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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Atypical iliac vein compression in patients with symptomatic May–Thurner syndrome

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PURPOSE
We aimed to investigate the incidence, etiology, treatment, and clinical course of atypical iliac vein compressions (AIVCs) among patients with May–Thurner syndrome (MTS).

METHODS
A total of 173 patients who presented with MTS were retrospectively analyzed at a single center. Computed tomographic venography (CTV) was used to diagnose MTS. An AIVC was defined as the compression of the left common iliac vein (LCIV) by structures other than the right common iliac artery (RCIA) or the compression of other venous structures in the pelvic cavity instead of the LCIV. The patients with AIVC were categorized into the LCIV compression group (category A) and non-LCIV compression group (category B).

RESULTS
Ten patients with AIVC were identified (5.8%; male/female, 5/5), five in category A and five in category B. The median age of patients was 76 years (range, 51–94 years), and the median follow-up duration was 388 days (range, 12–4694 days). In category A, the LCIVs were compressed by the left common iliac artery (LCIA) (n=2), uterine leiomyoma (n=1), LCIA aneurysm (n=1), and RCIA aneurysm (n=1). In category B, the right common iliac veins were compressed by the RCIA (n=4) and L5 osteophyte (n=1). Endovascular treatment, including balloon angioplasty and stent placement, was performed in six patients, three from each group. Three patients underwent conservative treatment due to their advanced age and comorbidities. Endovascular aneurysm repair was performed in one patient with RCIA aneurysm. Follow-up images were available for six patients, and all of them had patent venous flow.

CONCLUSION
The AIVC had an incidence of 5.8% (10/173) among symptomatic MTS patients and wide spectrum of etiologies. Pathogenesis-tailored endovascular treatments are safe and effective.

May–Thurner syndrome (MTS) manifests with clinical symptoms such as unilateral lower extremity edema, pain, varicosities, and venous ulcer due to the compression of the left common iliac vein (LCIV) between the right common iliac artery (RCIA) and the fifth vertebral body predisposing one to deep vein thrombosis (DVT) and chronic venous insufficiency (1). Many anatomical variations of MTS, called as atypical iliac vein compressions (AIVCs) in this article, including right-sided MTS (2), compression of the LCIV by the ipsilateral internal iliac artery (3), and compression of the distal inferior vena cava (IVC) and LCIV by the RCIA have been sporadically reported (4). However, the incidence of AIVC has not been investigated, and the anatomic potential etiology of AIVC remains unknown because of the lack of a study with a large population sample. The treatment of choice for AIVC is also not well established because there are only few case reports regarding the management of AIVC. However, most previous cases have been treated by balloon angioplasty and endovascular stenting at the corresponding locations.

The purpose of this study was to investigate the incidence of AIVC among patients with symptomatic MTS and to evaluate the safety and efficacy of endovascular treatments for AIVC. Anatomical causes of AIVC were also identified and classified.

