Doppler ultrasound and renal artery stenosis: An overview

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Abstract Renovascular disease is a complex disorder, most commonly caused by fibromuscular dysplasia and atherosclerotic diseases. It can be found in one of three forms: asymptomatic renal artery stenosis (RAS), renovascular hypertension, and ischemic nephropathy. Particularly, the atherosclerotic form is a progressive disease that may lead to gradual and silent loss of renal function. Thus, early diagnosis of RAS is an important clinical objective since interventional therapy may improve or cure hypertension and preserve renal function. Screening for RAS is indicated in suspected renovascular hypertension or ischemic nephropathy, in order to identify patients in whom an endoluminal or surgical revascularization is advisable. Screening tests for RAS have improved considerably over the last decade. While captopril renography was widely used in the past, Doppler ultrasound (US) of the renal arteries (RAs), angio-CT, or magnetic resonance angiography (MRA) have replaced other modalities and they are now considered the screening tests of choice. An arteriogram is rarely needed for diagnostic purposes only. Color-Doppler US (CDUS) is a noninvasive, repeatable, relatively inexpensive diagnostic procedure which can accurately screen for renovascular diseases if performed by an expert. Moreover, the evaluation of the resistive index (RI) at Doppler US may be very useful in RAS affected patients for predicting the response to revascularization. However, when a discrepancy exists between clinical data and the results of Doppler US, additional tests are mandatory.

Sommario La malattia nefrovascolare è un disordine complesso e le cause più comuni sono la malattia aterosclerotica e la displasia fibromuscolare. Classicamente si presenta in una delle seguenti tre forme: stenosi dell'arteria renale (SAR) asintomatica, associata a ipertensione nefrovascolare e/o con nefropatia ischemica. La SAR su base aterosclerotica è una malattia progressiva che può determinare in maniera asintomatica o paucisintomatica perdita graduale della funzione renale. Per tale motivo, la diagnosi precoce di SAR è un obiettivo clinico importante poiché la terapia interventistica può migliorare o curare l'ipertensione e preservare la

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funzione renale. Lo screening per SAR è indicato nel sospetto di ipertensione nefrovascolare o di nefropatia ischemica al fine di identificare i pazienti in cui è indicato un intervento di rivascolarizzazione. I test di screening per SAR sono migliorati considerevolmente durante l'ultimo decennio. Mentre la scintigrafia con test al captopril è stata utilizzata quasi esclusivamente nel passato, l'ecocolorDoppler delle arterie renali, l'angioTC e/o l'angioRM hanno sostituito le altre modalità di screening in molti centri. Per tale motivo l'arteriografia riveste sempre più un ruolo interventistico e solo di rado diagnostico. L'ecocolorDoppler è una procedura diagnostica non invasiva, ripetibile e relativamente economica che negli ultimi anni, in mani esperte, si è accreditata sempre più come ottimo strumento di screening di malattia nefrovascolare. Inoltre, la determinazione dell'indice di resistenza sembra essere utile nei pazienti con SAR per la capacità di predire la risposta alla rivascolarizzazione. Tuttavia, quando esiste una discrepanza fra i dati clinici e i risultati dell'ecocolorDoppler è indicato il ricorso ad altre procedure diagnostiche.

Introduction

Renal artery stenosis (RAS) is most commonly caused by either fibromuscular dysplasia or atherosclerosis, and it may occur alone (isolated anatomical RAS) or associated with hypertension, renal insufficiency (ischemic nephropathy) or both.

RAS due to atherosclerotic changes of the RAs has become a serious concern as a cause of hypertension and renal ischemia, resulting frequently in end-stage renal failure [1]. Several epidemiologic studies [1,2] have shown the elevated prevalence of ischemic nephropathy in elderly patients mainly due to atherosclerotic RAS. Over the past decade, data have accumulated implicating atherosclerotic RAS as an increasingly significant cause of end-stage renal disease (ESRD) ranging anywhere from 5% to 22% of incident ESRD patients [3,4]. RAS is the most common potentially reversible and curable cause of secondary hypertension and renal failure. Thus, early diagnosis of RAS is an important clinical objective since interventional treatment may improve or cure hypertension and preserve renal function [5]. Prevalence of RAS is estimated to range from 1% to 5% of all hypertensives in the general population up to 30% of a highly selected referral population (i.e. malignant hypertension, young patients with hypertension, the presence of an abdominal bruit, decreased serum potassium, unexplained azotemia, recurrent congestive heart failure or ''flash'' pulmonary edema) [6,7]. Clinical screening of hypertensive patients is therefore recommended before extensive investigation for renovascular disease is started. The pathologic causes of RAS include atherosclerosis, fibromuscular dysplasia (FMD), arteritis, dissection and neurofibromatosis. From a practical point of view, there are only two major diseases that affect the RAs: (a) atherosclerotic disease, the most common pathologic condition, which mainly affects the orifice and proximal portion of the RA; (b) FMD, much less common, which involves mid to distal portion of the RAs. Intimal and periarterial FMD is commonly associated with progressive dissection and thrombosis, whereas medial FMD progresses only in 30% of patients and is rarely associated with dissection and thrombosis. Atherosclerotic RAS is a progressive disease, particularly in patients with diabetes or other manifestations of atherosclerosis [5]. The ideal imaging procedure for RAS should identify the main RAs as well as the accessory vessels, localize the site of stenosis or disease, provide evidence for the hemodynamic significance of the lesion and identify associated pathologies (e.g., abdominal aortic aneurysm, renal mass, etc.) that may have an impact on the treatment of RAS. Angiography, once considered the ''gold standard'' for arterial imaging, is invasive, expensive and carries a small but not negligible risk of severe complications such as adverse contrast media reactions, cholesterol embolization or arterial dissection. Owing to its invasive character and the substantial costs involved, angiography is not used as a screening method but as a guide for therapeutic transluminal angioplasty. Furthermore, angiography provides no information on the functional significance of the stenosis. Thus, in recent years many less invasive or noninvasive diagnostic methods, such as captopril renal scintigraphy, color-Doppler ultrasonography (CDUS), computed tomography angiography (CTA) and magnetic resonance angiography (MRA) have been tested and compared to arteriography. Among these different methods, CDUS has been selected by many institutions as the principal screening tool used to detect RAS.

