ORIGINAL ARTICLE

CME

Descending Aorta Diastolic Retrograde Flow Assessment for Aortic Regurgitation Quantification

Evaluación del flujo retrógrado diastólico en la aorta descendente para cuantificar la insuficiencia aórtica

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ABSTRACT

Background: Diastolic retrograde flow in the descending aorta has been associated to the severity of aortic regurgitation; however, most of the parameters related to flow velocity are not validated with a reference imaging technique.
Objective: The aim of this study was to assess the usefulness of diastolic retrograde flow in the descending thoracic aorta and the abdominal aorta in the quantification of aortic regurgitation using magnetic resonance imaging as reference.
Methods: Forty consecutive patients were included in a prospective echocardiography and magnetic resonance study. The following parameters were analyzed by pulsed-wave Doppler: a) velocity-time integral of the diastolic retrograde flow and b) peak end-diastolic velocity of the regurgitant flow, both in the thoracic aorta, and c) holodiastolic flow reversal in the abdominal aorta. The cardiac magnetic resonance protocol included phase contrast sequences to calculate the regurgitant fraction. Values ≥30% were considered as severe aortic regurgitation.
Results: Eleven patients (30%) presented a regurgitant fraction ≥30%. The velocity-time integral of diastolic retrograde flow demonstrated the best diagnostic accuracy to detect severe aortic regurgitation: AUC=0.87, p<0.001. A cut-off value for the velocity-time integral of diastolic retrograde flow >15cm showed 91% sensitivity and 86% specificity to detect severe aortic regurgitation. Holodiastolic flow reversal in the abdominal aorta demonstrated excellent specificity (100%) but low sensitivity (50%) to detect severe aortic regurgitation.
Conclusions: Diastolic retrograde flow assessment in the thoracic aorta allows an accurate diagnosis of severe aortic regurgitation. Holodiastolic flow reversal demonstrated good specificity but low sensitivity.

Key words: Heart Failure - Echocardiography, Doppler - Magnetic Resonance Imaging

RESUMEN

Introducción: El flujo diastólico retrógrado en la aorta descendente se ha relacionado con la gravedad de la insuficiencia aórtica; sin embargo, la mayoría de los parámetros vinculados con la velocidad del flujo no se encuentran validados con una técnica de imágenes de referencia.
Objetivo: Evaluar la utilidad del flujo retrógrado diastólico en la aorta torácica descendente y la aorta abdominal en la cuantificación de la insuficiencia aórtica utilizando como referencia la resonancia magnética.
Material y métodos: Se incluyeron 40 pacientes consecutivos en un estudio prospectivo de ecocardiografía y resonancia magnética. Por Doppler pulsado se analizaron los siguientes parámetros: a) la integral velocidad-tiempo del flujo retrógrado diastólico y b) la velocidad máxima telediastólica del flujo regurgitante, ambos en la aorta torácica, y c) el flujo holodiastólico inverso en la aorta abdominal. El protocolo de resonancia magnética incluyó secuencias de contraste de fase para calcular la fracción regurgitante. Valores ≥ 30% se consideraron diagnósticos de insuficiencia aórtica grave.
Resultados: Once pacientes (30%) tenían una fracción regurgitante ≥30%. La integral velocidad-tiempo del flujo retrógrado diastólico demostró la mayor precisión en el diagnóstico de insuficiencia aórtica grave: ABC = 0,87; p < 0,001. Un punto de corte para la integral velocidad-tiempo del flujo retrógrado diastólico > 15 cm demostró una sensibilidad del 91% y una especificidad del 86% para detectar insuficiencia aórtica grave. El flujo pandiastólico inverso en la aorta abdominal mostró una excelente especificidad (100%) para el diagnóstico de insuficiencia aórtica grave, aunque con baja sensibilidad (50%).
Conclusiones: La evaluación del flujo retrógrado diastólico en la aorta torácica descendente permite un diagnóstico adecuado de la insuficiencia aórtica grave. El flujo holodiastólico inverso, aunque es poco sensible, muestra una alta especificidad.