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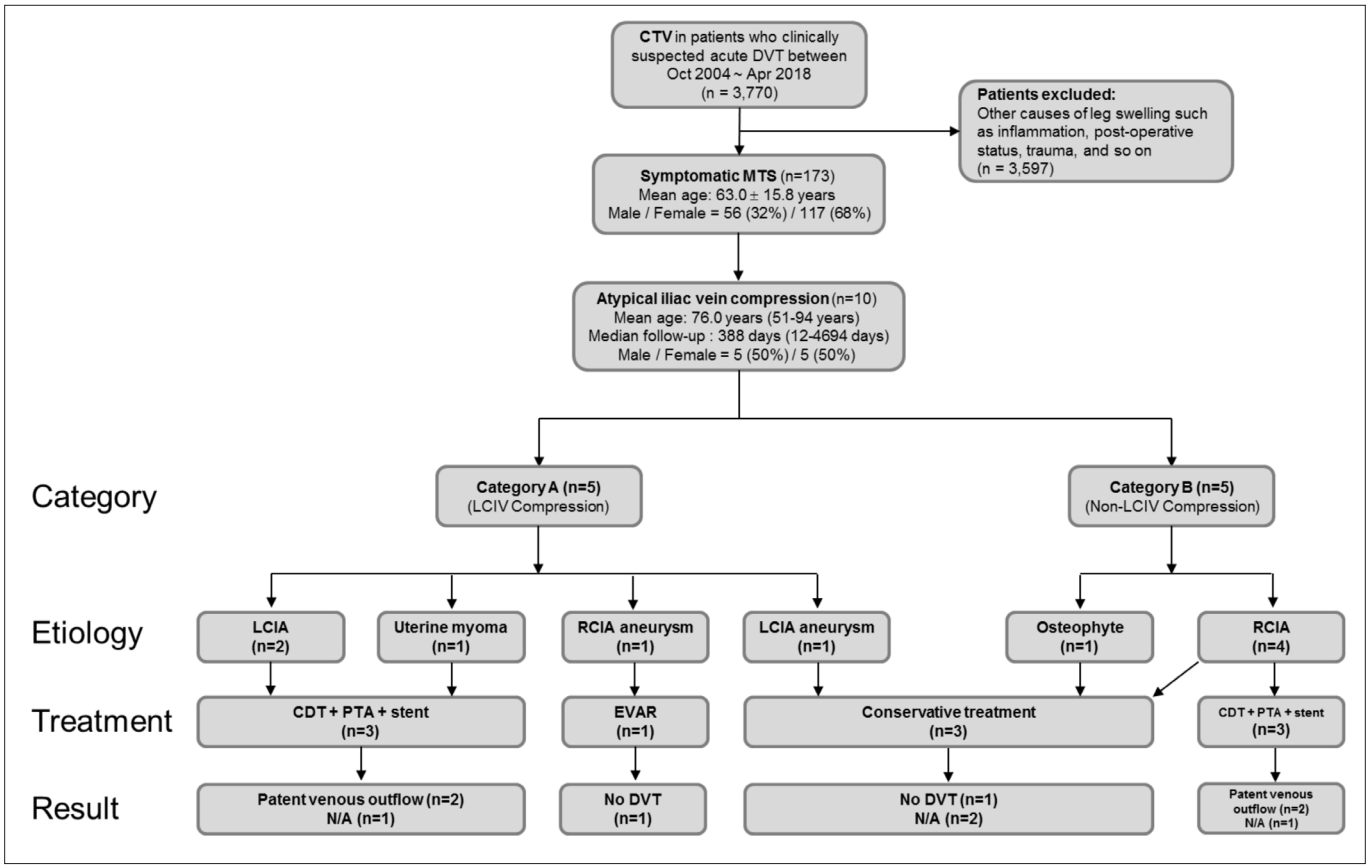

Figure 1. Flowchart of patient selection, etiology, treatment strategy, and outcomes. CTV, computed tomographic venography, DVT, deep vein thrombosis; MTS, May–Thurner syndrome; LCIV, left common iliac vein; LCIA, left common iliac artery; RCIA, right common iliac artery; CDT, catheter-directed thrombolysis; PTA, percutaneous aspiration thrombectomy; EVAR, endovascular aneurysm repair; N/A, not applicable.

Methods

Patient demographics

The institutional review board approved the protocol (approval number: 2020-05-004-000); the requirement of informed consent was waived because of the retrospective nature of this study. Patients with symptoms of acute DVT, including unilateral lower extremity edema, pain, and varicosities, were selected for this study and underwent computed tomographic venography (CTV). The results of CTV recorded between October 2004 and April 2018 in a single institution were retrospectively extracted from a database of medical charts and radiological reports. Out of 3770 patients who underwent CTV, 173 patients (32% males) with symptomatic MTS were detected by two interventional radiologists (with 19 and 16 years of experience) while investigating the anatomical causes of venous outflow obstruction, extent of venous thrombosis, presence of venous collaterals, and varicosity. The remaining 3597 patients with other causes of leg swelling, such as cellulitis, post-operative status, and trauma, were excluded from this study. The flowchart of patient selection was summarized in Fig. 1.

Main points

- The incidence of atypical iliac vein compression (AIVC) is relatively common (5.8%) among patients diagnosed with May–Thurner syndrome.
- Patients with AIVC have a wide spectrum of pathologies including tortuous vascular structure, leiomyoma, aneurysm, and prominent bony structure.
- Endovascular treatments tailored to the pathogenesis should be performed for the safe and effective management of AIVC.