Examination technique and normal findings

RAS scanning is very difficult, and it requires a great amount of skill due to the depth of the arteries, the motion imposed by respiration, and intraabdominal gas. The patients should therefore be examined early in the morning if at all possible after a 12-h overnight fast. This will diminish the amount of bowel gas and also ensure that the stomach is empty.

Examination technique and normal anatomy

The procedure begins with the patient in the supine position and the head of the bed elevated about 30 degrees. A low-frequency scanhead (2.5−5.0 MHz) is used to depict the abdominal aorta and renal arteries (RAs). The two main approaches for imaging the RAs are through the anterior abdominal wall and the flank. Which approach is used depends on the specific portion of the renal vasculature being investigated. In most cases the anterior approach is used to evaluate the main RAs. The flank approach (Fig. 1) may be used to image both the intrarenal vasculature and the main RAs. Each of these windows has limitations, which
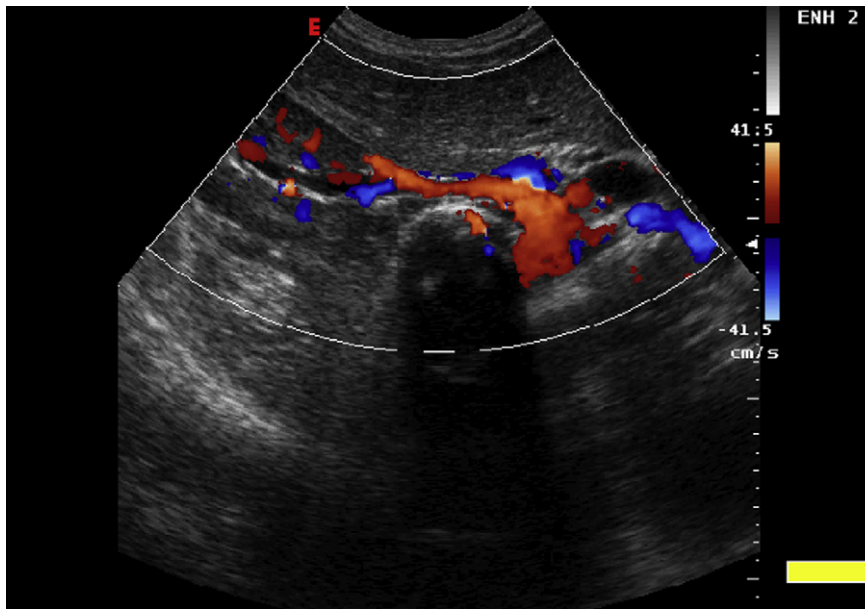
Fig. 1 Color-Doppler US image of the right kidney with the renal vessels. Good visualization of the entire renal vascular tree.

are dependent on individual body habitus and several other variables, such as the ability of the patients to hold their breath. In selected cases the posterior approach can be used [8,9].

The RAs originate from the lateral sides of the aorta (Fig. 2), typically at the level of the superior border of the second lumbar vertebra, directed slightly anteriorly, usually 1—2 cm below the superior mesenteric artery origin. The right RA originates from the anterolateral aspect of the aorta and immediately turns posteriorly to course beneath the inferior vena cava (IVC). The proximal right RA is not only deep in the abdomen but it also lies perpendicular to the Doppler beam in the usual transverse scan plane [8,9,10]. The right RA may also be difficult to separate from the overlying IVC in this plane, and in this case flank

approach is better. From this view, RA flow is in a direction that is parallel to the Doppler beam, optimizing signal reception. The patient usually needs to be placed in the opposite lateral decubitus position [8,10].

The left RA tends to originate from the posterolateral surface of the aorta and courses posteriorly the surface of the aorta and over the psoas muscle. An aid to locating the left RA is to first identify the left renal vein, which is usually large and easy to find [9,10]. Once the vein is identified, the artery will often be apparent as a smaller vessel directly behind it, coursing in the opposite direction. A pitfall that should be avoided is mistaking the origin of the inferior mesenteric artery (IMA) for that of the left RA. However, the IMA tends to have a high resistance spectral waveform, which is quite different from the normal low-resistance
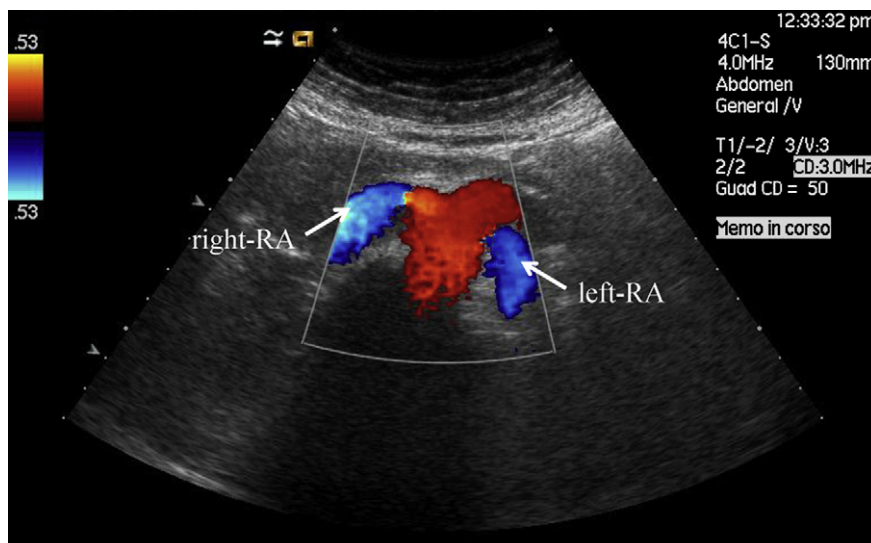

