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

Julio Garcia[1], Romain Capoulade[2], Lyes Kadem[3], Eric Larose[2], and Philippe Pibarot[2]

[1]*Radiology, Northwestern University, Chicago, Illinois, United States,* [2]*Laval University, Quebec, Quebec, Canada,* [3]*Concordia University, Montreal, Quebec, Canada*

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 showed that MPG measured by CMR systematically underestimates MPG obtained by TTE, mainly when transvalvular velocity greater than 4 m/s [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 from the left ventricular outflow tract (LVOT) to the location of the vena contracta, it is then decelerated and diverges within the ascending aorta (AAo). 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 and magnitude 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 energetic cost (in mmHg) between the LVOT and the AAo after pressure recovery and ω can be used to estimate the dissipation effects within the flow. Reynolds number (Re) indicates the transition from laminar flow 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 (0.60 cm^2≤EOA≤1.79 cm^2) underwent TTE and CMR. TTE measurements were performed according to the ASE guidelines [2]. CMR study was performed after TTE study 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 position (Ao) [3, 4]. Velocity flow imaging parameters consisted of: TR/TE of 4.60-4.92/2.76-3.05 ms, flip angle 15°, 24 phases, pixel spacing 1.32–2.07 mm, slice thickness 10 mm and acquisition matrix of 256 x 208. For each patient, MGP_{CMR} was 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 ($EL=V_{peak}^2\times[1-EOA_{CMR}/A_{AAo}]^2$), where V_{peak}^2 is the transvalvular aortic peak jet velocity and A_{AAo} is 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 $Re=\rho\times V_{average}\times D/\mu$, where ρ=1055 kg/m^3 is the blood density, μ =4.6 cp is blood dynamic viscosity and D is the LVOT diameter and ii) Strouhal number given by $St=(D_{average}/2)\times(f/[V_{peak}-V_{average}])$. To assess the discordance between MPG obtained by CMR and by TTE, the MPG relative error (in %) was computed as follows: MPG_{error} = ($[MPG_{TTE}-MPG_{CMR}]/MPG_{TTE})\times100$. 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_{CMR} underestimated MPG_{TTE}, this underestimation increased with AS severity (Figure 1). However, MPG_{TTE} and MPG_{CMR} correlated well (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=0.1) were significantly related to MPG_{error} (Table 1). In the multivariate analysis, adjusted to EOA_{CMR} and age, ω, St and EL were the factors independently associated with higher MPG_{error} (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_{error}. 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 unexplored 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 and highlighted their association with AS severity. Larger studies are needed to confirm the potential usefulness of CMR-derived fluid mechanic parameters in cardiovascular diseases and valve function.

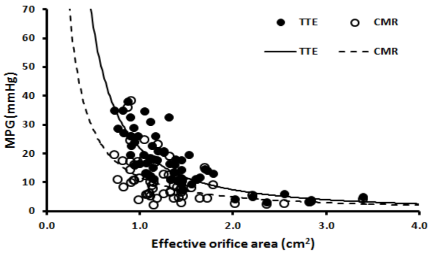

FIGURE 1: Effective orifice area and mean transvalvular pressure gradient. The aortic valve effective orifice area and mean transvalvular pressure gradient (MPG) plot using measurements from transthoracic echo-Doppler (TTE) and cardiovascular magnetic resonance (CMR).

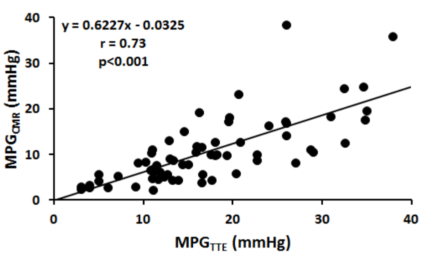

FIGURE 2: Regression fit of the transvalvular mean pressure gradient (MPG) measured by transthoracic echo-Doppler (TTE) and cardiovascular magnetic resonance (CMR).

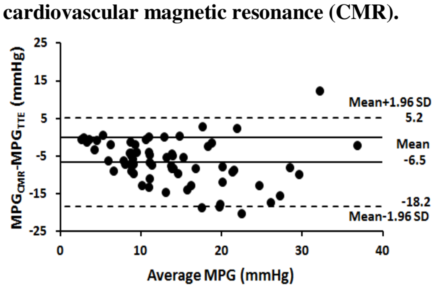

FIGURE 3: Bland-Altman agreement plot for both transthoracic echo-Doppler (TTE) and cardiovascular magnetic resonance (CMR) transvalvular mean pressure gradients (MPG).

TABLE 1. Univariate and multivariate determinants of transvalvular mean pressure gradient relative error.

Men transvalvular pressure gradient relative error = MRI-TTE/TTE (%)	Univariate Analysis			Multivariate Model		
	β coeff±SE	r	p-value	β coeff±SE	r	p-value
Age (years)	0.31 ± 0.197	0.193	0.123	-	-	0.82
Effective orifice area (cm^2)*	-5.34 ± 4.662	-0.143	0.256	-	-	0.23
Energy loss (mmHg)*	-1.06 ± 0.373	-0.337	0.006	-1.15 ± 0.36	-0.367	0.003
Peak Re number*	-0.01 ± 0.004	-0.373	0.002	-0.01± 0.003	-0.17	0.104
Strouhal number*	-1266 ± 809	-0.193	0.1	-3055 ± 920	-0.467	0.002
Mean systolic vorticity (1/s)*	-0.26 ± 0.086	-0.365	0.003	-0.37 ± 0.088	-0.501	<0.001

Legend: *Parameters computed from CMR. Multivariate model includes only variables that were significantly (p<0.1) associated with transvalvular mean pressure gradient relative error on univariate analysis. β coeff: regression coefficient β; SE: standard error.

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