Basic Science and Experimental Studies

Effects of an Interatrial Shunt on Rest and Exercise Hemodynamics: Results of a Computer Simulation in Heart Failure

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ABSTRACT

Background: A treatment based on an interatrial shunt device has been proposed for counteracting elevated pulmonary capillary wedge pressure (PCWP) in patients with heart failure and mildly reduced or preserved ejection fraction (HFpEF). We tested the theoretical hemodynamic effects of this approach with the use of a previously validated cardiovascular simulation.

Methods and Results: Rest and exercise hemodynamics data from 2 previous independent studies of patients with HFpEF were simulated. The theoretical effects of a shunt between the right and left atria (diameter up to 12 mm) were determined. The interatrial shunt lowered PCWP by ~3 mm Hg under simulated resting conditions (from 10 to 7 mm Hg) and by ~11 mm Hg under simulated peak exercise conditions (from 28 to 17 mm Hg). Left ventricular cardiac output decreased ~0.5 L/min at rest and ~1.3 L/min at peak exercise, with corresponding increases in right ventricular cardiac output. However, because of the reductions in PCWP, right atrial and pulmonary artery pressures did not increase. A majority of these effects were achieved with a shunt diameter of 8−9 mm. The direction of flow though the shunt was left to right in all of the conditions tested.

Conclusions: The interatrial shunt reduced left-sided cardiac output with a marked reduction in PCWP. This approach may reduce the propensity for heart failure exacerbations and allow patients to exercise longer, thus attaining higher heart rates and cardiac outputs with the shunt compared with no shunt. These results support clinical investigation of this approach and point out key factors necessary to evaluate its safety and hemodynamic effectiveness. (*J Cardiac Fail 2014;20:212−221*)

Key Words: Left atrial pressure, heart failure, diastolic dysfunction, heart failure with preserved ejection fraction, interatrial shunt, computer simulation.

Development of treatments for patients with heart failure and preserved ejection fraction (HFpEF) or mildly reduced ejection fraction is among the highest priority in cardiology today. These patients represent >50% of all patients with heart failure (HF) and experience rates of morbidity and mortality that are similar to patients with HF and reduced ejection fraction.[1−3] To date, there are no therapies that are proven to be effective in these patients. This could be

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Manuscript received June 25, 2013; revised manuscript received November 20, 2013; revised manuscript accepted January 3, 2014.

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Funding: Supported in part by DC Devices, Boston, Massachusetts, and a program grant (D.M.K.) from the National Health and Medical Research Council of Australia.

See page 219 for disclosure information.

1071-9164/$ - see front matter

http://dx.doi.org/10.1016/j.cardfail.2014.01.005

because these patients as a whole may have different underlying etiologies and varied numbers and severity of comorbid conditions, so that different therapies may be needed to address different patient subgroups. However, regardless of etiology or comorbid conditions, an overarching pathophysiologic mechanism is elevated pulmonary capillary pressure during HF exacerbations and during exertion and increased left atrial size. Accordingly, an approach that directly addresses this hemodynamic abnormality may be therapeutic across disparate patient subgroups.

Detailed characterization of rest and exercise hemodynamics in patients with HF has been performed by several groups[4,5] and most recently in patients with HFpEF.[6–11] Hemodynamic factors that have been suggested to contribute to exercise intolerance in HFpEF include blunted chronotropic response, inability to increase stroke volume, altered oxygen extraction by the periphery and dramatic increases of pulmonary capillary wedge pressure (PCWP) out of proportion to increases of right atrial pressure. To a certain extent, some of these abnormalities are indicative of deconditioning and may be overcome by exercise training[12–14]; however, such improvements do not appear to be linked to improvements in ventricular or vascular properties.[15,16] Despite somewhat different conclusions arrived at in these studies, one common finding is the marked exercise-induced increase of left atrial and pulmonary capillary pressures in HFpEF.