Fig. 2 Axial section of the midepigastric region showing the origin of both RAs.

pattern of the RA [8,10]. The IMA also originates much lower along the aorta than the left RA, unless the latter arises from an atypical location. A second approach to imaging the left RA is a variation of the flank approach described for the right RA above. In this case, the patient is placed in the right lateral decubitus position, and with scanning through the kidney, the main RA is followed back towards the aorta. The decubitus position is essential, because the kidney often falls towards the midline and acts as its own window [8,9]. Another method of identifying the main RAs, particularly the areas of the ostia (where most stenoses occur in elderly patients), has been termed the ''banana peel'' view (Fig. 3).

Also in this situation, the patient is turned to the opposite decubitus position from the vessel being examined. For the ''banana peel'' view, the transducer is oriented longitudinally [8]. The aorta is located, and the transducer is moved in an anterior-to-posterior direction until the RA is identified arising from it, coursing towards the transducer. Looking at the RAs and the aorta as a whole, some have likened this appearance to a half-peeled banana with its skin curved alongside. On the right, an additional aid in locating the RA is to image the IVC and to look posterior to it until a vessel crossing perpendicularly and of the opposite color is found [9]. This must be the right RA, because no other large vessel lies posterior to the IVC. Approximately 20—30% of patients have one or more accessory renal arteries (Fig. 4) [8—10]. The main RA divides at the hilum, either within or outside the kidney, into anterior and posterior branches that further divide into segmental and then interlobar arteries. The interlobar arteries further divide into a network of arcuate arteries that run at the corticomedullary junction and give off the cortical (interlobular) branches, which run radially towards the periphery, and the medullary branches, which supply the renal pyramids. The renal veins usually follow the course of the arteries running in a more ventral position.

The right renal vein runs in a posteroanterior direction, with a short course to reach the IVC. The left vein is more horizontal and passes between the abdominal aorta and the superior mesenteric artery before entering the IVC [8,9].

Normal findings

When the origins of the RAs are depicted with color Doppler in the transverse position, the flow of the first segment of the right RA is directed towards the transducer depicted in red color. Color change is seen shortly after the origin, where the direction of the flow is directed posteriorly. Most of the course of the vessels is then displayed in blue. If the origin of the RAs is imaged in the oblique longitudinal section, the right RA passes directly towards the transducer from the aorta and is red, whereas the left RA is directed away from the transducer and is blue. The normal waveform of the main renal artery demonstrates a low-resistance pattern similar to that found in all the parenchymal organs of the body (Fig. 5). Although the main RAs may be imaged from an anterior approach, the deep location in the abdomen often limits the resolution of the transducer that may be applied. Lower frequency transducers will have better sonographic penetration, but there is a trade-off of decreased spatial resolution. The highest frequency transducer that allows good demonstration of arterial waveforms is preferable. Doppler gain should be optimized to detect flow by increasing the gain to a level just below color artifact visualization in adjacent structures. The pulse repetition frequency, or velocity scale, is the frequency of sampling; undersampling may underestimate peak velocities. For spectral Doppler, the Doppler gate should be set to include the entire artery lumen and angled with the direction of flow. The angle of insonation should be maintained at 60 degrees or less. Although the exact angle should be reproduced for follow-up studies, this is not widely performed [8,11]. The frequency shift
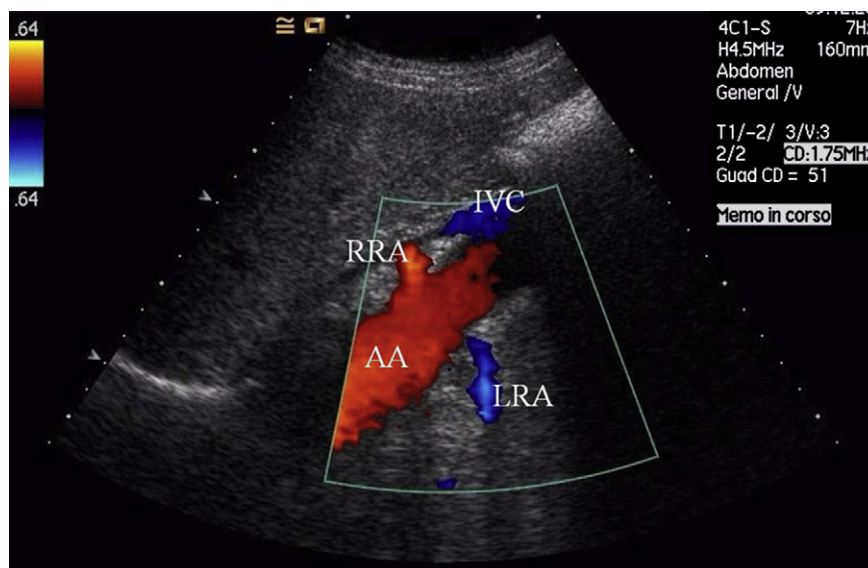

Fig. 3   Color image of the ostium (arrows) in both RAs arising from the aorta using the ''banana peel'' technique. The Doppler beam angle is optimized and close to zero. The right RA is depicted in red, the left RA in blue. Abdominal aorta (AA), left RA (LRA), right RA (RRA), inferior vena cava (IVC).

