New insights in the disagreement of transthoracic mean pressure gradient measured by transthoracic echo-Doppler and cardiovascular magnetic resonance in patients with aortic stenosis

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Introduction: Valve effective orifice area (EOA) and transvalvular mean pressure gradient (MPG) are the most frequently used parameters to assess aortic stenosis (AS) severity. Current ACC/AHA and ESC guidelines suggest an EOA<1.0 cm² and a MPG>40 mmHg as main criteria to define a severe AS [1,2]. Transthoracic Doppler-echocardiography (TTE) is the primary method to assess and grade AS severity. Cardiovascular magnetic resonance (CMR) has emerged as an accurate alternative method to corroborate AS severity when uncertain or discordant results are obtained at TTE [3,4]. However, previous studies have shown that MPG measured by CMR systematically underestimates MPG obtained by TTE, mainly when transvalvular mean pressure gradient is greater than 40 mmHg [3-5]. It was showed that this underestimation might be due to flow turbulence generated downstream the severe AS, local signal loss, background noise and phase wrap [3,5,6]. From a fluid dynamic point-of-view, when the blood flows through the aortic valve it is spatially accelerated by the left ventricular outflow tract (LVOT) to the location of the vena cava, it is then decelerated and diverges within the ascending aorta (A Ao). This flow generates turbulence when the aortic valve is severely stenotic and an irreversible heat dissipation process. Several parameters (energy loss [EL], vorticity magnitude [ω], Reynolds number [Re] and Strouhal number [St]) can give an insight on the presence of turbulence generated downstream of a severe aortic stenosis and may be useful for identifying potential sources of discordance between MPG measured by MRI and TTE. EL represents the energy cost (in mmHg) between the LVOT and the A Ao after pressure recovery and ω can be used to estimate the dissipation effects within the flow. Reynolds number (Re) indicates the transition from laminar to turbulent flow and Strouhal number (St) represents the dimensionless stroke volume through the aortic valve. The objectives of this study were: 1) to identify the fluid dynamic factors associated with MPG underestimation by CMR, 2) to investigate the association of those factors in the AS severity assessment by CMR. Methods: Eight (8) healthy control subjects and 60 patients with mild to severe AS (60 cm² EOA<1.79 cm²) underwent TTE and CMR. TTE measurements were performed according to the ASE guidelines [7]. CMR study was performed with the use of a 1.5 T scanner (Philips Achieva, Philips Healthcare, Best, The Netherlands). A standard LV and aortic examination were performed. In addition, through-plane phase-contrast imaging was performed in the LVOT upstream from the aortic valve annulus plane and in the vena contracta plane (Ao) [3,4]. Velocity flow imaging parameters were classified as: TR/T of 4.60-4.92/2.7-3.05 ms, flip angle 15°, 24 phases, pixel spacing 1.32-2.07 mm, slice thickness 10 mm and acquisition matrix 256 x 208. For each patient, MPG_CM is determined by simplified Bernoulli formula and valve EOA was calculated using jet shear layer detection method [7] from velocity field at Ao plane. The same plane was used to compute energy loss (EL = V̇/4 Ȧ (ω²)), where V̇ is the transvalvular aortic peak jet velocity and Ȧ is the aortic cross sectional area of the ascending aorta. Systolic absolute mean ω was used to consider both clockwise and anti-clockwise effects. Furthermore non-dimensional hemodynamic parameters were computed: i) Reynolds number given by Re = ρAV̇/μ, where ρ=1055 kg/m³ is the blood density, μ =4.6 cp is blood dynamic viscosity and D is the LVOT diameter and ii) Strouhal number given by St=(Ḋ V̇/2πf_0 (f_0 being the frame rate)). To assess the discordance between MPG obtained by CMR and by TTE, the MPG relative error (in %) was computed as follows: MPG_误差 = |MPG_CM - MPG_TTE|/MPG_TTE×100. Absolute error differences (|ΔMPG|) were classified in three groups: group A (|ΔMPG|<10 mmHg), group B (10 mmHg≤|ΔMPG|<20 mmHg) and group C (|ΔMPG|≥20 mmHg). Results: Sixty patients with mild to severe AS (65% men, age 64±15 years) and eight healthy subjects (75% men, age 34±8 years) were included in this study. Valve morphology was bicuspid in 27% of AS patients. Age, MPG, EOA, EL, ω and St were significantly higher (p<0.001) in AS patients compared with healthy control subjects. When comparing AS severity groups with healthy control subjects a significant difference (p<0.001) was found for MPG, EOA, EL, ω, peak Re and St. MPG_CM underestimated MPG_TTE, this underestimation increased with AS severity (Figure 1). However, MPG_CM and EOA_CM correlated well with TTE (r = 0.73, p<0.001, Figure 2). A Bland-Altman analysis showed a bias=-6.5 mmHg with limits of agreement from -18.3 to 5.2 (Figure 3). When considering |ΔMPG| groups, group A had 78% (n=53) of subjects, group B had 21% (n=14) of subjects and group C had 1% (n=1) of subjects. In the univariate analysis peak Re number (r=-0.37, p=0.002), ω (r=-0.36, p=0.003), EL (r=-0.33, p=0.006) and St (r=-0.19, p=0.01) were significantly related to MPG_误差 (Table 1). In the multivariate analysis, adjusted to EOA_CM and age, ω, St and EL were the factors independently associated with higher MPG_误差 (Table 1). Discussion and Conclusion: The main findings of this study are: 1) The identification of the fluid dynamic factors of MPG underestimation by CMR as compared to TTE; 2) The characterization of new fluid dynamic insights for the aortic valve hemodynamics with CMR. MPG_TTE underestimation by CMR is typically related to local signal loss, background noise, phase wrap and turbulence. However, as it was demonstrated with cardiac catheterization that other hemodynamic parameters affect MPG measurements, mainly Re [8], EL [9] and pressure recovery [8-10]. Those explanations should also apply to CMR given the theoretical background of the measurements. In this study, dimensionless hemodynamic parameters were used in the context of AS severity. Its role was important in the association analysis of MPG_误差. Inconsistencies on EOA and MPG measurements may lead to incorrect therapeutic/surgical decisions. It is important to avoid them and define consistent cut-offs (EOA and pressure gradients) valid on all imaging techniques used to assess AS severity. A recent substudy of SEAS cohort [11] showed the potential usefulness of EL for AS severity assessment, highlighting the importance of this parameter underexplored in CMR. A more accurate evaluation of EL may be performed using 4D flow time-resolved velocity measurements. Furthermore, vorticity magnitude may provide useful additional information of aortic valve hemodynamics and AS severity. In conclusion, this study showed that fluid mechanic factors are related to MPG discrepancies between CMR and TTE. Further studies are needed to confirm the potential usefulness of CMR-derived fluid mechanic parameters in cardiovascular diseases and valve function.