



Hydrodynamic Characteristics of Bovine Pericardial and Porcine Valves Using a Mock Circulatory System Mimicking the Aortic and Pulmonary Positions

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Purpose: Aortic prostheses are used in pulmonary positions due to structural similarities between the pulmonary and aortic valves. However, there are no available studies that have comprehensively evaluated the mechanism of bioprosthetic aortic valves under pulmonary conditions.

Materials and Methods: Using a mock circulatory system, we evaluated the hydrodynamic characteristics of bovine pericardial and porcine valves. Geometric orifice area, regurgitant and leakage volume, regurgitant fraction, peak pressure gradient, and forward flow volume were evaluated in different pulmonary pressure conditions (from 15/5 mm Hg to 75/35 mm Hg) and normal aortic pressure (110/80 mm Hg).

Results: Bovine pericardial valves were associated with larger opening area (0.93±0.01 vs. 1.70±0.01 for 23-mm valve; 0.99±0.01 vs. 1.75±0.01 for 25-mm valve; 1.58±0.01 vs. 2.25±0.02 for 27-mm valve; all $p<0.01$) and forward flow volume (42.27±0.05 vs. 64.79±0.14 for 23-mm valve; 46.41±0.06 vs. 64.28±0.18 for 25-mm valve; 72.64±0.17 vs. 73.25±0.07 for 27-mm valve; all $p<0.01$). Porcine valves were associated with incomplete opening, smaller opening area, and lower regurgitant fraction. Bovine pericardial valves demonstrated lower peak pressure gradients (15.75±0.14 vs. 12.57±0.47 for 23-mm valve; 14.85±0.05 vs. 12.87±0.28 for 25-mm valve; 15.72±0.32 vs. 7.91±0.03 for 27-mm valve).

Conclusion: Bovine pericardial and porcine bioprosthetic valves has different hydrodynamic characteristics under various pulmonary pressure conditions.

Key Words: Prosthesis, heart valve, pulmonary valve, bioprostheses

INTRODUCTION

Long-term pulmonary valve insufficiency leading to the development of right ventricular dilatation after a right ventricular outflow tract reconstruction is a common phenomenon. Pros-

Received: June 16, 2025 **Revised:** October 14, 2025

Accepted: November 4, 2025 **Published online:** February 6, 2026

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•The authors have no potential conflicts of interest to disclose.

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thetic valves were primarily designed for the aortic valve position; however, the structural similarities between the pulmonary and aortic valves allow the prosthetic valves, developed initially for the aortic valve position, to be used in the pulmonary position. Conversely, several reports have demonstrated different clinical outcomes of bioprosthetic valves when used in the aortic and pulmonary positions. Gao, et al.¹ reported better midterm durability of the pericardial valve and a lower rate of structural valve degeneration than that of the porcine valve in the aortic position. Dalmau, et al.² reported that the bovine pericardial valve showed hemodynamic superiority in the transvalvular pressure gradient compared with the porcine valve in the aortic position after 5 years. However, reports on the durability of bioprosthetic valves in the pulmonary position demonstrated disparate results. Kwak, et al.³ reported that the porcine valve

had long-term advantages in reducing the reoperation rate and prosthetic valve dysfunction in the pulmonary position. Yuen, et al.⁴ reported comparable midterm outcomes of the bioprosthetic valves regarding the rate of reintervention. The contrasting reports could be a result of the different valve degeneration modes.

Grunkemeier, et al.⁵ identified different causes of valve dysfunction in pericardial and porcine valves. The pericardial valve developed steno-insufficiency due to leaflet calcification and fibrosis, whereas the porcine valve mainly showed insufficiency resulting from leaflet tearing. Similarly, Persson, et al.⁶ reported different behaviors of porcine and bovine bioprosthetic valves at the aortic valve position. The porcine valve had a higher tendency for valve incompetence due to cusp tearing, whereas the bovine valve had a higher rate of valve stenosis. Several mechanisms have been identified in the pathogenesis of bioprosthetic valve degeneration; chemical, biological, immunological, and mechanical processes contribute to valve calcification and degeneration.⁷ Although the mechanisms of valve failure at the aortic and pulmonary positions remain unclear, the differing hydrodynamic characteristics of the arterial systems are a potential cause; however, no study has extensively examined this phenomenon.

Mock circulatory systems (MCS) are used to gather hydrodynamic data *in vitro* to develop a new heart valve. They are composed of tubing flow channels, compliance chambers, and a pump that mimics the arterial or venous circulatory system. Circulatory models simulate pressure/resistance changes in a physical system with flow and pressure monitoring. Real-time monitoring of flow in the loop provides hands-on feedback during manipulations of the cardiovascular system (without the need for animal subjects), allowing investigation of the hemodynamics of various cardiovascular devices such as stents, artificial pumps, or heart valves.^{8,9} The *in vitro* hydrodynamic performance obtained by MCS was similar to the hemodynamic performance of the valves. The study aimed to evaluate the *in vitro* hydrodynamic performance of bovine pericardial and porcine valves in the aortic and pulmonary settings. Pulmonary settings were evaluated at varying pressures to mimic the clinical scenario of patients with congenital heart disease requiring pulmonary valve replacement.

