Quantification of Multiple Mitral Regurgitant Jets: An In Vitro Validation Study Comparing Two- and Three-Dimensional Proximal Isovelocity Surface Area Methods

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Background: The accuracy of the proximal isovelocity surface area (PISA) method for the quantification of mitral regurgitation (MR), in the case of multiple jets, is unknown. The aim of this study was to evaluate different two-dimensional (2D) and three-dimensional (3D) PISA methods using 3D color Doppler data sets.

Methods: Several regurgitant volumes (Rvols) were simulated using a pulsatile pump connected to a phantom equipped with single and double regurgitant orifices of different sizes and interspaces. A flowmeter served as the reference method. Transthoracic (TTE) and transoesophageal echocardiography (TEE) were used to acquire the 3D data sets. Offline, Rvols were calculated by 2D PISA methods based on hemispheric and hemicylindric assumptions and by 3D integrated PISA.

Results: A fusion of the PISA was observed in the setting of narrow-spaced regurgitant orifices; compared with flowmeter, Rvol was underestimated using the single hemispheric PISA model (TTE: Bland-Altman bias ± limit of agreement, −17.5 ± 8.9 mL; TEE: −15.9 ± 7.3 mL) and overestimated using the double hemispheric PISA model (TTE: +7.1 ± 14.6 mL; TEE: +10.4 ± 11.9 mL). The combined approach (hemisphere for single orifice, hemicylinder with two bases for nonfused PISAs, and hemicylinder with one base for fused PISAs) was more precise (TTE: −3.4 ± 6.3 mL; TEE: −1.9 ± 5.6 mL). Three-dimensional integrated PISA was the most accurate method to quantify Rvol (TTE: −2.1 ± 6.5 mL; TEE −3.2 ± 4.8 mL).

Conclusions: In the setting of double MR orifices, the 2D combined approach and integrated 3D PISA appear to be superior as compared with the conventional hemispheric method, thus providing tools for the challenging quantification of MR with multiple jets. (J Am Soc Echocardiogr 2017;30:511-21.)

Keywords: Mitral regurgitation quantification, Multiple regurgitant orifices, 2D color Doppler echocardiography, 3D color Doppler echocardiography, Proximal isovelocity surface area

The accurate assessment of mitral regurgitation (MR) directly influences the optimal timing for valve repair. The best prognosis after surgical treatment, for severe primary MR, is obtained at an asymptomatic stage without echocardiographic signs of left ventricular volume overload.[1-4] The current guidelines recommend an integrated approach for the evaluation of the MR severity including, as the most robust two-dimensional (2D) color Doppler echocardiography (CDE) parameters, the regurgitant volume (Rvol) and the effective regurgitant area (EROA) obtained by the proximal isovelocity surface area (PISA) method, combined with a measurement of the vena contracta (VC).[2,5-7] However, the optimal tools for the quantitative assessment of secondary MR remain to be defined, and MR evaluation is technically difficult in this context.[7-9] Using 2D CDE, the recommended methods are based on geometric assumption of a circular orifice, which in the context of complex anatomical MR orifices often leads to inaccuracy.[10-13] Moreover, there is to date no recommendation for quantifying MR with multiple jets,[5] and the scientific literature on this topic is sparse.[14,15] Since the development of three-dimensional (3D) CDE, several studies have shown the accuracy of direct PISA measurement in the assessment of MR.[10,11,16-18] Brugger *et al.* recently validated a customized 3D PISA software and showed that the 3D PISA technique permits a more accurate MR assessment than conventional 2D PISA with cardiac magnetic resonance imaging (CMR) as the reference method.[19] The aim of the present study was to evaluate different 2D and 3D PISA methods in the presence of multiple MR orifices, using 3D CDE data sets obtained by transthoracic (TTE) and transoesophageal (TEE) echocardiography, in vitro, against a flowmeter, in order to determine which simple geometric assumption could best estimate the PISA surface and to confirm the accuracy of the integrated 3D PISA method.

