International Journal of Cardiology 166 (2013) 688–695

Contents lists available at SciVerse ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

A novel fully automated method for mitral regurgitant orifice area quantification ☆,☆☆

Michela Moraldo [a,*], Corinna Bergamini [b], Anura S.N. Malaweera [a], Niti M. Dhutia [a], Punam A. Pabari [a], Keith Willson [a], Resham Baruah [a], Charlotte Manisty [a], Justin E. Davies [a], Xiao Y. Xu [c], Alun D. Hughes [a], Darrel P. Francis [a]

[a] International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College, 59-61 North Wharf Road, London W21LA, UK
[b] Department of Medicine, Division of Cardiology, Ospedale Civile Maggiore, University of Verona, Piazzale Stefani 1, 37126 Verona, Italy
[c] Department of Chemical Engineering, Imperial College London, SW72AZ, UK

ARTICLE INFO

Article history:
Received 17 October 2011
Accepted 27 November 2011
Available online 2 January 2012

Keywords:
Mitral valve regurgitation
Echocardiography
Blood flow velocity
Automated analysis

ABSTRACT

Background: Effective regurgitant orifice area (EROA) in mitral regurgitation (MR) is difficult to quantify. Clinically it is measured using the proximal isovelocity surface area (PISA) method, which is intrinsically not automatable, because it requires the operator to manually identify the mitral valve orifice. We introduce a new fully automated algorithm, ("AQURO"), which calculates EROA directly from echocardiographic colour M-mode data, without requiring operator input.

Methods: Multiple PISA measurements were compared to multiple AQURO measurements in twenty patients with MR. For PISA analysis, three mutually blinded observers measured EROA from the four stored video loops. For AQURO analysis, the software automatically processed the colour M-mode datasets and analysed the velocity field in the flow-convergence zone to extract EROA directly without any requirement for manual radius measurement.

Results: Reproducibility, measured by intraclass correlation (ICC), for PISA was 0.80, 0.83 and 0.83 (for 3 observers respectively). Reproducibility for AQURO was 0.97. Agreement between replicate measurements calculated using Bland-Altman standard deviation of difference (SDD) was 21,17 and 17mm^{2}for the three respective observers viewing independent video loops using PISA. Agreement between replicate measurements for AQURO was 6, 5 and 7mm^{2}for automated analysis of the three pairs of datasets.

Conclusions: By eliminating the need to identify the orifice location, AQURO avoids an important source of measurement variability. Compared with PISA, it also reduces the analysis time allowing analysis and averaging of data from significantly more beats, improving the consistency of EROA quantification.

AQURO, being fully automated, is a simple, effective enhancement for EROA quantification using standard echocardiographic equipment.

1. Introduction

Quantification of effective regurgitant orifice area (EROA) is an important aspect of evaluating mitral regurgitation (MR), but is difficult to achieve consistently in day-to-day clinical practice. The root cause of this difficulty is the intrinsic impossibility of automating the standard recommended technique, the proximal isovelocity surface area (PISA) method [1–3], because a human operator must measure the distance *r* between the flow convergence shell and the orifice. Both the selection of a suitable frame and judgement of the orifice position are required to measure *r*, preventing automatic measurement.

In busy clinical practice, there is often not time to measure multiple replicates [4]. Commonly few measurements are made; sometimes only one. Therefore variability (within and between observers) is high because of within-patient biological variability and (especially if only 1 beat is measured) it may be as large as the difference between patients.

Operators, noticing the random variability between measurements, and suffering the time-consuming process of acquisition and analysis, understandably respond by reducing the proportion of time invested in its measurement rather than increasing it. Thus, despite recommendations [5,6], most clinical echocardiographic studies for MR do not include quantitative assessment of EROA by conventional PISA.

