

Trans-abdominal Color Doppler US versus Direct Multi-detector Computed Tomography Venography in the Diagnosis of May-Thurner Syndrome

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ABSTRACT

Background: Early recognition and treatment of May-Thurner Syndrome (MTS) is critical in order to avoid the potential complications and irreversible sequelae that may result in lifestyle limitations. The diagnosis of MTS depends on both clinical and imaging findings. The study aimed to compare the efficacy of transabdominal Color Doppler US (CDUS) with that of direct multi-detector computed tomography venography (MDCTV) in the diagnosis of MTS using conventional venography and intravascular ultrasound (IVUS) as gold standard.

Patients and Methods: One-hundred patients with clinically suspected MTS were graded by Clinical Etiological Anatomical Pathological (CEAP) classification. All patients underwent transabdominal CDUS of the deep pelvic and lower limbs veins followed by direct MDCTV. Based on venography and IVUS results, the diagnostic performances of both imaging modalities in diagnosing MTS and detecting associated iliofemoral DVT, synechia, and venous collaterals were quantified. Finally, the degree of agreement between each imaging method and the gold standard and between both modalities was calculated.

Results: Conventional venography and IVUS confirmed the MTS diagnosis in 77 out of 100 patients. There was a predominance of females (62%), young and middle-aged (83%), and overweighted patients (60%). MDCTV showed significantly higher accuracy (100%) in diagnosing MTS than that of CDUS (91%) ($p=0.008$). There was no significant difference between MDCTV and CDUS regarding the detection of iliofemoral thrombus, synechia, and venous collaterals (all $p>0.05$). MDCTV and CDUS showed substantial agreement in the detection of venous stenosis, iliofemoral thrombus, and synechia ($k=0.78, 0.77, \text{ and } 0.72$) and almost perfect agreement regarding venous collaterals ($k=0.91$).

Conclusions: Direct MDCTV is a valuable reference in the diagnosis and preoperative workup of MTS with comparable accuracy to that of the more invasive venography and IVUS. Due to its low accuracy in iliac veins evaluation, trans-abdominal CDUS should not be used as the sole investigative tool to confirm or ruled out MTS and combined MDCTV is mandatory.

Keywords: May-Thurner syndrome, Transabdominal Color Doppler ultrasound, Direct multi-detector computed tomography venography, Conventional venography, Intravascular ultrasound.

INTRODUCTION

May-Thurner syndrome (MTS), is an anatomical and pathophysiologic condition in which there is an extrinsic compression of the left common iliac vein (LCIV) between right common iliac artery (RCIA) and the underlying spine ^(1,2).

Venous compression may be clinically insignificant with no symptoms but overtime the chronic pulsatile compression of the LCIV leads to an intimal damage with formation of intraluminal fibrotic adhesions, and partial or complete venous obstruction with or without DVT ⁽¹⁻³⁾. MTS is highly prevalent in young and middle-aged females and should be kept in mind whenever a young patient presents with an acute left lower limb swelling ⁽⁴⁾. Recurrent DVT, chronic unexplained edema, pain, claudication, varicosities, or ulcerations of the left lower limb should also raise the suspicion in MTS. Right sided or bilateral symptoms are rare presentations of the syndrome ^(3,5-7).

Currently, the Clinical Etiological Anatomical Pathological (CEAP) scoring system is an accepted worldwide standard to perform an accurate diagnosis and consequently correct treatment of patients with venous disorders ⁽⁸⁾.

Once MTS is clinically suspected, imaging should be undertaken to confirm the presence of the anatomical variant and to decide the best treatment option ⁽⁹⁾. Multiple imaging modalities can be employed in the diagnosis, preoperative workup, and follow-up of MTS including Color Doppler ultrasonography (CDUS), multi-detector computed tomography venography (MDCTV), magnetic resonance venography (MRV), conventional venography, and intravascular ultrasound (IVUS) ^(2,9,10).