Definition and categorization of AIVC

An AIVC was defined as the compression of the LCIV by structures other than the RCIA or the compression of pelvic veins instead of the LCIV. Based on the CTV findings, the patients with AIVC were then divided into category A with LCIV compression and category B with non-LCIV compression. Patient demographic characteristics, clinical symptoms, extent of DVT, anatomical causes of DVT, comorbidities, treatment strategy, and clinical outcomes were recorded.

General consideration of endovascular procedure

The treatment plan for each patient was determined by multidisciplinary discussion among the interventional radiologist, vascular surgeon, and physicians based on the patient's condition, past medical history, and anatomical variations of AIVC according to the CTV findings. All endovascular procedures were performed by a single interventional radiologist with 16 years of experience. Low-molecular-weight heparin and enoxaparin sodium (Clexane 1 mg/kg; Sanofi-Aventis) were administered to most patients before and during the procedure except in those with a high risk of hemorrhagic complications such as intracranial hemorrhage and gastrointestinal bleeding. Ultrasound-guided puncture of the corresponding popliteal vein with a micropunc-

Table. Clinical characteristics of patients with atypical iliac vein compressions

Category	Sex/ Age (yrs)	Initial symptoms	Extent of DVT	Etiology	Comorbidities	Treatment	Type of stent (diameter × length, mm)	Interval of last CTV (days)	Result of last CTV
A	M/94	Edema in left lower extremity	Right CIV to calf vein	LCIA	Angina	CDT + PTA + Stent	Nitinol (14×60)	N/A	N/A
	M/55	Pain in left lower extremity	Left CIV to popliteal vein	LCIA	Hypertension	CDT + PTA + Stent	Nitinol (12×60)	4694	Patent
	F/51	Edema in left lower extremity	Left CIV to calf vein	Uterine leiomyoma	Schizophrenia	CDT + PTA + Stent	Nitinol (14×90)	2352	Patent
	M/76	Pain in both lower extremity	Left CFV	RCIA aneurysm	Lung cancer	EVAR	N/A	1661	No DVT
	F/77	Right hip pain	Bilateral CFV and SFV	LCIA aneurysm	Polycystic kidney disease, hypertension, right total hip replacement	Conservative treatment with IVC filter	N/A	601	No DVT
B	M/90	Edema in right lower extremity	Right CIV to calf vein	Lumbar osteophyte	Hypertension, cerebral infarction	Conservative treatment with IVC filter	N/A	N/A	N/A
	F/75	Edema in right lower extremity	Infrarenal IVC to right calf vein	RCIA	Diabetes mellitus, hypertension, asthma sepsis	Conservative treatment without IVC filter	N/A	N/A	N/A
	F/83	Edema in right lower extremity	Right CIV to popliteal vein	RCIA	Diabetes mellitus, hypertension, chronic kidney disease, dementia	CDT + PTA + Stent	Nitinol (12×80)	N/A	N/A
	F/76	Edema in right lower extremity	Right CIV to calf vein	RCIA	None	CDT + PTA + Stent	Wallstent (14×90)	1813	Patent
	M/52	Edema in right lower extremity	Right CIV to calf vein	RCIA	None	CDT + PTA + Stent	Nitinol (14×60)	175	Patent

DVT, deep vein thrombosis; CTV, computed tomographic venography; M, male; F, female; CIV, common iliac vein; LCIA, left common iliac artery; CDT, catheter-directed thrombolysis; PTA, percutaneous transluminal angioplasty; N/A, not applicable; CFV, common femoral vein; SFV, superficial femoral vein; RCIA, right common iliac artery; EVAR, endovascular aneurysm repair; IVC, inferior vena cava.

ture set (Cook Medical) was performed for vascular access. To confirm the extent and severity of DVT, diagnostic venography was performed after inserting a 6 F sheath. An intravenous bolus dose of 100 000 IU of urokinase (UK) was administered into the thrombi, and percutaneous aspiration thrombectomy (PAT) was performed with an 8 F guiding catheter (Envoy, Cordis). Catheter-directed thrombolysis (CDT) with UK (1000–2000 IU/kg/h) if necessary was performed for 6 h or overnight via catheters with multiple side holes in patients with ilio-femoral DVT. The endpoint of the thrombolytic treatment was near completely dissolved thrombi as evaluated on follow-up venogram. Finally, endovascular treatment, such as balloon angioplasty and stent placement, was performed according to the main cause of AIVC. Wallstent (Boston scientific) and nitinol stent (SMART, Cordis) were implanted for the dilatation of venous stenosis.

