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Original Article

Radiology Section

Diagnostic Performance of the Modern Imaging Modalities in Renovascular Disease: An Evaluation

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ABSTRACT

Introduction: Renal artery stenosis is a very important cause of Renovascular disease. Atherosclerosis has been identified as a most common etiology for renal artery stenosis. Long standing renal artery stenosis can cause irreversible changes in kidney hence, it is imperative to identify the disease at early stage and treat.

Aim: To evaluate the diagnostic accuracy of Color Doppler US, CT Angiography(CTA), and GD-enhanced MR Angiography (MRA) compared with digital subtraction angiography(DSA) for the detection of renal artery stenosis in patients with clinically suspected renovascular hypertension and to select the most appropriate non-invasive modality as alternate diagnostic tool compared with the invasive intra-arterial digital subtraction angiography.

Materials and Methods: Fifty patients were prospectively recruited from the internal medicine outpatient clinics over the period of two years. All the hypertensive patients between 20 and 80 years of age with an arterial systolic blood pressure over 140 mmHg and diastolic over 90 mmHg were screened for predefined clinical clues indicating renal artery stenosis. Patients who exhibited at least 1 clinical clue were included in the study. All the recruited patient further underwent Color Doppler US, CTA and GD-enhanced MRA followed by DSA. DSA was considered gold standard.

Results: Sensitivity, specificity, positive and negative predictive value for diagnosis of renal artery stenosis were 75%,90%, 60% and 95%, respectively, for color Doppler US; 90%, 93%,75%, and 97.9%, respectively, for CTA; and 90%,95%, 82%, and 98%, respectively, for GD-enhanced MRA.

Conclusion: Diagnostic accuracy of CTA and GD enhanced MRA is almost similar to exclude the renal artery stenosis. Color Doppler US can be used as screening modality and CTA or MRA to further confirm the findings or as primary investigating modality where color Doppler US findings were equivocal. DSA is considered gold standard hence it can be utilized for the case with disagreement or case where therapeutic interventions are indicated.

Keywords: Color Doppler, CT angiography, Digital subtraction angiography, MR angiography, Renal artery stenosis,

INTRODUCTION

Secondary hypertension due to renovascular cause is considered the common cause of potentially treatable secondary hypertension. It is found in 1–2% of the general hypertensive population [1]. The most common causes of renovascular disease are atherosclerotic disease in 60% and fibromuscular dysplasia in 35%. The early intervention of renal artery stenosis is mandatory in order to treat it adequately. This will lead to reduction in the incidence of end stage renal disease in these patients. Hence, it is very important to detect the renal artery stenosis at early stage. The radiological investigations play very vital role to precisely determine the pathology of renal arteries and guide appropriate treatment.

Doppler ultrasonography, conventional angiography, and CT and MR angiography are crucial in diagnosing renal artery stenosis [2,3]. The diagnostic role of conventional angiography continues to shrink as non-invasive CT and MR angiography techniques are refining [2,4]. However, conventional angiography is still considered gold standard and plays active role in treatment [5].

The aim of the study was to compare these four imaging methods in a patient diagnosed with renovascular hypertension so that imaging protocol can be suggested for these patients.

MATERIALS AND METHODS

This prospective comparative study was carried out in 50 patients during a period of two years at a tertiary care hospital after approval from institutional ethical committee. The study included 50 patients from 21-85 years of age group with mean age of 48.9 yrs. 36 (72%) patient were male and 14 (28%) were female among study group. Patients were prospectively recruited from the internal medicine outpatient clinics (including cardiology & nephrology subspecialty clinic). The written informed consent was obtained from all participants. At the clinics, all hypertensive patients between 20 and 80 years of age with an arterial systolic blood pressure over 140 mmHg and diastolic over 90mmHg were routinely screened for predefined clinical clues indicating renal artery stenosis. Patients were eligible for participation in the study if they exhibited at least 1 clinical clue of the following clinical inclusion criteria:

