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# Usefulness of triggered non-contrast-enhanced magnetic resonance angiography in assessing lower extremity venous disease

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## Abstract

Although venous duplex ultrasonography (USG) is reliable for diagnosing lower extremity venous disease (LEVD), cross-sectional imaging studies were usually required before intervention or surgery. Patients of LEVD with renal insufficiency usually restrict the use of contrast-enhanced imaging modalities. In seeking an alternative imaging solution for these patients, we explore the clinical utility of triggered angiography non-contrast-enhanced magnetic resonance imaging (TRANCE-MRI) in the assessment of LEVD.

We collected data from patients presenting to a tertiary wound-care center with symptoms of LEVD from April 2017–November 2019. Each participant underwent baseline USG followed by TRANCE-MRI on a 1.5T MR scanner (Philips Ingenia, Philips Healthcare, Best, The Netherlands). Inter-rater reliability was measured using Cohen's kappa ($\kappa$).

All 80 participants (mean age, 61.9 ± 14.8 years; 35 males, 45 females) were assessed and were classified into one of five disease groups, deep vein thrombosis (n = 38), venous static ulcer (n = 16), symptomatic varicose veins (n = 18), recurrent varicose veins (n = 3), and lymphoedema (n = 5). The inter-rater reliability between TRANCE-MRI and doppler USG showed substantial agreement ($\kappa$, 0.73). The sensitivity, specificity, and accuracy of TRANCE-MRI were 90.5%, 88.1%, and 88.8%, respectively. In 59 (73.8%) USG-negative patients, we were able to diagnose positive findings (deep venous thrombosis, n = 7; varicose veins, n = 15; lymphedema, n = 10; iliac vein compression with thrombosis, n = 6; external venous compression, n = 5; vena cava anomaly, n = 2; occult peripheral artery disease, n = 5; ccluded bypass graft, n = 1) by using TRANCE-MRI. Of these, 9 (15.3%) patients underwent additional vascular surgery based on positive TRANCE-MRI findings.

TRANCE technique provides the limb's entire venous drainage in clear images without background contamination by associated arterial imaging. Additionally, simultaneous evaluation of bilateral lower extremities can help determine the lesion's exact site. Although TRANCE-MRI can provide MR arteriography and MR venography, we recommend performing only MR venography in symptomatic LEVD patients because the incidence of occult arterial disease is low.

**Abbreviations:** 3D = three-dimensional, CT = computed tomographic, CTA = computed tomographic angiograph, DVT = deep venous thrombosis, FOV = field of view, LEVD = lower extremity venous disease, MRI = magnetic resonance imaging, NC-MRA = non-contrast MRA, STIR = short tau inversion recovery, TRANCE-MRI = triggered angiography non-contrast-enhanced magnetic resonance imaging, TSE = turbo spin-echo, USG = ultrasonography.

**Keywords:** deep vein thrombosis, lower extremity, magnetic resonance imaging, non-contrast-enhanced, triggered angiography non-contrast-enhanced, venous disease

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## 1. Introduction

Lower extremity venous disease (LEVD) is a common condition, which usually has a long-standing course associated with pain and discomfort. LEVD included anatomic and functional abnormality of the whole venous systems and the associated clinical illness.[1] Long-standing anatomic abnormality may lead to the venous system's advanced functional abnormality such as deep vein thrombosis (DVT), venous static ulcers, varicose veins, or lymphoedema.[2–4] Clinical symptoms of LEVD including a broad spectrum of manifestation, ranging from mild leg swelling, achiness, eczema, and hemosiderosis, to nonhealing venous leg ulcer.[5] Adults with venous leg ulcers usually experience pain, fatigue, depression, loneliness, and social isolation. Associated psychological distress had reduced the quality of life of long-term patients.[6] LEVD also causes a significant health care problem and cost. According to an extensive epidemiological survey, the prevalence of venous disease accounts from 51.9% in the Asian area to 70.18 in eastern Europe.[7] The refractory nature of LEVD negatively affects the ability to work and causes frequent visits for health care. The cost of LEVD is very high in terms of productivity loss, the high price of dressing, and health care. The mean total cost of treating venous ulcers was reported as $15,732 in a one-year-follow-up study.[8] The above economic study demonstrated that surgical intervention did not significantly increase total cost but significantly reduced recurrence rates. If the underlying venous pathology is diagnosed, most patients with lower-limb venous disease can either be managed with treatments targeted towards the superficial venous system or stenting the affected deep vein.[9]

Ultrasonography (USG) is usually the first-line diagnostic tool used in patients presenting with LEVD. In the past, conventional venography was considered the gold standard for evaluating venous thromboembolism.[10] Further, the detection of venous pathology during conventional venography enabled immediate vascular intervention during the same session. However, this procedure is invasive, time-consuming, involve exposure to ionizing radiation, and requires contrast media. While computed tomographic angiography (CTA) is less invasive than conventional venography, it still requires intravenous injection of a contrast agent and radiation imaging, thus exposing patients to associated risks.[11] Contrast-enhanced magnetic resonance angiography has emerged as a highly sensitive imaging modality for detecting vascular pathology without exposing the patient to adverse effects of ionizing radiation. However, the use of a gadolinium-based contrast medium for MRA has its own risk of complications, for example, "nephrogenic systemic fibrosis," which has been reported worldwide.[12–14]

