Radionuclide Venography in the Diagnosis of Deep Vein Thrombosis of the Lower Extremities : A Comparison to Contrast Venography

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Abstract

Radionuclide venography (RNV) and contrast venography (CV) were compared in 72 limbs of 59 patients being clinically suspected of deep vein thrombosis (DVT) of the lower extremities. The criteria of positive RNV for DVT regarding flow pattern abnormailty included (1) nonfilling or nonvisualization of a deep vein, (2) interruption of the flow, (3) irregular or asymmetric filling of a deep vein, and (4) presence of abnormal collateral vessels. The overall accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and positive likelihood ratio (LR+) were 90 per cent, 88 per cent, 96 per cent, 98 per cent, 79 per cent, and 20.8 respectively. These figures are even higher when we focused on the major veins of the thigh and pelvis. They were 97 per cent, 95 per cent, 98 per cent, 98 per cent, 95 per cent, and 61 respectively. The results indicates that radionuclide venography, while technically simple, is a reliable test for detection of DVT particulary of the major veins of the lower extremities. Combined radionuclide venography and perfusion lung scan can also be performed in the same setting if Tc99m-MAA is used. Contrast venography which is an invasive procedure, should be reserved for questionable cases or those with suspected isolated calf vein thrombosis.

The diagnosis of deep vein thrombosis (DVT) on the clinical grounds alone is difficult and inaccurate[1-3], requiring evaluation by diagnostic or imaging techniques. Contrast venography (CV), while generally accepted as the "gold standard" for the diagnosis, is an invasive procedure, requires a skilled medical team and has morbidity due to complications or adverse reactions produced by the contrast medium[4,5]. Frequently the procedure cannot be performed because of difficulty to obtain

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the injection in patients with swollen legs and inability to perform in patients who have allergy to the contrast material. Thus, CV is not recommended for routine use[6].

There are many non-invasive tests for the evaluation of DVT, including impedance pethysmography (IPG), Doppler ultrasound and duplex sonography. However, the former two studies do not provide anatomical image details and duplex sonography, even providing venous images, requires a lot of skill for performing and interpretation. Radionuclide venography (RNV), on the other hand, is a minimally invasive procedure but it provides a nice picture of the whole deep venous system of the leg upto the inferior vena cava (IVC) similar to that seen from CV which is much easier for clinicians to understand. It is also simpler, less invasive and has no such risks from the contrast medium as compared with CV. So it has gained a widespread acceptance in the diagnosis of DVT[7-9].

Objective :

The main objective of the current study is to determine the accuracy of RNV performed in our laboratory for many years compared to the contrast venographic findings.

MATERIAL AND METHOD

Eighty nine patients with clinical suspicion of DVT and/or pulmonary embolism (PE) (Table 1) who were submitted to both RNV and CV were reviewed. Twenty six patients (29%) had no contrast study while only four (4%) had no radionuclide study due to technical failure. These 26 and another four patients who had incomplete clinical information or poor image quality for the interpretation were excluded from the project. Therefore, 59 patients, including 72 limb studies remained for the analysis. They were 35 women and 24 men whose age ranged from 13-82 years (mean age = 54±16 years) (Table 2). Most of the patients had leg swelling with clinical suspicion of DVT (Table 3). They had experienced symptoms for various durations as shown in Table 4.

Totally 72 limb studies were included in the series. Both RNV and CV were compared on the right side alone in 24 patients (24 legs), on the left side alone in 20 cases (20 legs) and on both sides in the remaining 14 cases (28 legs). The interval between the tests varied from the same day to 44 days (mean = 8 ± 9 days). Only eight patients had performed both studies in more than two weeks apart.

Table 1. Indication(s) for investigation.

Indications for investigation	Cases
1. Clinical suspicion of DVT	51
2. Clinical suspicion of PE	3
3. Clinical suspicion of both conditions	5

Table 2. The patient population : age and sex.

