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Renal artery blood flow: quantification with breath-hold or respiratory triggered phase-contrast MR imaging

M. W. de Haan[1], M. Kouwenhoven[3], A. G. H. Kessels[2], J. M. A. van Engelshoven[1]

[1] Department of Diagnostic Radiology, University Hospital Maastricht, P. Debyelaan 25, P. O. Box 5800, NL-6202 AZ Maastricht, The Netherlands
[2] Department of Epidemiology, University Hospital Maastricht, P. Debyelaan 25, P. O. Box 5800, NL-6202 AZ Maastricht, The Netherlands
[3] Philips Medical Systems, Department of Clinical Science MR, P. O. Box 10 000, NL-5680 DA Best, The Netherlands

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Abstract. The aim of this study was to evaluate the validity and reproducibility of breath-hold and respiratory triggered phase-contrast (PC) MR imaging techniques in the measurement of renal artery blood flow. In 12 healthy subjects cardiac-gated PC flow measurements were obtained in the renal arteries using a breath-hold and a respiratory-triggered technique. The flow measurements were repeated in each renal artery separately. Comparison between the sum of flow measurements in the renal arteries and the difference in aortic flow measurements above and below the renal arteries served as an internal control. The flow measurements showed a good reproducibility both with the breath-hold ($r = 0.92$, $p < 0.0001$) and with the respiratory-triggered ($r = 0.91$, $p < 0.0001$) technique. The validity of both methods was good and there was no statistically significant difference. Reproducible quantitative measurements of renal artery blood flow are possible with respiratory controlled, cardiac-gated, PC MR imaging.

Key words: Renal arteries – MR imaging – Flow dynamics – Phase imaging

Introduction

Renal artery stenosis is the most frequent cause of secondary hypertension, with an estimated prevalence of 3–5 % in the general population of people with hypertension [1, 2]. Identifying hypertensive patients with renovascular disease could allow for potential curative therapy. Correction of arterial stenoses by means of percutaneous transluminal angioplasty (PTRA) or surgical techniques shows normalization or improvement of the hypertension in the majority of these patients [3, 4, 5]. However, in 10–30 % there is no response to these therapeutic regimens [5, 6] and it is unpredictable in terms of who will respond and who will not. Moreover, many aortograms obtained for other reasons demonstrate renal artery stenosis in normotensive patients.

Up to now the decision to correct renal artery stenosis in hypertensive patients has predominately been based on morphologic information (stenosis > 50 %) provided by current imaging techniques including digital subtraction angiography (DSA), computed tomographic angiography, and MR angiography [7, 8]. Doppler sonography is used for noninvasive detection of renal artery stenosis with varying results concerning diagnostic accuracy, because quantification of renal artery blood flow is influenced by a variety of errors inherent in the indirect calculation of Doppler parameters [9, 10, 11]. Various functional tests, e. g., para-aminohippuric acid (PAH) clearance, venous renin sampling, and radionuclide renography, are either indirect measures of disease or yield only total renal flow, rather than unilateral flow to each kidney [12, 13, 14].

Knowledge of blood flow in the individual renal artery in patients with hypertension would provide a better understanding of the pathophysiology of renovascular hypertension, and this information might be important in the therapeutic management of these patients. Furthermore, measurements of renal artery blood flow could serve as a noninvasive test for follow-up after PTRA or surgical reconstruction and for evaluation of various vasoactive agents.

Recent publications indicate that high-resolution 3D gadolinium-enhanced MR angiography is the preferred MR angiography technique for morphologic assessment of the renal arteries. Other MR angiographic techniques (i. e., phase-contrast and time-of-flight) show limitations in depicting small-caliber vessels and distal renal artery segments [15]. However, phase-contrast MR imaging (PC MR), which goes beyond morphologic imaging by allowing quantitative evaluation of flow dynamics, can be used to determine the hemodynamic significance of renovascular disease. Flow quantification with PC MR

Correspondence to: M. W. de Haan

uses the velocity-dependent phase shifts of flowing spins [16]. In combination with cardiac triggering, flow rates can be determined at specified phases of the cardiac cycle. This enables the flow rates to be studied as a function of time. The accuracy of PC flow measurement has been validated in vitro and in vivo [17, 18].

In the past few years, several phase-contrast MR techniques have been proposed for quantification of blood flow in the renal arteries [19, 20]. However, the reported results show varying success in renal blood flow measurement compared with results obtained by means of para-aminohippurate (PAH) clearance. Respiratory motion, which causes the renal arteries to move during data acquisition, appears to be a considerable source of error in these measurements [20, 21,22]. Synchronization with respect to respiratory motion, along with cardiac triggering, seems to be necessary to obtain accurate, reproducible flow data [22, 23].