Fig. 4 Color image of the ostium (arrows) in both RAs arising from the aorta using the ''banana peel'' technique. The Doppler beam angle is optimized and close to zero. The right RA is depicted in red, the left RA in blue. Abdominal aorta (AA), left RA (LRA), right RA (RRA), inferior vena cava (IVC), accessory right RA (aRRA).
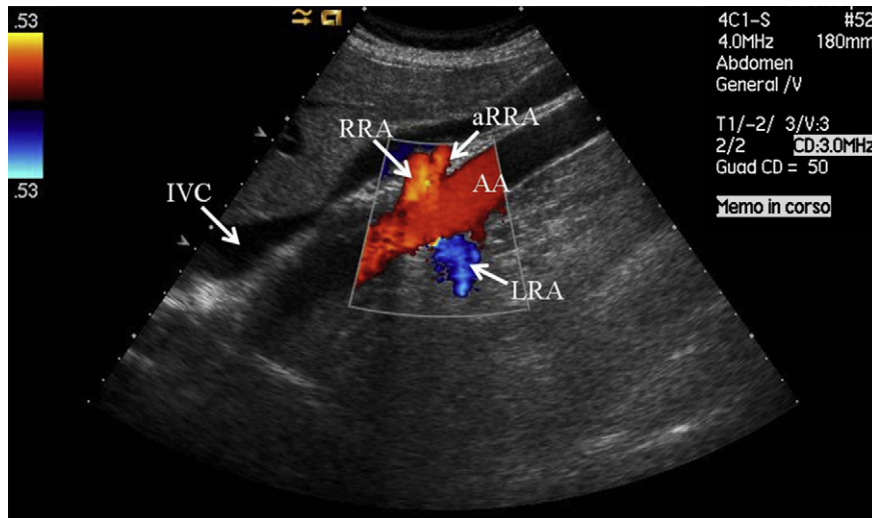
depends on the angle between the vessel and the ultrasound (US) beam, and on the frequency of the transducer used. If the course of the main RAs is well recognized, angle-corrected velocity estimates can be made. The peak systolic velocity (PSV) in the main RA and its branches should be less then 120 cm/s [11]. The velocity slowly decreases in the intrarenal arteries as they branch into the kidney. The resistive index (RI) measures the degree of intrarenal arterial impedance and is calculated using the following formula: ([PSV − end-diastolic velocity]/PSV). RI values measured in healthy subjects show a significant dependence on age and the area sampled. The values in the main RA are higher in the hilar region (0.65 ± 0.17) than in the more distal small arteries, and they are lowest in the interlobar arteries (0.54 ± 0.20) [8,10,11]. Intrinsic renal

diseases (i.e. nephroangiosclerosis, hypertension, tubular-interstitial disease, diabetes mellitus, and severe bradycardia) can cause an increase of RI, even in the presence of normal serum creatinine levels [12]. In clinical practice the value of RI 0.7 is used to discriminate between normal and pathologic resistance to flow. Various authors [8,9,11] currently think that the best signals for evaluation come from the large segmental or interlobar arteries as they course directly towards the transducer. In this location, signals are the strongest and most reproducible. Weak signals from peripheral (arcuate arteries) should be avoided [12,13]. Modern sonographic equipment has practically overcome problems due to obesity and bowel gas, so it is possible to study about 90% of the patients who are referred for investigation [14]. In one study, direct
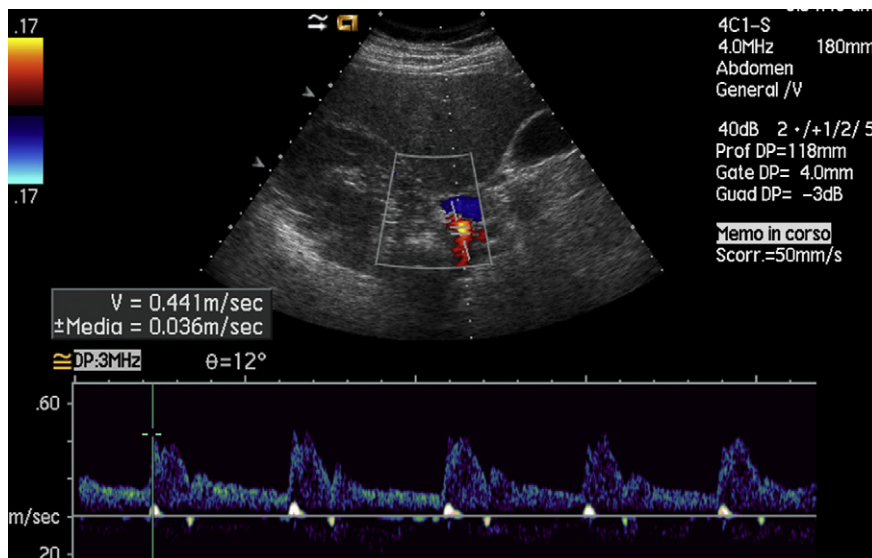

Fig. 5 Spectral Doppler US image of the right RA in a normal subject. Note the small spike occurring at the end of the systolic rise. This feature is seen only in a normal main RA.

visualization of both main RAs was possible in 84% of patients, right renal artery in 91% and left renal artery in 85%. In 5% non-visualization was due to total occlusion of the renal artery, as suspected by absent intrarenal color-Doppler signals and as confirmed by angiography [15].

Doppler criteria for diagnosis of RAS

Doppler US criteria of RAS can be divided into two groups based on direct findings obtained at the level of the stenosis (proximal criteria), or on flow changes observed in the renal vasculature distal to the site of stenosis (distal criteria).