MATERIALS AND METHODS

Bioprosthetic valves

A Carpentier-Edwards Perimount Magna Ease valve (Edwards Lifesciences, Irvine, CA, USA) was used as the bovine pericardial valve, and a Hancock II valve (Medtronic, Minneapolis, MN, USA) was used as the porcine valve. Prosthetic valves were tested in various sizes, ranging from 21 to 27 mm. Valves were mounted on the silicone mold of the mock circulatory system using continuous polypropylene sutures.

Mock circulatory system

1) The aortic and pulmonary pressure systems were simulated using a commercial pulse duplicator system (HDTi-6000 Heart Valve Pulse Duplicator, BDC Laboratories, Wheat Ridge, CO, USA) equipped with a PD-1100 pulsatile pump (BDC Laboratories, Wheat Ridge, CO, USA) (Supplementary Fig. 1, only online). Each chamber of the pulse duplicator system was filled with distilled water. The flow rate, beat rate, and driving waveform shape were controlled using the Statys[®] HDTi software (BDC Laboratories, Wheat Ridge, CO, USA) interface.

2) A Transonic 9PXL perivascular ultrasound probe (Transonic Systems, Ithaca, NY, USA) was used for the flow measurements. The flow probe was connected to a Transonic TS410 tubing flow meter (Transonic Systems). The pressures upstream and downstream of the valve were measured using a pressure transducer. Each test run was reported as a 10-cycle measurement average using Statys[®] HDTi software (BDC Laboratories) to determine the geometric orifice area (GOA) and mean pressure gradient. Moving images were obtained using HDTi-6000 Vision Cameras at 600 fps.

Accelerated wear test

An accelerated wear test (AWT) was used to investigate the durability of each valve in aortic and pulmonary settings *in vitro* (Supplementary Fig. 2, only online). The AWT of prosthetic heart valves allows the simulation of wear and fatigue sustained by the replaced heart valves and enables estimation of their life expectancy in the human body.¹⁰ Valves were cycled at 20 Hz for 200 million cycles, corresponding to 5 years of actual valve use. During accelerated wear testing, the 25-mm bovine pericardial valve showed no leaflet motion under pulmonary pressure conditions, likely due to limited movement at the high test frequency (20 Hz). Therefore, the 21-mm valve—which demonstrated stable opening and closing motion—was used for the AWT.

Test conditions

First, the bovine pericardial and porcine valves were tested in the aortic settings as a reference, and then in the pulmonary setting. Various pressure settings were applied considering the variation in the right ventricular pressure (resulting from pulmonary arterial development and resistance) of patients with congenital heart disease. As systolic and diastolic pressures were gradually increased from low (15/5 mm Hg) to high (75/35 mm Hg), the hydrodynamic performance of the valves was recorded (Supplementary Table 1, only online). Ten consecutive pressure and flow recording cycles were performed in individual tests, with the tests repeated five times for validation using the same valve installation. The aortic and pulmonary settings were based on the ISO 5840-1 guidelines.¹¹ In addition, the following variables were evaluated: 1) transvalvular pressure difference: pressure difference across the prosthetic valve during forward flow (mm Hg); 2) forward flow volume:

flow volume ejected through a prosthetic valve in the forward direction (mL); 3) closing reverse flow: volume that flows in the reverse direction during the closing period (mL); 4) leakage volume: volume that flows in the reverse direction after the end of the closing period until the beginning of leaflet opening (mL); 5) GOA: minimal cross-sectional area of the flow jet downstream of the aortic valve (cm²); 6) regurgitant volume: fluid volume that flows through a prosthetic valve in the reverse direction during one cycle (mL); and 7) regurgitant fraction: regurgitant volume expressed as a percentage of the forward flow volume (%)

Statistical analysis

Continuous variables are presented as the mean±standard deviation. Values were compared using independent t-tests. All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Flow and pressure curves

Fig. 1 shows the flow and pressure profiles of the 21-mm valve generated under normotensive pulmonary conditions. Some

resonance was observed in the pressure curves of the Hancock valve. This finding was consistent with the fluttering leaflet motion observed in the 21-mm Hancock valve.

Valve leaflet motion by pressures and valve sizes

During testing under normal pulmonary conditions, all Hancock valves showed an incomplete opening, regardless of size. Restricted motion of one or two leaflets among the three cusps caused incomplete opening. Magna valves did not show incomplete opening; however, sequential rather than simultaneous opening of leaflets was observed. In addition, the GOA of the Hancock valve was smaller than that of the Magna valve for all valve sizes (0.67±0.01 vs. 1.41±0.01 cm² for 21-mm valve; 0.93±0.01 vs. 1.70±0.01 cm² for 23-mm valve; 0.99±0.01 vs. 1.75±0.01 cm² for 25-mm valve; 1.58±0.01 vs. 2.25±0.02 cm² for 27-mm valve; all $p<0.01$). Accordingly, the transvalvular peak pressure gradient was higher, and the forward flow volume was smaller in the Hancock valve for all sizes (Table 1).

