Prevalence of May-Thurner Syndrome in Patients with Deep Vein Thrombosis at a Large Medical Referral Center

Prävalenz des May-Thurner-Syndroms bei Patienten mit iliofemoraler tiefer Venenthrombose an einem universitären Zentrum

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Key words
iliac vein compression syndrome, May-Thurner syndrome, prevalence, iliofemoral deep vein thrombosis

received 09.08.2018
accepted 01.06.2019

Bibliography
DOI https://doi.org/10.1055/a-0959-6230
Published online: 4.7.2019
Fortschr Röntgenstr 2019; 191: 1107–1117
© Georg Thieme Verlag KG, Stuttgart · New York
ISSN 1438-9029

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ABSTRACT

Objective We set out to investigate the prevalence of May-Thurner syndrome (MTS) in a cohort of patients diagnosed with iliofemoral deep vein thrombosis at a large medical referral center.

Materials and Methods We retrospectively analyzed a cohort of 496 patients who were referred to the emergency unit of a large medical referral center with suspected venous thromboembolism (VTE) and were diagnosed with deep vein thrombosis of the iliac veins and/or the thigh on ultrasound. We retrospectively assessed the presence of MTS in the primary ultrasound examination and on additional imaging (available in n = 193 patients).

Results Across all 496 patients with iliofemoral deep vein thrombosis, the median age was 70 years. 238 patients (48 %) were female. The thrombosis was left-sided in 263 cases (53 %), right-sided in 208 cases (42 %) and bilateral in 24 cases (5 %). In the subgroup of patients with left-sided and bilateral thrombosis, the growth pattern was classified as ascending in 142 patients (50 %), descending in 104 patients (36 %) and unclear in 41 patients (14 %). Additional imaging tests were available in 193 patients: 119 patients (41 %) underwent CT, 18 patients (6 %) MRI and 30 patients (10 %) underwent phlebography. Within the subgroup of patients with left-sided and bilateral thrombosis, MTS was confirmed in 88 patients (31 %), and the imaging findings in 17 patients (6 %) were highly suspicious of MTS. Differentiation was not possible in 86 patients (30 %) and MTS was excluded in 96 patients (33 %).

Conclusion Underlying MTS is not uncommon in the selected cohort of patients with deep iliofemoral vein thrombosis at a large referral center and should be excluded by imaging.

Key Points:
- May-Thurner syndrome (MTS) is a relatively frequent cause of deep vein thrombosis.
- MTS should be excluded in patients with left-sided or bilateral iliofemoral thrombosis.
- Cross-sectional imaging is helpful in this setting.
- Approximately one third of patients in this subgroup show signs of MTS.

Citation Format

ZUSAMMENFASSUNG

Ziel In der vorliegenden Arbeit wurde untersucht, mit welcher Häufigkeit bei Patienten mit einer tiefen Becken-Beinvenenthrombose an einem Universitätsklinikum ein May-Thurner-Syndrom (MTS) vorliegt.

Material und Methoden Wir untersuchten retrospektiv ein Kollektiv von 496 Patienten, die mit der Verdachtsdiagnose einer tiefen Beinvenenthrombose in den Jahren 2013 – 2017 in der Notaufnahme eines Klinikums der Maximalversorgung vorgestellt wurden und bei denen eine tiefe Becken-Oberschenkel-Venenthrombose mittels farbcodierter Duplexsono-
Introduction

May-Thurner syndrome is a condition in which the left common iliac artery is compressed by the right common iliac artery causing the formation of an endoluminal lesion, known as a pelvic venous spur [1]. The endoluminal changes are assumed to be the result of constant mechanical irritation of the vein caused by the pulsation of the overlying artery. Various forms have been described (▶ Fig. 1, 2): In the first lateral form, the pelvic venous spur projects into the lumen like a curtain resulting in a membranous constriction of the lumen. The central spur as the second form divides the lumen into different compartments while the lumen is almost fully occluded in the third form [2].