Age range (yrs)	Female	Male	Total
< 30	3	0	3
30-39	5	3	8
40-49	9	4	13
50-59	7	4	11
60-69	5	7	12
> 70	6	6	12
Total	35	24	59

Table 3. Symptom - Leg swelling.

Side of swollen leg	Cases
Right leg only	21
Left leg only	26
Both legs	9
Total	56

Table 4. Duration of leg swelling (56 cases).

Duration	Cases
Less than 1 week	17
>1-4 weeks	17
>1-3 month	13
>3 month	9

Radionuclide Venography (RNV)

Radionuclide venography was performed using SIEMENS or TOSHIBA (Model GCA-901A) gamma camera with low-energy, general-purpose (LEGP) collimator. The studies were acquired as

multiple overlapping static images or a whole-body scan. The static images were recorded for 90 seconds/ frame including calf, thigh, and pelvic regions. The whole-body image was acquired at the rate of 40 cm./ min. covering the same areas. Initially the patient lay on the scanning table and the tourniquets were applied above the ankles to enhance the isotopic material into the deep veins. After that a 25G butterfly needle which was attached with a three-way stopcock connected to a 20-ml syringe containing normal saline and the other syringe containing 5 mCi of Tc99m-MAA or Tc99m-phytate was inserted into a dorsal vein of each foot. The radioactive marker was placed at the level of the knee. The radiotracer was injected in divided doses followed by saline flushing and the imaging from the calf level upto the pelvic region including the lower part of the IVC was obtained. The procedure was repeated once again in the same manner after the tourniquets were released.

Contrast Venography (CV)

Contrast venography was also obtained in the supine position with the injection of 80 ml of Ioxaglate *via* a 20G butterfy needle into the dorsal foot vein under application of a tourniquet above the ankle. Overhead imagings of leg, thigh, and pelvis were obtained during the contrast infusion. When those images were completed, AP and lateral films of the leg were performed immediately after the tourniquet was taken off.

The Interpretation :

1. Radionuclide Venography :

RNV images were interpreted blindly by two nuclear medicine physicians (JM and SC) without knowledge of the clinical data or CV findings. The interobserver agreement was evaluated. If the results were discordant, the third observer (PP) would make the final diagnosis. The normal RNV is seen as a single channel of deep vein from calf upto the distal IVC with bilateral and symmetrical filling of the radioactivity. This normal configuration resembles a wishbone or an inverted Y with long arms (Fig. 1).

The criteria of positive RNV for DVT regarding flow pattern abnormailty include the following.

1. Nonfilling or nonvisualization of a deep vein
2. Interruption of the flow
3. Irregular or asymmetric filling of a deep vein
4. Presence of abnormal collateral vessels

2. Contrast Venography :

The criterion of positive CV for DVT was the presence of constant intraluminal filling defects with or without collateral vessels, abrupt termination of the opaque column of contrast material, or persistent nonfilling of a venous segment despite adequate technique in at least two projections.

The statistical analysis

The interobserver agreement was evaluated by using Kappa measurement. The accuracy, sensitivity, specificity, positive predictive value (PV+), negative predictive value (PV-), and positive likelihood ratio (LR +) of RNV were achieved in comparison with CV as a gold standard.

RESULTS

The total of 72 limbs of 59 patients were analyzed. Most of the patients (43/59 = 73%) had underlying diseases or predisposing conditions which were risk factors for developing DVT e.g.