In terms of valve closing, the results were the opposite. All Hancock valves closed completely under normal pulmonary pressure conditions; however, Magna valves showed incomplete central closure, except for the 27-mm valve (Fig. 2). For valve sizes ranging from 23 mm to 27 mm, the closing reverse flow was greater in the Magna valve (0.20±0.02 vs. 0.65±0.29

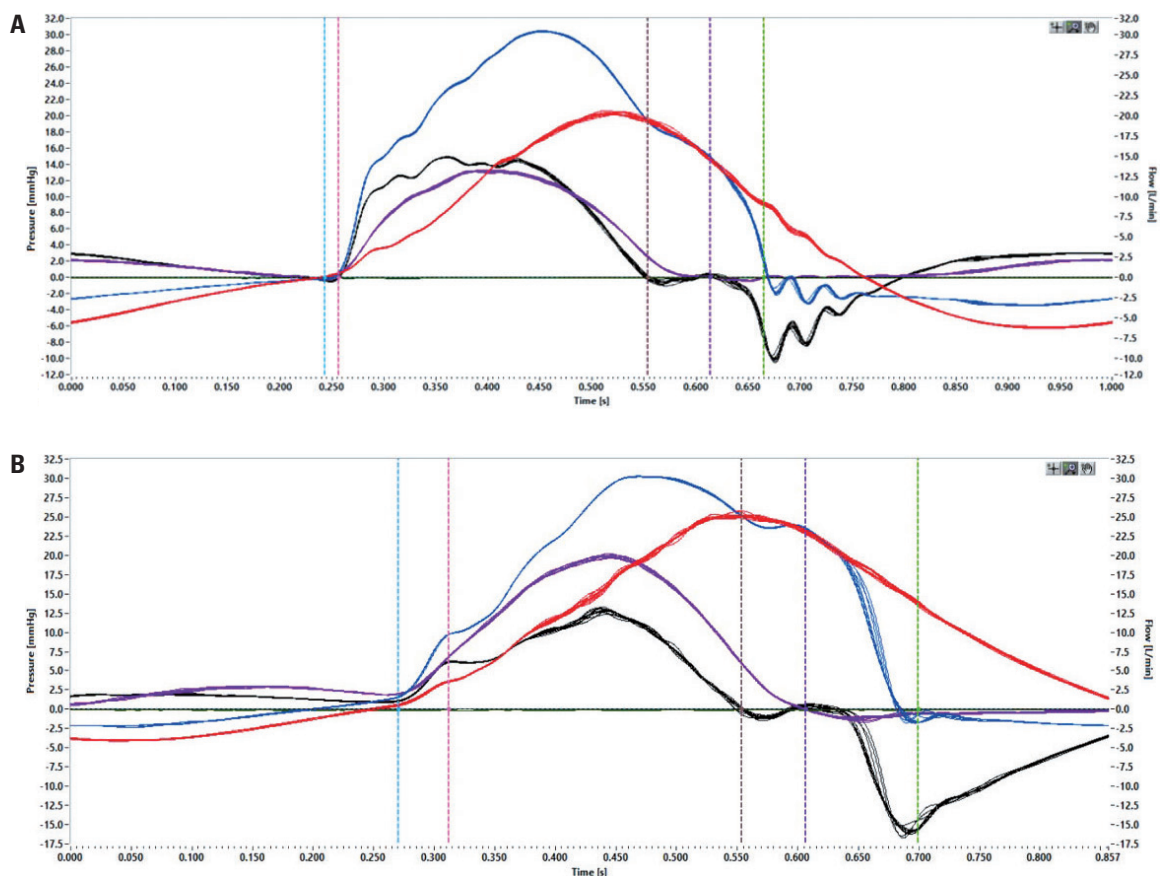


Fig. 1. Pressure and flow output for the pulmonary normotensive condition of the 21-mm valve. (A) Hancock valve. (B) Magna valve. Blue line, ventricular pressure; red line, arterial pressure; purple line, flow; black line, mean pressure difference.

Table 1. Hydrodynamic Variables Under Normotensive Pulmonary Pressure Conditions (30/10 mm Hg)

	21 mm		23 mm		25 mm		27 mm	
	Hancock	Magna	Hancock	Magna	Hancock	Magna	Hancock	Magna
Transvalvular peak pressure gradient, mm Hg	20.78±0.38	18.36±0.34	15.75±0.14	12.57±0.47	14.85±0.05	12.87±0.28	15.72±0.32	7.91±0.03
Forward flow volume, mL	35.27±0.05	64.67±0.12	42.27±0.05	64.79±0.14	46.41±0.06	64.28±0.18	72.64±0.17	73.25±0.07
Closing reverse flow, mL	0.38±0.03	0.57±0.18	0.20±0.02	0.65±0.29	0.17±0.03	1.32±0.11	0.83±0.09	3.56±2.27
Leakage volume, mL	0.67±0.05	1.34±0.22	0.04±0.02	1.97±0.23	0.04±0.02	1.24±0.20	1.11±0.43	8.18±1.74
Regurgitant fraction, %	1.84±0.22	2.95±0.32	0.58±0.09	4.04±0.44	0.44±0.08	3.98±0.43	2.67±0.64	16.02±5.44
GOA, cm ²	0.67±0.01	1.41±0.01	0.93±0.01	1.70±0.01	0.99±0.01	1.75±0.01	1.58±0.01	2.25±0.02

GOA, geometric orifice area.

Data are presented as mean±standard deviation. *p*<0.01 for all parameters.