One key advantage of MRA is that, unlike CTA, it can reconstruct the vascular model during imaging acquisition without using a contrast medium. Non-contrast MRA (NC-MRA) is a broad spectrum of MR techniques, which has been widely developed and applied in different vascular scenario for decades.[15,16] According to the literature, most NC-MRA studies were focused on the application of arterial disease. Triggered angiography non-contrast-enhanced magnetic resonance imaging (TRANCE-MRI) is an NC-MRA technique, which exploits differences in vascular signal intensity during the cardiac cycle, for subsequent image subtraction, without the use of a contrast agent. Both venograms and arteriograms can be acquired using this technique. This imaging method has been used in patients with renal insufficiency and various vascular diseases that preclude intravenous contrast.[17,18] However, the clinical utility of TRANCE-MRI remained unclear. A few reported studies of this technique focused on its application only for arterial disease and had a small sample size.[19–22]

Although venous duplex USG is the most reliable noninvasive test to diagnose the LEVD. Cross-sectional imaging studies were usually needed to confirm the lesion territory and venous anatomy before interventional treatment or surgery. Conventionally, contrast-enhanced CTA and contrast-enhanced magnetic resonance angiography can be used to image vessels in the entire lower extremity. Clinically, patients of LEVD with renal insufficiency usually restrict contrast agents for enhanced imaging. A positive correlation between chronic kidney disease and venous thromboembolism has been reported.[23,24] There is a need for alternative cross-sectional imaging solutions for patients with renal insufficiency. Thus, we conduct this TRANCE-MRI study with a large sample size to assess LEVD in a novel way. The results of this study will supplement related application reports and help establish the diagnostic criteria for LEVD combined with renal insufficiency.

## 2. Methods

### 2.1. Patients

In this cross-sectional study, conducted from April 2017 to November 2019, we prospectively collected data from patients visiting a wound-care center in a tertiary hospital. Patients who were willing to sign a written consent, who were >30-years of age (to minimize the influence of the geriatric population), who were aware of the diagnosis, and who were able to understand the study protocol, were included in the study. Pregnant/breastfeeding women, patients with in-vivo devices incompatible with MRI, those with severe claustrophobia/poor compliance resulting in an inability to lie still during the MRI scan, were excluded from the study. The complete lower-limb venous system (including femoral veins, great saphenous veins, popliteal veins, and perforating calf-veins) in all patients was examined using baseline USG, following a TRANCE-MRI was performed. Standard duplex sonography and color Doppler imaging were performed on the same device and reported by two sonographers (YHT, YKH), using defined morphological and hemodynamic criteria. The two sonographers are specialized cardiovascular surgeons and have eight years of experience (YHT) and twelve years of experience (YKH) in the field of ultrasound examination, respectively. As pelvic veins were difficult to assess in patients with obesity or edema, these were not assessed in the regular ultrasound survey.[25] computed tomographic (CT) angiography, radionuclide lymphoscintigraphy, and conventional venography were also performed, as applicable, according to the USG findings. The Institutional Review Board of Chang Gung Memorial Hospital approved this study (Institutional Review Board number: 201700389B0, 201900448B0). All participants provided written, informed consent for participation in the study.

### 2.2. TRANCE MRI technique

All images were acquired using a 1.5T MR scanner (Philips Ingenia, Philips Healthcare, Best, The Netherlands), reported by a specialized radiologist (CWC) who has six years of experience in vascular imaging. Patients underwent imaging in a supine position along with simultaneous monitoring using a peripheral

