Effective Orifice Area during Exercise in Bileaflet Mechanical Valve Prostheses

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Background: The aims of this study were to investigate the evolution of the transprosthetic pressure gradient and effective orifice area (EOA) during dynamic bicycle exercise in bileaflet mechanical heart valves and to explore the relationship with exercise capacity.

Methods: Patients with bileaflet aortic valve replacement (n = 23) and mitral valve replacement (MVR; n = 16) prospectively underwent symptom-limited supine bicycle exercise testing with Doppler echocardiography and respiratory gas analysis. Transprosthetic flow rate, peak and mean transprosthetic gradient, EOA, and systolic pulmonary artery pressure were assessed at different stages of exercise.

Results: EOA at rest, midexercise, and peak exercise was 1.66 ± 0.23, 1.56 ± 0.30, and 1.61 ± 0.28 cm^2, respectively (P = .004), in aortic valve replacement patients and 1.40 ± 0.21, 1.46 ± 0.27, and 1.48 ± 0.25 cm^2, respectively (P = .160), in MVR patients. During exercise, the mean transprosthetic gradient and the square of transprosthetic flow rate were strongly correlated (r = 0.65 [P < .001] and r = 0.84 [P < .001] for aortic valve replacement and MVR, respectively), conforming to fundamental hydraulic principles for fixed orifices. Indexed EOA at rest was correlated with exercise capacity in MVR patients only (Spearman ρ = 0.68, P = .004). In the latter group, systolic pulmonary artery pressures during exercise were strongly correlated with the peak transmitral gradient (ρ = 0.72, P < .001).

Conclusion: In bileaflet mechanical valve prostheses, there is no clinically relevant increase in EOA during dynamic exercise. Transprosthetic gradients during exercise closely adhere to the fundamental pressure-flow relationship. Indexed EOA at rest is a strong predictor of exercise capacity in MVR patients. This should be taken into account in therapeutic decision making and prosthesis selection in young and dynamic patients. (J Am Soc Echocardiogr 2016;■:■-■.)

Keywords: Mitral valve replacement, Aortic valve replacement, Mechanical valve prostheses, Exercise echocardiography, Hemodynamics

Mechanical valve prostheses are the prostheses of choice for aortic valve replacement (AVR) and mitral valve replacement (MVR) in young patients (<60 and <65 years of age for AVR and MVR, respectively) if long-term anticoagulation is not contraindicated.[1,2] In this young and dynamic population, optimal performance of the prosthesis is required not only at rest but during physical activities as well.[3] Knowledge of the hemodynamic behavior of these mechanical valve prostheses during dynamic exercise, with increasing heart rate and flow, therefore remains of timely importance. Although the geometric orifice area of a mechanical prosthesis is fixed, the orifice area that is effectively used by the "contracting" flow through the orifice (effective orifice area [EOA]) exerts large interindividual variation for the same prosthesis size[4,5] and is significantly lower than the geometric area for aortic and mitral valve prostheses.[6,7] It remains unclear whether EOA during dynamic exercise is fixed as well or whether changes in flow contraction during exercise might occur, causing EOA to increase, thereby attenuating the rise in transprosthetic pressure gradients at increasing flow rate. Pulsatile in vitro assessment of mechanical valves in aortic position showed no change in EOA with increasing stroke volume.[8] However, in vivo studies measuring EOA before and after dynamic exercise,[9,10] during dobutamine infusion,[11,12] and during rapid ventricular pacing[13] have rendered conflicting results in both mitral and aortic positions.

The aim of this study was to investigate in vivo the stepwise evolution of the transprosthetic pressure gradient and EOA during dynamic

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Abbreviations

AVR = Aortic valve replacement

EOA = Effective orifice area

LV = Left ventricular

LVOT = Left ventricular outflow tract

MVR = Mitral valve replacement

RER = Respiratory exchange rate

Vo_2max = Maximal oxygen uptake

bicycle exercise in bileaflet mechanical heart valves, in both mitral and aortic valve positions. In addition, the impact of EOA at rest and during exercise on the respective exercise capacity was evaluated.

METHODS

Study Design and Population

Consecutive patients who underwent mechanical bileaflet AVR at a single tertiary care center (Ziekenhuis Oost-Limburg, Genk, Belgium) between January 2008 and August 2014 ($n = 42$) were screened for participation in the study protocol. In addition, all patients with St. Jude Medical (St. Paul, MN) bileaflet mitral prostheses who were in active outpatient follow-up at our center on October 1, 2012 ($n = 34$), were screened for participation. Eligible patients were invited to undergo a prospectively organized study visit comprising resting transthoracic echocardiography followed by semisupine bicycle exercise transthoracic echocardiography with cardiopulmonary exercise testing. Exclusion criteria were (1) inability to undergo a bicycle exercise test at our center, (2) more than mild aortic regurgitation (vena contracta width > 3 mm), and (3) subaortic stenosis or left ventricular (LV) outflow tract (LVOT) obstruction impeding correct Doppler assessment of LV stroke volume. The study complied with the Declaration of Helsinki and was approved by the local ethics committee, and written informed consent was obtained from all participating patients.