The exact incidence of symptomatic May-Thurner syndrome is not known. The data regarding prevalence varies. McMurrich showed endothelial changes in 33% of cases in a series of 107 autopsies and May and Thurner showed such changes in 22% of 430 autopsies [2, 3]. In the presence of additional thrombogenic factors, these changes can manifest as acute May-Thurner syndrome with a left-sided descending thrombosis in the majority of cases (up to 80%). In the chronic form, signs of chronic venous obstruction are seen such as one-sided painful leg swelling, ulcer cruris, or post-thrombotic syndrome [4]. The syndrome was primarily described in women between the ages of 20 and 40 years.

Among the 20–25% of the normal population with May-Thurner anatomy, only 1–5% will develop symptomatic May-Thurner syndrome. Based on this, approx. 16–20 million people in Germany have the condition and 480,000–800,000 have the syndrome. Approx. 77% of patients with May-Thurner syndrome develop iliofemoral deep vein thrombosis and 23% develop venous claudication, resulting in significant costs for the healthcare system [2, 5–9]. Up to 5% of all cases of deep vein thrombosis are caused by the syndrome and approx. 3–4% of cases with chronic venous insufficiency are associated with May-Thurner syndrome [6, 10, 11]. Some of the currently available modern endovascular treatment methods for treating thrombosis and for correcting the underlying morphological pathology are a topic of debate [8, 12–14].

The goal of the present study is to provide new insight into the prevalence of the syndrome in a selected high-risk patient cohort and to compare this data to the data from the literature. From this, conclusions can be made for the selected high-risk patient cohort of a university hospital regarding the frequency of the disease, the required diagnosis, and the number of patients that can be considered for modern interventional treatment methods.

Materials and Methods

In this retrospective diagnostic cohort study, we analyzed patients with iliofemoral deep vein thrombosis detected on duplex ultrasound for the presence of May-Thurner syndrome. In addition to the ultrasound findings, any available CT or MRI scans were also examined.

Inclusion and exclusion criteria

For possible inclusion in this study, all patients who were referred by the emergency room of our university clinic to the radiology department for duplex ultrasound imaging due to suspicion of iliofemoral deep vein thrombosis (n = 6293) were retrospectively examined over a period of 5 years (January 1, 2013 to December 31, 2017). The patients were retrospectively identified based on the ultrasound findings documented in the radiology information system (RIS, Centricity 5.0, GE Healthcare). 496 patients with deep vein thrombosis of the iliac veins and/or the thigh diagnosed on duplex ultrasound were included in the analysis. Patients with a negative ultrasound finding or isolated deep vein thrombosis of the lower leg were excluded.

Clinical setting

As a maximum care hospital, our facility is responsible for the inhabitants of a medium-sized city and the surrounding areas. The radiology department provides duplex ultrasound services 24/7 for all outpatients and inpatients. In accordance with the guidelines all patients with clinical suspicion of an acute or chronic thromboembolism and with a pathological Wells score and/or elevated D-dimer level (>0.5 mg/l) underwent duplex ultrasound examination.

Sonography

Sonographic examinations for ruling out iliofemoral deep vein thrombosis were performed as a combination of color-coded...
Fig. 1 Endovascular changes in May-Thurner syndrome. VCI = inferior vena cava; Ao = abdominal aorta; AICD = right common iliac artery; VICS = left common iliac vein; P = promontorium.

Fig. 2 CT scan of May-Thurner syndrome with compression of the left common iliac vein a and venography of May-Thurner syndrome (after thrombectomy) b.
duplex ultrasound, compression ultrasound, and B-mode ultrasound from the groin to the lower leg by a radiology specialist using a high-end ultrasound device (Aplio XG, Toshiba) and a linear transducer (PLT 604 AT, 6 MHz, Toshiba). In the case of suspicion of deep vein thrombosis of the iliac veins, the iliac veins were additionally examined using a convex transducer (PVT 375 BT, 3.5 MHz, Toshiba). The images were stored in the digital image archive (PACS). The examination report was archived in the RIS.