Proximal criteria (direct evaluation of the stenosis)

Proximal criteria are direct signs obtained at the site of the stenosis. Four criteria are used to diagnose significant proximal stenosis or occlusion of the RA. The first and most important sign is the increase in PSV. Velocities higher than 180 cm/s suggest the presence of a stenosis of more than 60% (Fig. 6), while an end-diastolic velocity greater than 150 cm/s suggests a degree of stenosis greater than 80%. Using a cut-off value of 180 cm/s and RA diameter reduction of more than 50%, Radermacher et al. [15] evaluated 226 patients using CDUS and arteriography reaching a sensitivity of 96.7% and a specificity of 98%. In another study, Hua et al. [16] used a cut-off value of 200 cm/s and RA diameter reduction of more than 60% in a series of 107 patients reaching a sensitivity of 91% and a specificity of 75%. A PSV greater than 200 cm/s has been suggested as the threshold for Doppler diagnosis of 60% reduction of the RA diameter [17,18]. This criterion yielded a positive predictive value (PPV) of 60%, a negative predictive value (NPV) of 95%, and an overall accuracy of 79%. In a recent study [19], PSV >200 cm/s resulted in a sensitivity of 97%, specificity of 72%, PPV of 81% and NPV of 95% in terms of diagnostic accuracy for RAS. In a meta-analysis, PSV was the best predictor of RAS, with a sensitivity and specificity of 85% and 92%, respectively [20].

The second criterion is the comparison of PSV values obtained in the prerenal abdominal aorta with those measured in the RAs, the so-called renal/aortic ratio (RAR) [21]. The use of the RAR instead of the absolute PSV value is preferable since hypertension itself can cause increased PSV velocities in all the vessels in hypertensive patients [8]. In normal conditions, RAR is lower than 3.5. If PSV obtained in the prerenal abdominal aorta is abnormally low (less than 40 cm/s), RAR cannot be used. In one study, a RAR of 3.5 or greater identified hemodynamically significant lesions with a sensitivity and specificity of 91—92% and 75—95%, respectively [21,22]. In another study by Chain et al. [23], a diagnosis of severe RAS based on RAR >3 yielded a sensitivity of 77%, specificity of 90%, PPV of 90% and NPV of 76%. In a recent study, RAR > 3.5 yielded a sensitivity and specificity of 91% and 91%, respectively [24]. Technical failure is reported to be due to severe obesity, the use of older US devices, excessive bowel gas or poor flow in the main RA due to severe renal impairment. For the identification of RAS ≥ 50%, Soares et al. [25] reported that renal-segmental ratio (RSR), i.e. a ratio of PSV measured in the renal artery to that obtained in the segmental artery, was the best parameter (sensitivity 93.33%; specificity 89.47%). Other authors [26] found that renal-interlobar ratio (RIR), i.e. a ratio of PSV measured in the renal artery to that obtained in the interlobar artery, was more accurate (sensitivity 88%; specificity 88%). Chain et al. [23] proposed a new direct-method Doppler parameter, the renal renal ratio (RRR), which was defined as the rate between renal artery peak systolic velocity (RPSV) at the proximal or mid segment of the RA and RPSV measured at the distal segment of the renal artery (RRR = RPSV (proximal or mid RA)/RPSV (distal RA). It is based on the fact that increased blood flow velocity through the stenosis and the immediate post-stenotic segments and the observed decrease in blood flow velocity distal to the stenosis is proportional to the degree of stenosis. The intra-examiner variability was good
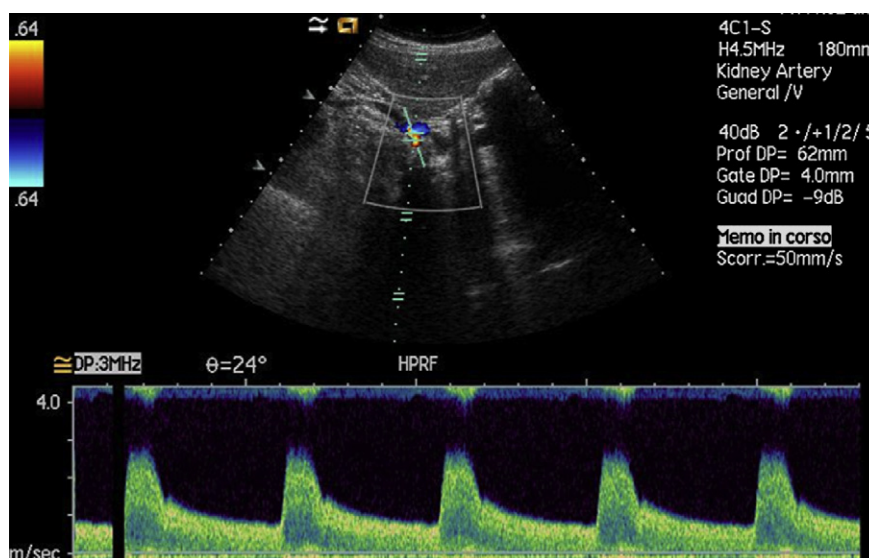

Fig. 6 Spectral Doppler waveform of the stenotic area in the right RA. Increased peak systolic velocities are seen (PSV 286 cm/s); Mosaic flow is seen within the stenotic area.