Follow-up strategy

All patients with AIVC were prescribed Warfarin, a vitamin K antagonist, for 6 months after discharge to achieve a target international normalized ratio (INR) of 2.3. As an alternative treatment strategy since 2015, all patients received a 15 mg twice-daily dose of rivaroxavan (Xarelto, Bayer Pharma AG) for the first three weeks and then a 20 mg once-daily dose for 6 months. After 6 months, an antiplatelet agent (aspirin 100 mg/day or clopidogrel 75 mg/day) was prescribed. Follow-up CTV was performed at 6 months and 1 year after the procedure, and, then annually, if possible.

Statistical analysis

Non-normally distributed continuous variables are presented as median and range, whereas normally distributed continuous variables are presented as mean ± standard deviation. Categorical variables are shown as count and percentage.

Results

Atypical iliac outflow obstruction was present in 10 patients out of 173 (5.8%; men/women, 5/5; category A/ B, 5/5). The median age of the patients was 76 years (range, 51–94 years). The median age of patients was 76 years (range, 51–94 years). The median follow-up duration was 388 days (range, 12–4694 days). All patients with symptomatic AIVC presented with DVT in the corresponding lower extremities. In category A, the LCIVs were compressed by a tortuous left common iliac artery (LCIA) (n=2), aneurysm of the LCIA (n=1), aneurysm of the RCIA (n=1), and uterine leiomyoma (n=1). In category B, the main cause of AIVC was compression of the right common iliac vein (RCIV) inducing right-sided DVT by a tortuous RCIA (n=4) and a large prominent osteophyte of the vertebral body (n=1). Patient characteristics, initial symptoms, extent of DVT, anatomical causes of venous

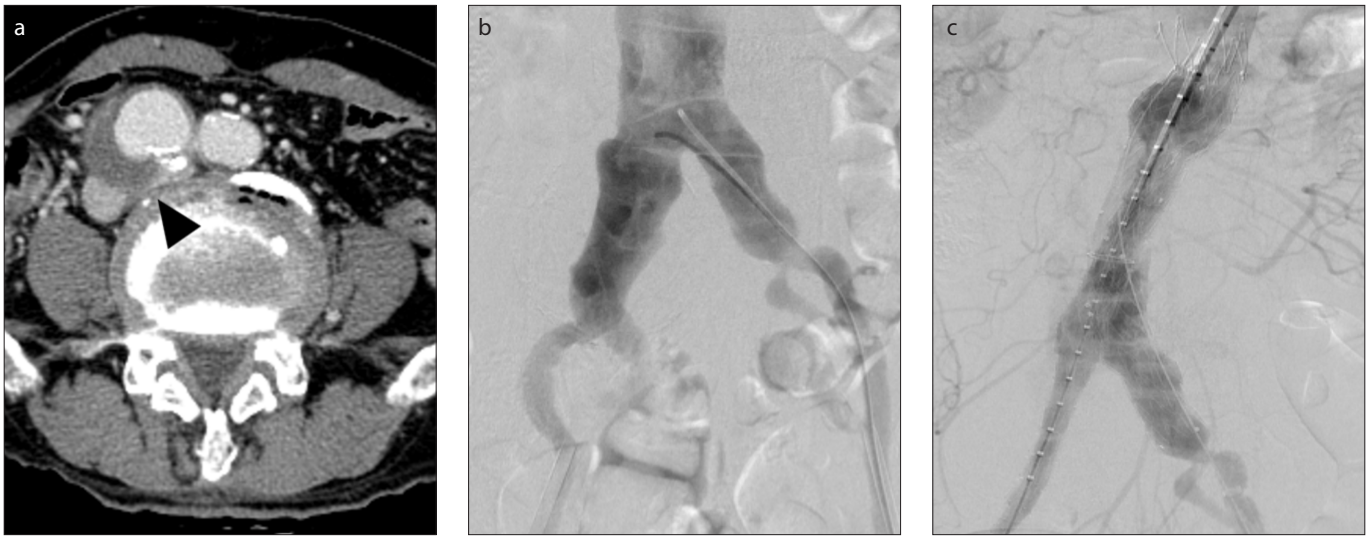

Figure 2. a–c. A 76-year-old man visited the outpatient clinic for an aortic aneurysm detected in a routine health checkup. Axial CT venogram **(a)** shows a severe compression of the left common iliac vein by a large aneurysm of the right common iliac artery (RCIA) *(black arrowhead)*. Abdominal aortogram **(b)** demonstrates a RCIA aneurysm with a concurrent left common iliac artery aneurysm and infrarenal abdominal aortic aneurysm. Endovascular aneurysm repair was performed **(c).**