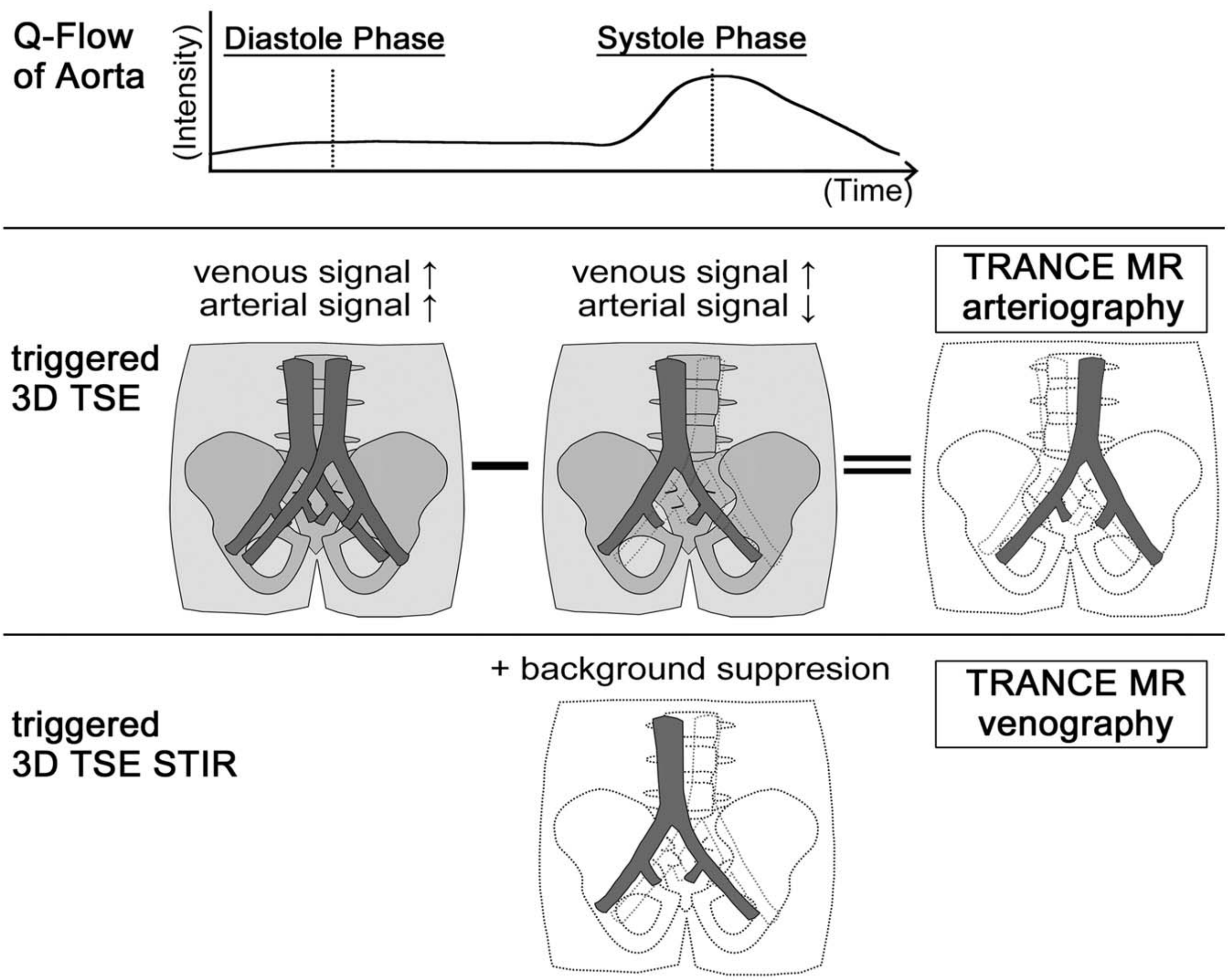


**Figure 1.** Triggered angiography non-contrast-enhanced magnetic resonance imaging (TRANCE-MRI) principle. A, Quantitative Flow (Q-Flow) scan of the abdominal aorta was routinely performed to determine the appropriate triggering time-intervals. Arterial blood flows rapidly, leading to the creation of flow-voids during cardiac systole. Using three-dimensional (3D) turbo spin-echo (TSE) sequences, subtraction of the diastolic-phase, and systolic-phase scans allow reconstruction of a 3D dataset with only arterial vasculature (arteriography). Conversely, using 3D TSE short tau inversion recovery sequence (STIR), systolic-phase scans allow reconstruction of a 3D-dataset with only venous structures (venography), because the sequence enables additional background suppression of fatty and bony tissue.

pulse unit or electrocardiography. A quantitative flow scan of the abdominal aorta was routinely performed to determine the appropriate triggering times for systolic and diastolic phases. After examining venous drainage at 4-levels (abdominal, pelvic, thighs, knees, and legs), the data were reconstructed into a three-dimensional (3D) dataset comprising of all infra-diaphragmatic vascular structures. Images of arterial structures were acquired using a 3D turbo spin-echo (TSE) sequence during systolic and diastolic phases, using the following parametric ranges: repetition time, 1 beat; echo time, shortest; flip angle, 90°; voxel size, 1.7 x 1.7 x 3 mm; field-of-view (FOV), 350 x 420 mm. During systole, arterial vessels appeared dark due to rapid intravascular blood-flow, which exerted a flow-void effect. Conversely, during diastole, both arterial and veno-lymphatic vessels appeared bright, because of slower blood-flow. Subtraction of the two phased scans resulted in a 3D-dataset with only arterial vasculature (MR arteriography). Images of veno-lymphatic structures were acquired using a 3D TSE short tau inversion recovery (STIR) sequence during the systolic phase, using the following parametric ranges: repetition time, 1 beat; echo time, 85-ms; inversion recovery delay time, 160-ms; voxel size, 1.7 x 1.7 x 4 mm; FOV, 360 x 320 mm. Using STIR sequence imaging enabled additional background suppression of fatty and bony tissue while allowing arteries to be visualized as dark structures during cardiac systole. The result was a 3D dataset with only veno-lymphatic structures (MR venography). Figure 1 summarizes the principles of the TRANCE-MRI technique. All images were acquired without using a gadolinium contrast medium (Fig. 2). The MR protocol used in this study required 60-minutes for image-acquisition, consisting of 25 and 35 minutes for venography and arteriography, respectively.