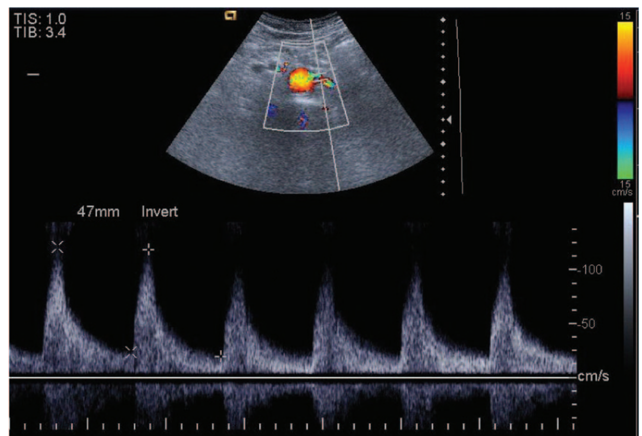
- Onset of hypertension before the age of 30 or after the age of 50.
- Severe hypertension refractory to standard medical treatment associated with progressive renal failure.
- Sudden onset of arterial hypertension with predominant increase of diastolic pressure.
- Rapidly progressive arterial hypertension.

Exclusion criteria were known allergy to iodinated contrast agents, pregnancy or breast feeding, severely impaired renal function with serum creatinine over 1.8 mg/dl, history of single functioning kidney, collagenoses, vasculitides or other systemic disease and general contraindication for CT,MRI or intervention if any.

The participant belonged to a mixed ethnic and socioeconomic group. Every patient who fulfilled the criterion was scheduled for all four diagnostic tests. The order of examination was Color Doppler, CTA, MRA and the reference standard DSA. No treatment which could affect the test results was given to the selected patients before all tests were completed. The examination was performed at least 12 hours apart from each other and completed at maximum within 2 weeks. Independent panels of radiologists compared Color Doppler, CTA and MRA image data and were blinded to all other results. DSA images were evaluated by Interventional Radiologist. All patients were also evaluated for renal parameter (serum creatinine) post CT angiography after 48-72 hrs.

The color Doppler was performed using 3.5 MHz curvilinear array transducer by using high end Doppler ultrasound machine following bowel preparation with patient in the supine position to visualize the origin and proximal course of the main renal arteries and accessory renal arteries (extra renal arteries).

Doppler sonographic studies included imaging of the main renal arteries and an effort was made to identify the accessory renal arteries, if any. The selected angle of insonation was between 30° and 60° and the age of the patient was taken into consideration in order to obtain meaningful data. The measurements included peak systolic velocities within main renal arteries, Renal Aortic Ratio (RAR), and intrarenal blood flow measurements. Peak Systolic Velocities (PSV) more than 100 cm/sec were considered abnormal. It was further classified in to mild stenosis (<50% narrowing) and severe stenosis (50-99% narrowing) on the basis of PSV. PSV between 100 to 200 cm/sec and more than 200 cm/sec were suggestive of mid stenosis and severe stenosis respectively. RAR greater than 3.0 was suggestive of significant renal artery stenosis [Table/Fig-1].



[Table/Fig-1]: Color Doppler shows normal Peak systolic velocity suggestive of normal flow.

Intrarenal vasculature were studied with the patient in the lateral decubitus position.

Prolonged acceleration time (more than 0.07 seconds) and a slow rising with low PSV spectral pattern (Tardus-Parvus pattern) were suggestive of severe stenosis of the extrarenal arteries.

Subsequently, all patients underwent renal CT angiography using nonionic contrast (ioversol injection, Optiray 350, Tyco health) on 4 slice CT scanner (Somatom Sensation 4, Siemens). The acquisition started with a localizing dynamic scan to determine the level of the renal arteries, and the study was performed in a craniocaudal direction. The examination protocol included axial images at the level of the renal arteries with a FOV 220 mm. A total volume of 100-120 ml non-ionic contrast material was then injected via a pressure injector at a rate of 3 ml/sec through an antecubital intravenous 18 G catheter. The slice thickness was 1.5 mm; pitch, 2 mm; scan time, 1.5 sec; kVp, 120; mA, 130; and the reconstruction index, 1 mm. A fixed delay time of 22 sec was used. Following the examination, the axial source images were analyzed on the Syngo workstation to obtain maximum intensity projection (MIP) and multiplanar reconstruction (MPR).