Database creation

Patients were identified in the radiology information system based on their findings. All duplex ultrasound findings regarding the lower extremities were analyzed, patients with thrombosis of the iliac veins or thigh were recorded in a database (Microsoft Excel 2010) and a search of the RIS and PACS (Agfa Impax 6.5.3) for the presence of additional pelvic examinations was performed. The analysis included the age and sex of the patients, the location and type of thrombosis, whether additional imaging was performed and if applicable, which type of imaging was performed.

Identification of additional imaging

The PACS was checked for additional imaging for all patients with iliofemoral deep vein thrombosis. Cross-sectional imaging or a venography examination with clear criteria at the time of diagnosis was required for the retrospective diagnosis of May-Thurner syndrome. Only cross-sectional images acquired before or during a single inpatient stay during which the thrombosis was diagnosed were used. Therefore, MTS could not be reliably ruled out in patients who did not undergo additional imaging when DVT was diagnosed. Additional imaging included either non-contrast or contrast-enhanced computed tomography (Aquilion 64, Toshiba) or magnetic resonance imaging (Magnetom Avanto 1.5 Tesla or Magnetom Verio 3.0 Tesla, Siemens Healthineers). Moreover, images from external examiners stored in the PACS were used. Available cross-sectional imaging was used regardless of whether it was acquired in connection with the thrombotic event provided that the degree of stenosis of the iliac veins could be reliably measured. Venography was performed using a Fluorospot Top (Siemens Healthineers). As a rule, it was only performed in patients who underwent venous recanalization.

Evaluation of imaging

The radiology findings and the image data were evaluated in an interdisciplinary context by a physician specialized in both radiology and angiology with over 25 years of professional experience and many years of experiences as a specialist in angiography and duplex ultrasound.

Evaluation of the initial ultrasound examination

Due to the obstructed flow in the common iliac vein, May-Thurner syndrome usually manifests as left-sided, proximal, descending thrombosis. Therefore, the thrombosis location was initially classified as left-sided, right-sided or bilateral. The growth pattern of the thrombus was classified as descending, ascending, or unclear in the next step. This was performed according to the following criteria: in the case of descending thrombi, the thrombus projects distally into the vascular lumen (stalactite sign, ▶ Fig. 3a). If the veins of the lower leg are normal, descending growth of the thrombus can also be assumed. In the case of the ascending type, the location of the thrombus is usually crural, popliteal, and possibly femoral and the thrombus extends cranially with its head having a proximal orientation (cupola sign, ▶ Fig. 3b).

Evaluation of the available cross-sectional imaging

In all cases with left-sided or bilateral thrombosis, any available additional cross-sectional imaging was analyzed in a targeted manner regarding the presence of MTS. To calculate the degree...
of stenosis, the diameter of the ipsilateral common iliac vein caudal to the stenosis and the vessel diameter at the narrowest point at the level of the May-Thurner point were independently measured by two radiologists (Fig. 4). The degree of stenosis was measured on axial views since thin-slice data for multiplanar reconstruction was not always available. In the case of discrepancies between the two radiologists, the measurement was repeated in consensus. The degree of stenosis was then calculated as a percentage: $1 - \frac{\text{diameter on the level of the stenosis/prestenotic diameter}}{\times 100\%}$.

Evaluation of available venography results

Venography results were used to evaluate the collateral circulation (Fig. 5). In MTS, drainage into other venous areas typically occurs to the opposite side via presacral or pudendal collaterals or in a central direction via epigastric or paravertebral veins. An increased iliac vascularity or a thrombus filling defect was considered evidence of May-Thurner syndrome. Since the venography examinations were performed in connection with endovascular revascularization involving correction of the thrombosis and
treatment of the underlying stenosis with balloon angioplasty and stent implantation if needed, the location and presence of MTS can be reliably confirmed or ruled out here.