CDUS is the first imaging modality usually used for the evaluation of lower limb venous insufficiency, as it can assess the venous anatomy as well as the amount and direction of blood flow. CDUS is superior to other imaging methods in being widely available, time and cost-effective, non-invasive, and safe real-time modality with no radiation exposure, so can be utilized in emergency cases and repeated as frequently as needed ^(2, 11-13). On the other hand, CDUS is operator dependent, and needs long experience. Moreover, the bladder, bowel gas, and abdominal soft tissue makes US evaluation of the pelvic veins technically difficult, especially in obese patients ^(13,14).

Some authors advocated the use of cross-sectional imaging when CDUS fails to make the diagnosis in case of suspected pelvic vein abnormalities while others preferred to use CDUS as a screening test and if positive, the patient should undergo further evaluation by MDCTV or MRV^(13,15). MDCTV showed high sensitivity and specificity in confirming MTS with many advantages over other imaging modalities; including lack of operator dependence, clearer thin section, and shorter acquisition-time⁽¹⁶⁻¹⁸⁾. Besides, multiplanar reformation (MPR), three-dimensional volume rendering, and maximum intensity projection (MIP) help in the visualization of vascular anatomy⁽¹³⁾.

Nevertheless, MDCTV has two main disadvantages, which are the radiation exposure and the large amount of contrast used⁽¹⁷⁾. Similarly, MRV is highly sensitive and specific in the detection of DVT. But, in addition to being expensive and of limited availability; the primary disadvantage of MRV is that the vessels above bifurcations has non-laminar flow, which can lead to confusion in MTS^(13,19).

Conventional venography is the usually used gold standard in cases of MTS as it allows simultaneous diagnostic and therapeutic interventions. However, conventional venography has many drawbacks such as the invasiveness, cost, time radiation exposure, and the use of intravenous iodinated contrast^(6, 13, 16, 20). Likewise, IVUS allows imaging from within the vessel lumen but still an invasive method and does not provide extravascular information^(6,16,21,22). But, IVUS can document the degree and morphology of venous stenosis including; wall thickening, intraluminal spurs, webs, and chronic thrombotic change^(21,22).

To the best of our knowledge, no studies have compared the diagnostic performances of CDUS of MDCTV in MTS patients. In the current study, we aimed to compare the efficacy of transabdominal CDUS with that of direct MDCTV in the diagnosis of MTS using conventional venography and IVUS as a gold standard.

PATIENTS AND METHODS

One-hundred patients with clinically suspected MTS were graded by Clinical Etiological Anatomical Pathological (CEAP) classification. All patients referred to the Diagnostic Radiology Department from the Vascular Clinic of Assiut University Hospital with acute onset of lower limb swelling and a clinical diagnosis of acute iliofemoral DVT with suspected MTS were included in the study, during the period from January 2019 to January 2021.

Patients <15 years or those with chronic or isolated lower leg DVT, DVT caused by lower limb fracture, history of previous lower limb venous stenting, or pelvi-abdominal tumors causing extrinsic compression of the iliac veins were excluded from the study. Pregnancy, impaired renal functions, and

hypersensitivity to contrast media were also from the exclusion criteria.

All patients were subjected to detailed history taking, comprehensive clinical examination, CDUS of the deep pelvic and lower limbs veins followed by blinded direct MDCTV, and finally conventional venography and IVUS as gold standard.

1. Clinical evaluation:

In all patients, a full clinical history was obtained by a single expert vascular surgeon (O.M.A., 8 years' experience) followed by comprehensive visual assessment of the affected and contralateral lower limbs under bright light. The limbs were then graded by the clinical score of CEAP classification system⁽⁸⁾ as follow; C0: No visible or palpable signs of venous disease. C1: Telangiectasias and reticular veins. C2: Varicose veins. C3: Edema. C4a: Brown pigmentation ochre dermatitis and/or eczema. C4b: Lipodermatosclerosis or atrophie blanche. C5: Healed venous ulcer, and C6: Active venous ulcer.

2. Imaging:

After clinical evaluation, the patient was referred to the Department of Diagnostic Radiology for assessment by transabdominal CDUS and direct MDCTV.

Patient Preparation:

The patients were instructed to fast for at least 6 hours and to take an anti-foaming agent to reduce the colonic gaseous distension prior to CDUS evaluation. On the other hand, all patients performed renal function tests and underwent good hydration before MDCTV examination.