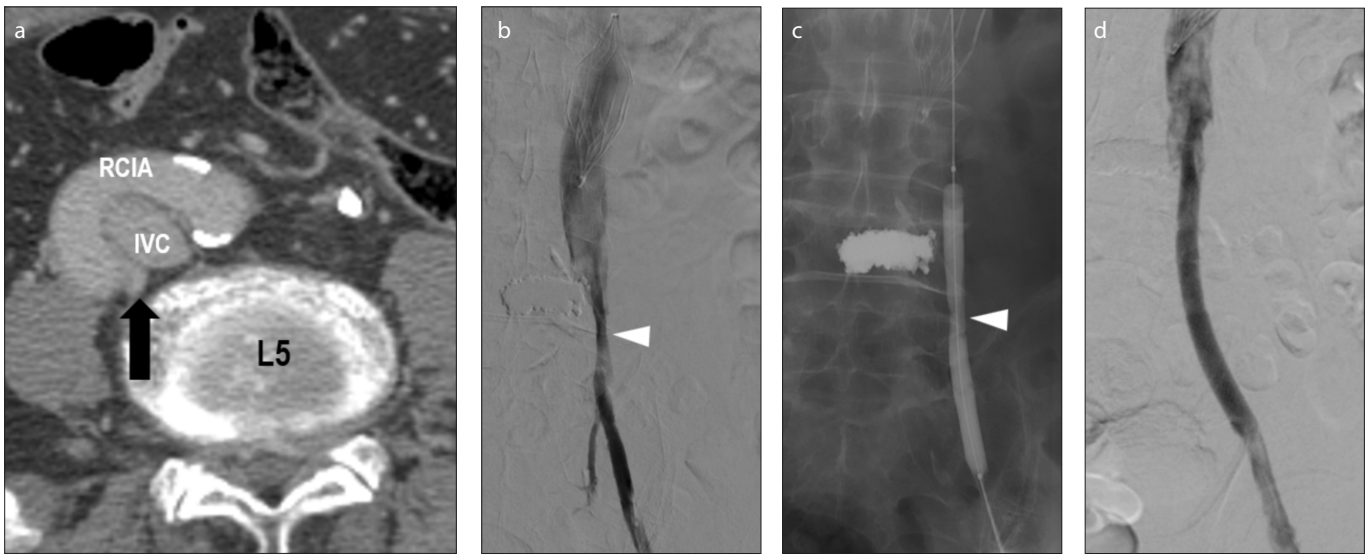

Figure 3. a–d. A 76-year-old man visited the outpatient department of vascular surgery with a complaint of swelling in his right lower extremity and back pain. Axial CT scan **(a)** with venous phase demonstrates compression of the right common iliac vein *(black arrow)* by a tortuous right common iliac artery (RCIA) and L5 vertebral body. Post-thrombolysis venogram **(b)** reveals severe stenosis *(white arrowhead)* in the proximal RCIA corresponding to a waist seen during balloon angioplasty (**c,** *white arrowhead*). A Wallstent was deployed to maintain venous outflow **(d)**.

stenosis, treatment strategies, and clinical outcome are summarized in the Table.

Six out of the 10 patients with AIVC underwent endovascular treatment including CDT, balloon angioplasty, and stent placement in both category A (n=3) and B (n=3). Five nitinol stents were used in three patients in category A and two patients in category B, and one Wallstent was used in category B.

In category A, endovascular aneurysm repair was performed in one patient with AIVC due to concurrent abdominal aortic aneurysm and bilateral common iliac artery aneurysm (Fig. 2). In category B, manual thromboaspiration and balloon angioplasty for venous stenosis were performed in one patient with a compressed RCIV by a tortuous RCIA. After that, a Wallstent was deployed in the residual waist using a venogram (Fig. 3). Another patient in category B with a compressed RCIV by a prominent osteophyte of the lumbar vertebrae underwent conservative management using medication and insertion of an IVC filter because of advanced age and comorbidities (Fig. 4). In category A, IVC filters were also used in a patient in the conservative treatment group due to impaired renal function.