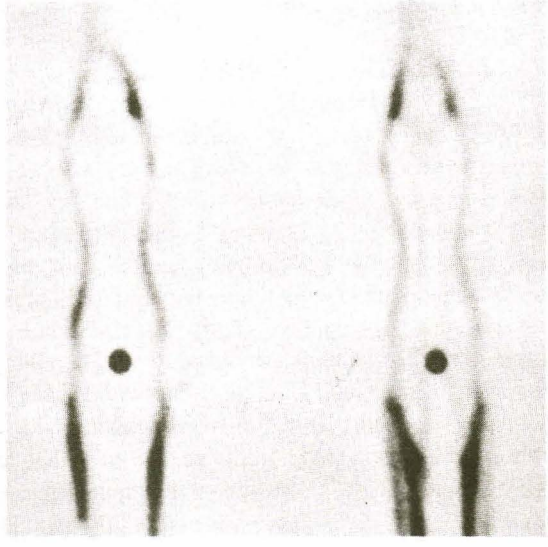


Fig. 1. Normal whole-body RNV images of the lower extremities; on-tourniquet (left) and off-tourniquet (right) : good and symmetrical flow of the radioactivity in the deep veins of both legs upto IVC with filling of the radioactivity in the superficial veins when the tourniquets are released.

Table 5. Underlying diseases/ conditions of the patients.

Underlying diseases or conditions	Cases
1. Medical diseases	38
1.1 Diabetes mellitus	10
1.2 Hypertension	8
1.3 Renal diseases	4
1.4 Heart diseases	3
1.5 Hepatic diseases	3
1.6 Hematologic diseases	2
1.7 Autoimmune diseases e.g. SLE	2
1.8 Cerebrovascular disease	1
1.9 Miscellaneous	5
2. Postoperation	5
2.1 Abdominal surgery	2
2.2 Gynecological surgery	2
2.3 Orthopaedic surgery	1
3. Malignancies	14
3.1 Lung cancer	4
3.2 Cervical cancer	4
3.3 Carcinomatosis peritonei (adenocarcinoma), unknown primary	3
3.4 Breast cancer	1
3.5 Urinary tract cancer	1
3.6 Gallblader cancer	1
4. Immobilization	3

Note : One patient may have more than one underlying diseases/ conditions

Table 6. Interobserver agreement for interpreting RNV.

Regions	Agreement	Kappa
Calf	0.861	0.721
Popliteal	0.902	0.801
Femoral	0.931	0.859
Iliac	0.917	0.821

Table 7. Sites and numbers of DVT detected by CV and RNV.

Site of DVT	Numbers detected by CV	Numbers detected by RNV
Calf vein	48	37
Popliteal vein	43	38
Femoral vein	43	41
Iliac vein	20[a]	19 + 7[b]
IVC	2	2 + 4[c]

a CV could not provide good visualization of the iliac veins in 17 studies.

b 7/17 studies that CV had inadequate information, RNV gave a positive result for iliac thrombosis

c In these four patients, RNV could detect IVC obstruction while CV could not.

Table 8. The results of RNV *vs* CV ; overall and in separate locations.

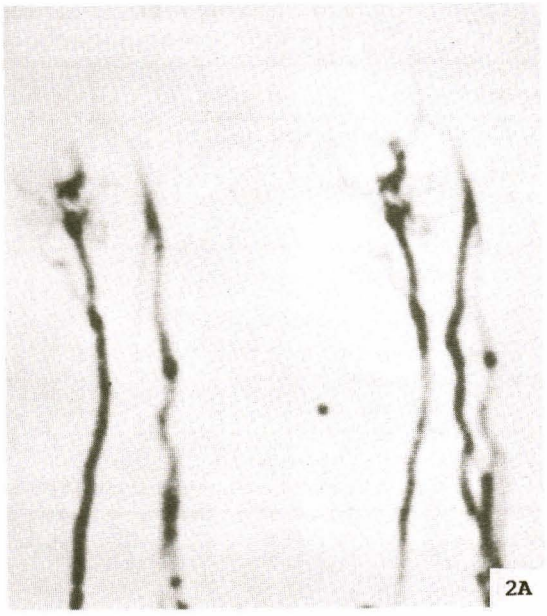
	Overall		Calf		Popliteal		Femoral		Iliac*	
	CV +	CV-	CV +	CV-	CV +	CV-	CV +	CV-	CV +	CV-
RNV +	42	1	37	1	38	3	41	0	19	1
RNV -	6	23	11	23	5	26	2	29	1	34

* N = 55

medical diseases, postoperation, malignancies, and immobilization (Table 5). We found that the prevalence of DVT in this group was 42/72 limbs (58%). The results interpreted by two observers were evaluated for separate regions i.e. calf, popliteal, femoral, and iliac. The interobserver agreement and Kappa measurement for each region are shown in Table 6. The sites of the abnormalities considered positive for DVT detected by CV and RNV are compared in Table 7.