The MR Angiography of the renal arteries were performed on a 1.5 Tesla whole body superconducting magnet equipped with a powerful gradient system (gradient strength 40 mT/meter, rise time 200 msec) and a circular polarized phased array surface coil. First, localizer sequence were performed, which consisted of three imaging stacks oriented in the transverse, sagittal and coronal planes, a coronal 2D FLASH sequence was performed for localization of the origin of the renal arteries. Next, a transverse breath hold fat suppressed 3D FLASH sequence was performed. Coronal 3D fast spoiled gradient-echo (Turbo-Flash, Siemens) breath-hold sequence with fat saturation were performed before and after intravenous administration of bolus of paramagnetic contrast {Gadodiamide (GdDTPA-BMA), 0.287mg /ml, Omniscan, GE healthcare}. The imaging parameters were TR, 4.0 ms; TE, 1.6 ms; flip angle, 30°; slab thickness, 64 mm; effective thickness, 1.78 mm; FOV, 360mm and matrix, 256×156; acq time,19sec. A total volume of 20 ml of nonionic paramagnetic contrast {Gadodiamide (Gd DTPA-BMA), 0.287mg /ml, Omniscan, GE healthcare} was administered through a 20 G antecubital venous catheter via a power injector (SpectrisMedrad, Dual Head) at a rate of 2 ml /sec (0.2mmol/Kg). Images were analysed after post processing.

CTA and MRA image sets were separately analysed in a double-blind fashion. The number of main and accessory renal arteries and the degree of renal artery stenosis were recorded. The stenosis were graded on the basis of measuring the ratio between the diameter of the narrowest portion and normal segment of the same artery used as reference. The grading of renal stenosis was defined as mild when the reduction of the caliber was <50%, severe when the reduction was between 50–99%, and total occlusion. The measurements are taken at ostia, mid one third and distal one third of main renal artery. The angiographic definition of hemodynamically significant renal artery stenosis is stenosis of 50% or more which is most widely used definition of stenosis [5].

The digital subtraction angiography (DSA) of the renal arteries was performed on polystar uniplanar system, Siemens. The examination was performed by trained interventional radiologist. The aortogram of the abdominal aorta using a 5F pigtail catheter and nonionic contrast (16 ml/sec) was acquired first with transfemoral approach. Selective renal angiography was acquired in posteroanterior and lateral view, systematically with a hydrophilic catheter (Cobra SF, Terume, Belgium). The volume of the contrast medium was 8 ml (3 ml/sec). According to the grading scheme used at MRA and CTA, numbers of accessory renal arteries were determined and the presence of stenosis or other pathology was noted and graded.

STATISTICAL ANALYSIS

The statistical analysis was done using SPSS 12.0. Sensitivity, specificity, and positive and negative predictive value were calculated for each diagnostic modality individually with DSA as the reference standard. Statistical exact two-sided confidence intervals for binomial proportions at the 95% level for the above parameters were calculated.

RESULTS

The results are summarized in [Table/Fig-2] regarding the finding of all utilized imaging methods. DSA which is considered the gold standard, revealed 106 arteries (100 main renal artery and 06 accessory arteries) in the 50 patient examined. Multiple renal arteries were detected in 06 patients [Table/Fig 3].

DSA revealed 20 renal arteries with stenosis and FMD (16 and 04 respectively) and 86 renal arteries to be free of stenosis [Table/Fig-2,4].

Color Doppler US corresponded to a sensitivity of 0.75 (95% CI: 0.56 < Se < 0.94), a specificity of 0.9 (95% CI: 0.836 <Sp< 0.957), a positive predictive value of 0.6 (95% CI: 0.408 < pp

Findings	US	CTA	MRA	DSA
Normal Renal Artery	76	76	78	80
Normal Accessory Artery	0	02	04	6
Atherosclerotic MRA Stenosis	16	20	18	16
FMD	04	04	04	04
Invisible Accessory Artery	06	04	02	0
Total No. of Examined Arteries	96	102	104	106

[Table/Fig-2]: Summary of results.
*Total sum of arteries is calculated after excluding the no. of invisible accessary arteries, as they were not examined.

[Table/Fig-3]: Volume rendered image showing no evidence of stenosis and left accessory renal artery.

	Stenosis <50	Stenosis 50-90%	FMD	Total
US	0	8	4	12
CTA	1	13	4	18
MRA	1	13	4	18
DSA	2	14	4	20

[Table/Fig-4]: Severity of stenosis in detected cases.