Technique of CDUS:

Assessment of all patients were accomplished by a single expert radiologist (M.K.M., 20 years' experience in CDUS) using the same high-resolution US- machine (Philips-Affiniti-50G, Philips medical systems, Amsterdam, the Nederland B.V). The patient was positioned in supine or semi sitting position with the affected limb relaxed, externally rotated and slightly flexed at the knee. In order to rule out iliofemoral, femoral, or popliteal DVT; the examination was started by gray scale (B-mode) evaluation of the lower limb deep veins from the groin to the lower leg using the linear-array transducer (5-12MHz). Then, Color-Doppler interrogation and spectral analysis were performed during which the scale level was reduced, the color gain was increased, and the angle was adjusted at <60°. In case of suspected iliac venous compression or DVT, the iliac veins were examined using the convex transducer (4-5MHz) with axial measurement of the stenotic site and pre-stenotic dilatation. The iliac vein was also evaluated for intraluminal synechiae, thrombus, or collaterals. Multiple images and videos were obtained during each patient' examination and were stored on the US-machine DICOM viewer (Philips US DICOM viewer R2.1).

Protocol of Direct MDCT Venography:

Direct MDCTV examination was performed using one of two MDCT scanners ("Aquilion 64-slice; Toshiba" or "Somatom Definition 128-slice; Siemens"). The two scanners' technical parameters were adjusted to optimize the image quality and minimize the patient irradiation. The parameters were as follows: tube voltage, 100-120 kVp; tube current, 150-250 mAs; section thickness, 1-2.5mm; increment, 0.33mm; beam collimation, 0.625mm; effective pitch, 0.6; field of view, 300mm; and matrix, 1024 X 1024 pixels. The rotation time was 0.3-0.5sec and the total scan time was approximately 10-20sec with an average CT dose index volume (CTDI-vol.) of 8.15-22.50mGy. The patient was placed supine with feet first. Frontal and lateral projection scouts were obtained and the scanning box was adjusted to cover from the toes distally up to the diaphragm (L1 vertebral body) proximally. The contrast solution was prepared by dilution of a nonionic iodinated contrast material (Ultravist, 370mg/ml) by sterile saline (1:1) in order to prevent artifact formation. Above and below knee tourniquets were placed bilaterally in order to force the contrast medium into the deep veins. Then, using an automatic pump, bilateral simultaneous contrast injection was performed through a Y-shaped 16-gauge IV line inserted into the dorsal foot veins or into the varices of the legs or thighs. The injection rate was 3.5ml/sec with a total amount of 100ml. The bolus tracking technique was employed so that the ascending acquisition was started automatically when the contrast reached the femoral veins. After scan completion, the examination data were transferred to the dedicated 3D-workstation. For data analysis, oblique coronal, sagittal and axial reconstructions were generated with no reconstruction interval for axial images and a 0.5mm or less reconstruction interval for the oblique coronal and sagittal images. Lastly, all images were stored on the dedicated picture archiving and communication system (PACS) for later review.

Image Assessment:

Two senior radiologists (M.S. and A.H.A., with 10 and 15 years' experience in vascular imaging; respectively) randomly and independently reviewed the images of MDCTV and CDUS. The evaluation was performed in four separate sessions so as to each examination was analyzed by the two radiologists. Each radiologist was blinded to the findings of the other imaging modality and to the other radiologist's report for the same examination. In the images of both modalities, the lower limb deep veins, particularly the iliac veins were assessed for the presence or absence of abnormal venous stenosis, wall thickening, synechiae, DVT, or venous collaterals. The degree of stenosis was determined in the axial views by measuring the narrowest venous diameter at the May-Thurner point and the diameter of ipsilateral common

iliac vein distal to the stenosis. In case of initial discrepancy between the two radiologists' measurements, a third senior radiologist (M.K.M.) or an expert vascular surgeon (O.M.A.) blindly repeated the measurement and a final consensus was obtained in each modality. The percentage of the stenosis was calculated by the following equation; $1 - \frac{\text{the diameter at level of stenosis}}{\text{prestenotic diameter}} \times 100\%$ ⁽⁴⁾. Iliac vein stenosis >50% was used as the primary diagnostic evidence of MTS. The presence of venous collaterals was considered an additional secondary indicator for significant iliac vein compression ⁽¹⁸⁾.

