing – original draft. **Vito Racanelli:** Supervision. **Nicola Susca:** Supervision. **Nicola Martinelli:** Supervision, Writing – original draft. **Alberto Maino:** Conceptualization, Data curation, Formal analysis, Writing – original draft.

Table 2
Summary of the clinical characteristics and outcomes of the cases included in the systematic review by the dose of DOAC administered. n: number; DOAC: direct oral anticoagulant; full dose: rivaroxaban 20 mg once daily, apixaban 5 mg two times a day, dabigatran 150 mg two times a day; prophylactic dose: rivaroxaban 10 mg once daily, apixaban 2.5 mg two times a day.

	All cases	DOAC full dose	DOAC prophylactic dose	Dose not reported
Patients, n	33	12	11	10
DOAC				
rivaroxaban	24	10	7	7
apixaban	8	1	4	3
dabigatran	1	1	/	/
Male sex (%)	72.7	83.3	63.6	70.0
DVT first localization*				
limbs bilateral		7	7	6
limbs unilateral		4	4	2
abdomen		2	0	1
Age at first DVT, years (min–max)	26 (13–64)	24.5 (13–48)	20 (17–64)	33.5 (19–47)
Mean follow-up, years (min–max)	1.0 (0–10)	1.5 (0–10)	2.0 (0–7)	1.0 (0–1)
Thromboembolic recurrence, n	1	0	0	1
Bleedings, n	0	0	0	0
Thrombotic recurrences, n	1	0	0	1

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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