Palabras clave: Insuficiencia aórtica - Ecocardiografía Doppler - Imagen por resonancia magnética

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Abbreviations

3D	Three-dimensional	**HDF-AbAo**	Holodiastolic flow in the abdominal aorta
AR	Aortic regurgitation	**JW**	Jet width
CMR	Cardiac magnetic resonance imaging	**LVOT**	Left ventricular outflow tract
DRF-VTI	Diastolic retrograde flow velocity-time integral	**PISA**	Proximal isovelocity surface area
DRF-VTI/SAF-VTI	Diastolic retrograde flow/systolic anterograde flow velocity-time integral ratio	**RF**	Regurgitant fraction
ED-RFVm	Maximum end-diastolic retrograde flow velocity	**RV**	Regurgitant volume

INTRODUCTION

Aortic regurgitation (AR) is a relatively common valve disease, secondary to intrinsic aortic valve disorder, a disease of the ascending aorta or both. In young patients it is often associated with the presence of bicuspid aortic valve or to genetic pathology of the aorta and, with age, to degenerative aortic sclerosis or to ascending aortic dilatation secondary to atherosclerosis or high blood pressure. Echocardiography is the reference technique both for the etiologic diagnosis as for the assessment of AR severity and its impact on the left ventricle. Quantification of AR by Doppler echocardiography remains controversial because most of the methods have some limitation to estimate its severity. It is well established that the slope of the flow curve determined by continuous-wave Doppler echocardiography is heavily influenced by left ventricular end-diastolic pressure. The color apical area is subject to a large inter-group variability and it depends on the gain and the Nyquist limit. Recent guidelines recommend the use of vena contracta width associated with quantitative methods such as the proximal isovelocity surface area (PISA) to better assess its severity. However, quantitative methods require high expertise, are highly operator-dependent and considerably lengthen study time. Although 3D echocardiography can solve some of the current limitations, (1, 2) the temporal resolution of color Doppler still remains its main limitation. From a clinical point of view there is need for a secondary method supporting the quantification determined by jet width (JW). Reverse end-diastolic flow velocity in the descending thoracic aorta >20 cm/sec was suggested as criterion of AR severity. (3, 4) Yet, this velocity depends significantly on the duration of diastole, so the quantification of diastolic retrograde flow velocity-time integral (DRF-VTI) in the descending thoracic aorta seems more appropriate. To date no study has defined its accuracy or cutoffs values for a proper estimation of AR severity. (5)

The aim of this study was to assess the usefulness of diastolic reverse flow in the descending thoracic aorta and the abdominal aorta in the quantification of AR using cardiac magnetic resonance (CMR) imaging as reference.

METHODS

Study population

Forty consecutive patients (29 men and 11 women; mean age 59±17 years) with AR, referred for aortic valve disease assessment, were prospectively included in the study. Inclusion criteria were the presence of more than minor aortic regurgitation, sinus rhythm, acceptance to perform CMR imaging study and less than one week interval between the two studies. Patients with poor echocardiographic window or with contraindication for CMR due to pacemaker or manifest claustrophobia were excluded.

Doppler echocardiography protocol

A Vivid q General Electric ultrasound machine with 3 MHZ probe was used. A full Doppler echocardiography was performed according to the established recommendations. (3, 6, 7) For severe AR quantification, vena contracta width >6 mm, ratio between JW and left ventricular outflow tract (JW/LVOT) >65% and absolute value of JW >10 mm were considered. For the proximal descending thoracic aorta flow study the transducer was placed in the suprasternal notch with the body in supine position and the head hyperextended backwards. Using pulsed-wave Doppler, the sample volume was positioned in the aortic isthmus, immediately below the origin of the left subclavian artery (Figure 1A) in the center of the aortic lumen to avoid any increase in flow velocity generated by the aortic wall. The proximal abdominal aorta flow was also assessed by pulsed-wave Doppler with the ultrasound beam as parallel as possible to the direction of blood flow. The following parameters were analyzed: 1) diastolic retrograde flow velocity-time integral in the descending thoracic aorta (DRF-VTI), 2) maximum end-diastolic retrograde flow velocity in the descending aorta (ED-RFVm) (Figure 1B) and 3) diastolic retrograde flow/systolic anterograde flow velocity-time integral ratio (DRF-VTI/SAF-VTI). Reverse flow velocities in the abdominal aorta were then evaluated assessing whether the signal was holodiastolic.. (HDF-AbAo)

Cardiac magnetic resonance imaging protocol

The images were acquired with a 1.5-T HDX (General Electric System), using a 36-channel cardiac coil. Contrast phase images were taken in the aortic root immediately above the annulus for flow quantification. Flow sequence parameters were: echo time (ET) = 3.2 ms; repetition time (RT) = 7.6 ms, field of view (FOV) = 40 mm; matrix = 256 × 160, number of phases/cardiac cycle = 30, number of excitations (NEX) = 1, and slice thickness (ST) = 8 mm. Coding velocity was adjusted individually according to flow velocity starting at 200 cm/s.