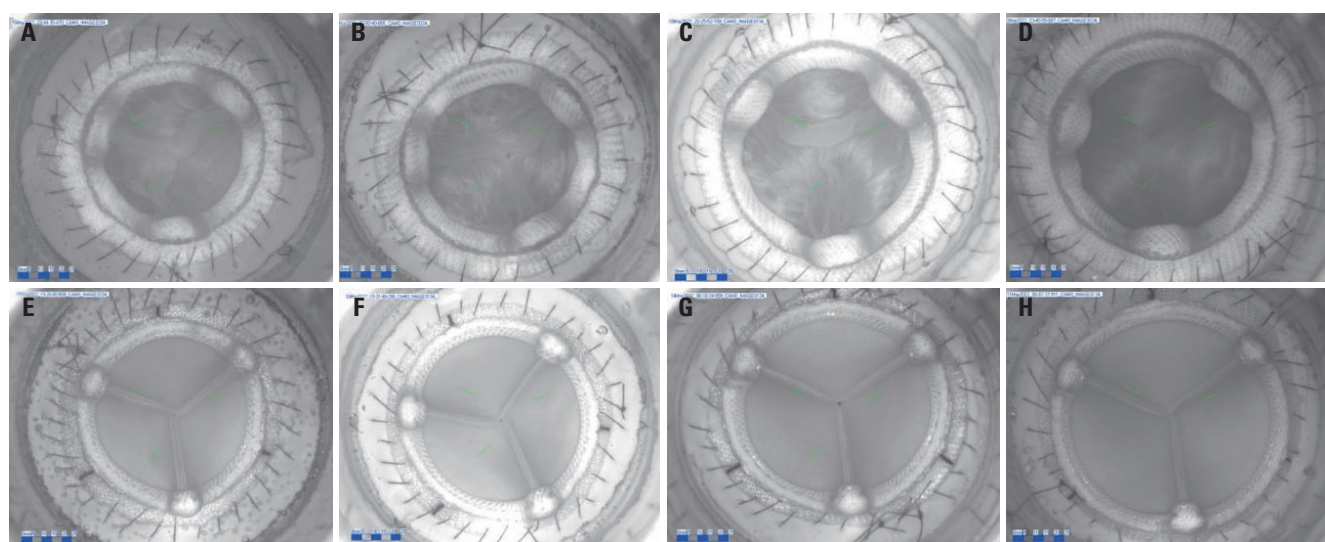


Fig. 2. Closing of the bioprosthetic valves under normal pulmonary pressure conditions (30/15 mm Hg). (A) 21-mm Hancock valve. (B) 23-mm Hancock valve. (C) 25-mm Hancock valve. (D) 27-mm Hancock valve. (E) 21-mm Magna valve. (F) 23-mm Magna valve. (G) 25-mm Magna valve. (H) 27-mm Magna valve.

for the 23-mm valve; 0.17±0.03 vs. 1.32±0.11 for 25-mm valve; 0.83±0.09 vs. 3.56±2.27 for 27-mm valve; all *p*<0.01). In addition, leakage volume was larger in Magna valves in all sizes; therefore, the regurgitant fraction was higher in Magna valves (Table 1). Under pulmonary hypotensive conditions, the opening motion of the Hancock valve was reduced. For the 21-mm valve, one leaflet was fixed, and another was partially opened, resulting in only a single leaflet moving properly. For valves from 23 mm to 27 mm, a single leaflet did not open, and the remaining leaflets opened sequentially rather than simultaneously. Altered leaflet movements were observed in all three sizes of the Hancock valve with each beat. The Magna valves exhibited different motions under pulmonary hypotensive pressure; the leaflets opened sequentially, and eventually, all leaflets opened completely (Table 2). The forward flow was greater in Magna valves of all sizes, whereas the Hancock valve showed reduced GOA in all sizes. During pulmonary hypotensive testing, none of the Magna valves closed completely at the center; consequently, leakage volume and regurgitant fraction were higher (Table 3).

At pulmonary hypertensive pressures of 50/20 mm Hg and 75/35 mm Hg, the Magna valves showed simultaneous open-

Table 2. Completeness of Opening and Closure of 25-mm Valves

Pressure	Hancock		Magna	
	Opening	Closing	Opening	Closing
15 mm Hg	-	-	+	--
30 mm Hg	-	+	+	--
50 mm Hg	+	+	+	-
75 mm Hg	+	+	+	+
110 mm Hg	+	+	+	+

-, incomplete; --, severely incomplete; +, complete.

ing and complete closure of the leaflets. However, the Hancock valves showed different motions relative to size. One leaflet of the 21-mm Hancock valve did not open at 50 mm Hg, whereas all leaflets opened at 75 mm Hg. A fluttering motion of the leaflets was observed at 75 mm Hg. For the 23-mm to 27-mm Hancock valves, simultaneous but asymmetrical leaflet opening was observed during pulmonary hypertensive testing. For valve sizes 21 mm and 23 mm, the forward flow volume was higher in the Hancock valve (Table 4). For the 25- and 27-mm valves, the forward flow volume was higher in the Magna valves. The GOA was higher for all Magna valve sizes. The incomplete

Table 3. Hydrodynamic Variables Under Hypotensive Pulmonary Pressure Conditions (15/5 mm Hg)