3. Conventional Venography and Intravascular Ultrasound (IVUS):

All patients subsequently underwent conventional venography followed by IVUS to confirm the diagnosis of MTS. A single vascular surgeon (O.M.A.) using the same operating room with ceiling-mounted International Surgical Systems performed both procedures. The hard copy of the patient's MDCTV and the detailed report and images of her/his CDUS examination were available to the surgeon while performing intervention. Retrievable IVC filters were applied during intervention to safeguard against any embolization. The venous access was obtained under US-guidance by cannulation of the ipsilateral PV (or common femoral vein in case of thrombus restricted to the iliac vein). Then, a guidewire was inserted and a sheath was introduced. Limbs with acute iliac or iliofemoral DVT underwent mechanical or pharmaco-mechanical thrombolysis of the thrombus. Subsequently, a single-plane antegrade venography was done using a power injector with 8ml/s ejection rate, 900-psi pressure, and a total volume of 15ml. The presence or absence of collaterals was documented during phlebography. Next, an over-the-wire IVUS investigation was performed with evaluation of the iliac and common femoral veins for the anatomic cause of obstruction, degree of stenosis, presence of intraluminal synechiae. A 50% stenosis of the iliac vein was considered significant in both interventional procedures. Finally, balloon angioplasty of the stenotic segment was accomplished and a self-expanding stent was implanted if needed. The resolution of the stenosis and the stent patency were then confirmed by IVUS. The findings were then recorded in a standard format.

Ethical consent:

The Ethical Review Board of faculty of medicine, Assiut University (approval number: 17100327), approved this prospective single-institution study and all patients signed written informed consent. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical Analysis:

Data were collected and analyzed using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). Nominal data were presented as frequency and percentage while continuous data were expressed as mean ± SD. Using the findings of conventional venography and IVUS as gold standard, the diagnostic performances of transabdominal CDUS and direct MDCTV in confirming the presence of iliac stenosis, iliofemoral DVT, intraluminal synechia, and venous collaterals were quantified by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. The exact McNemar test was applied to test for any statistically significant difference between the diagnostic performances of MDCTV and CDUS. In addition, the nonparametric Kruskal–Wallis test was used to compare the two modalities regarding the percentage of the measured venous stenosis. The degree of agreement between transabdominal CDUS, direct MDCTV, and interventional techniques was calculated using kappa coefficient (k) (k 0.00= no agreement, 0.01-0.20= slight agreement, 0.21-0.40= fair agreement, 0.41-0.60= moderate agreement, 0.61-0.80= substantial agreement and 0.81-1= almost perfect agreement). The level of confidence was kept at 95% and the statistical significance was set at p-value ≤0.05.

RESULTS

During the period of the study, 120 patients were referred to the diagnostic radiology department with suspected MTS. Based on the aforementioned inclusion and exclusion criteria; the final study population was 100 patients (40 males and 60 females, with a mean age of 34.9±10.5 years and age range 20-70 years). The mean body mass index of the patients was 28±3.2 kg/m². Isolated left lower limb affection was observed in 61% of the patients while bilateral affection was encountered in the remaining 39%. Patients were frequently manifested with multiple clinical signs and spanned variable CEAP clinical classes. Leg edema and varicose veins were the most frequently detected signs (83% and 58% of the patients, respectively). Skin changes and venous ulcers were encountered in only 20% and 10% of the study population, respectively. Using CEAP classification, the clinical class of the disease severity was as follow: CEAP 3 (n=70; 70%); CEAP 4 (n=20; 20%); CEAP 5 (n=4; 4%); and CEAP 6 (n=6; 6%). The demographic characteristics of the study population are presented in Table 1.

Table (1): Demographics of the total study populations.