(correlation 0.86, coefficient of variation 8.9%). The best estimated cut-off value for the new RRR was 2.7. The RRR values, when compared to the other direct-method parameters (PSV > 200 cm/s and RAR > 3) showed a sensitivity and specificity of 97% and 96%, respectively. The main limitation of this study was that Chain et al. [23] evaluated only the main RAs because these vessels have a more important role in renovascular diseases and could be submitted to endovascular treatment, while results obtained by other authors [10] using the parameters PSV and RAR included accessory RAs detected at arteriography. Recently, Li et al. [27] found that receiver operating characteristic (ROC) curve analysis for RAS ≥ 50% showed that the areas under the curve (AUCs) for RPSV, RAR, RRR, RSR, and RIR were 0.92, 0.87, 0.90, 0.93, and 0.94, respectively, and the optimal threshold values of the five parameters were 170 cm/s, 2.3, 2.0, 4.0, and 5.5, respectively. The authors [27] state that in RAS diagnosis it was possible and necessary to measure 3 representative hemodynamic parameters (RAR, RPSV and RIR or RSR) in the diagnosis of ≥50% RAS. PSVs in the abdominal aorta and RA can be affected by factors other than RAS, which may decrease the accuracy of RAR. However, post-PSV ratios are little affected by PSV in the abdominal aorta or by an equal proportional change in PSVs in the RA trunk and its intra-renal RAs; therefore, the use of post-PSV ratios overcomes some limitations of RAR. In the detection of RAS, it is helpful to notice the degree and location of stenosis, arterial tortuosity and factors that influence PSVs in the abdominal aorta and RA. Accessory RAs are quite common, seen in approximately 25—30% of cases [23]. Two or more RAs are common, although typically one is dominant. It may be difficult or impossible to see accessory RAs, leading some to conclude that US evaluation for RAS is not sufficiently sensitive. However, the occurrence of hemodynamically significant stenosis isolated to an accessory RA was 1—1.5% in a retrospective review of renal angiograms obtained in patients who underwent workup for renovascular hypertension [21], thus decreasing the significance of non-visualized accessory RAs [22].

However, when is investigation of accessory RAs required? In angiographic investigations, the caliber of the single renal artery originating from the abdominal aorta was found to measure between 5 and 10 mm in adults, with values for women in the lower part of the range [23]. Aytac et al. [24] showed that if the diameter of a RA measured by US is 4.65 mm or less, the presence of an accessory renal artery can be established with 80% sensitivity and 80.5% specificity. If the diameter of the renal artery is 4.15 mm or smaller, the presence of an accessory renal artery is extremely probable, with 98.8% specificity. It was also interesting that in kidneys with a main RA diameter of 5.5 mm, no accessory RAs were encountered.

The third criterion is identification of RAs with no detectable Doppler signal, a finding than indicates occlusion. The fourth criterion is the visualization of color artifacts such as aliasing at the site of the stenosis and the presence of turbulence at Doppler evaluation indicating the presence of a significant stenosis upstream. Usually, these two patterns are the first and immediate signs of a stenosis [25]. These criteria permit classification of RA narrowing into the four categories listed in Table 1.

Table 1 Criteria for the classification of RA stenosis by color-Doppler US from Zieler and Strandness (Am J Hypertens, 1996).

Renal artery diameter reduction	Renal artery PSV	RAR
Normal[a]	<180 cm/s	<3.5
<60%	>180 cm/s	<3.5
≥60%	>180 cm/s	≥3.5
Occlusion	No signal	Indeterminable

[a] PSV = 100 ± 20 cm/s.

A stenosis is important when it is more than 60%. In this case, the stenosis produces a significant decrease in renal blood flow.

Distal criteria (indirect evaluation of the stenosis)

The difficulties related to the direct evaluation of the stenosis (the mean examination time was 69 min for the complete examination and 14 min for the distal evaluation) have led several investigators [28] to search for and to identify waveform alterations, other than increased velocity, distal to the stenosis in arterial segments more accessible with Doppler US (i.e. hilar or interlobar arteries). Many distal quantitative criteria have been proposed in the literature [27,29] (loss of early systolic peak; acceleration index (AI) lower than 3 m/s^2; acceleration time (AT) < 0.07 s; a difference between the kidneys in RI > 5% or in pulsatility index >0.12). Correlative studies using angiography are confusing because of the variability in criteria and in the corresponding degree of stenosis. Interobserver and intraobserver variability using these criteria is high [29,30]. The rationale is that the flow at the renal hilum downstream to a hemodynamically significant stenosis should become damped and show a slow rise to the peak systole [26]. This phenomenon has been called the ''tardus—parvus'' effect. Tardus means slow and late and parvus means small and little. Tardus refers to the fact that systolic acceleration of the waveform is slow with consequent increase in time to reach the systolic peak. Parvus refers to the fact that the systolic peak is of low height, indicating a slow velocity (Fig. 7). However, although the presence of this finding is helpful in forming the diagnosis, its absence does not exclude RAS. In patients with atherosclerosis, vessel compliance may be reduced, making the parvus—tardus waveform morphology less obvious [31,32]. Several articles have shown excellent results with this indirect technique [9,10,11,14,17] and a slow systolic upstroke or AI (the upstroke of the systolic peak adjusted to the transmitted frequency), an increase in AT (the interval measured in seconds between the onset of the wave and the initial systolic peak) and loss of the early systolic peak (ESP) appear to be the most useful parameters [27].