Data analysis

Flow analysis was performed in a working console (Advantage Windows 4.4, General Electric). Flow was manually quantified tracing a region of interest on the aortic root, just above the annulus, using phase contrast sequence. Regurgitant aortic volume (RV) was directly estimated from the aortic flow curve through the retrograde aortic flow time integral. Aortic regurgitant fraction obtained by CMR (RF-CMR) was calculated as the ratio between RV and aortic anterograde volume (8, 9) (Figure 2). Aortic regurgitation severity was established as follows: RF-CMR <15% mild, RF 15-29% moderate and RF>30% severe AR. (10-12)

Statistical analysis:

Continuous variables were expressed as mean ± standard deviation and categorical variables as percentages. The Kolmogorov-Smirnov test was used to assess the normal distribution of variables. In the case of categorical variables the chi-square test was applied if the distribution was normal and Fisher's exact test if the distribution was not normal, and for continuous variables Student's t test or the Mann-Whitney U test were used, respectively. The correlation between continuous variables was assessed with Pearson correlation coefficient (r) for normal distribution, while Spearman's correlation coefficient was applied to non-normal distributions. Interobserver variability was estimated using the intraclass correlation coefficient. The concordance between the different methods used for assessing AR severity was evaluated with the kappa index. The DRF-VTI cut-off point was determined with the receiver operating characteristic curve, and sensitivity and specificity were estimated. A p valued <0.05 was considered as statistically significant. SPSS version 23.0 (Chicago, Illinois, USA) software package was used for statistical analysis.

Ethical considerations

The protocol was approved by the hospital Ethics Committee.

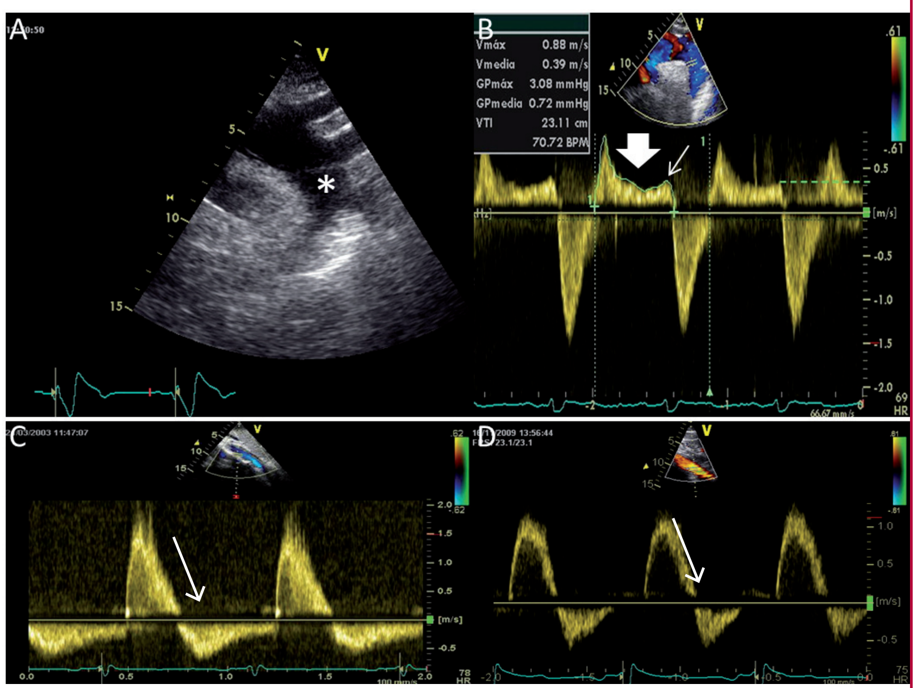

Fig. 1. A. Aortic isthmus (*asterisk*), where the sample volume for pulsed-wave Doppler is placed to obtain proximal descending thoracic aorta flow. **B.** Pulsed-wave Doppler in the descending aorta. The *broad arrow* points DRF-VTI and the *thin arrow* indicates ED-RFVm in severe AR. **C.** Pulsed-wave Doppler in the abdominal aorta in the case of severe AR where the presence of holodiastolic retrograde flow is observed (*arrow*). **D.** Pulsed-wave Doppler in the abdominal aorta in the case of non-severe AR where absence of holodiastolic reverse flow is observed (*arrow*).