Table 8 summarizes the overall results of RNV including accuracy, sensitivity, specificity, PV+, PV-, and LR+ of RNV in the diagnosis of DVT compared with CV findings.

RNV could pick up DVT in 42 of 48 abnormal limbs. Most of the studies showed similar findings between RNV and CV procedures (Fig. 2). However, false negative RNV results still existed which mainly occurred in the veins below the knee (Fig. 3). For the non-DVT group, only one patient



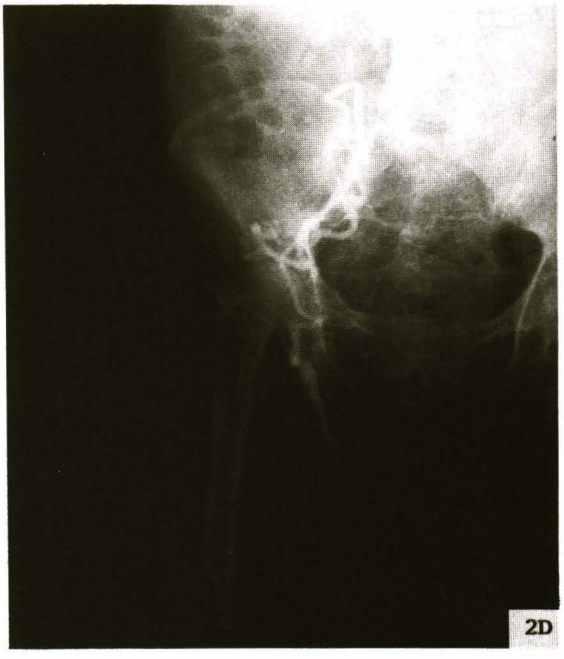


Fig. 2. Extensive DVT of the right lower extremity. (A) RNV showed nonvisualization of the deep veins of the whole right leg with partial filling of the right external iliac vein and multiple collaterals at the thigh and around the ilio-femoral junction. (B-D) CV showed multiple filling defects in the deep veins of the right calf, popliteal veins., nonfilling of right superficial femoral and external iliac veins with collaterals corresponding to the RNV results.

Fig. 4. RNV showed occlusion of both iliac veins and IVC with multiple abnormal collateral vessels which should not truly represent a false-negative result. (In this case CV was performed on the left side and reported as no DVT involvement of the iliac vein, probably due to inadequate technique resulting in missinterpretation).

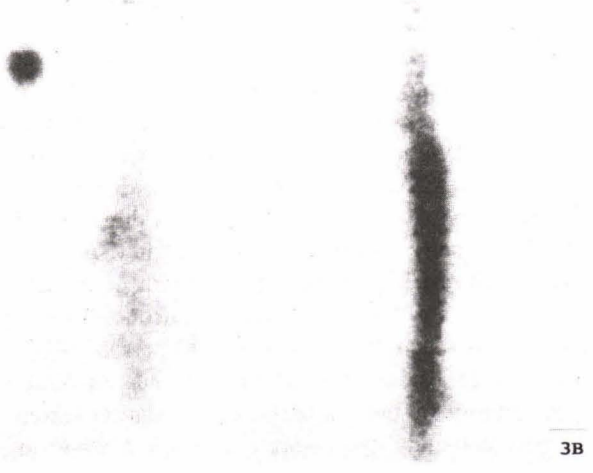


Fig. 3. (A) CV of the left calf region showed no opacification of distal two-thirds of the posterior tibial vein, multiple filling defects in the peroneal and the anterior tibial veins. There were also filling defects in soleus and perforating veins as well. (B) RNV of the left calf region appeared normal. (false-negative RNV result)