Assessment of the presence of May-Thurner syndrome

Based on all available data, a physician specialized in both radiology and angiology with over 25 years of professional experience then classified the patients into four categories: MTS confirmed, MTS highly likely, unclear, MTS ruled out. The degree of stenosis of the left common iliac vein on MRI or CT and the detection of venous collaterals by venography served as central criteria for this classification. In patients without any available cross-sectional imaging and venography findings, the growth pattern of the thrombus suspected on imaging and additional clinical findings were used as further criteria.

Statistical analysis

Descriptive data analysis was performed using SPSS (IBM, Version 22). Since normal distribution could not be assumed, the median and range were calculated for the numeric parameters (age of the patients, number of levels affected). The distribution of the age and sex of the patients, the growth pattern of the thrombosis (ascending, descending, not able to be classified), location (right, left, bilateral) were analyzed. The availability of additional imaging (CT, MRI, angiography) was documented with the degree of stenosis. These parameters were related to the four diagnostic categories (MTS verified, MTS highly likely, unclear, MTS ruled out). The prevalence of MTS in the study population was calculated.

Results

Patient cohorts

In the period from January 2013 to December 2017, thrombosis with involvement of the deep iliac and/or thigh veins was diagnosed on ultrasound. The percentage of women was 48% (n = 238, Table 1). The median age was 70 years (1–99 years), with a peak of 60–80 years in men and 75–85 years in women.

Distribution of location and growth pattern

Left-sided (n = 263, 53 %), right-sided (n = 208, 42 %) and bilateral (n = 24, 5 %) thrombi were seen. The subgroup of left-sided and bilateral thrombosis (n = 287) included ascending thrombi in 50 % of patients (n = 142) and descending thrombi in 36 % of patients (n = 104). The growth pattern could not be clearly determined in 14 % of patients (n = 41).

Availability of additional imaging

In the same subgroup of left-sided and bilateral thrombosis (n = 287), additional imaging was not available for 140 patients (49 %), a CT examination was available for 119 patients (41 %), a venography examination was available for 30 patients (10 %), and an MRI examination was available for 44 patients (15 %) (Table 1).

At least one additional imaging examination was available for 147 patients (51 %) with data from two modalities available for 21 patients and from three modalities for one patient.

Prevalence of May-Thurner syndrome

Based on the ultrasound findings together with the additional imaging, MTS was able to be confirmed in 88 patients (33 %), MTS was determined to be highly likely in 17 patients (6 %), differentiation was not possible in 86 patients (30 %), and MTS was able to be ruled out in 96 patients (33 %). In the group of patients with confirmed MTS (n = 88), the average degree of stenosis of the left common iliac vein was 67 ± 15 %. The average vessel diameter at the narrowest point was 3.6 mm. Among the 30 patients with left-sided or bilateral thrombosis who underwent venography, the suspicion was confirmed in 22 patients. All of these 22 patients also exhibited venous collateralization. 18 patients were treated with balloon angioplasty and 8 were additionally treated with stent implantation.

Demographic characterization of patients with MTS

In the group with left-sided and/or bilateral thrombosis (n = 287), 143 patients (50 %) were female. The median age was 69 (1–99) years. In the smaller subgroup of patients with confirmed MTS (n = 88), the median age was 69 (15–91) years and the percentage of women was 56 %. The age and sex distribution did not differ significantly from the other patients in the study population (Table 2).

Discussion

In this study we were able to show in a large patient population that MTS should be considered as the cause of ileofemoral deep vein thrombosis and this should be confirmed or ruled out after initial ultrasound by additional imaging.