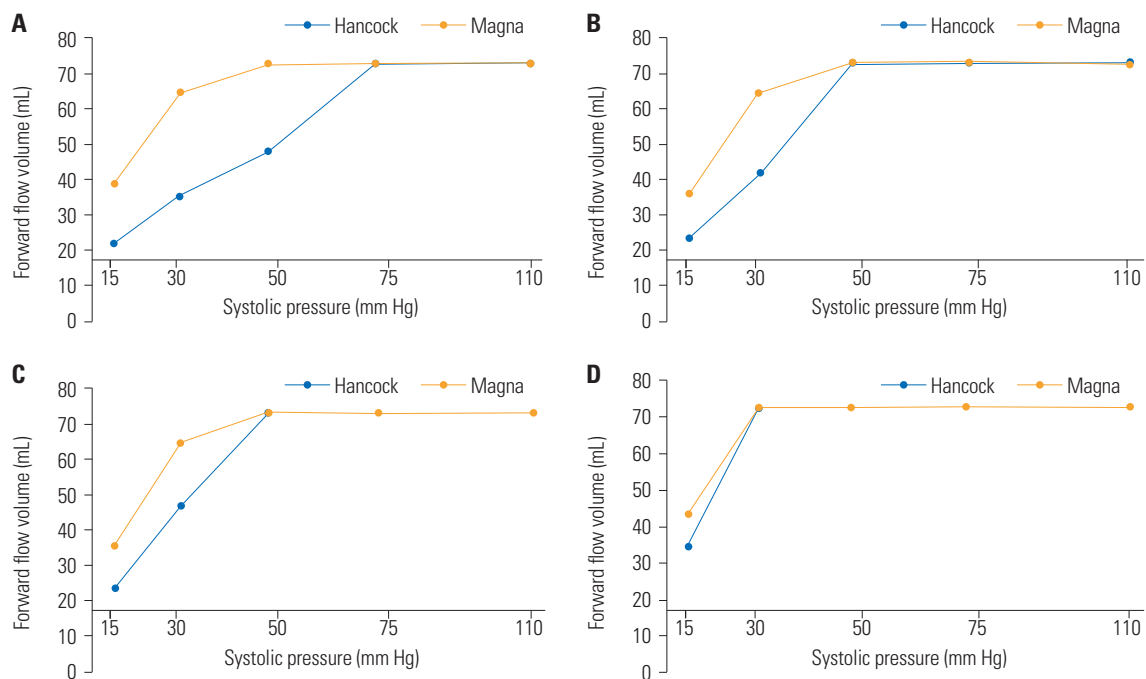
	21 mm		23 mm		25 mm		27 mm	
	Hancock	Magna	Hancock	Magna	Hancock	Magna	Hancock	Magna
Transvalvular peak pressure gradient, mm Hg	9.46±0.08	6.92±0.09	6.70±0.06	5.76±0.04	9.15±0.06	5.77±0.03	6.30±0.04	5.77±0.05
Forward flow volume, mL	21.70±0.05	39.01±0.10	24.20±0.06	36.64±0.06	23.19±0.03	34.97±0.06	34.88±0.08	43.76±0.13
Closing reverse flow, mL	0.44±0.02*	0.41±0.06*	0.19±0.02	0.82±0.13	0.17±0.01	0.66±0.07	0.59±0.03	1.68±0.08
Leakage volume, mL	0.69±0.02	0.15±0.09	0.01±0.01	0.31±0.12	0.01±0.01	0.17±0.03	0.09±0.02	0.45±0.05
Regurgitant fraction, %	2.36±0.12	1.45±0.28	0.83±0.11	3.08±0.24	0.79±0.07	2.37±0.22	1.94±0.15	4.87±0.24
GOA, cm ²	0.61±0.01	1.32±0.01	0.77±0.01	1.73±0.01	0.73±0.01	1.40±0.01	1.29±0.01	2.22±0.01

GOA, geometric orifice area.

Data are presented as mean±standard deviation. $p < 0.01$ for all parameters except as noted.* $p = 0.01$.**Table 4.** Hydrodynamic Variables Under Hypertensive Pulmonary Pressure Conditions (50/20 mm Hg)

	21 mm		23 mm		25 mm		27 mm	
	Hancock	Magna	Hancock	Magna	Hancock	Magna	Hancock	Magna
Transvalvular peak pressure gradient, mm Hg	35.77±0.23	24.15±0.64	33.71±0.31	16.31±0.48	29.04±0.32	13.77±0.35	15.81±0.14	7.39±0.14
Forward flow volume, mL	48.43±0.05	73.06±0.09	73.31±0.12	72.95±0.06	72.55±0.10	72.75±0.10	72.64±0.17	73.25±0.07
Closing reverse flow, mL	0.31±0.03	0.57±0.14	0.39±0.16	0.62±0.10	0.57±0.07	0.91±0.16	0.83±0.09	3.56±2.27
Leakage volume, mL	0.12±0.05	5.31±0.14	1.69±0.36	12.42±0.37	2.64±0.25	11.58±0.36	1.11±0.43	8.18±1.74
Regurgitant fraction, %	0.89±0.14	8.05±0.24	2.83±0.49	13.81±0.44	4.42±0.35	17.17±0.48	2.67±0.64	16.02±5.44
GOA, cm ²	0.71±0.01	1.47±0.01	1.12±0.01	1.71±0.01	1.17±0.01	1.81±0.01	1.58±0.01	2.25±0.02

GOA, geometric orifice area.