was overdiagnosed to have calf and popliteal vein thrombosis. Very few false negative results occurred at the femoral or iliac region. These should be due to DVT producing incomplete occlusion of the blood flow. Only one case that RNV provided a discordant interpretation at the iliac region demonstrated occlusion of both iliac veins and IVC with multiple abnormal collateral vessels (Fig. 4). Moreover, RNV could detect asymptomatic iliac and/or femoral DVT of the opposite limb in another nine patients on whom CV had not beeen carried out (Fig. 5). In addition, RNV also detected iliac vein thrombosis in seven studies and diagnosed IVC obstruction in six patients (Fig. 6) while CV could not provide good opacification of the iliac veins and could diagnose only two cases of IVC obstruction. No significant side effects or complications due to the RNV procedure were observed.

We also further compared RNVand CV findings for separate locations including calf, popliteal, femoral, and iliac regions. The results are

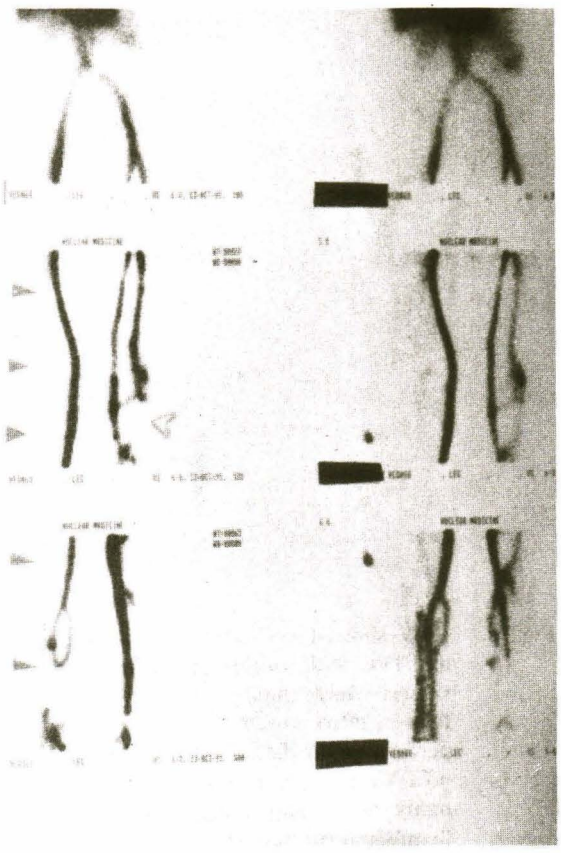


Fig. 5. A 58-year-old woman who had had a swollen right leg for two weeks. RNV which was performed bilaterally detected extensive DVT on the right side (arrows) confirmed by CV and also picked up femoropopliteal DVT of the contralateral limb which was asymptomatic (open arrow).

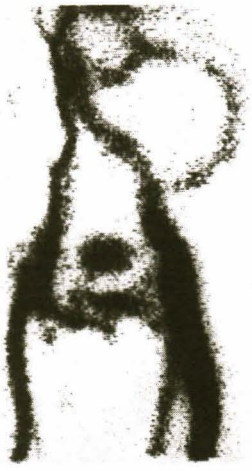


Fig. 6. RNV showed IVC obstruction, complete occlusion of right external and common iliac and partial occlusion of left external iliac vein with presence of abnormal collaterals. Cross pelvic and abdominal collateral pathways were clearly demonstrated. (In this case CV could not provide the information about IVC obstruction.)

shown in Table 9. When we focused on the DVT of the large veins of the thigh and pelvis i.e. iliofemoral DVT, the accuracy, sensitivity, specificity etc. of RNV were excellent, approaching 100 per cent (Table 9). Thus, for separate locations, the diagnostic accuracy of RNV was highest at the major veins of the thigh and pelvis and lowest at the calf veins.