Parameter	N=100 patients
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Age (years) Mean ± SD (Range)	34.9±0.5 (20-70)
Sex - Male - Female	40 (40%) 60 (60%)
Body mass index (kg/m²) Mean ± SD (Range)	28±3.2 (22.7-36.5)
Laterality of lower limb affection Isolated left Isolated right Bilateral	61/100 (61%) 0 (0%) 39/100 (39%)
Clinical signs Edema Varicose veins Skin changes Venous ulcers	83/100 (83%) 58/100 (58%) 20/100 (20%) 10/100 (10%)
CEAP clinical classes - C3 - C4 - C5 - C6	70 (70%) 20 (20%) 4 (4%) 6 (6%)

Based on the combined results of conventional venography and IVUS, the suspicion of MTS was confirmed in only 77 of the included patients whereas the remaining 23 patients were recognized as either primary varicose veins or anti-phospholipid syndrome. With exception of one case in which the LCIV compression was caused by the LCIA, all cases were attributed to compression of the LCIV by the RCIA (Figures 1 & 2). As expected, there was a predominance of female gender (n=48/77, 62%) and most of them were multipara and had a history of hormonal contraception (81% and 93.8%, respectively). Moreover, the majority of the confirmed cases were 25-65years of age and 60% were overweight. Associated acute iliofemoral DVT, intraluminal synechia, and venous collaterals were detected in 55.8% (43/77), 33.8 (26/77), and 69% (53/77) of the confirmed cases, respectively. Sixty cases were treated by balloon angioplasty only but 17 cases needed endovascular implantation of a stent. The demographic data and the interventional findings of the patients with confirmed MTS are shown in Table 2.

Table 2: Demographic data and venography and IVUS findings of the patients with confirmed MTS.

Parameter	N=77 patients
Age (years) - Mean (Range) - Groups: 25-45 years 46-65 years 66-85 years	54±8.85 (25-85) 29/77 (38%) 35/77 (45%) 13/77 (17%)
Sex - Male - Female Hormonal contraception Multipara	29 (38%) 48 (62%) 39/48 (81%) 45/48 (93.8%)
Body mass index (kg/m²) - Mean (Range) - Groups: Normal Overweight Obese	28±3.2 (23-35) 26/77 (33.8%) 46/77 (60%) 5/77 (6.2%)
Findings of conventional venography and IVUS Location of compression RCIV LCIV Caval Bifurcation Cause of Compression RCIA LCIA Aortic Bifurcation Associated findings Iliofemoral DVT Intraluminal synechiae Venous collaterals	0/77 (0%) 77/77 (100%) 0/77 (0%) 76/77 (98.7%) 1/77 (1.3%) 0/77 (0%) 43/77 (56%) 26/77 (33.8%) 53/77 (69%)

Direct MDCTV correctly diagnosed all venography and IVUS-proved MTS cases with an accuracy of 100% and perfect agreement with both interventional procedures (k=1). However, CDUS could not detect the venous stenosis in nine of the 77 confirmed cases with 88.3% sensitivity, 100% specificity, 91% accuracy, and substantial agreement with conventional venography and IVUS (k=0.78). There was a statistically significant difference between the accuracies of the two imaging modalities in the diagnosis of iliac venous stenosis (p=0.008). However, there was no significant difference between the mean percentage of iliac vein stenosis calculated from MDCTV measurements (64.3±6.96%) and that calculated from CDUS measurements (63±6.7%) (p=0.2) (Figures 1 & 2).



Figure (1): 45 years-old female presented with left lower limb swelling, transabdominal CDUS revealed compression of the left CIV by the right CIA (typical MTS) with significant stenosis (74%) as confirmed by direct MDCTV (74.2%). (a and b) axial gray-scale US and axial MDCTV showing the stenotic site measuring 2.6 mm and 2.5 mm, respectively. (c and d) axial gray-scale US and axial MDCTV showing the pre-stenotic dilatation of LCIV measuring 10 mm and 9.8 mm, respectively. (e) Color Doppler interrogation of the compressed left CIV showing reduction of its lumen. (f) 3D-reconstruction of MDCTV revealed the left CIV compression site (arrow). (g and h) conventional venography and IVUS confirmed the diagnosis of MTS.

