

# Quantification of Aortic Valve Regurgitation by Pulsed Doppler Examination of the Left Subclavian Artery Velocity Contour: A Validation Study with Cardiovascular Magnetic Resonance Imaging

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**Background:** Reflux of the aortic regurgitation (AR) causes an increased diastolic reverse flow in the aorta and its branching vessels. We aimed to evaluate the feasibility and accuracy of Doppler measurements in the left subclavian artery (LSA) for quantification of AR in a cardiovascular magnetic resonance imaging (CMR) validation study.

**Methods:** Systolic and diastolic flow profiles of the LSA (subclavicular approach) were evaluated prospectively by use of pulsed wave Doppler in 59 patients ( $55.5 \pm 15$  years; 44 men), 47 with a wide spectrum of AR and 12 as control group. Using CMR phase-contrast sequences (performed 1 cm above the aortic valve), the AR was divided into three groups: mild, regurgitant fraction (RF) < 20% ( $n = 17$ ); moderate, RF 20%-40% ( $n = 10$ ); and severe, RF > 40% ( $n = 20$ ). The LSA Doppler-derived RF was calculated as the ratio between diastolic and systolic velocity-time integrals (VTI).

**Results:** Quality LSA Doppler signal could be obtained in all cases. Patients with CMR severe AR had higher values of LSA Doppler-derived RF ( $51\% \pm 9\%$  vs  $36\% \pm 11\%$  vs  $16\% \pm 8\%$ ;  $P < .0001$ ). LSA Doppler showed a good correlation with CMR, with a sensitivity of 95%, specificity of 89%, and diagnostic accuracy for severe AR of 91.5%. Finally, Bland-Altman plots showed agreement in the group with moderate to severe AR (mean bias =  $-2.2\% \pm 8\%$ , 95% CI,  $-17.7$  to  $13.3$ ;  $P = .145$ ) but differed in mild AR.

**Conclusions:** Measurements of the RF for quantification of AR using LSA Doppler are comparable to those of CMR, highlighting the potential role of LSA Doppler as an adjunctive technique to assess the severity of AR. (J Am Soc Echocardiogr 2017; ■: ■ - ■.)

**Keywords:** Aortic valve, Regurgitation, Left subclavian artery, Diastolic flow reversal, Doppler quantification, CMR

Echocardiography is the method of choice to evaluate the aortic valve regurgitation (AR), but it is still challenging especially in patients without optimal acoustic windows or in those with multiple or eccentric jets. Qualitative assessment of AR severity by echocardiography has been shown to be unreliable when compared with cardiovascular magnetic resonance (CMR) measurements of regurgitant fraction (RF).<sup>1</sup> Current echocardiographic guidelines recommend a multiparametric

approach.<sup>2,3</sup> Efforts should be made to use semiquantitative and quantitative parameters (i.e., vena contracta width and proximal isovelocity surface area [PISA] method) whenever possible. Adjunctive parameters help to consolidate the evaluation of the severity of AR, particularly when there is discordance between the quantified degree of AR and the clinical context. AR leads to diastolic flow reversal in the descending aorta (DA) and its branches. As the degree of the regurgitation increases, the duration and the velocity of the reversal flow during diastole increases. Thus, the measurement of the diastolic flow reversal in the aorta is recommended, when assessable, and should be considered as the strongest additional parameter for evaluating the severity of AR.<sup>2</sup> However, Doppler examinations are often restricted to the DA, where a high-quality Doppler signal acquisition is usually challenging, allowing only a qualitative or a semiquantitative assessment.<sup>4</sup> On the other hand, the examination of the left subclavian artery (LSA) by pulsed Doppler can be easily performed,<sup>5</sup> and a quantitative assessment of the RF by examination of the velocity contour can be attempted,<sup>6,7</sup> as was suggested for the first time by Boughner.<sup>8</sup> Nevertheless, this method

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Conflicts of Interest: None.

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## Abbreviations

<b>AR</b> = Aortic regurgitation
<b>b-SSFP</b> = Balanced steady-state free precession
<b>CMR</b> = Cardiovascular magnetic resonance
<b>DA</b> = Descending aorta
<b>EF</b> = Ejection fraction
<b>LSA</b> = Left subclavian artery
<b>LV</b> = Left ventricular
<b>LVOT</b> = Left ventricle outflow tract
<b>PISA</b> = Proximal isovelocity surface area
<b>RF</b> = Regurgitant fraction
<b>RVol</b> = Regurgitant volume
<b>TE</b> = Echo time
<b>TR</b> = Repetition time
<b>TTE</b> = Transthoracic echocardiography
<b>VTI</b> = Velocity-time integral

has never been validated and compared with the highly accurate and reproducible CMR measurements of aortic RF. Therefore, we sought to evaluate the feasibility and accuracy of LSA Doppler measurements for AR quantification in a prospective study using CMR as a reference standard.

**METHODS****Study Population**

We prospectively enrolled 59 patients (55.5 ± 15 years; 44 men), 47 with a wide spectrum of AR of the native valve referred to our center for evaluation of the pathology (AR group) and 12 patients without any apparent AR on transthoracic echocardiography (TTE) or CMR with clinical indication for a CMR study other than heart valve disease (control group). Patients were eligible if they had sinus rhythm during the study. Patients with

an associated cardiac valve lesion of more than moderate, with a significant aortopathy (i.e., ascending aorta diameter ≥55 mm or aortic coarctation), or with typical contraindications for CMR imaging were excluded.