Transthoracic Echocardiography

Resting and exercise echocardiography was performed using a commercially available system (iE33; Philips Medical Systems, Andover, MA). Standard two-dimensional and Doppler echocardiographic images were acquired in the left lateral decubitus position using a phased-array transducer in the parasternal and apical views and stored digitally for offline analysis using CardioView software (TomTec Imaging Systems, Unterschleissheim, Germany). Each echocardiographic measurement was averaged from three consecutive cardiac cycles for patients in sinus rhythm and from five consecutive cycles in those with atrial fibrillation. LVOT dimension was measured from a zoomed parasternal long-axis acquisition. LV volumes and ejection fraction were calculated using the modified Simpson biplane method for apical windows.[14] LV stroke volume was measured using pulsed-wave Doppler in the LVOT; cardiac output was calculated as the product of heart rate and LV stroke volume. Color Doppler flow images were obtained in the parasternal and apical views to assess valve regurgitation. Peak and mean transprosthetic gradients were calculated using the modified Bernoulli equation on the continuous-wave transprosthetic Doppler signal. Importantly, care was taken to acquire the continuous-wave Doppler velocities through the side orifices of the bileaflet prosthesis whenever possible and not through the central orifice, because of the higher pressure recovery phenomenon.[15] Prosthetic valve EOA was measured using the continuity equation,[16] that is, dividing LV stroke volume by the velocity-time integral of the transprosthetic flow. Because patients with more than mild aortic regurgitation were excluded, mean transmitral flow rate was estimated by dividing the LV stroke volume by the diastolic filling time measured on Doppler echocardiography. Mean transaortic flow rate was calculated by dividing LV stroke volume by the systolic ejection time. Systolic pulmonary artery pressure was calculated using the modified Bernoulli equation on the transtricuspid continuous-wave Doppler signal, while adding an estimate of right atrial pressure.[17]

Exercise Testing

All participating patients underwent symptom-limited graded bicycle tests in semisupine position on a tilting exercise table. Workload was initiated at 20 W, with increments of 20 W every 3 min. At each stage of exercise, Doppler echocardiography assessing LV stroke volume, peak and mean transprosthetic gradient, EOA, transprosthetic flow rate, and systolic pulmonary artery pressure was performed. In addition, blood pressure, 12-lead electrocardiogram, and ergospirometry (JAEGER, Würzburg, Germany) was measured throughout the exercise test.

Transprosthetic Pressure-Flow Relationship

Doppler echocardiography measurements at rest and during exercise were analyzed with respect to fundamental hydraulic notions derived from the Bernoulli equation and the principle of continuity.[18,19] Briefly, the pressure gradient, ΔP, across an effective stenotic orifice, EOA, is a function of the flow rate, F, squared,[18,20] as displayed in equation 1.

$$\Delta P = \left(\frac{F}{50.4 \times EOA}\right)^2. \qquad (1)$$

The numeric constant 50.4 in this equation results from the conversion of pressure metric units from dynes per square centimeter to millimeters of mercury and includes blood density.[18]

Statistical Analysis

Continuous variables are expressed as mean ± SD if normally distributed and otherwise as median (interquartile range). Normality was assessed using the Shapiro-Wilk statistic. Repeated-measures analysis of variance was used to compare Doppler hemodynamics at rest, midexercise, and peak exercise. Linear regression models were used to assess the relationship between the mean transprosthetic gradient and the square of transprosthetic flow rate. The Spearman ρ statistic was used to assess potential correlations between indexed EOA and exercise capacity in AVR and MVR patients. Statistical significance was set at a two-tailed probability of $P < .05$. All statistical analyses were performed using SPSS release 20.0 (SPSS, Chicago, IL).

RESULTS

Study Population

Of the 42 screened AVR patients, a total of 24 patients were able to participate. Reasons for exclusion of 18 patients were refusal to participate, loss to follow-up, or distance to the hospital. In addition, one participating patient was excluded because of LVOT obstruction with significant flow acceleration during the exercise test. Of the 34 screened MVR patients, 16 were eligible for study participation. Reasons for exclusion were aortic regurgitation ($n = 2$), refusal to