Data are presented as mean±standard deviation. $p < 0.01$ for all parameters.**Fig. 3.** Forward flow volume of each valve according to testing systolic pressure. (A) 21 mm. (B) 23 mm. (C) 25 mm. (D) 27 mm.

closure of the Magna valve observed under hypotensive conditions was not apparent in the hypertensive setting. Furthermore, a higher regurgitant fraction was noted in Magna valves compared to Hancock valves.

Valve performance by pressure elevation

The forward flow volume of the valves increased proportionally with increasing test pressure and reached a peak where further pressure increase could not alter it (Fig. 3). The Magna valve achieved maximum forward flow volume at pressures above 50 mm Hg (30 mm Hg for the 27-mm valve). The Han-

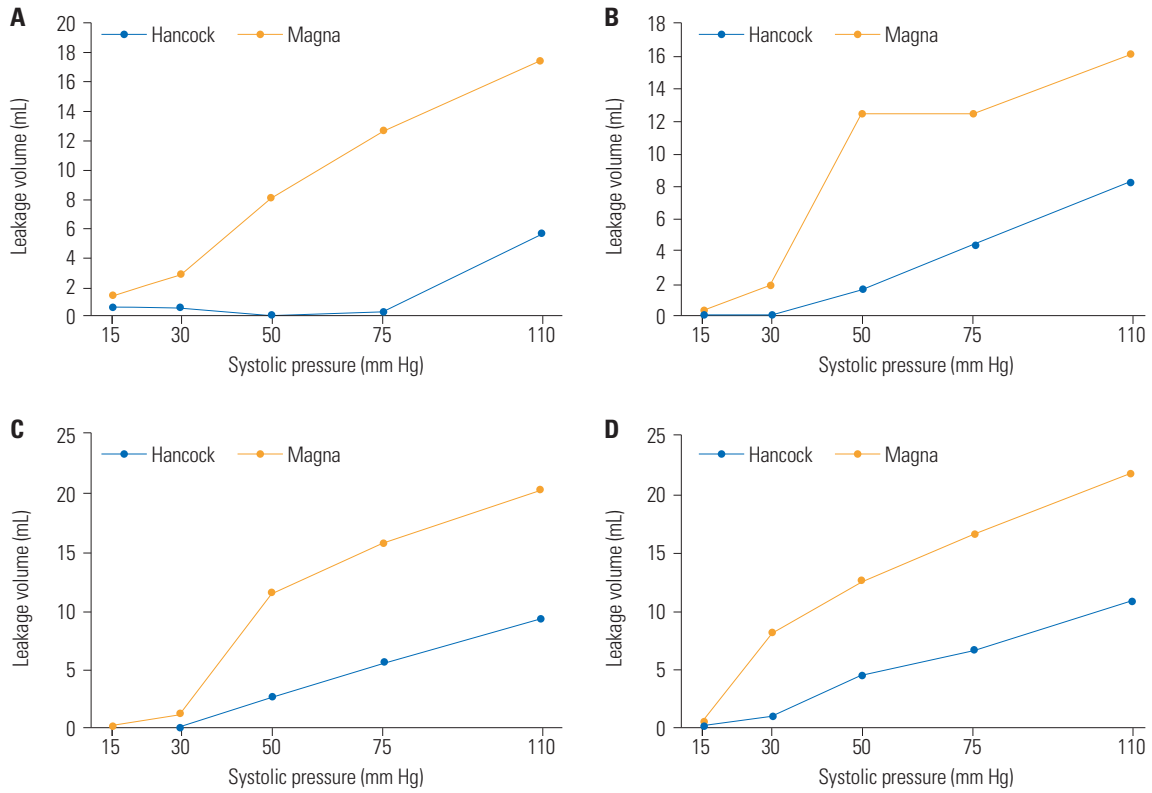


Fig. 4. Leakage volume of each valve according to testing pressure. (A) 21 mm. (B) 23 mm. (C) 25 mm. (D) 27 mm.

cock valve reached a plateau in forward flow volume at 75 mm Hg for the 21-mm valve. The forward flow volume of the Hancock valve was lower than that of the Magna valve under normotensive and hypotensive testing conditions. The closing reverse flow of the valves did not increase consistently with rising pressure; however, the leakage volume and regurgitant fraction differed. The leakage volume for the Hancock valve did not increase under normotensive and hypotensive pressure conditions. In addition, the leakage volume for the Magna valve increased simultaneously with pressure (Fig. 4).

Accelerated wear test

The 25-mm valves could not be tested in the AWT circuit. One leaflet of the Magna valve did not move at 20 Hz; however, the motion of the Hancock valve was normal. Therefore, the valve size was changed to 21 mm, which functioned normally during testing. After 200 million cycles, no damage or deformation of the valves was observed (Fig. 5).