Usually, patients underwent both CMR imaging and TTE within 12 hours (in 38 patients of the AR group, the period was <12 hours, with an overall median delay between TTE and CMR examination <1 day [95% CI, 0.14 to 2.6]). All baseline characteristics were prospectively collected. Finally, on the basis of CMR quantification, the AR group was divided into three groups (i.e., mild, RF < 20%; moderate, RF 20%-40%; and severe, RF > 40%), and comparison with LSA Doppler-derived quantification was carried out using the identical severity grading.

**Pulsed Doppler of the LSA Velocity Contour**

The systolic and diastolic flow profiles of the LSA were evaluated by use of pulsed wave Doppler ultrasound (3.4-9 MHz linear probe). Patients were examined in a supine position with a subclavicular approach. Higher frequencies (>7 MHz) were used for assessment of the morphology, and lower frequency (<7 MHz) was preferred for Doppler examination. LSA was documented with gray-scale imaging and color Doppler to rule out relevant stenosis. The depiction of the LSA was modified to align the Doppler angle parallel to the vector of blood flow and to avoid the Doppler signal of the adjacent vein. The sample volume was placed just near the origin of the LSA. Patients with vascular shunts of the left upper arm were excluded.

We routinely used angle correction applying the following formula:  $\Delta f = 2f_0 V \cos \theta / C$  ( $\Delta f$  = Doppler shift frequency,  $f_0$  = transmitted ultrasound frequency,  $V$  = the velocity of red blood cells,  $\theta$  = angle between the transmitted beam and the direction of blood flow within the blood vessel, and  $C$  = speed of sound in the tissue). To avoid spectral broadening, the Doppler angle should not exceed 60° (the preferred angle was 50° ± 5°), the position of the sample volume

box should be in the mid lumen parallel to the vessel wall, and the size of the sample volume box should be 2-3 mm. Color velocity scale was set between 30 and 40 cm/sec, sweep speed between 50 and 100 mm/sec, and forward and backward velocity-time integrals (VTI) profiles were traced using an adjusted flow velocity scale for more precise measurements. The outer edge of the dense (bright) envelope of the spectral recording (i.e., modal velocity) was used to measure the VTI.<sup>9</sup> The RF was calculated as follows: RF(%) = LSA-derived diastolic reversed flow VTI × 100/LSA systolic forward flow VTI (Figure 1). At least two measurements were performed. The LSA Doppler examination was carried out blinded to the results of echocardiography and the CMR evaluation of AR.

**Standard Echocardiography**

All TTE were performed by experienced echocardiographers using commercially available ultrasound machines (Vivid E9, General Electric Healthcare, Wauwatosa, WI; or Acuson SC2000, Siemens Healthcare GmbH, Erlangen, Germany) equipped with M5S or 4V1c two-dimensional TTE probes. All recordings were stored digitally for offline analysis. Left ventricular (LV) volumes and ejection fraction (EF) were calculated using the biplane Simpson disk method. Doppler measurements were evaluated as the average of at least three cycles. An effort was made to perform the flow convergence (or PISA) method, from apical views or, in the case of eccentric jets, from parasternal long-axis views. The AR severity was graded according to current recommendations,<sup>2,3</sup> with a special focus on semiquantitative parameters like diastolic flow reversal in the DA measured by pulsed wave Doppler. Additionally, the same LSA Doppler scale and method described above to calculate the RF were used at the level of the DA. Finally, an integrative approach was applied to grade the AR, which was classified into one of three grades: mild, moderate, or severe. Evaluation of AR was performed by an experienced echocardiographer (R.A.S.) with >10 years of experience in echocardiography with European Society of Cardiology certification, who was blinded to the results of the CMR exam.

**Cardiovascular Magnetic Resonance**

All CMR examinations were performed in our cardiology department on a 1.5-T magnetic resonance imaging system (Ingenia, Philips Healthcare, Best, the Netherlands) equipped with a 28-element array coil with full in-coil signal digitalization combined with optical transmission. All scans were accomplished without sedation. Image data acquisition and subsequent analysis were carried out according to current guidelines. For cine imaging, a balanced steady-state free precession (b-SSFP) sequence with retrospective gating was used during short periods of breath holding. All standard cardiac geometries were acquired (multiple, gapless short-axis slices covering the entire left ventricle and two-, three- and four-chamber views). Imaging parameters were chosen as follows: echo time (TE) and repetition time (TR) were set to shortest, resulting in an average TR of around 4 msec and a TE of 2 msec, with a reconstructed in-plane resolution of 1.0 × 1.0 mm<sup>2</sup>; the slice thickness was 8.0 mm. The typical temporal resolution of the cine b-SSFP sequences was 30-25 msec depending on the heart rate. The imaging plane for the through-plane phase-contrast flow measurement was placed in the ascending aorta approximately 10 mm above the aortic valve and positioned perpendicular to the flow direction. On a coronal image of the aorta together with the three-chamber view, the CMR operator checked that the image plane was truly perpendicular to the

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