### 2.3. Statistical analysis

This study used both Doppler ultrasound and TRANCE-MRI for detecting DVT in thigh vessels. Cohen's kappa coefficient (κ) was

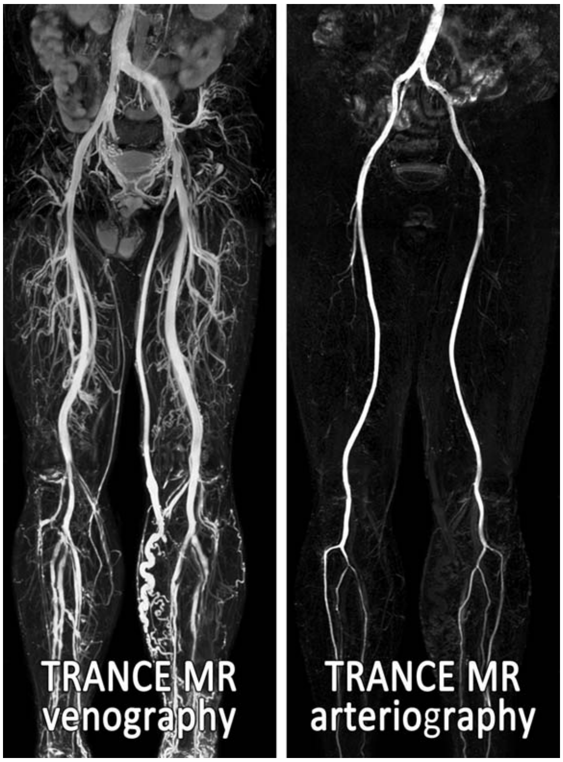


**Figure 2.** Triggered angiography non-contrast-enhanced magnetic resonance venography and magnetic resonance arteriography. A large field-of-view is one of the advantages of TRANCE-MRI. Simultaneous presentation of bilateral lower extremity vasculature in the same high-resolution image can help determine the lesion location, and in evaluating its surrounding vascular territory and associated newly-formed collaterals. In this figure, a large varicose vein from the territory of the left great saphenous vein can be observed.

used to measure the inter-rater reliability between both tests. Examination results of doppler USG (standard reference) were considered the true outcome to evaluate the comparative sensitivity, specificity, and accuracy of TRANCE-MRI.

## 3. Results

Of the total 80 participants (mean age, 61.9 ± 14.8 years) included in this study, 35 and 45 were males and females, respectively. All participants underwent a baseline physiological assessment and based on their diagnosis, were classified into one of five disease groups, deep vein thrombosis (Fig. 3), venous static ulcer, symptomatic varicose veins, recurrent varicose veins, and lymphoedema, consisting of 38 (48.5%), 16 (20%), 18 (22.5%), 3 (3.8%), and 5 (6.3%) cases, respectively. Of these, 15 (18.8%) patients had received anticoagulant therapy previously, due to the history of thromboembolism or ischemic infarction. Totally, 24 (30%) patients had undergone relevant operative procedures such as stripping the great saphenous vein, truncal ablation of the great saphenous vein, and angioplasty axillary-bifemoral bypass, hip/knee-joint replacement, or flap reconstruction of the affected leg. Three (3.8%) patients had received radiation therapy for pelvic malignancy. The baseline characteristics of all study patients have been summarized in Table 1.

All patients diagnosed with DVT involving the thigh region were first assessed using doppler USG as the reference standard, the results of which were further cross-referenced with TRANCE-MRI findings. Inter-rater reliability between TRANCE-MRI and doppler USG showed substantial agreement (κ, 0.73). The sensitivity, specificity, and accuracy of TRANCE-MRI were 90.5%, 88.1%, and 88.8%, respectively. Using TRANCE-MRI, we were able to diagnose 7 (11.9%), 15 (25.4%), 10 (16.9%), 6 (10.2%), 5 (8.5%), 2 (3.4%), 5 (8.5%), and 1 (1.7%) USG-negative patients (n = 59) with DVT, varicose veins, lymphedema,