DISCUSSION

The bovine pericardial and porcine valves are the most frequently used bioprosthetic valves. Off-label use of bioprosthetic valves (designed for aortic valve surgery) in the pulmonary valve position is common practice in congenital heart surgery. However, the outcomes and failure modes of bioprostheses

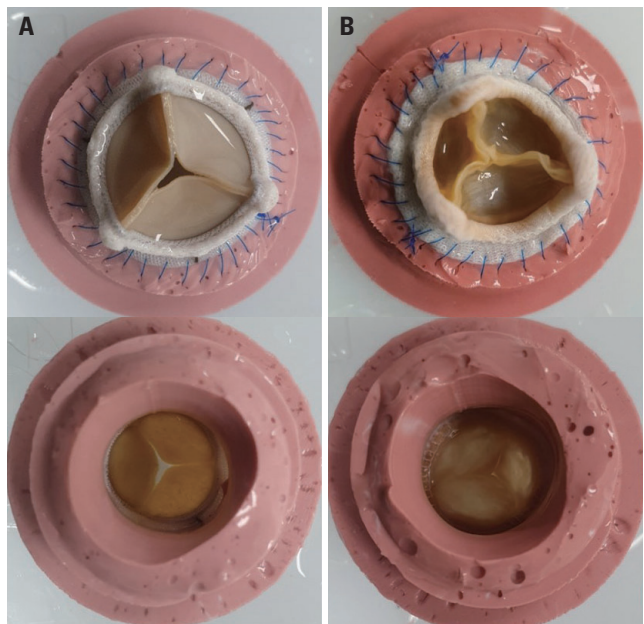


Fig. 5. Pulmonary arterial side (upper panel) and ventricular side (lower panel) of the 21-mm Magna valve (A) and Hancock valve (B) after completion of 200 million cycles of the accelerated wear test.

vary depending on the pulmonary valve position. In addition, the hemodynamic performance of prostheses in a pulmonary setting is poorly understood. To investigate the differences in hydrodynamic performance between the aortic and pulmo-

nary positions of the bovine pericardial and porcine valves, we used a mock circulatory system. Unfavorable hemodynamic parameters of prosthetic valves (such as high transventricular pressure gradient and valve regurgitation) are risk factors for valve deterioration, reintervention, and poor survival.¹² The *in vitro* hydrodynamic performance observed using the MCS mimicked the hemodynamic performance of a valve and additionally revealed the mechanical components of the valve degeneration mechanism.

Leaflet motion during the cardiac cycle showed that bovine pericardial valves did not close completely during diastole under normotensive and hypotensive pulmonary pressures; conversely, full closure was attained under high pulmonary or aortic pressure conditions. In a study describing the *in vitro* behavior of a bileaflet mechanical valve in a low-pressure system, low impedance produced incomplete prosthesis closure, correlating with findings in a high-pressure system.¹³ A similar phenomenon was observed in the bovine pericardial valve under pulmonary pressure conditions; incomplete valve closure occurred in the pulmonary system, in contrast to the aortic pressure system.¹⁴ High leakage volume and regurgitant fraction were associated with the bovine pericardial valve. Incomplete closure of the valve is associated with reduced leaflet motion, consequently influencing leaflet fixation.¹⁴ Incomplete closure may contribute to leaflet calcification and fibrosis, which represent potential primary mechanisms causing stenosis of the bovine pericardial valve.⁷ Therefore, this study provides mechanistic insights into valve degeneration. However, the effect of incomplete opening observed in the porcine valve under mock circulation conditions remains to be elucidated. Parameters such as incomplete opening, low forward flow volume, and small orifice area may increase the heart rate required to obtain optimal cardiac output, consequently accelerating the degeneration of prosthetic valves.

Conversely, the porcine valve demonstrated an incomplete opening and a smaller GOA. Leaflet tearing has been suggested as a mechanism of porcine valve degeneration in the aortic valve position.^{7,8} The transvalvular pressure gradient was higher in the porcine valve than in the bovine pericardial valve under the same pressure conditions; the systolic pressure increased the difference in the transvalvular pressure gradient between the two valves. The high transvalvular pressure gradient of the porcine valve observed under aortic pressure may be associated with leaflet tearing; however, leaflet tearing may not affect prosthesis performance under normal pulmonary pressure and an appropriate transvalvular pressure gradient.

The bovine pericardial valve demonstrated higher forward flow volume under normal pulmonary pressure, consistent with previous reports in the aortic valve position.^{15,16} The Magna valve has been reported to have superior hydrodynamic properties, particularly in effective orifice area and pressure gradient, compared with porcine valves under aortic conditions;¹⁷ using a bovine pericardial valve in the pulmonary position could

be beneficial in this effect. The small porcine valve demonstrated suboptimal forward flow in pulmonary normotensive and hypotensive conditions; the difference in forward flow volume between the porcine and bovine pericardial valves was more pronounced for the 21-mm valve. Moreover, small-sized porcine valves demonstrated inefficient hydrodynamic performance in both opening motion and area during systole. In contrast, the bovine pericardial valve required a lower systolic pressure to reach the maximum forward flow. Therefore, small-sized porcine valves should not be considered suitable for pulmonary prosthetic use under normotensive conditions. The valve size and various pressure environments (the degree of pulmonary hypertension) may affect bioprosthesis behavior in the pulmonary position.