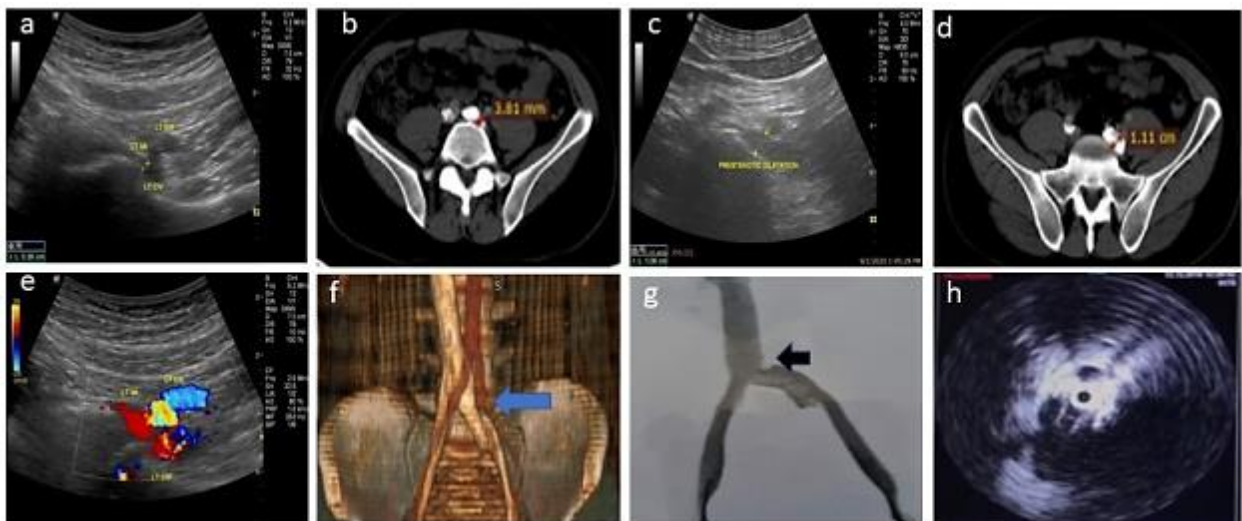


Figure (2): Male patient 50 years-old complaining of recurrent left lower limb swelling. Transabdominal CDUS and direct MDCTV revealed compression of the left CIV by the Left IIA (atypical MTS). (a and b) axial gray-scale US and axial MDCTV showing the stenotic site measuring 2.8 mm and 3.8 mm, respectively. (c and d) axial gray-scale US and axial MDCTV showing the pre-stenotic dilatation of LCIV measuring 10.8mm and 11.1mm, respectively. (e) Color Doppler interrogation showing reduced lumen with turbulent flow inside the compressed left CIV. The calculated percentage of stenosis was 72% by CDUS and 66% by MDCTV. (f) 3D-reconstructed MDCTV revealed compression of the left CIV by the left IIA (arrow). (g and h) conventional venography and IVUS confirmed the diagnosis of MTS.

Considering detection of the acute iliofemoral thrombus, the sensitivity, specificity, and accuracy of MDCTV were 95.4%, 100%, and 97.4% with almost perfect agreement with venography and IVUS ($k=95$), while those of CDUS were 81.4%, 97%, and 88.3%, with substantial agreement with venography and IVUS ($k=0.77$) and no significant difference between the diagnostic performance of both modalities ($p=0.22$). For synechiae detection, MDCTV showed almost perfect agreement with conventional venography and IVUS ($k=0.88$) and its sensitivity, specificity, and accuracy were 88.5%, 98%, and 95%, respectively. Nevertheless, CDUS has missed the identification of synechiae in five limbs with iliofemoral DVT and incorrectly reported two cases as having synechiae with 81% sensitivity, 96% specificity, 91% accuracy, and substantial agreement with venography and IVUS ($k=0.79$) with no significant difference between its diagnostic efficacy and that of MDCTV ($p=0.5$). MDCTV matched the gold standard in the detection of venous collaterals with 100% accuracy and perfect agreement with conventional venography ($k=1$) but CDUS could not visualize the collaterals in three cases with an accuracy of 96% and almost perfect agreement with the gold standard ($k=0.91$) ($p=0.25$) (Table 3 and 4).