As a rule, MTS is to be diagnosed on ultrasound only in exceptional cases if the course of the left common iliac vein can be visualized despite the limited visibility [15]. In particular, the compression by the artery or the pelvic venous spur cannot be reliably visualized. Due to low sensitivity in the visualization of the iliac vessels, additional imaging should be performed in the case of suspicion of MTS. Compression of the common iliac vein as a manifestation of MTS can be visualized on CT or MR venography, invasive venography, or intravascular ultrasound [16]:

Collateralization and iliac vessels as well as masses or other anatomical changes that could also be responsible for compression of the vein can be evaluated on contrast-enhanced CT. The method can differentiate between non-thrombotic and thrombotic MTS. In addition to the filling defect, direct thrombus detection, precisely definable stenosis, and prestenotic dilatation, perivascular infiltration and differences in leg circumference are indirect indications of MTS with associated thrombosis. However, the pelvic venous spur can be overlooked in the case of an unsuitable slice thickness of greater than 5 mm [6, 15, 17–19].

Venous obstruction of the iliac vein, collateralization, and a possible external cause of compression can also be visualized on
non-contrast and contrast-enhanced magnetic resonance imaging. MRI can be used to detect intraluminal thrombosis and vein wall inflammation can be evaluated on contrast-enhanced sequences [8, 16, 20 – 24].

The visualization of flow dynamics is comparatively difficult and rather unusual in the clinical routine with both of these non-invasive methods. An advantage of cross-sectional imaging methods is the ability to determine the degree of stenosis and the minimum vein diameter at the compression point, both of which are risk indicators for the occurrence of deep vein thrombosis or the presence of MTS [25 – 27]. In addition, cross-sectional imaging methods allow visualization of the tissue surrounding the vessel.

In venography, a vascular occlusion, compression, collateralization, or a lesion of the intima can be initially visible or become visible after thrombolytic treatment [8, 18, 20 – 22]. According to some authors, stenosis can be underestimated in venography, making intravascular ultrasound (IVUS) a more suitable method for evaluating intraluminal and mural changes and the degree of stenosis. As an invasive method, IVUS is reserved for complicated cases with simultaneous endovascular therapy [11, 17, 28 – 30].

In studies to date, the vessel diameter was measured in patients with DVT knowing that a reduced diameter is an independent risk factor for thrombosis. In a case control study, vessel diameters in patients with thrombosis were compared to those of a healthy population. Similarly reduced diameters as in our population (3.6 mm in our population and 4 mm in the case control study) were seen [26]. It must be taken into consideration when evaluating these results that the size (mm) at which the risk increases has not been precisely defined. In addition, isolated evaluation of vessel diameter can result in small deviations if measurements were not performed on the corresponding plane. Such deviations can be minimized by using thin slice thicknesses and careful repeated measurement. However, the degree of filling of the iliac veins can vary greatly thus presenting like May-Thurner syndrome.

To qualify the assumption that vessel diameter is a highly thrombogenic risk factor, studies in which the diameter of the left common iliac vein was measured in asymptomatic patients must be taken into consideration. Therefore, a retrospective analysis of abdominal CT scans of 50 patients with neither clinical nor
diagnostic signs of thrombosis showed an average compression of the left iliac vein of 35%. Compression of > 50% was measured in a quarter of these asymptomatic patients and stenosis of the vessel of at least 23% was seen in two-thirds of these patients. The high incidence of vein compression compared to the low incidence of deep vein thrombosis indicates that additional factors must be involved in the formation of a thrombus [6]. Raju confirmed this: The constriction of the iliac vein would first become symptomatic with the occurrence of additional pathologies like venous reflux, cellulitis, or trauma [11]. Nazzahl et al. examined 300 asymptomatic patients in a similar manner and determined that stenosis of over 70% was present in 30% of the patients. Women had a higher incidence. From these results they concluded that stenosis alone does not cause symptoms. There is even a hypothesis that a reduced diameter of the iliac vessels acts as a natural filter and can reduce the risk for symptomatic pulmonary embolism [26].