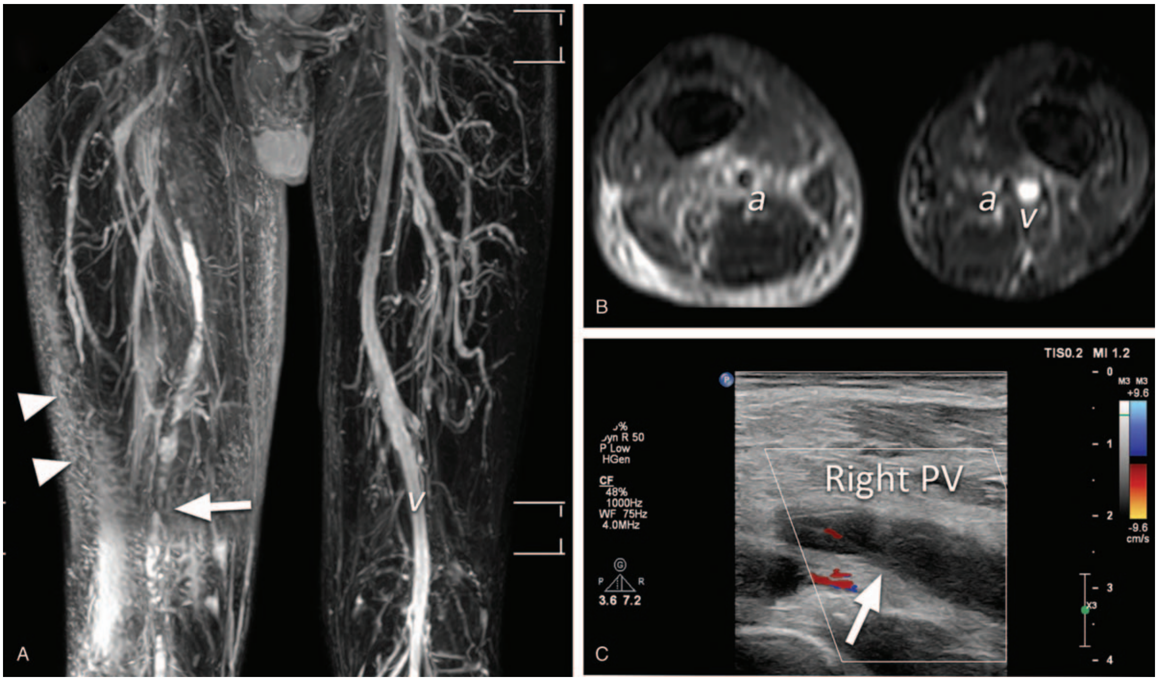


**Figure 3.** Deep vein thrombosis (DVT). (A) Coronary image showing the filling defects (arrow) due to DVT of the right popliteal vein (PV) along with superficial reticulation (arrowheads) indicating lymphedema of the right thigh. (B) The axial image shows that the arteries (a) are dark because of the flow-void effect. Right thigh shows prominent lymphedema without obvious, associated signal-intensity of underlying veins (v). (C) Doppler scan shows thrombosis causing distension of the right popliteal vein.

**Table 1**

**Baseline characteristics of study participants (n = 80).**

| Variables | Values |
|---|---|
| Demographic variables | |
| Gender, male, No. (%) | 35 (43.8%) |
| Age, mean ± SD, y | 61.9 ± 14.8 |
| BMI, mean ± SD, kg/m$^2$ | 26.6 ± 5.3 |
| Initial assessment of venous pathology | |
| Deep vein thrombosis, No. (%) | 38 (48.5%) |
| Venous static ulcer, No. (%) | 16 (20%) |
| Symptomatic varicose vein, No. (%) | 18 (22.5%) |
| Recurrent varicose vein, No. (%) | 3 (3.8%) |
| Lymphoedema, No. (%) | 5 (6.3%) |
| History of anticoagulation and vascular procedure | |
| Anticoagulant therapy, No. (%) | 15 (18.8%) |
| Varicose vein stripping, No. (%) | 7 (8.8%%) |
| Varicose vein truncal ablation, No. (%) | 10 (12.5%) |
| Balloon angioplasty, No. (%) | 1 (1.3%) |
| Axillary-bifemoral bypass, No. (%) | 1 (1.3%) |
| Artificial joint replacement, No. (%) | 2 (2.5%) |
| Free flap reconstruction, No. (%) | 3 (3.8%) |
| Radiation therapy, No. (%) | 3 (3.8%) |
| Imaging modalities | |
| Doppler ultrasonography in venous system, No. (%) | 80 (100%) |
| TRANCE MR arteriography, No. (%) | 80 (100%) |
| TRANCE MR venography, No. (%) | 80 (100%) |
| CT angiography, No. (%) | 4 (5%) |
| Radionuclide lymphoscintigraphy, No. (%) | 1 (1.3%) |
| Conventional venography, No. (%) | 1 (1.3%) |
| Further vascular procedure after examination No. (%) | 15 (18.8%) |

BMI = body mass index, CT = computed tomography, SD = standard deviation, TRANCE MR = triggered angiography non-contrast-enhanced sequence magnetic resonance.

**Table 2**

**Detailed cross-tabulated triggered angiography non-contrast-enhanced sequence magnetic resonance imaging findings and doppler ultrasonography data for diagnosis of deep venous thrombosis of the thigh.**

| | TRANCE-MRI | | |
|---|---|---|---|
| | Present | Absent | Total |
| Doppler ultrasonography (as reference standard) | | | |
| Present | 19 | 2 | 21 |
| Absent | 7 | 52 | 59 |
| Total | 26 | 54 | 80 |
| Inter-rater reliability between TRANCE-MRI and ultrasonography | | | |
| Cohen's kappa | 0.73 | | |
| Performance of TRANCE-MRI | | | |
| Sensitivity | 90.5% | | |
| Specificity | 88.1% | | |
| Accuracy | 88.8% | | |
| Detected MRI pathologies in ultrasonography-negative cases (n = 59): | | | |
| Deep venous thrombosis | 7 | 11.9% | |
| Varicose veins | 15 | 25.4% | |
| Lymphoedema | 10 | 16.9% | |
| Iliac vein compression with thrombosis | 6 | 10.2% | |
| Other venous compression | 5 | 8.5% | |
| Vena cava anomaly | 2 | 3.4% | |
| Occult peripheral artery disease | 5 | 8.5% | |
| Occluded bypass graft | 1 | 1.7% | |
| Further vascular procedure after MRI | 9 | 15.3% | |