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Abbreviations

2D = Two-dimensional

3D = Three-dimensional

AROA = Anatomic regurgitant area

AUC = Area under the ROC curve

CDE = Color Doppler echocardiography

CMR = Cardiac magnetic resonance imaging

CW = Continuous wave

EROA = Effective regurgitant area

MR = Mitral regurgitation

mRvol = Mean Rvol

PISA = Proximal isovelocity surface area

ROC = Receiver operating characteristic

Rvol = Regurgitant volume

TEE = Transoesophageal echocardiography

TTE = Transthoracic echocardiography

VC = Vena contracta

VTI = Velocity time integral

METHODS

In Vitro Model

The in vitro model has been described elsewhere.[19] The phantom was 3D printed using the plastic material WaterShed (DSM, Elgin, IL; Figure 1). It consisted of a "ventricle" and an "atrium" submerged in a commercially available "Doppler test fluid" solution (model 707, ATS Laboratories Inc., Bridgeport, CT). A pulsatile pump (ViVitro Systems Inc., Victoria, British Columbia, Canada), mimicking the cardiac cycle, was connected to the "ventricle," using four connectors, to assure a symmetrical pressurization of the cavity (pump frequency at 60 beats per minute). Mitral valve models with one or two orifices, different interspaces between the orifices (10 or 20 mm), and different anatomic regurgitant orifice areas (AROA: 15, 30, 50, or 70 mm^2) were used (Figure 2). All orifices were circular. A flowmeter (transit-time ultrasonic flow probe, Transonic Systems, Inc., Ithaca, NY) was placed on the tube connecting the ventricle to the pump. A second flowmeter was placed on the "outflow tract" of the ventricle, where a safety valve prevented pressure overload in the test bench (Figure 1). The flow measured during one beat was then integrated in order to obtain the volume per beat. The difference between the volume passing through the entry tube and the volume passing through the exit tube gave the Rvol passing through the mitral valve, which served as reference method. Rvols acquired during five consecutive beats were averaged.

Echocardiographic Acquisition

TTE (X5-1 transducer, frequency range 1–5 MHz, harmonic imaging mode activated, imaging depth 9 cm, on "ventricular" side) and TEE (X7-2t transducer, frequency range 2–7 MHz, harmonic imaging mode deactivated, imaging depth 6 cm, on "atrial" side) echocardiography (iE33 Phillips Healthcare, Zurich, Switzerland) were performed after setting of the same stroke amplitudes. In order to render the in vitro model similar to the human heart, the distance between the TEE probe and the "mitral" valve was two thirds of the distance between the TTE probe and the valve. After optimization of the depth and narrowing of the image sectors on two perpendicular planes, electrocardiogram-triggered (six beats) 3D volumes focused on MR-PISA were acquired during three cardiac cycles. The peak velocity (*V*max) and velocity time integral (VTI) were obtained with continuous wave (CW) Doppler.

Quantification of MR

Color Doppler pyramidal volumes were analyzed on orthogonal planes using QLAB (Koninklijke Philips Electronics, Eindhoven, the Netherlands). Usually, a Nyquist velocity between 20 and 40 cm/sec (range, 11–51 cm/sec) permitted us to obtain an optimal shape of the PISA, and the visually biggest PISA was chosen at midsystole. Three groups were defined according to the presence of one or two MR orifices and according to the presence or absence of a fusion

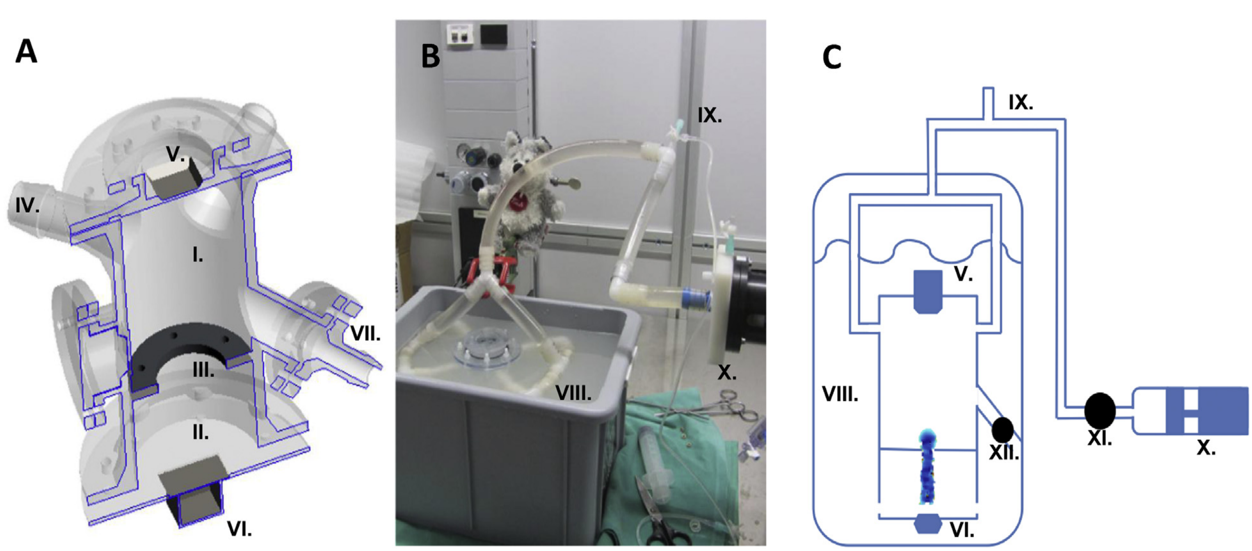

Figure 1 **(A)** Three-dimensional representation of long-axis section of the test bench. **(B)** Photograph of the experimental apparatus. **(C)** Schema of the whole in vitro model. I, left ventricle; II, left atria; III, annulus permitting the attachment of different mitral regurgitant orifices; IV, accesses for the piston pump; V, window for the TTE probe; VI, TEE probe holder; VII, outflow tract with unidirectional safety valve; VIII, bath containing a "Doppler test fluid"; IX, vacuum tap; X, piston pump; XI, main flowmeter between piston pump and "ventricle"; XII, auxiliary flowmeter on outflow tract.