Hausberg et al. and Rabbia et al. [32,33] confirm the usefulness of AI and AT but report that a simple pattern recognition of the Doppler waveform from the segmental arteries (persistence of the ESP) may be more valuable than calculating AI and AT with 95% sensitivity, 97% specificity, and 96% accuracy for stenosis greater than 60%. On the
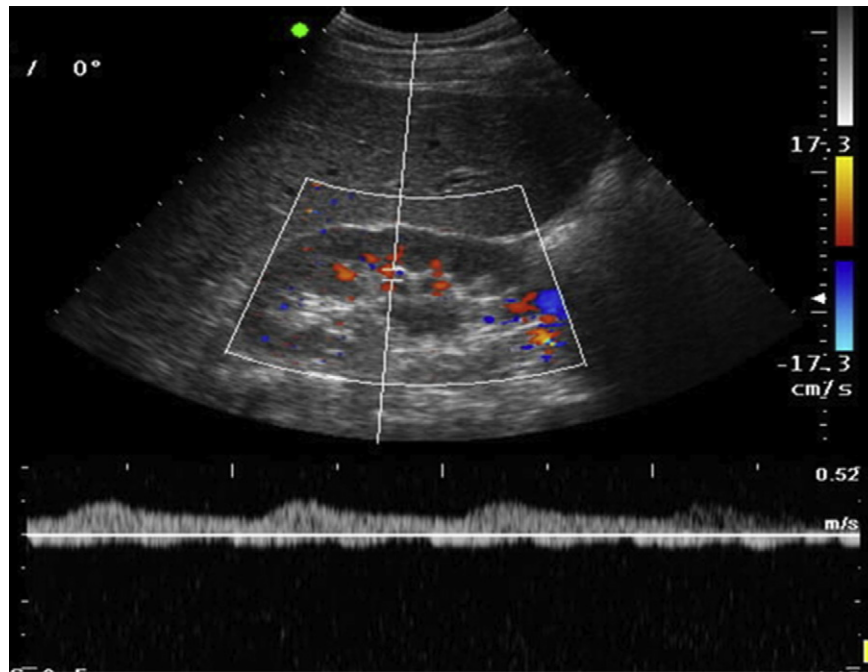
Fig. 7 Tardus—parvus waveform in a patient with RA stenosis. Note the delayed and dampened upstroke yielding a rounded appearance to the waveform.

other hand, in a comprehensive review, the authors [19,34] found for AT and AI a sensitivity of 80% and 74% and a specificity of 88% and 85%, respectively. Many factors influence systolic acceleration and may make the test non-specific. Extrarenal factors such as aortic and mitral valvular diseases, left ventricular dysfunction or even cardiovascular medication might affect systolic accelera-tion. Numerous factors, such as age, hypertension and diabetes affect vessel compliance. Such variables may explain why some authors have not been able to reproduce these results [30,35]. Therefore, these criteria are used only when obvious on spectral traces, when quantifying the stenosis as severe ($>75\%$), or when identifying a down-stream pattern of a stenosis on a segmental or an accessory artery that has been missed [28,36]. Most accrediting organizations recommend the use of a combination of intra- and extrarenal parameters, as it results in an overall sensitivity of 89% and specificity of 92% [11,37].

Bardelli et al. [38] recently introduced new intrarenal echo-Doppler velocimetric indices for the diagnosis of RAS. The maximal acceleration index (AI_{max} s^{-1}, defined as the maximal slope of the systolic acceleration corrected for the relative district flow regimen, as stated by the PSV). The sensitivity and specificity of AI_{max} at the best cut-off value of 9.0 s^{-1} was found to be 88% and 89%, respectively, for stenoses $\geq50\%$, 93% and 84% for stenoses $\geq60\%$ and 92%, and 82% for stenoses $\geq70\%$. However, the study design did not provide comparative analyses of the new intrarenal indices and of the proximal ones. Thus, it cannot be established from the present data which of the two approaches is better. Furthermore, the accuracy of this new index for the diagnosis of RAS has not been evaluated in other studies.

A great difference in RI values obtained on the 2 kidneys ($>0.05-0.07$) is another criterion for diagnosis of RAS as the post-stenotic flow in the RA beyond the region of stenosis will often have low-resistance waveforms [37—39]. However, this criterion is not commonly used in our practice. Unlike obstructive uropathy [40,41], the abnormal kidney will show reduced RIs beyond the point of stenosis [42].

Another advantage of US over other modalities is its ability to predict which patients will benefit from thera-peutic correction of RAS. Radermacher et al. [43] showed in a large prospective study that symptoms and urinary values do not improve after stenting in patients with elevated RI > 0.80. The authors [43] therefore suggested that repair of the stenosis is not warranted in these patients. However, a subsequent study showed that 29% of patients with renal insufficiency and RI > 0.80 showed improved renal function after revascularization, and 50% had improvement of hypertension [28].

Evaluation in assessing restenosis of renal artery stents

Several studies [44,45] have shown good technical success rates immediately after the procedure, but restenosis rates approximately from 2% to 36% at 6—12 months follow-up. Assessment of restenosis of RA stents is important in the clinical management of individual patients to determine the long-term benefits of the procedure. MRA and spiral CTA are less suitable for assessing restenosis because of artifacts caused by the stent material. CDUS follow-up to assess for restenosis may be warranted in patients after stent placement for RAS, even in the absence of clinical signs of restenosis (Fig. 8a,b). Girndt et al. [44] reported a sensitivity and specificity of 100% and 74%, respectively, using the published threshold value of in-stent PSV >180 cm/s. If the published threshold value of RAR >3.5
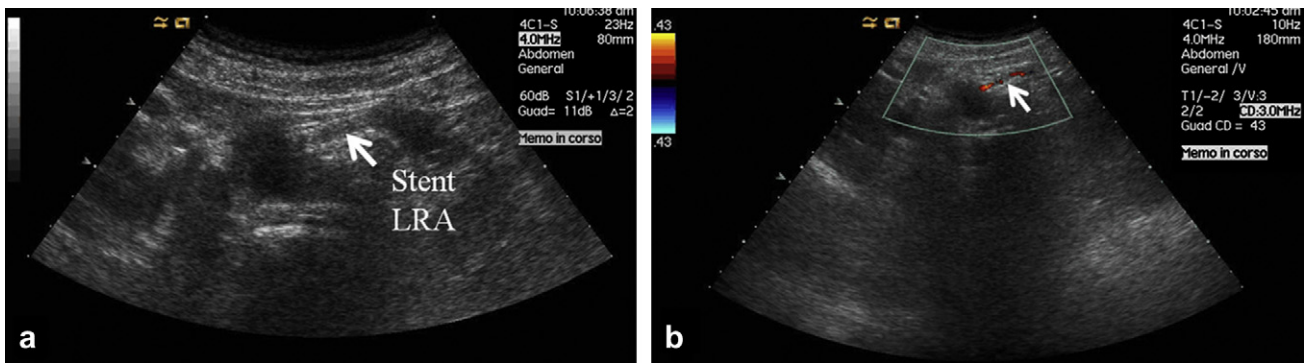
Fig. 8 (a) Gray-scale US examination showed a stent in the left RA (arrow); (b) Color US examination showed restenosis in the left RA (arrow).