MRI = magnetic resonance imaging, TRANCE MRI = triggered angiography non-contrast-enhanced magnetic resonance.

iliac vein compression with thrombosis, venous compression (caused by pelvic lymphadenopathy, hip prosthesis, or knee joint effusion), vena cava anomaly, occult peripheral artery disease, and occluded bypass graft, respectively. Of these, 9 (15.3%) patients underwent additional vascular surgery based on the positive TRANCE-MRI findings. Detailed cross-tabulated data to both investigative modalities are listed in Table 2.

## 4. Discussion

The present study showed that findings of non-contrast-enhanced MR angiography, performed using the TRANCE technique, were reliable for diagnosing deep venous pathology, and demonstrated substantial agreement with results of the first-line imaging modality (doppler USG) for detecting lower-extremity venous thrombosis. In addition, TRANCE-MRI enabled detection of venous pathology even in patients who did not show any abnormality on doppler USG. Varicose veins and lymphedema were the lesions most likely detected by TRANCE-MRI, in patients with negative USG results. It may be due to the smaller FOV assessable during USG, which may make it difficult to investigate the entire veno-lymphatic system of the lower extremity thoroughly. TRANCE-MRI allows for detecting venous pathology in USG-negative patients with various venous symptoms, which can be corrected using further vascular surgeries. These results demonstrated the efficiency and value of TRANCE-MRI for evaluating patients with renal insufficiency, which increases the risk of contrast-induced nephropathy and nephrogenic systemic fibrosis.[26]

The primary purpose of this study was to assess the clinical utility of non-contrast-enhanced MRI in assessing lower-limb, veno-lymphatic pathology, in patients presenting with engorged varicose veins, unhealed static ulcers, and unilateral leg-swelling.[2,4,27,28] Doppler USG is usually the first diagnostic tool used in patients presenting with symptoms suggestive of lower-limb vascular insufficiency, especially in those with concurrent renal impairment. Patients with chronic renal disease may be at increased risk for DVT.[29] However, USG is not a particularly sensitive investigative modality in patients with obesity, edema, or localized tenderness.[25] This study revealed that TRANCE-MRI could detect veno-lymphatic pathology in one-fourth of USG-negative cases. Further analysis of the false-negative cases showed that MRI enabled detection of smaller-sized, dilated varicose veins and of lymphoedema that was more symmetrical in distribution, signs that may be difficult to detect on doppler USG. Assessment of a larger FOV is one of the advantages of TRANCE-MRI, which can be used for detailed evaluation and mapping of the territory and distribution of vascular lesions, in case further vascular surgery is considered for management. It is difficult to assess the entire venous system, especially that supplying pelvic and abdominal areas, using only USG. It may be difficult to detect venous compression using only ultrasound, if the veins within the thigh are not concurrently thrombosed (Fig. 4).

Contrast-enhanced CT scans or MRI can be performed to assess the entire lower-limb venous system, including that draining deep-seated pelvic and abdominal areas. Cross-sectional imaging modalities are usually used for further evaluation of iliac venous pathology. Ideally, both contrast-enhanced CT and MRI can identify both stenotic lesions or the specific cause of external venous compression that gives rise to