Techniques have been proposed [7–11] based on variants of the conventional PISA formula, to quantify the mitral regurgitation *if* the

☆ The British Heart Foundation supports: DPF (FS/10/038/28268), MM (PG/08/115), PP (PG/08/114), KW (PG/07/065).
☆☆ No relationships with industry.
* Corresponding author at: ICCH building, 59-61 North Wharf Road, London W21LA, UK. Tel.:+44 7964729272; fax: +44 2075941706.
E-mail address: michela.moraldo@gmail.com (M. Moraldo).

0167-5273
doi:10.1016/j.ijcard.2011.11.104

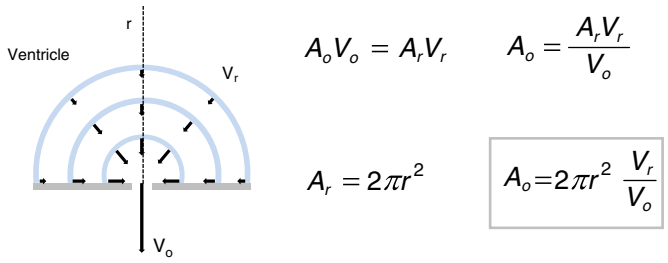

Fig. 1. Conventional PISA method equations to calculate EROA.

position of the orifice is known unambiguously. However, the exact location of the orifice is often difficult to identify. Can we quantify EROA without a human measuring the radius *r*?

In this study we explore a new technique, AQURO, which does not require manual measurement of *r* and can therefore be performed automatically, making it easy to obtain multiple independent measurements. It is based on an in-vitro study [12] arising from a simple rewriting of the conventional PISA mathematical equation. It uses a transformed slope of the velocity profile in the flow convergence zone to calculate orifice area without operator intervention. We compare AQURO with conventional PISA in subjects with known mitral regurgitation, in order to assess the validity of the technique for clinical application.

2. Method

2.1. Subjects

Twenty stable subjects with MR, identified from the echocardiography laboratory of Imperial College Healthcare NHS Trust, underwent transthoracic echocardiography. Inclusion criteria were the presence of mild, moderate or severe MR as judged by a conventional clinical echocardiogram and a recognisable PISA in the 4-chamber apical view. Patients were excluded if they had moderate or severe disease of tricuspid or pulmonary valves (3 patients), any aortic valve disease graded mild or higher, a prosthetic aortic valve (2) or atrial fibrillation (4). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a *priori* approval by the institution's human research committee and written informed consent was obtained.

2.2. Echocardiography

Echocardiographic data were acquired with the patient in the left lateral decubitus position using a Philips iE33 echocardiography system. Continuous wave (CW) Doppler, colour Doppler and colour M-mode images were acquired with simultaneous ECG, and stored digitally. Images were acquired in the apical view, using a 30°colour Doppler sector. CW Doppler velocity across the mitral valve was acquired co-axially with the regurgitant jet; the peak velocity was then measured.

2.3. Proximal isovelocity surface area method

Currently, conventional PISA is the recommended method for MR quantification [1]. The PISA method is based on the continuity principle that flow converges toward the regurgitant orifice approximately symmetrically from all directions (at least near the orifice). Progressively closer to the orifice, blood must accelerate because the surface area of the notional hemisphere through which it passes becomes progressively smaller, while flow rate (in ml/min), equalling velocity × area, is conserved because blood is incompressible. The downwards aliasing velocity is typically chosen for V_r (velocity at distance *r* from the orifice), because it can be read directly from the colour bar on the scanner. The radius *r* is the distance from the orifice to the onset of aliasing. Velocity at the orifice (V_o) is determined separately by continuous wave Doppler. The orifice area (A_o) is then calculated (Fig. 1).

The flow convergence region was visualized by colour Doppler velocity mapping. The aliasing velocity was kept at 31.9 cm/s, suitable for PISA. Quadruplicate loops of 2 beats each were acquired (acquisition time = 5 s). Three operators spent an average of 15 s measuring the radius for each conventional PISA EROA measurement, blinded to each others' findings. The operators were required to select the frame from which to take the measurements, as well as to choose the exact location of the orifice from where to measure *r*, and calculate EROA. The 4 EROAs took a total of ~80 s for acquisition and analysis.