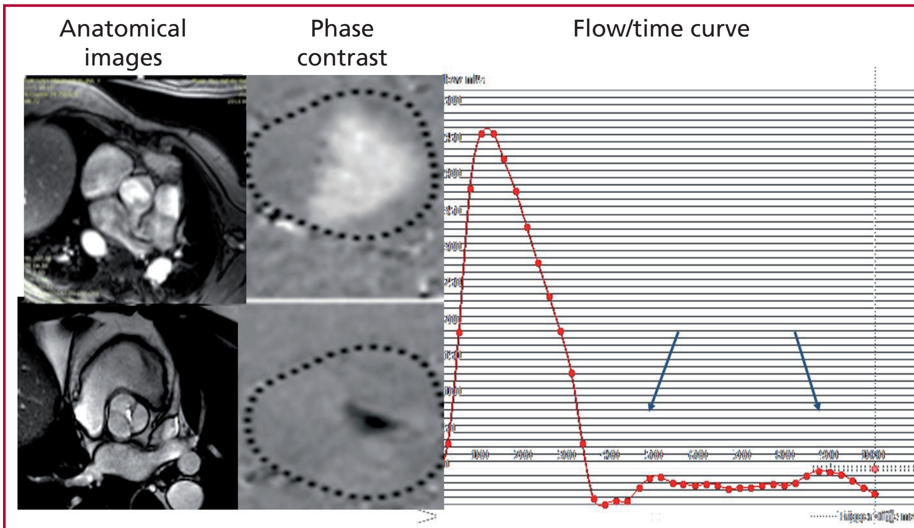

Fig. 2. Quantification of aortic regurgitation by cardiac magnetic resonance imaging. Left: Anatomical images obtained in the aortic root during systole (*top*) and diastole (*bottom*). Center: Area of interest traced for the phase contrast sequence also in systole and diastole, with anterograde (*white*) and retrograde (*black*) aortic flow visualization. Right: Flow/time curve with anterograde flow marked above the timeline (the x-axis of the graph) and retrograde flow below it to calculate the aortic regurgitant fraction.

RESULTS

Among the 40 patients included in the study one case was excluded due to poor Doppler flow signal in the descending aorta. Mean age was 59.6 (±17.5) years (range: 19-82): 7 patients (18%), between 20 and 40 years, another 7 (18%) between 40 and 60 years and 25 (64%) >60 years. Seven patients (18%) were hypertensive. The RF-CMR stratified AR severity into three groups: 13 patients with mild AR (32%), 15 patients with moderate AR (38%) and 11 patients with severe AR (30%). The etiology of AR assessed by echocardiography was degenerative or due to valvular sclerosis in 13 patients (33.3%), bicuspid valve in 12 patients (30.8%), sigmoid prolapse in 1 patient (2.5%), and idiopathic in 12 patients (30.8%). Among patients with bicuspid valve, the outflow jet was markedly eccentric in 10 (83%). Table 1 shows clinical demographic and echocardiographic data.

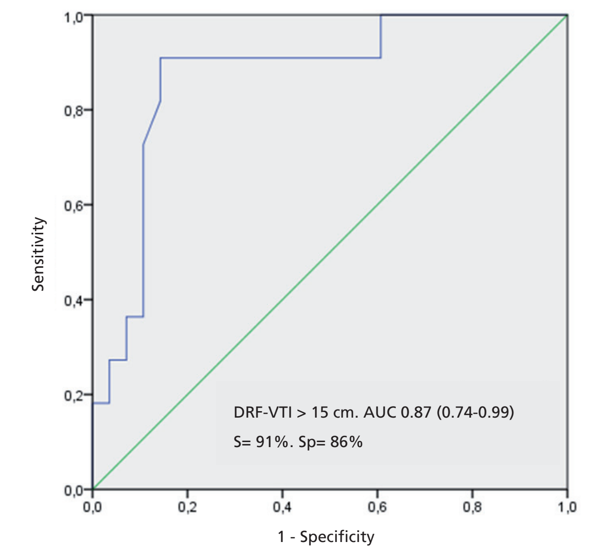

Fig. 3. ROC curve showing the diagnostic accuracy of diastolic retrograde flow velocity-time integral in the quantification of severe aortic regurgitation.