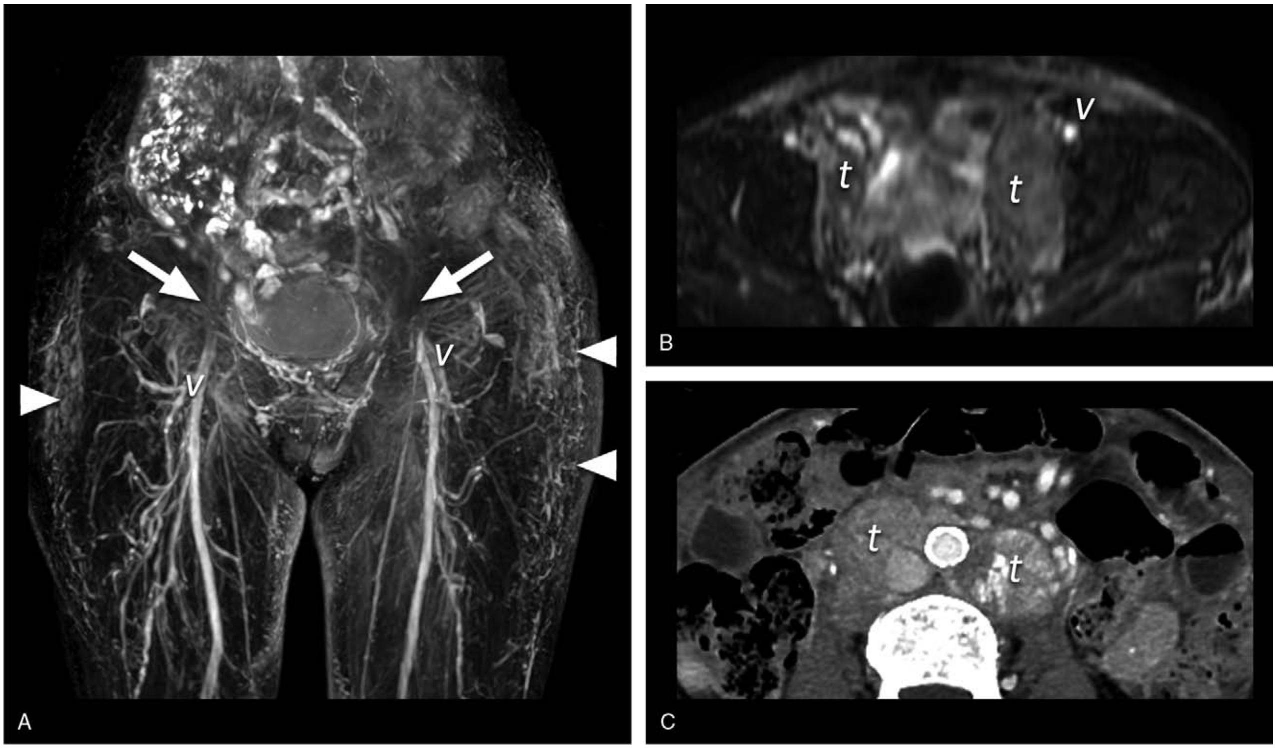


**Figure 4.** Pelvic tumors were causing pelvic veins compression. Triggered angiography non-contrast-enhanced magnetic resonance imaging performed in an ultrasonography-negative case. (A) Coronal image showing patent bilateral common femoral veins (v) but associated obliteration of pelvic veins. Associated lymphoedema is also observed. Axial (B) magnetic resonance image and (C) computed tomography scan show retroperitoneal and pelvic tumors (t) compressing pelvic veins.

symptoms.[30] However, the main challenge with both these imaging methods is that it is difficult to estimate the correct duration required to attain optimal contrast opacity of the target vein.[31] While this universal technical issue applies to all contrast-enhanced vascular imaging modalities, it is especially trickier to surmount in the evaluation of the iliac venous system. Intrinsic patient factors (e.g., cardiac output) or an external compressive force exerted on the affected vein/s can alter the contrast transit-time to varying degrees. These variable factors may result in determining an incorrect acquisition time-interval, which limits image resolution and makes detection of subtle lesions difficult. Conversely, MR venography performed using the triggered 3D TSE STIR sequence can suppress static background tissue and eliminate arterial signals. This sequence facilitates an angiographic image acquisition, which shows only high-resolution venous vasculature without contamination by the accompanying arterial vessels. We can achieve an excellent signal-to-noise ratio with this technique, producing vivid vascular images, which make it an excellent imaging tool for diagnosing obstructive iliac venous pathology (Fig. 5) and vena cava anomalies (see Video, **Supplemental Video** {Supplemental Video. Video that demonstrates the three-dimensional rotating projection in a patient with double inferior cava by using non-contrast-enhanced magnetic resonance venography, 4 seconds, 8.4MB}, http://links.lww.com/MD2/A115, which demonstrates the three-dimensional rotating projection in a patient with double inferior cava). More importantly, this modality is particularly suitable for patients who are vulnerable to the adverse effects of contrast agents.

However, ultra-clear vascular images also pose new diagnostic challenges. Firstly, we noticed that some subjects who were initially suspected of having DVT showed equivocal interruption of the left common iliac vein without associated venous thrombosis or collateral vessel formation. Due to the anatomical narrowing of the left common iliac vein, it may be sandwiched between the common iliac arteries and the spine. Further research is needed to explore the correlation between the false-positive imaging findings and the eventual clinical results. Secondly, while TRANCE-MRI can detect DVT with associated collateral-formation and lymphedema, we did not use its findings to distinguish between acute and chronic thrombosis in the course of this study. Distinguishing acute from chronic venous thrombosis is a potential advantage of TRANCE-MRI, with irregular wall thickening findings in the presence of collaterals and diminutive lumen being suggestive of chronic DVT.[25] We recommend further research to substantiate this hypothesis.