The aim of this study was to determine the feasibility and reproducibility of two respiration-controlled PC MR techniques: one breath-hold sequence, and one respiratory triggered sequence, to measure blood flow in the individual renal arteries.

Materials and methods

Subjects

Twelve subjects (8 men and 4 women; mean age 35.0 years, age range 23–48 years) were recruited. All volunteers were normotensive without known underlying renal disease. Criteria for participation in the study included willingness to give informed consent, and lack of standard contraindications to MR imaging (e.g., pacemaker, claustrophobia, or ocular metallic fragments). The study was approved by the ethical review board of our institute.

MR imaging technique

All images were acquired on a 1.5-T whole-body MR system (ACS II, Philips Medical Systems, Best, The Netherlands), using the quadrature body coil for signal transmission and reception. No abdominal compression was used.

To localize the renal arteries, a T1-weighted gradient-echo multistack scout view was obtained at the level of the kidneys (TR/TE: 22.0/7.0 ms, flip angle 20°, 15.0-mm slice thickness, FOV 500 mm, 256 × 256 matrix). Images were obtained in the coronal and transverse planes.

Subsequently, a non-cardiac-gated 3D phase-contrast MR angiographic (PC MRA) sequence was performed for morphological assessment of the renal arteries [8].

T1-weighted, gradient-echo images were obtained in the transverse plane with the following parameters: TR/TE = 27.0/8.5 ms; flip angle 20°; two signals averaged; 75% partial echo sampling; FOV 200 × 140 mm; 128 × 103 acquisition matrix, using a 256 reconstruction matrix; and 45 cm/s flow-encoded velocity. Fourier interpolation was used to reconstruct sections thinner than those acquired. In the sequence performed without gating, 32 sections of 4 mm were acquired, reconstructed to 64 slices of 2.0 mm. The outer 10% on both sides was discarded resulting in 50 slices of 2 mm.

To reduce the venous signal from the inferior vena cava, a transverse presaturation slab (60.0 mm thick) was placed inferior to the lower pole of the kidneys. The maximum intensity projection (MIP) algorithm was used to create angiographic projections in the transverse, coronal, and sagittal planes. Both the MIPs and the original transverse images were used to select an image plane perpendicular to the studied artery for flow quantification.

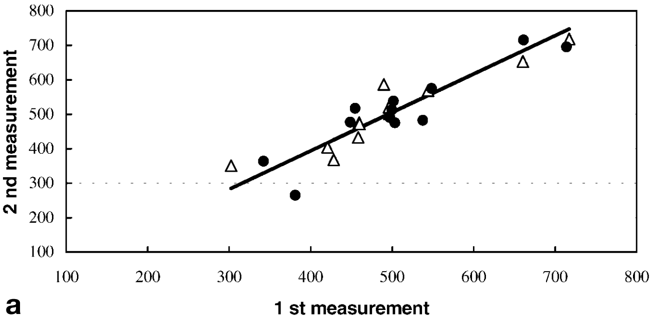
A flow-compensated turbo gradient-echo PC MR technique was used for flow data acquisition with the following parameters: FOV 180 × 90; TR/TE = 12.0/7.0 ms; flip angle 25°; 7.0-mm slice thickness; two signals averaged allowing fold-over suppression in the phase-encoding direction (anterior–posterior); 128 × 96 acquisition matrix, using a 128 reconstruction matrix; in-plane voxel size 1.4 × 1.9 mm; cardiac triggering; eight phases per cardiac cycle; linear profile order; ten profiles per heart phase; flow-encoded velocity 120 cm/s. Electrocardiography was used for cardiac synchronization. Flow quantification was performed both with a breath-hold (acquisition time 30 s) and a respiratory-triggered technique (acquisition time 2 min). Images were obtained perpendicular to the right and left renal artery 8–15 mm from their aortic origin.

In order to acquire information about the reproducibility of the flow measurements, flow quantification in each separate renal artery was repeated within 5 min in each subject without changing the scan parameters and/or off-centers.

As an internal validation of the measurements, flow data were obtained in each renal artery separately and in the abdominal aorta superior and inferior to the origins of the renal arteries. To avoid inclusion of the superior mesenteric artery, the position of the slices was carefully planned on the MIPs of the non-gated 3D PC MRA sequence. Postulating that no other (major) vessel originates from the involved aortal segment means that, with accurate flow measurements, the sum of flow volumes in the renal arteries and inferior aorta is the same as in flow volume measured in the aorta superior to the renal artery origins.