	True Positive	True Negative	False Positive	False Negative
US	12	72	8	4
CTA	18	76	6	2
MRA	18	80	4	2

[Table/Fig-5]: True positivity, true negativity, false positivity and false negativity with US, CTA and MRA.

	Sensitivity	Specificity	Positive predictive value	Negative predictive Value
US	75%	90%	60%	95%
CTA	90%	93%	75%	97.4%
MRA	90%	95%	82%	98%

[Table/Fig-6]: Sensitivity, specificity, positive predictive value and negative predictive value of US, CTA and MRA.

< 0.792), and a negative predictive value of 0.95 (95% CI: 0.857 < np < 1.035) [Table/Fig-5,6].

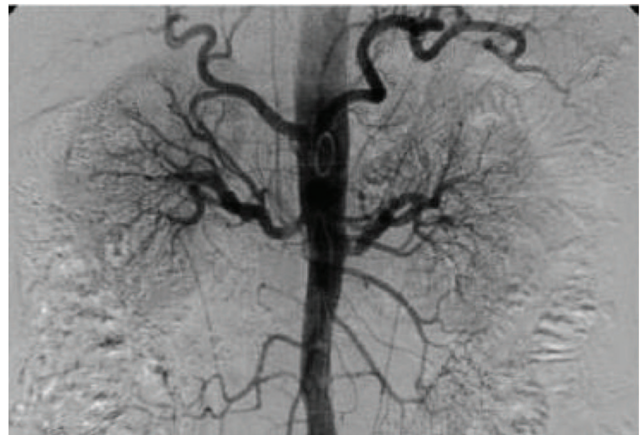
CT angiographic findings corresponded to a sensitivity of 0.90 (95% CI: 0.668 < Se < 0.982), a specificity of 0.93 (95% CI: 0.841 <Sp<0.969), a positive predictive value of 0.75 [95% CI: 0.529 < pp <0.893], and a negative predictive value of 0.97 (95% CI: 0.901 < np <0.995) [Table/fig-5,6]. In this study 16 renal arteries showed plaque involving ostia and proximal one third of main renal artery which summarized in [Table/Fig-7].

The findings of MR GD-enhanced angiography corresponded to a sensitivity of 0.9 (95% CI: 0.668 < Se < 982), a specificity of 0.95 (95% CI: 0.875 <Sp<0.984), a positive predictive value

	Calcified	Noncalcified	Concentric	Eccentric
At ostia and proximal 1/3	14	02	5	11
Mid and distal 1/3	Nil	Nil	Nil	Nil

[Table/Fig-7]: Renal artery plaque detected with CTA.

[Table/Fig-8]: CT angiography maximum intensity images show typical string of beads appearance in bilateral mid and distal two third both main renal arteries.



[Table/Fig-9]: IA DSA confirm FMD.

of 0.82 (95% CI: 0.589 < pp <0.940), and a negative predictive value of 0.98 (95% CI: 0.906 < np <0.995) [Table/Fig-5,6].

Color Doppler US depicted both patients with bilateral findings suggestive of fibromuscular dysplasia, [Table/Fig-8,9] namely mid- to distal flow derangement and velocity augmentation. Both CTA and MRA depicted these two patients correctly. CTA was unable to detect one mild stenosis, and MRA failed to detect one mild stenotic and one severe stenotic main renal artery.

DISCUSSION

Color Doppler US has the benefit of being easily available, cost effective, reproducible and well-tolerated method. Color Doppler US might be suitable as screening modality for suspected renal artery pathology [6]. Although, there are a number of limitations involved with this modality [7,8]. We have concluded that 2/16 (12.5%) polar renal arteries were detected with US which was normal but 2 of the undetected polar arteries were stenotic that were seen by DSA. It has been reported that stenosis of a polar artery may be the cause of hypertension [9]. Hence, it is important to exclude stenosis in main as well as polar renal arteries [10].

Multiple studies that investigated the usefulness of CTA comparing with DSA have suggested that it is a noninvasive useful modality in cases of renal artery stenosis [11,12]. Severe allergic reactions to iodinated contrast media and X-ray exposure are considered as limitation of CTA. This modality has edge over other modalities due to its increased spatial resolution and rapid acquisition time. It has been reported that CTA is superior in demonstration of accessory renal arteries [13].