It has recently been proposed that creation of a small permanent opening in the interatrial septum to allow left-to-right shunting of blood could provide a means of limiting left atrial pressure rises, thus potentially improving exercise tolerance and protecting a patient from episodes of acute pulmonary edema. Such a shunt might be especially effective when the pressure gradient between left and right atria is increased, as occurs during exercise in HFpEF patients.

Preclinical evaluation of the hemodynamic effects of such a device is difficult, especially for the case of severe HF with relatively well preserved ejection fraction, because there is no accepted large animal model and, in addition, invasive exercise studies are difficult to conduct in large animal models. To circumvent this problem, we used a computer model to simulate rest and exercise hemodynamics typically encountered in HF. This model has been used before to prospectively predict and/or retrospectively explain different aspects of HF pathophysiology and the effects of treatment.[17–21] For the present simulation, we used hemodynamic data from two published studies of patients with HFpEF[9,10] and then simulated the impact of the presence of an interatrial shunt. The results show the potential benefits, suggest potentially important aspects of patient selection, and point out potential limitations of this approach.

Methods

Patient Population

Rest and exercise hemodynamic data used in the present simulation-based study were previously published by Maeder et al[4] and Borlaug et al.[5] Borlaug et al[5] included 32 patients with EF ≥50% evaluated for effort intolerance and normal resting hemodynamics and B-type natriuretic peptide (BNP), and without significant coronary artery disease, valvular heart disease, hypertrophic or infiltrative cardiomyopathy, constrictive pericarditis, or vascular disease. In that study, patients were also included if PCWP increased to ≥25 mm Hg during exercise. Use of this exercise-PCWP criterion identifies patients who have an unambiguous hemodynamic abnormality contributing to their symptomotology, at least during exercise. Maeder et al studied 14 patients who had EF ≥50%, New York Heart Association functional class II or III signs, and symptoms and objective evidence of impaired exercise capacity but no evidence of myocardial ischemia. To be consistent with the selection criteria of Borlaug et al,[9] we also selected data from 7 of these patients in whom PCWP increased to ≥25 mm Hg during exercise.

Participants in both of these studies underwent detailed echocardiographic and invasive hemodynamic evaluation at rest and during exercise. Right heart catheterization monitoring was performed to assess intracardiac pressures and cardiac output by the thermodilution or direct Fick method. Exercise was performed on a cycle ergometer in the supine position.

Hemodynamic Simulation

We used a previously developed real-time model of the cardiovascular system to simulate hemodynamics at rest and during exercise.[17–21] The equations underlying the model have been provided in detail previously,[17,18] and an overview is provided in Appendix 1. In brief, contractile properties of each heart chamber was modeled as a time-varying elastance, which has been validated for both the ventricles[22] and the atria.[23–29] The systemic and pulmonary vascular beds were modeled by series of resistance and capacitance elements. Parameter values of the model were adjusted by a custom-designed algorithm to fit the average hemodynamic conditions at rest and exercise as defined by the clinical studies noted above.[4,5] Parameters that were varied included right and left ventricular (RV and LV, respectively) chamber systolic properties, vascular resistance, vascular compliance for the systemic vascular beds, and stressed blood volume (which correlates with overall fluid status of the patient). The model was then modified to simulate the presence of a shunt between the right and left atria according to the equation governing instantaneous flow through an orifice as detailed in Appendix 1. Flow = $K \cdot Area \cdot \Delta P$, where Area (in cm^2), ΔP is the pressure gradient across the orifice (in mm Hg), and K = 2.66. The effects of varying shunt sizes up to 12 mm in diameter were also modeled.

Aortic, pulmonary arterial, ventricular, and atrial pressure waveforms, as well as pressure-volume (PV) loops of each of the 4 chambers were constructed for baseline and exercise conditions. The pressure waveforms and pressure-volume loops were also assessed with and without the interatrial shunt.

Results

Although there are limited data available for detailed validation specifically of the atrial simulation aspects of the model used, it is striking that rather detailed aspects of the atrial pressure and volume curves and the impact of acute opening/closing of an atrial septal defect (ASD) can be simulated. For example, see the tracings presented in Figure 1. The left atrial pressure tracing from a patient