Evaluation and statistics

To ensure optimal vessel demarcation and measurement reproducibility, all phase-contrast flow data were analyzed in a contour detection program, on an off-line workstation (Sun Microsystems, Mountain View, Calif.). The employed automated region of interest (ROI) definition algorithm defined the region on the phase-contrast MR images bounded by an operator-defined ellipsis drawn generously around the vessel on the modulus images. Instantaneous flow (milliliters per second)



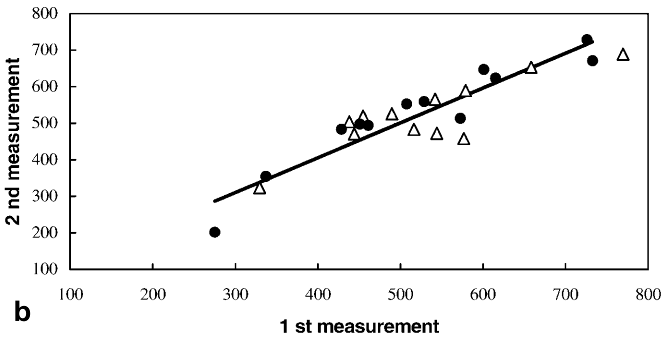


Fig. 1 a, b. Scatterplot of the first and second renal flow measurements with orthogonal regression line. **a** Breath-hold; **b** respiratory triggered. △ right renal artery, ● left renal artery

was calculated from the individual velocity images by integrating velocity (centimeters per second) across the area (square centimeters) of the vessel. Mean flow in each vessel was calculated as the average of instantaneous flows across the cardiac cycle.

The interobserver agreement was determined by calculating the Pearson correlation coefficients for both the breath-hold and the respiratory-triggered flow measurements.

Validity assessment of both techniques was based on differences between the in- and outgoing flows.

Results

Non-gated 3D PC MRA revealed a total of 26 renal arteries in the 12 subjects. Two subjects showed an accessory renal artery. None of the visualized arteries showed renovascular disease on the non-gated 3D PC MRA images. The waveforms in the renal arteries showed a continuous forward-flow characteristic of an arterial system with low peripheral resistance. The aortic waveforms showed a more pulsatile flow pattern with a phase of retrograde flow during diastole.

The flow measurements in the renal arteries showed a good reproducibility with Pearson correlation coefficients of 0.92 and 0.91 ($p < 0.0001$) for the breath-hold and respiratory-triggered technique, respectively (Fig. 1).

The residual flow, i. e., the difference between flow measured in the superior aorta (inflow) and the sum of measurements of both renal arteries and inferior aorta (outflow), should be equal to zero. The standard deviations of this residual flow with the mean set to zero were for the breath-hold and respiratory triggered 11.4 and 9.3, respectively. These values did not differ significantly (F-test: $p = 0.23$).

In one subject a relatively large residual flow was noted: 680.6 ml/min using the breath-hold technique and 434.0 ml/min with the respiratory triggered technique, probably caused by poor positioning of the flow-acquisition slices. If these deviating results would have been omitted, the difference in standard deviations for the breath-hold and the respiratory triggered technique, namely 4.2. and 8.6, respectively, would have been statistically significant ($p = 0.01$), thus favoring the breath-hold technique.

Likewise, the independent MRA measurements of the total renal blood flow (RBF) calculated from the sum of renal artery flows concurred well with the RBF calculated from the aortic difference (Fig. 2).

Discussion

Respiration-controlled MR phase imaging promises to be reliable technique for non-invasive measurement of blood flow in the renal arteries. The obtained absolute flow measurements in the renal arteries and abdominal aorta correspond well with results of other published studies [20, 21, 22, 23, 24].

Comparison between the in- and outgoing flows, i. e., flow in the superior abdominal aorta vs flows in the renal arteries and inferior abdominal aorta, served as an internal control from which information was derived about the accuracy of the MR technique. The degree of reproducibility, which to our knowledge has not been addressed in recent literature, was evaluated by repeating the separate flow measurements in the renal arteries without changing scan parameters and/or off-centers. Thus, 12 separate flow measurements, i. e., 6 with the breath-hold and 6 with the respiratory-triggered technique, were performed in each individual. In this study methods these independent measurements yielded overall concurring and reproducible results with both the breath-hold and the respiratory-triggered technique.