The sensitivity and specificity of MRA were 90% and 94.1% respectively in this series. Contrast-enhanced MRA has been projected as a noninvasive diagnostic modality alternative to DSA. Several studies have reported sensitivity >96% and specificity >92% of this modality [4,14,15]. However, the main drawback of MRA includes inability of the patients to maintain breath-hold, poor arterial phase timing and small imaging volume. Hence, MRA is considered good alternative modality for the patients who are not having contraindication to MRI [16,17].

This study has concluded that CTA and MRA failed to depict accessory renal arteries that were seen with DSA. Small calibre, angulations of the vessels, and misinterpretation as the early division of the main renal artery were responsible for the above result. Hence, it is interpreted that US, CTA and MRA may be unable to detect all cases of polar renal arteries. However it is pertinent to mention that both MRA and CTA detected hemodynamically significant stenosis which decide prognosis of patients with renovascular disease.

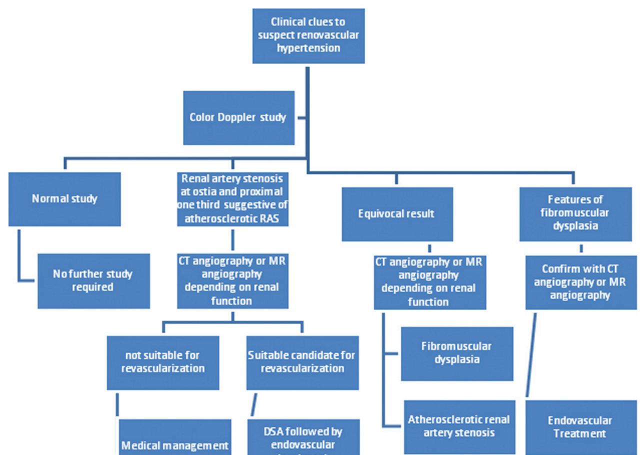
This study was able to detect all cases of fibromuscular dysplasia of four renal arteries. The advanced pattern which was clear and apparent by all methods may explain the excellent performance reported. However the data vary significantly from published data [18].

As negative predictive accuracy was very high for both CTA (99%) and MRA (98%). CTA performs slightly better in term of accuracy related to the exclusion of any pathology in renal arteries. However, the positive predictive value of MRA, CTA and US were 75, 71% and 60% respectively in this study. High number of false positive cases of our study group was responsible for the low value. This needs attention as it is crucial in cases that need to be further evaluation by DSA.

It was concluded that CTA and MRA may be utilized for imaging investigation of renal arteries with effective alternate to DSA with limitation as discussed. This was comparable with previously reported meta-analysis [19,20] of all these three modalities which concluded that contrast enhanced MRA and CTA could be the preferred methods applied in patients referred for the evaluation of renovascular hypertension.

DSA was accepted as a gold standard method with 100% sensitivity and specificity in this study. However, it is not supported by the published data [19] but we have not included cases with controversial DSA findings. Hence, we can depend on the data provided from DSA studies.

The imaging investigation in a patient with suspected renal artery pathology should be tailored best suited for the single patient. As we all are aware about limitation of ultrasound hence it is not ideal for an obese patient but would be reliable screening for a younger patient. CTA or MRA can be second line investigation. Hence, it may be suggested that the combined agreement of US and either CTA or MRA is adequate to determine pathology related to renal arteries and can be used in the routine clinical practice. The combination is particularly useful in cases of hemodynamically significant renal artery stenosis. DSA can be reserved for cases with major discrepancy between the two modalities, for those with negative imaging findings and unexplained hypertension and those suitable for active intervention [Table/Fig-10].



[Table/Fig-10]: Proposed Algorithm for investigation of renovascular disease.

CONCLUSION

Renal artery stenosis is a major reversible cause of Renovasuclar hypertension. Long standing RAS can cause permanent damage to kidney hence it is essential to diagnose RAS timely. Considering all the available and affordable modalities it is appropriate to use color Doppler US as screening test and CTA or MRA as second step investigation. DSA can be reserved for the case where therapeutic intervention is required or major disagreement between two modalities has been reported.

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