Table (3): Calculated sensitivity, specificity, positive and negative predictive values, and accuracy of MDCTV and CDUS in correlation with venography and IVUS findings.

Type of Finding	Direct MDCTV					Transabdominal CDUS					p- value*
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	
Presence of iliac venous stenosis	100	100	100	100	100	88.3	100	100	72	91	0.008**
Iliofemoral DVT	95.4	100	100	94.4	97.4	81.4	97	97.2	80.5	88.3	0.22
Intraluminal Synechiae	88.5	98	96	94.3	95	81	96	91.3	91	91	0.5
Venous collaterals	100	100	100	100	100	94.3	100	100	89	96	0.25

* P-value calculated with the exact McNemar test and Binomial distribution.

** P ≤0.05=statistically significant difference.

The degree of agreement between direct MDCTV and transabdominal CDUS was substantial regarding the detection of venous stenosis (k=0.78), iliofemoral thrombus (k=0.77), and intraluminal synechiae (k=0.72) whereas it was almost perfect as regards the venous collaterals recognition (k=0.91) (Table 4).

Table (4): Degree of agreement between direct MDCTV, CDUS, and interventional findings in the confirmed MTS cases.

Parameter	Agreement	Direct MDCTV versus venography and IVUS	Transabdominal CDUS versus venography and IVUS	MDCTV versus CDUS
Iliac vein stenosis		1	0.78	0.78
Iliofemoral DVT		0.95	0.77	0.77
Intraluminal Synechiae		0.88	0.79	0.72
Venous collaterals		1	0.91	0.91

Data are kappa coefficients: k 0.00= no agreement, 0.01-0.20= slight agreement, 0.21-0.40= fair agreement, 0.41-0.60= moderate agreement, 0.61-0.80= substantial agreement and 0.81-1= almost perfect agreement.

DISCUSSION

MTS was initially described as a rare pathophysiologic anatomical variant and was poorly recognized for many years because there were no standardized clinical criteria to confirm or exclude the anatomical variant (1,2). Recently, the diagnosis of MTS became more frequent due to the modern advances in imaging techniques and the increased clinical awareness for the syndrome (3,9). There are multiple imaging methods that can be used to evaluate patients with MTS and the radiologists must be able to recognize the diagnostic criteria of the syndrome because the management of DVT with an underlying iliac vein compression is different from that without (2,10).

Despite it has been stated that CDUS has low accuracy in the evaluation of abdominopelvic veins (1,3,23) some reports advocated its use as a radiation free, cost and time-effective imaging method in the evaluation of patients with MTS as it can provide anatomical and hemodynamic information about the veins (1,2,7,23-25). Recent advances in computer technology make MDCTV the primary imaging tool in venous diseases (24). MDCTV can distinguish between non-thrombotic and thrombotic MTS, and identify intraluminal spurs and collateral pathways (2,3,9,10). The

high spatial, contrast, and temporal resolution are further advantages of MDCT (26).

The purpose of the current study was to compare the efficacy of transabdominal CDUS with that of direct MDCTV in the diagnosis of MTS using venography and IVUS as gold standard.

The direct MDCTV protocol was chosen in this study rather than the indirect technique because direct injection of diluted contrast into the foot veins with ascending acquisition of imaging leads to more distension and efficient contrast enhancement of the venous network, without enhancement of the surrounding tissues and hence provides outstanding details (24).

Iliac vein stenosis of MTS may not always be observed in conventional venography, especially in limbs that had subtle radiologic findings (27). On the other hand, IVUS is limited in the evaluation of extravascular findings of MTS such as the venous collaterals (16). Furthermore, a recent study concluded that the treatment plan was changed in many patients when the IVUS findings were added to those of conventional venography (22). Therefore, we preferred to use the combined findings of conventional venography and IVUS as the gold standard of the present study.

Although the possibility of MTS should not be excluded based on bilaterality or right-sided involvement, most researchers including Virchow who first described the syndrome, documented the left-sided predominance of MTS with a left-right ratio of 3-5:1 (2,9,19,26-28). In agreement with the former results, in the current work all proved cases of MTS were attributed to the LCIV compression; by the RCIA in 76 cases and by early bifurcation of the LCIA in one case.