The application of TRANCE-MRI for lower extremity venous pathology has many advantages. Firstly, the TRANCE technique can help visualize the entire venous drainage of the limb, producing clear images without background-distortion, and without contamination by associated arterial imaging. This is valuable for assessing the pathophysiology of DVT, which may occur due to either an intravascular cause such as venous thrombus-formation or as secondary to extravascular venous compression by surrounding arteries, lymph nodes, or other structures. Secondly, a larger FOV can help assess the entire vascular territory and distribution of lesions. Simultaneous evaluation of bilateral lower extremities within the same high-


**Figure 5.** Iliac vein compression syndrome. Iliac vein compression syndrome can be observed in a patient with recurrent deep venous thrombosis of the left leg. (A) Turbo spin-echo (TSE) sequence triggering during cardiac diastole is used to acquire venous and arterial images simultaneously. The tortuous right common iliac artery (CIA) covering the left common iliac vein (CIV) can be seen. (B) TSE short tau inversion recovery sequence triggering during cardiac systole can be used to acquire solely venous images. Interruption (arrow) of flow within the left CIV and filling defects (*) involving the left femoral vein (FV) are consistent with a diagnosis of iliac vein compression syndrome.

resolution image can help determine the exact site of the lesion. Besides allowing precise determination of the lesion's location, assessing the involved vascular territory and associated collaterals is also essential for pre-interventional imaging. In this study, small variceal veins and lymphedema were other most likely lesions to be detected on TRANCE-MRI in patients with negative ultrasonographic results. Thirdly, this modality of vascular imaging is radiation-free and does not require intravenous contrast agents. It is precious to evaluate patients with renal insufficiency, as impaired renal function increases the risk of developing contrast-induced nephropathy and nephrogenic systemic fibrosis. Finally, we used a prospective study design and included a sizeable study-group, which helps provide detailed information on the clinical utility of TRANCE-MRI. Our findings provide robust preliminary evidence for the application of this technology in patients with venous diseases.

This study had certain limitations. Firstly, the major limitation of this investigation is that it was a nonrandomized study with few patients. Further studies with a larger sample size and randomized trial should be conducted. Secondly, it lacked a healthy control-group, as all participants visited our wound-care center to resolve symptoms that were likely to have been caused by a vascular pathology. It may have led to selection bias, which may have increased the calculated incidence of various vascular pathologies. Thirdly, we did not compare the inter-observer variability because the same radiologist was responsible for interpreting all TRANCE images. Comparative studies between TRANCE-MRI and contrast-enhanced CT are also lacking.

Further studies designed to assess this comparison are needed to fully explore the values and pitfalls of TRANCE technique. Fourthly, a long imaging time-interval is not feasible for regular clinical application. The MRI protocol used in this study took 60-minutes to acquire images of all infra-diaphragmatic (including abdomen, pelvis, thighs, knees, and legs) vascular structures. MR venography takes 25-minutes, while MR arteriography takes 35-minutes. Thus, it is not a suitable modality for imaging of critically ill or irritable patients. It may not always be necessary to perform the whole TRANCE-MRI protocol, which may be suitably altered and abbreviated according to individual clinical presentation. Our study revealed that occult, peripheral arterial occlusive disease is rarely found in patients initially suspected of having venous disease (5/80, 6.3%). Therefore, we recommend that sole TRANCE MR venography be given priority in patients with suspected venous disease, making this diagnostic modality more applicable in the clinical setting. Finally, a non-contrast-enhanced MR sequence for vascular imaging is an expensive, time-consuming imaging modality, which is unavailable for routine use in many institutions and countries. Further studies on its clinical application are indicated to discover and establish the potential capability and utility of this noninvasive imaging method.

Considering these drawbacks of TRANCE-MRI encountered in this study, we suggest that Doppler ultrasound should be used primarily for assessing suspected lower-limb venous lesions because it is both noninvasive and cost-effective. However, USG has limited utility for detecting small varicose veins, lymphedema, and lesions of deep-seated pelvic and abdominal veins. Suppose a patient is suspected of having a pelvic vein pathology, intricate lower-limb varicose veins, or is suffering from concurrent renal impairment. In that case, we recommend a TRANCE-MRI for further evaluation. We also recommend TRANCE-MRI as a pre-interventional assessment method because it allows the clinician to delineate the lesion site, its associated vascular territory, and newly-formed collaterals. This technique may provide more useful information, allowing optimal therapeutic protocols for treating complicated vascular diseases.

## 5. Conclusion

TRANCE-MRI facilitates vascular imaging of the lower extremity veins and the deep-seated pelvic and abdominal vasculature. While examining iliac veins, using TRANCE-MRI may yield false-positive results. Compared to those obtained with USG, the newer technique allows for better recognition of small varicose veins and lymphoedema involving lower extremities. It can be used to discern deep venous pathology in the pelvis and abdomen. Further evaluation with TRANCE-MRI can help identify venous anomalies missed on doppler ultrasound. The detailed imaging data can help the clinician correct the condition via vascular surgery, as needed. Thus, with further study, TRANCE-MRI could prove to be a powerful tool for treating lower-extremity venous disease.

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## Author contributions

All authors were involved with study conception and design. YCW, SCW, YHT and YKH were involved with the acquisition of data. CWC, HT, PYC, and JCW were involved with the analysis and interpretation of data. CWC and YKH were responsible for funding acquisition. All authors participated in the drafting of the manuscript and critical revision. All authors read and approved the manuscript and agreed to be accountable.

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