The optimal method for flow data acquisition and evaluation in the renal arteries is not yet certain. Several published reports show reliable flow measurements using MR techniques without respiratory synchronization [19, 21, 24, 25], whereas others identify respiratory motion as a significant potential source of error in quantitative flow assessment in the renal arteries [20, 22, 23]. This contrast could be related to differences in the location of the parasagittal imaging plane with respect to the aorta, since respiration is likely to have a more significant influence on motion of the renal vessels in the periphery than in their central segment.

Misalignment between slice direction and vessel axis and partial volume effects due to the limited in-plane resolution are other potential sources of error. Great care was taken to localize the renal arteries on MR angiography, using both MIPs in three different planes and

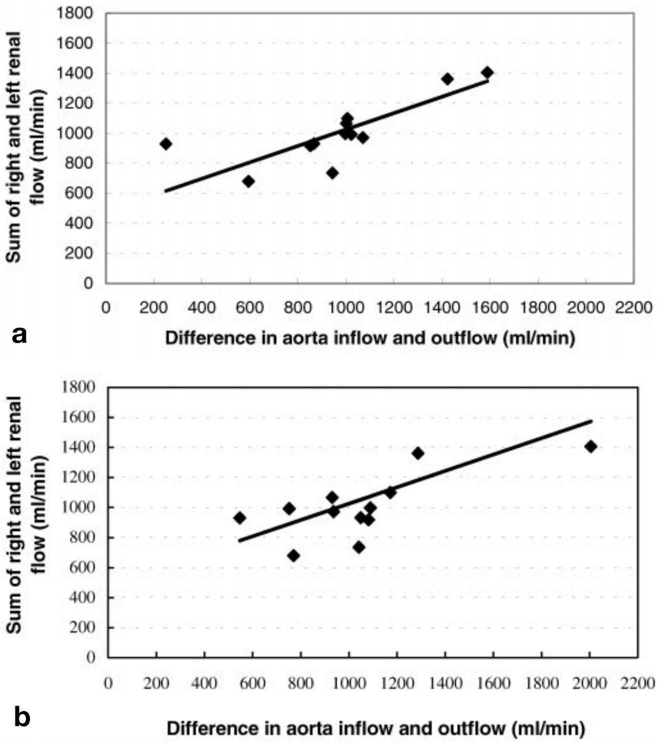


Fig. 2 a,b. Scatterplot of the total renal bloodflow calculated from the sum of renal artery flows and from the aortic difference. **a** Breath-hold; **b** respiratory triggered

the original transverse images, and (double-) angulating the slice perpendicular to the flow axis.

With a typical R-R interval of 850 ms (70 bpm), respiratory synchronization, along with cardiac triggering, permitted a temporal resolution of only approximately 107 ms, allowing reproducible assessment of the mean renal artery blood flow. However, the relative low temporal resolution of this technique does not allow qualitative analysis of flow profiles, which might be necessary in patients with more complex flow patterns. In a recent publication Schoenberg et al. [26] described a cardiac-gated cine PC MR technique, without respiratory synchronization, with a temporal resolution from 32 to 16 ms. This technique enabled them to analyze the pulsatile properties of the renal artery waveform and to identify different segments of the flow profile. However, reduction of the mean renal blood flow proved to be the only statistically significant parameter in accurate differentiation between hemodynamically relevant high-grade (> 50 %) stenosis and low-grade (≤ 50 %) stenosis. Maximum velocity and time to systolic maximum were more sensitive to changes at lower degrees (< 50 %) of stenosis.

Published reports indicate that differences from right to left in excess of 15 % (calculated by dividing the difference from right to left by the average of the two) are abnormal [18]. Measurements in this study showed asymmetry in all subjects to some extent: mean differences of 8.6 and 13.0 % for the breath-hold and respiratory triggered techniques, respectively. In two subjects a mean right-to-left difference greater than 15 % was noted with the breath-hold technique, as opposed to three subjects with the respiratory-triggered technique.

In summary, quantitative assessment of renal artery blood flow may prove to be important in the clinical evaluation of patients with renal artery pathology. Furthermore, measurement of renal blood flow could serve as a non-invasive test for follow-up after PTRA or surgical reconstruction, and for evaluation of various vasoactive agents.

This preliminary study shows that reproducible quantitative measurements of renal artery blood flow are possible with respiratory controlled, cardiac-gated, PC MR imaging. Our data show a slight preference for the breath-hold technique compared with the respiratory-triggered technique. However, the study was limited by the small sample size ($n = 12$) and the composition of the subject group (i. e., healthy, relatively young volunteers), which makes extrapolation of the results to daily practice difficult. Further and larger studies in (hypertensive) patients comparing different MRA techniques mutually and with other methods, and studies which address the reproducibility of the various techniques, would be worthwhile.

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