was used, sensitivity and specificity were 50% and 89%, respectively. In another study, Bakker et al. [46] used an optimal threshold value of 226 cm/s rather than 180 cm/for in-stent PSV and an optimal threshold value for the RAR of 2.7 rather than 3.5, and reported a sensitivity of 100% for both parameters and a specificity of 90% for in-stent PSV and 84% for RAR.

Finally, the number of technically inadequate US examinations may be reduced by searching for alterations in Doppler waveforms in areas of renal vasculature distal to a stenosis, instead of directly insonating the RA. However, the results of these indirect methods are controversial and several investigators question their usefulness [44,46].

Contrast-enhanced ultrasound and renal artery stenosis

Contrast-enhanced ultrasound (CEUS) has recently added new possibilities to CDUS in the detection or RAS as it improves visualization of the main RAs and accessory vessels and reduces the number of equivocal examinations (Fig. 9). US contrast agent increases the intensity of the Doppler signals, thus producing a more rapid and complete visualization of the RAs. Main indications include cases

where Doppler trace is difficult to obtain in basal conditions because of the overlying tissues, calcifications or weakness of the signal.

Missouris et al. [47] showed that renal duplex scanning using contrast enhancement produces more reproducible spectral waveforms, improves accuracy and reduces the time needed for the examination. They demonstrated a sensitivity of 85% and a specificity of 79% without contrast enhancement, and a sensitivity of 94% and a specificity of 88% with contrast enhancement, besides an important reduction in the duration of the procedure. In another study, Claudon et al. [48] showed that the number of examinations with successful results was increased by CEUS examination compared to non-enhanced Doppler US, also in patients affected by obesity or renal dysfunction. However, the sensitivity and specificity of Doppler US examination did not substantially increase. Teixeira et al. [49] showed that CEUS does not improve the accuracy despite a reduced duration of the procedure and an increase in specificity based on one Doppler criterion. CEUS imaging of the RAs is safe but not routinely required when Doppler US is performed by an experienced sonographer. However, CEUS may increase visualization and accuracy in patients affected by stenosis and in patients whose vessels are not initially visualized. Although increased velocities are seen
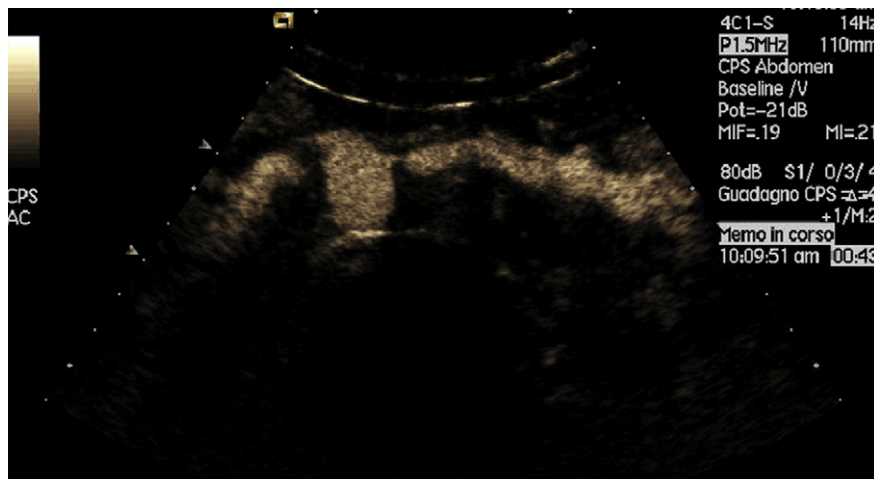

Fig. 9 Contrast-enhanced US examination showed proximal stenosis in the left renal artery (arrow).

when contrast agent is used, this does not appear to necessitate different Doppler criteria [50].

The feasibility of US examination depends on the quality of the equipment, and the injection of contrast agent does not add advantages if the performance of the US equipment is excellent. Contrast agents (microbubbles) do not undergo renal filtration or tubular excretion and, on the whole, they can be considered as purely vascular tracers.

Following recent improvements in CEUS techniques, a quantitative time-intensity analysis of the wash-in wash-out enhancement curve of tissues is currently feasible [51]. Time-intensity enhancement curves show the variation of the average pixel power over time within a box that is sized and shaped to match the target organ and enables direct and immediate quantitative evaluation of curve-related parameters such as time to peak, maximum peak concentration and the area under the curve [8,31,52]. CEUS is a new promising method of screening, and a renewal of interest in Doppler techniques is therefore to be expected. At present, however, only preliminary results have been presented in the literature, and further studies are needed before the introduction of this technique in clinical practice.

Conflict of interest statement

The authors have no conflict of interest.

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