DISCUSSION

It is known that CV is the most reliable diagnostic tool for accurate localization of DVT, however, it is invasive and has risks for developing complications[4,5]. RNV, on the other hand, is less invasive, simpler and more generally accepted among the patients. In addition, it provides good images of the deep venous system of the lower extremities upto IVC in a similar manner to those seen from CV with good visualization of both iliac veins and IVC quite well in the same setting compared to the CV findings which may be disappointing in the pelvic region due to contrast dilution and overlying bony structure. Sometimes it requires a larger contrast load or pelvic venogram or inferior venacavogram for better opacification of these veins. It is much more convenient to perform RNV even bilaterally compared with CV due to better accessibility of the dorsal vein cannulation. From our current study, the failure rate of CV (29%) was much higher than that of RNV (4%). Apart from the simpler technique, RNV is also a safe procedure without producing any significant side effects, unlike CV which could produce local symptoms from the contrast injection and/or contrast leakage.

Our study showed that the overall correlation between RNV and CV was quite high (90%) and even higher when we focused on the major

Table 9. Summary of diagnostic accuracy of RNV for separate locations.

Location	No. of studies	Accuracy	Sensitivity	Specificity	PV +	PV -	LR +
Overall	72	90	88	96	98	79	20.8
Calf	72	83	77	96	97	68	18.4
Popliteal	72	89	88	79	93	84	8.6
Femoral	72	90	95	100	100	94	-
Iliac	55	96	95	97	95	97	31.7

Blank space = no false positive RNV

Table 10. Diagnosis of DVT by 99mTc-MAA RNV.

Authors	Year	Number of studies	Sensitivity (%)	Specificity (%)	Correlation (%)	Site of DVT
Webber (11)	1972	13	77	-	77	Overall
Webber (12)	1974	30	65	92	77	Overall
Henkin (13)	1974	25	100	86	96	Proximal veins
Van Kirk (14)	1976	19	100	95	95	Overall
Vlahos (15)	1976	52	100	100	100	Pelvis
		98	89	100	97	Thigh
		98	92	97	95	Calf
Ennis (16)	1977	154	90	89	95	Overall
Cordoba (17)	1977	44	100	80	94	Overall
Ryo (18)	1977	47	89	66	89	Overall
Gomes (19)	1982	51	88	65	67	Overall
Mohamadiyeh (20)	1993	32	90	73	89	Proximal veins
Mangkharak	1996	72	88	96	90	Overall
		55	95	97	96	Pelvic
		72	95	100	90	Thigh
		72	77	96	83	Calf

veins of the thigh and pelvis (ilio-femoral veins), the correlation was excellent (97%). These veins are quite large and clearly demonstrated by the radionuclide method. RNV not only provides impressive images of the deep veins in these regions, but also the visualization of collateral vessels as seen in Fig. 2, 4, and 6. On the other hand, CV could not provide adequate information about iliac veins in 17/72 (24%) studies while RNV results were satisfactory and provided a more accurate extent of iliac involvement in seven patients. In addition, RNV could diagnose six cases of IVC obstruction while CV could be demonstrated in only two. Thus, RNV probably has advantages in the pelvic region, as well as in the evaluation of IVC thrombosis over CV performed by a similar technique. Furthermore, as we routinely performed RNV bilaterally at the same time, we could detect asymptomatic proximal DVT of the opposite limb in an additional nine cases that CV was performed only in the symptomatic limbs.

The most common site of the interpretation error is at the calf region where RNV has the lowest sensitivity due to variations and multiplicity of calf vessels[4]. CV, on the other hand, has highest accuracy at this location and should be the investigation of choice for detecting calf vein disorders, particulary isolated calf vein thrombosis rather than any other non-invasive modalities e.g. Doppler ultrasound, duplex sonography, IPG .