Multiple previous studies showed the high prevalence of MTS in young and middle-aged women (3,4,9,23,26,27). Moreover, some authors have considered multiple pregnancies, postpartum period, and contraceptive therapy among risk factors that accelerate the hemodynamic implications in MTS patients (3,29,30). In concordance with the aforementioned studies, the current results revealed that the majority of cases with confirmed MTS were young and middle-aged multiparous females with a history of hormonal contraceptive intake. This could be attributed to the more pronounced females' lumbar lordosis, particularly during pregnancy, causing more compression of the LCIV against the RCIA. The alteration in the female pelvic anatomy and in the uterine size under the effect of repeated hormonal changes could be another explanation (9,28,31). In addition, 60% of the confirmed cases were overweight. Obesity raise the intra-abdominal pressure leading to an increased venous pressure with consequently larger venous diameter and more venous insufficiency (32).

In venous abnormalities with acute iliofemoral DVT, Chung observed a high correlation between CT venography and conventional venography (33). Moreover, a series of studies with relatively similar contrast timing protocols (21-23,26,29,30) demonstrated the high sensitivity and specificity MDCTV in the diagnosis and evaluation of the anatomical characteristics of MTS. Our data are concordant with the preceding studies, in stating that direct MDCTV was highly accurate in the identification of LCIV compression, iliofemoral DVT, intraluminal synechiae, and pelvic venous collaterals with almost perfect to perfect agreement between MDCTV findings and those of conventional venography and IVUS.

In his study, Barry concluded that transabdominal CDUS is a very beneficial tool in diagnosing MTS (25) and in a previous case report, MTS was initially diagnosed by transabdominal CDUS alone and then confirmed by CT and conventional venography (7). Similarly, Metzger *et al.* noted a high degree of agreement between CDUS and IVUS in the detection of significant venous obstructions (34). It has been previously reported that CDUS can usually identify iliofemoral DVT, a common association with MTS (5,13). Conversely, it has been reported that the accuracy of CDUS in patients with MTS is low due to its lower sensitivity in the evaluation of iliac veins stenosis (79% for the external iliac and 47% for the common iliac veins) and its associated flow or structural abnormalities (35).

In our study, the accuracy of trans-abdominal CDUS regarding the detection of the iliac vein compression was significantly lower than that of direct MDCTV with substantial agreement between it, direct MDCTV, and both interventional procedures. Moreover, the sensitivity, specificity and accuracy of CDUS in the identification of the intraluminal spurs, iliofemoral thrombus, and venous collaterals were relatively lower than those of direct MDCTV but with high degree of agreement and no significant difference between both imaging modalities. The current study results showed no significant difference between the mean percentage of iliac venous stenosis calculated from the images of MDCTV and those of transabdominal CDUS.

A number of potential limitations should be considered in this study. First, this work was conducted as a single-center study on a relatively small sample size necessitating the confirmation of our conclusions by a long-term multi-centric study with large sample size. Second, only patients who met the inclusion criteria and accepted the participation in the study were included and this might have led to selection bias. Third, because the images of each imaging modality were analyzed by two radiologists in consensus we did not assess inter or intra-observer variability. Fourth, although conventional venography and IVUS were the best reference standards available for this study, both remain operator-dependent methods that have inter-observer or even intra-observer variability. However, the experience of the vascular surgeon might have enhanced the results of our study. Lastly, because the decision to perform conventional venography and IVUS was based not only on the clinical findings but also on the preoperative imaging findings, a verification bias might have been introduced. Moreover, the findings of conventional venography and IVUS might have been biased by the availability of the MDCTV and CDUS findings to the vascular surgeon.

CONCLUSION

Direct MDCTV is a valuable reference in the diagnosis and preoperative workup of MTS with comparable accuracy to that of the more invasive conventional venography and IVUS. Despite of being widely available time and cost-effective radiation-free imaging test, transabdominal CDUS has low accuracy in the identification of iliac vein compression, should not be used as the sole investigative tool to confirm or ruled out the possibility of MTS, and combined direct MDCTV is mandatory to establish the diagnosis.

Conflict of interest: The authors declare no conflict of interest.

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