Quantitative assessment of aortic regurgitation by diastolic flow in the descending aorta

The comparison of thoracoabdominal aortic flow evaluation results by pulsed-wave Doppler with RF-CMR showed that DRF-VTI in the descending thoracic aorta had good accuracy in the quantification of AR severity. DRF-VTI presented an area under the curve of 0.87 (p<0.001) (Figure 3). The DRF-VTI >115 cm cutoff point showed high sensitivity (91%) and specificity (86%) to identify patients with severe AR. ED-RFVm >20 cm/s showed poorer accuracy to diagnose severe AR with 73% sensitivity and 64% specificity. Moreover, the DRF-VTI/SAF-VTI ratio was also unable to discriminate between severe and mild to moderate AR. The pandiastolic reverse flow in the abdominal aorta showed excellent specificity (100%) to detect severe AR, albeit with low sensitivity (50%).

DRF-VTI presented a slightly negative correlation with age and systolic blood pressure both in groups with severe and non-severe AR. This correlation suggests that this parameter may be partially influenced

Table 1. Population characteristics and echocardiographic data related with the severity of aortic regurgitation assessed by cardiac magnetic resonance imaging

Variable (n=39)	Mild-moderate AR (RF<30%) [n=28 (72%)]	Severe AR (RF>30%) [n=11 (28%)]	p
Demographic data			
Men, n (%)	19 (68)	10 (91)	0.228
Age, years	58.9±18,9	61.2±13.7	0.727
SBP, mmHg	133.4±15.9	134.5±15.2	0.833
DBP, mmHg	73.6±12.7	68.6±8.4	0.236
HR, beats/minute	72.2±5.7	72.9±4.7	0.7
Echocardiography			
Aortic root, mm	37±6	43±10	0.091
Ascending aorta, mm	40±8	42±12	0.514
Bicuspid valve, n (%)	7(25)	4(36)	0.694
Thoraco-abdominal Doppler parameters			
DRF-VTI, cm	12.6±4.4	19.2±5.6	0.001
ED-RFVm, cm/s	17.9±4.8	26.2±7.2	0.001
DRF/SAF VTI	0.81±0,.33	0.87±0.23	0.571
HDF-AbAo, n (%)	0	5(50)*	0.002

Values express mean±standard deviation or the number of patients and percentage [n (%)].
RF: Regurgitant fraction of aortic flow obtained by cardiac magnetic resonance imaging. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. HR: Heart rate. DRF-VTI: Diastolic retrograde flow velocity-time integral in the descending aorta. ED-RFVm: Maximum end-diastolic retrograde flow velocity in the descending aorta. DRF/SAF VTI: Diastolic retrograde flow/systolic anterograde flow velocity-time integral ratio in the descending thoracic aorta. HDF-AbAo: Holodiastolic flow in the abdominal aorta. * Unable to assess in 1 case.

by age and blood pressure (Table 2).

Quantitative assessment of aortic regurgitation with other Doppler methods

The JW/LVOT ratio and JW could not be adequately assessed in 6 patients (15.3%) and neither vena contracta in 11 patients (28.2%). The comparison of results between the different parameters of Doppler echocardiography in AR quantification evidenced good correlation of DRF-VTI with vena contracta, JW/LVOT and JW (Table 2). A good concordance was observed between these Doppler methods with AR quantification by CMR (Table 3).

Parameter reproducibility

Interobserver variability in the acquisition and consecutive measurement of Doppler variables in 15 patients showed an excellent intraclass correlation coefficient for JW (0.89, 95% CI 0.73-0.96) and DRF-VTI (0.85, 95% CI 0.70-0.99), acceptable for vena contracta (0.70, 95% CI 0.52-0.88) and poor for ED-RFVm (0.50; IC 95 % 0.11-0.89) and JW/LVOT (0.44, 95% CI 0.10-0.90). The concordance for the semiquantitative estimation of HDF-AbAo was acceptable with kappa=0.67; 95% CI 0.26-1.00.

DISCUSSION

The results of this study demonstrate that diastolic retrograde flow assessment in the proximal descending thoracic aorta is a good method to quantify AR. It is not only easy to obtain but has good accuracy and reproducibility in the diagnosis of severe AR. The main limitation of the method is that it is partly influenced by age and blood pressure.

Aortic regurgitation quantification is not always easy. Guidelines (3, 13, 14) recommend the implementation of qualitative, semi-quantitative and quantitative variables to assess AR. All Doppler parameters have limitations in AR quantification, so it is advisable to use more than one method to define its severity. Vena contracta has been established as one of the reference methods, but it is not always adequately visualized and its reproducibility is questionable. (15, 16) In our study it could not be properly defined in 28% of cases and the reproducibility was suboptimal. Moreover, although JW normalized by LVOT diameter has been one of the reference methods for AR quantification, (17) the results of this study confirm our previously published findings in which the absolute value of JW in the outflow tract allows for better results than normalized for LVOT diameter. (18) In this prior study, color jet area evaluated by apical approach was used as second method. Although this method is suitable in patients with stable chronic AR, the significant variability in results with different equipments precludes its use in clinical practice.