Other authors have postulated that up to 5% of all cases of deep vein thrombosis are caused by May-Thurner syndrome. The significantly higher percentage in our study can be explained by the fact that we focused our analysis on patients with thrombosis in the iliac veins and/or thigh region (iliofemoral thrombosis). In our population of 495 patients, MTS was able to be confirmed in 88 patients and was considered highly likely in 17 patients. In total, this corresponds to 105 patients, i.e., approximately one-fifth of all patients with iliofemoral thrombosis (n = 495) and approximately one-third of all patients with left-sided or bilateral thrombosis (n = 287). If it is taken into consideration that only approximately half of the patients underwent additional imaging allowing further differentiation and that the findings were unclear in 30% of the examined individuals, the actual percentage of MTS patients in our population is probably higher.

The balanced gender distribution of iliofemoral deep vein thrombosis in our population coincides with the data in the literature cited above. However, even in the subgroup of patients with confirmed MTS in our study, a balanced sex ratio and a median age of 69 years was seen, while earlier studies described the syndrome predominantly in female patients between 20 and 40 years old [13]. This may be able to be explained by the fact that May-Thurner syndrome was examined specifically in young patients in other studies. In our population, the majority of patients with left-sided or bilateral thrombosis were 60–65 years old (men) or 80–85 years old (women).

### Table 2 Subgroup analysis of patients with left-sided or bilateral thrombosis.

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<th>May-Thurner syndrome</th>
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Vessels

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The results of the study have particular clinical relevance in the context of new treatment methods for endovascular recanalization and venous stent implantation (Fig. 6). The goal of these methods is to avoid a new manifestation as May-Thurner syndrome or chronic venous insufficiency. Our cohort also reflects the clinical reality in that MTS is often diagnosed retrospectively because the clinical picture and its treatment options are not common knowledge among both referring physicians and radiologists so that additional diagnostic and therapeutic measures like cross-sectional imaging and angioplasty with stent implantation are not performed enough.

**Limitations**

The analysis was performed retrospectively for a selected patient population at a university hospital. Additional CT or MRI examinations as well as intravascular ultrasound, direct or indirect venous pressure measurement, or diagnostic venography was not performed in all patients to diagnose May-Thurner syndrome. In addition, the majority of available CT and MRI examinations were per-
formed for other indications. The heterogeneity of the imaging modalities and protocols is a limitation of our study. The degree of stenosis was measured on axial views since thin-slice data for multiplanar reconstruction was not always available. However, only examinations in which the degree of stenosis of the iliac veins could be reliably measured were included in the analysis. A limitation of our retrospective study is that only a few patients were examined with venography or intravascular ultrasound. Therefore, many patients were not definitively diagnosed with May-Thurner syndrome with confirmation of a spur. As a further limitation, conventional risk factors for venous thromboembolisms and the patients’ medical history with regard to prior thromboembolisms could not be systematically recorded due to the retrospective study design.

Conclusion
May-Thurner syndrome (MTS) is a relatively common cause of iliofemoral deep vein thrombosis in the selected patient population at a German university hospital. In patients with left-sided or bilateral iliofemoral thrombosis and a descending growth pattern, MTS should be considered and ruled out. This requires a detailed sonographic examination of the thrombosis and additional cross-sectional or invasive imaging. MTS is found in approximately one-third of patients in the subgroup with left-sided or bilateral iliofemoral thrombosis.

CLINICAL RELEVANCE OF THE STUDY
- May-Thurner syndrome (MTS) is a relatively common cause of deep vein thrombosis.
- MTS should be considered in the case of left-sided or bilateral thrombosis and ruled out via additional cross-sectional imaging.
- Without treatment, MTS can result in a serious post-thrombotic syndrome.
- The results of the study have particular clinical relevance in the context of new treatment methods for endovascular recanalization and venous stent implantation.

Conflict of Interest
The authors declare that they have no conflict of interest.

References