2.4. AQURO method

It is not essential to measure the radius of a shell to calculate EROA with the flow convergence concept. The flow convergence pattern contains valuable information that could help calculate the EROA. The *rate of increase of velocity with distance* can replace the separate measurement of velocity and distance. Although this entails making more measurements, the whole method can be automated.

The origin of this method is a rewriting [12] of the conventional PISA mathematical equation so that, in the case of hemispheric isovelocity surfaces, the relationship between $\sqrt{V_o/V_r}$ and *r* is linear with a slope $\sqrt{2\pi/A_o}$, where V_o is the peak velocity at the regurgitant orifice (obtained from CW Doppler measurements), and V_r is the profile of velocity measurements obtained at distances *r* from the orifice. The EROA can be calculated directly from this slope (Fig. 2).

Just as for conventional PISA, the flow convergence region was imaged by colour Doppler flow mapping. The beam was positioned along the centreline of the regurgitant orifice. Flow velocities were acquired as colour M-Mode images. For each AQURO measurement we used an average of 20 s of data (to create a fair comparison with PISA). Typically this time was spent acquiring 10 still frames of 2–3 beats each. Quadruplicate AQURO measurements (a total of 40 still frames per patient) were acquired with 55 cm/s aliasing velocity, which is the optimal velocity for AQURO analysis.

Software then automatically calculated EROA beat-by-beat. The program first identifies regurgitant areas for each image (Fig. 3a). Because of the movement of the mitral valve though systole it then shears the image to allow averaging of flow velocities at equivalent distances across the sequential lines of the colour M-mode image (Fig. 3b). It then calculates the rate at which velocity declines with increasing distance from the orifice along each scan line.

The program converts colour pixel data to velocities using the colour scale bar, and then analyses all vertical scan lines of each beat. It plots $\sqrt{V_o/V_r}$ against *r* for series of time points (Fig. 3c). The analysis distance in the *r* direction is fixed at 1 cm (chosen after pilot data analysis). The shape of the relationship between $\sqrt{V_o/V_r}$ and *r* is expected to be linear near the valve. The program calculates the slopes of scan lines where this relationship is linear, rejecting scan lines where linearity is poor because they most likely reflect noisy instants or instants at the very beginning or end of systole; the number of scan lines actually used per beat was 28 ± 15. The software then calculates the average of the slopes of those lines, and hence the EROA, defined as $2\pi/slope^2$ (Fig. 3d). The entire process is repeated for each beat and for all 10 colour M-Mode images in a single AQURO measurement. The average of all these individual $2\pi/slope^2$ values is taken to be the single AQURO EROA from the 20 s of acquired data (typically 20–25 beats).

2.5. Statistical analysis

The intraclass correlation coefficient (ICC) was used to analyse the quadruplicate measurements (conventional PISA and AQURO). It quantifies whether measurements differ between patients because of true difference between patients or random measurement noise (Fig. 4). The ICC value lies between 0 (all noise, no signal) and 1 (all signal, no noise).

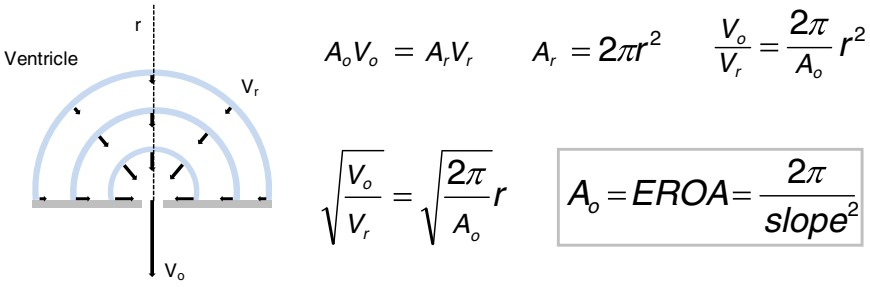

Fig. 2. AQURO method equations to calculate the EROA.