One of the limitations of vena contracta or JW in the outflow tract is that the regurgitant orifice is not always circular, especially in the very frequent eccentric jets found in AR secondary to bicuspid valve or aortic sigmoid prolapse. In the absence of a better temporal resolution with 3D echo, these measurements may condition a systematic underestimation of AR with eccentric jet. In this regard, the guidelines recommend quantifying the regurgitant orifice area with the PISA method, whenever possible. However, in clinical practice the adequate hemispherical shape is obtained in only 50% of cases, it needs a high level of expertise, significantly prolongs the study time and has high inter-acquisition variability. (19-21)

Quantification of AR severity by end-diastolic flow velocity in the descending aorta has been described in previous publications. (4, 22) However, it has not been replicated and has been seldom used in clinical practice. In the present study, ED-RFVm >20 cm/sec (3, 4) has shown poor diagnostic accuracy and poor reproducibility to detect severe AR. Conversely, DRF-VTI correlated better with CMR results and had good reproducibility; hence, it is a good method with different limitations than those influencing JW by color Doppler. In the present as in other studies, (2, 8, 9) HDF-AbAo was highly specific for severe AR, albeit with low sensitivity.

Few studies have evaluated the limitations of retrograde flow in the descending aorta related with variables that may affect the biomechanics of the aortic wall. One of our patients had severe dilation of the ascending aorta (80 mm); excluding this case, our results would have increased the diagnostic sensitivity of DRF-VTI (from 93% to 100%). In patients with dilated ascending aorta (>45 mm) we found a negative correlation (-0.45) between the diameter of the aortic root and DRF-VTI. This underestimation of VTI may be explained by the reduced elasticity of the aortic wall and therefore of flow recoil during diastole.

Table 2. Correlation between descending thoracic aorta Doppler parameters and other variables.

Correlations	DRF-VTI in the thoracic aorta[n=28 (72%)]	p
Age	-0.442	0.005
SBP	-0.281	0.084
DBP	-0.056	0.735
VC	0.667	<0.001
JW/LVOT	0.556	<0.001
JW	0.676	< 0.001
RF-CMR	0.568	<0.001

Data express Pearson's correlation and p value.
DRF-VTI: Diastolic retrograde flow velocity-time integral. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. VC: Vena contracta. JW/LVTO: Jet width/left ventricular outflow tract ratio. JW: Regurgitant jet width. RF-CMR: Aortic regurgitant fraction obtained by cardiac magnetic resonance imaging.

Limitations

The study has some limitations that must be consid-

	JW	JW/LVOT	VC [n=28 (72%)]	DRF-VTI	HDF-AbA
n (%)	37(94.9)	37(94.9)	28(71.8)	39(100)	30(76.9)
% Conc	89	78	92	77	83
Kappa	0.70	0.26	0.80	0.58	0.57

n (%): Number of patients (percentage) % Conc: Percent concordance or agreement between methods to diagnose severe aortic regurgitation. Kappa: Cohen's concordance coefficient.
JW: Regurgitant jet width. JW/LVTO: Jet width/left ventricular outflow tract ratio. VC: Vena contracta. DRF-VTI: Diastolic retrograde flow velocity-time integral. HDF-AbAo: Holodiastolic flow in the abdominal aorta.

Table 3. Concordance of Doppler methods with cardiac magnetic resonance in the diagnosis of severe aortic regurgitation

ered. The number of cases included is too small to analyze whether the DRF-VTI cut-off values are similar in different age groups, aortic dimensions or heart rate. For the same reason, the analysis has been restricted to the diagnosis of severe and non-severe lesions.

CONCLUSIONS

Diastolic retrograde flow assessment in the proximal descending thoracic aorta allows adequate quantification of AR. A VTI >15 cm is indicative of severe AR. The integration of this method's results to the measurement of vena contracta or JW in the LVOT allows an appropriate strategy to quantify regurgitation. However, more extensive studies are needed to confirm these results, especially in young populations or with aortic biomechanical disorders.

Conflicts of interest

None declared
(See authors' conflicts of interest forms in the website/ Supplementary material)

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