Under pulmonary normotensive conditions, a high forward flow volume and a low transvalvular pressure gradient of the bovine pericardial valve are advantageous. A high leakage volume may be deleterious to hemodynamic performance, and incomplete closure may contribute to leaflet fixation, thereby reducing the durability of the bovine pericardial valve. The porcine valve showed a low forward flow volume and a low transvalvular pressure gradient, which may prevent leaflet tearing over the long term. This hydrodynamic phenomenon may partly explain the improved durability of the porcine valve in the pulmonary position.⁵ However, under pulmonary hypertensive conditions, the bovine pericardial valve showed complete closure, eliminating concerns of leaflet fixation and demonstrating a higher forward flow volume than the porcine valve. For porcine valves, low forward flow volume is unfavorable for hemodynamic efficiency, and a high transvalvular pressure gradient may contribute to leaflet tearing, similar to that observed in the aortic valve position. Therefore, considering hydrodynamic data, the bovine pericardial valve may be used for pulmonary prostheses under pulmonary hypertensive conditions.

Under hypotensive pulmonary pressure conditions, the bovine pericardial valve showed markedly reduced values for forward flow and related parameters. This finding appears to be associated with the sequential, rather than simultaneous, opening of individual leaflets observed at low driving pressures, which may result in delayed valve opening and reduced flow performance.

After 200 million cycles of the AWT under pulmonary pressure conditions, no damage or deformation of the valve leaflets was observed. This result suggests that etiologies other than hydrodynamic wear were responsible for valve degeneration. However, further studies with longer test cycles equivalent to 10 or 20 years of lifespan are required to clarify the hydrodynamic influence on the prosthesis.

Valves designed for the left heart demonstrated aberrant behavior similar to that of pulmonary valves when subjected to alterations in pulmonary vascular resistance *in vitro*.¹ *In vitro* testing of bovine and porcine valves under different pressure conditions may help investigate the effects of valve type on

performance and durability while controlling for other confounding factors. However, extreme caution is warranted when applying the *in vitro* hydrodynamic test results to clinical practice. Other factors, such as calcification and thrombosis, that are significantly associated with the valve degeneration process need to be considered. In addition, further studies are required to evaluate the potential association between these findings and the increased risk of prosthetic valve degeneration under pulmonary conditions.

This study has several limitations. First, the experiments were performed using distilled water rather than a blood-analog fluid. Although this approach allowed for precise control of flow and pressure conditions in the mock circulatory system, the viscosity and density of water differ from those of blood and may influence hydrodynamic behavior. Therefore, future studies are planned using a blood-mimicking fluid with physiological rheological properties to validate and expand the present findings under more realistic *in vivo*-like conditions. Second, the testing was performed in a linear cylindrical tube, which differs from the natural right ventricular outflow tract anatomy. The influence of anatomical factors, such as the sinus of Valsalva and pulmonary artery bifurcation, on hydrodynamic performance could not be demonstrated in the present study. Finally, in a clinical *in vivo* setting, the hemodynamic performance of prosthetic valves is affected by pulmonary artery pressure, ventricular function, heart rate, and other underlying patient conditions. Therefore, it may not reflect the exact situation in the human body.

Bovine pericardial and porcine bioprosthetic valves exhibit different hydrodynamic characteristics under various pulmonary pressure conditions. Porcine valves were associated with incomplete opening and smaller forward-flow volume and GOA, whereas bovine pericardial valves were associated with incomplete closure and a higher regurgitant fraction.

Although the patient population requiring pulmonic valve replacements is generally smaller than that requiring aortic valve replacement, understanding the hydrodynamic characteristics of the valves and selecting the appropriate type of prosthetic valve for each cardiac position can help achieve optimal clinical outcomes in these patients.

ACKNOWLEDGEMENTS

This manuscript is based on the doctoral dissertation titled “Comparison of hydrodynamic characteristics between bovine pericardial and porcine valve using a mock circulatory system mimicking the pulmonary position” by Dr. Yu Rim Shin.

All data needed to evaluate the conclusions in the paper are present in the paper and the supplementary materials.

AUTHOR CONTRIBUTIONS

Conceptualization: Yu Rim Shin and Sak Lee. **Data curation:** Yu Rim Shin and Yongwoo Kim. **Formal analysis:** Yu Rim Shin, Seung-Hyun

Lee, Jae-Kwang Shim, and Sak Lee. **Funding acquisition:** Sak Lee. **Investigation:** Yu Rim Shin, Seung-Hyun Lee, Jae-Kwang Shim, and Sak Lee. **Methodology:** Yu Rim Shin, Yongwoo Kim, Seung-Hyun Lee, and Sak Lee. **Project administration:** Yu Rim Shin and Sak Lee. **Resources:** Yu Rim Shin, Yongwoo Kim, Seung-Hyun Lee, and Sak Lee. **Software:** Yu Rim Shin, Yongwoo Kim, Seung-Hyun Lee, and Sak Lee. **Supervision:** Jae-Kwang Shim and Sak Lee. **Validation:** Yu Rim Shin, Seung-Hyun Lee, Jae-Kwang Shim, and Sak Lee. **Visualization:** Yu Rim Shin and Sak Lee. **Writing—original draft:** Yu Rim Shin and Sak Lee. **Writing—review & editing:** Seung-Hyun Lee, Jae-Kwang Shim, and Sak Lee. **Approval of final manuscript:** all authors.

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