Follow-up CTV images were available in six patients (median time of CTV follow-up, 41 months; range, 6–125 months). Among them, four patients who underwent endovascular stent placement showed patency of venous flow, and the other two patients,

Figure 4. a–c. A 90-year-old man was initially brought to the emergency department because of a traffic accident. A CT venogram was performed because the patient complained of right calf pain 1 month after hospitalization. Axial **(a)**, coronal **(b)**, and sagittal **(c)** curved reconstruction images show right-sided deep vein thrombosis with right common iliac vein compression (**a,** *black arrow*; **b, c,** *white arrow*) by the right common iliac artery and prominent L5 osteophyte.

who underwent endovascular aneurysm repair and conservative treatment, did not show recurrent DVT on follow-up CTV. Four patients did not undergo follow-up CTV and duplex ultrasound because of poor renal function and general condition (n=3) and death due to unknown cause (n=1) during the follow-up.

Discussion

The present study revealed the incidence, anatomical etiologies, treatment, and clinical outcomes of AIVC. In this study, the incidence of AIVC was 5.8% among patients with symptomatic MTS. Several case reports have sporadically described various causes of AIVC, secondary to vascular and bony structures (2, 3, 5) similar to the etiologies observed of this study. However, no study on the exact incidence of AIVC has been reported.

In contrast to traditional MTS, which is more common in the younger population (6), AIVC can be found in the elderly population (median age of patients with AIVC, 76 years). This discrepancy could be attributed to the aging process, atherosclerosis (7), and complex comorbidities such as aneurysmal changes of vessels (8), vascular tortuosity (9), and prominent osteophyte of the lumbar spine. In category B, the major cause of stenosis in the RCIV was a tortuous RCIA except in one patient who showed RCIV compression by large osteophytes. These results also suggest etiologies different from those presented in previous case reports mainly showing associations with transposition of the IVC (2, 10, 11). These previous studies described unusual right-sided MTS, in which the RCIV was compressed by the LCIA in association with a congenitally left-sided IVC. Conversely, none of the presented cases in this study showed caval variants, but tortuous RCIA and a lumbar osteophyte were the only etiological results for right-sided DVT. In previous studies, the majority of the study sample comprised pediatric patients or young adults with right-sided MTS, whereas the mean age of our study population in category B was 75.2 years. As mentioned above, the association of RCIA tortuosity with the aging process and atherosclerosis may be the main reason for the difference in patient age between this study and previous case reports.

Five patients in category A had the same clinical symptoms, such as edema and pain in the left lower extremity due to the corresponding DVT, as patients with typical MTS. However, different pathologies were associated with each of the identified radiological findings including compression of the LCIV by the LCIA, uterine leiomyoma, and aneurysm of the CIA instead of the typical RCIA in patients with MTS. Therefore, AIVC should be considered as the potential etiology when left-sided ilio-femoral DVT is detected in patients with advanced age, and CTV should be performed for the evaluation of anatomical problems.

Endovascular stent placement after CDT and PAT has been considered as a treatment of choice for venous outflow obstruction because it is safe and effective in ensuring long-term patency, restoring venous stenosis, and preventing recurrent DVT in patients with symptomatic MTS (12–15). There is no established treatment strategy for AIVC because of the associated broad spectrum of etiologies. Nevertheless, in many previous case reports, investigators performed endovascular stent placement with or without CDT and PAT regardless of the etiology of venous stenosis (2, 3, 5, 10, 11). Therefore, awareness regarding different anatomical causes of AIVC is essential for accurate diagnosis via CTV and conventional angiography. After accurate diagnosis, endovascular treatment tailored to the pathogenesis should be performed for the safe and effective management of AIVC.

This study has several limitations. First, it was a single-center retrospective study. Second, all patients did not undergo follow-up CTV, and the follow-up interval was heterogeneous. Other limitations include a relatively small sample size and the lack of a hereditary predisposition assessment.

In conclusion, the incidence of AIVC among patients with symptomatic MTS

was 5.8% (10/173) and the wide spectrum of pathologies of AIVC were detected in the presented study. Endovascular treatments tailored to the pathogenesis should be performed for the safe and effective management of AIVC.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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