The second most common site of error by RNV is at the popliteal region. At this region RNV had the lowest specificity due to high false positive results. These should result from over stretch-

ing of the vein which commonly mimics the defect. Imaging during bending of the knee is helpful to clarify this phenomenon[10].

However, there are some disappointing views for RNV in the evaluation of the pelvic region in obese patients or cases with massive ascitis or huge pelvic mass due to attenuation problem. On the other hand, the deep veins of the thigh (superficial femoral vein) are located more superficially thus, probably result in better delineation. Nevertheless, false-negative RNV results of a few patients with femoral and iliac vein thrombosis still occurred but in cases that the venous flow is not interrupted. Only one case in our study showed discordant interpretation between RNV and CV at the iliac region. The occlusion of both iliac veins and IVC with multiple abnormal collateral vessels were clearly demonstrated by the radionuclide method. The contrast images probably showed poor visualization due to contrast dilution and/or inadequate technique, so positive findings might be missed. Thus, this should not be a real false-negative RNV result. On the contrary, false positive RNV for DVT of these veins was quite rare if flow defect and abnormal collaterals are clearly demonstrated.

The current study confirmed that the result was comparable to those reported previously in the literature[11-20] (Table 10). However, there were some variations of the techniques and criteria for the diagnosis.

Another important advantage of RNV if Tc99m-MAA is used is the ability to perform perfusion lung scan immediately after the completion of venous study to evaluate a concomitant pulmonary embolism (PE). Thus, DVT and prevalence of associated PE, which is quite a common complication, can be evaluated in the same setting.

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การใช้ Radionuclide Venography ในการวินิจฉัย ภาวะหลอดเลือดดำของขาอุดตัน เปรียบเทียบกับ Contrast Venography

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ผู้รายงานได้ทำการศึกษา การใช้ radionuclide venography (RNV) ในการวินิจฉัยภาวะหลอดเลือดดำของขาอุดตัน โดยเปรียบเทียบกับ contrast venography (CV) ในผู้ป่วยที่มีอาการทางคลินิกสงสัยว่ามีภาวะนี้ จำนวน 59 ราย รวม 72 ข้าง ผลของ RNV โดยรวม สำหรับค่าความแม่นยำ, ความไว, ความจำเพาะ, positive predictive value (PPV), negative predictive value (NPV) และ positive likelihood ratio เป็น 90%, 88%, 96%, 98%, 79%, และ 20.8 ตามลำดับ โดยค่าความแม่นยำต่าง ๆ ดังกล่าวจะยิ่งเพิ่มสูงขึ้น ถ้าพิจารณาเฉพาะในส่วนของหลอดเลือดดำใหญ่บริเวณต้นขา และในอุ้งเชิงกราน จากผลการศึกษา บ่งว่า RNV นอกจาก จะเป็นการตรวจที่ทำได้ง่ายและปลอดภัยแล้ว ยังให้ความน่าเชื่อถืออย่างมากสำหรับการวินิจฉัย ภาวะหลอดเลือดดำของขาอุดตัน โดยเฉพาะที่เกิดกับหลอดเลือดดำใหญ่ดังกล่าว รวมทั้งสามารถถ่ายภาพ perfusion lung scan เพื่อตรวจหาภาวะ pulmonary embolism ที่อาจเกิดแทรกซ้อนได้ด้วย ถ้าใช้สาร Tc99m-MAA ในการตรวจ ส่วน CV ซึ่งเป็นการตรวจที่ invasive มากกว่า ควรใช้เฉพาะในกรณีที่ การตรวจอื่นไม่ชัดเจน หรือให้ผลไม่ตรงกับอาการทางคลินิกของผู้ป่วย หรือกรณีสงสัยภาวะหลอดเลือดดำของขาอุดตันบริเวณน่องเท่านั้น

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