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Comparison of hydrodynamic characteristics  
between bovine pericardial and porcine valve  
using a mock circulatory system mimicking the  
pulmonary position

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Comparison of hydrodynamic characteristics  
between bovine pericardial and porcine valve  
using a mock circulatory system mimicking the  
pulmonary position

Directed by Professor Sak Lee

Doctoral Dissertation  
submitted to the Department of Medicine,  
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in partial fulfillment of the requirements for the degree of  
Doctor of Philosophy in Medical Science

Yu Rim Shin

December 2022

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December 2022

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## ABSTRACT

### **Comparison of hydrodynamic characteristics between bovine pericardial and porcine valve using a mock circulatory system mimicking the aortic and pulmonary position**

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(Directed by Professor Sak Lee)

**Background:** The most frequently used bioprosthetic cardiac valves have initially been designed for aortic positions. But, these prosthesis has been used in the pulmonary part due to structural similarities in each great artery's valve structure. No comprehensive evaluation was reported regarding the functioning of tissue prosthetic valves under pulmonary conditions.

**Methods:** Using a Mock circulatory system, a pulse duplicator, we evaluated the hydrodynamic characteristics of bovine pericardial and porcine valves (21, 23, 25, and 27 mm sized Magna and Hancock valve). Geometric orifice area, regurgitant volume, leakage volume, regurgitant fraction, peak pressure gradient, and forward flow volume were

evaluated. This procedure was performed under different pulmonary pressure conditions (from 15/5 mmHg to 75/35 mmHg) and normal aortic pressure (110/80 mm Hg) as a reference. In vitro longevity of each type of bioprosthetic valve in pulmonary system was identified by accelerated wear testing.

**Results:** Under normal and hypotensive pulmonary pressure conditions, bovine pericardial valves showed incomplete closure in contrast to the aortic condition. Bovine pericardial valves were associated with larger opening area ( $0.67 \pm 0.01$  vs  $1.41 \pm 0.01$  for 21 mm valve;  $0.93 \pm 0.01$  vs  $1.70 \pm 0.01$  for 23 mm valve;  $0.99 \pm 0.01$  vs  $1.75 \pm 0.01$  for 25 mm valve;  $1.58 \pm 0.01$  vs  $2.25 \pm 0.02$  for 27 mm valve, all  $p < 0.01$ ) and forward flow volume ( $35.27 \pm 0.05$  vs  $64.7 \pm 0.12$  for 21 mm valve;  $42.27 \pm 0.05$  vs  $64.79 \pm 0.14$  for 23 mm valve;  $46.41 \pm 0.06$  vs  $64.28 \pm 0.18$  for 25 mm valve;  $72.64 \pm 0.17$  vs  $73.25 \pm 0.07$  for 27 mm valve, all  $p < 0.01$ ). Porcine valves were associated with incomplete opening and smaller opening area, and lower regurgitant fraction. In terms of transvalvular pressure gradient, bovine pericardial valve demonstrated lower peak pressure gradient ( $20.78 \pm 0.38$  vs  $18.36 \pm 0.34$  for 21 mm valve;  $15.75 \pm 0.14$  vs  $12.57 \pm 0.47$  for 23 mm valve;  $14.85 \pm 0.05$  vs  $12.87 \pm 0.28$  for 25 mm valve;  $15.72 \pm 0.32$  vs  $7.91 \pm 0.03$  for 27 mm valve). After accelerated wear test, there was no change in hydrodynamic data for both types of valves.

**Conclusion:** Bovine pericardial and porcine bioprosthetic valves have different hydrodynamic characteristics under various pulmonary pressure conditions. Bovine pericardial valve was associated with incomplete closure, larger opening area, and greater forward flow volume. Porcine valve showed incomplete opening, smaller opening area, and lower regurgitant fraction. Further research is needed to evaluate whether or not these results are associated with potential increased risk of prosthetic valve degeneration in the pulmonary condition.

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Key words: mock circulatory system, pulmonary valve, bioprosthetic valve, hydrodynamic

# **Comparison of hydrodynamic characteristics between bovine pericardial and porcine valve using a mock circulatory system mimicking the aortic and pulmonary position**

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## **I. Introduction**

Long-term pulmonary valve insufficiency leading to right ventricular dilatation is a common situation following right ventricular outflow tract reconstruction. Because most prosthetic valves are designed for aortic valve position and because of the structural similarities between the pulmonary and aortic valves, the commercial valves that were developed initially for the aortic valve position have been used in the pulmonary position. However, various reports have demonstrated opposite clinical outcomes of these bioprosthetic valves when used in the aortic and pulmonary positions. Gao and colleagues reported better midterm durability of the pericardial valve and a lower rate of structural valve degeneration than that of the porcine valve in aortic position<sup>1</sup>. Dalmau and colleagues found that the bovine pericardial valve had hemodynamic superiority in trans-valvar pressure gradient to the porcine valve in the aortic valve position at five years<sup>2</sup>. Meanwhile, reports of the durability of bioprosthetic valves in the pulmonary position demonstrated

disparate results. Kwak and colleagues found that the porcine valve had long-term advantages in reducing reoperation rate and prosthetic valve dysfunction in the pulmonary position<sup>3</sup>. Yuen and colleagues reported the comparable midterm outcomes of both types of bioprosthetic valves regarding the rate of freedom from reintervention<sup>4</sup>. These contrasting findings may be explained by different degeneration modes of the valves. Grunkemeier and colleagues found different causes of valve dysfunction in pericardial and porcine valves. The pericardial valve developed stenoin sufficiency by leaflet calcification and fibrosis, whereas the porcine valve mainly showed insufficiency by leaflet tearing<sup>5</sup>. Similarly, Persson and colleagues reported different behavior of porcine and bovine bioprosthetic valve in the aortic valve position. Porcine valve had higher tendency of valve incompetence by cusp tear, while bovine valve had higher rate of valve stenosis<sup>6</sup>. Several mechanisms have been identified as pathogenesis of bioprosthetic valve degeneration. Chemical, biological, immunological, and mechanical process commonly result in valve calcification and degeneration<sup>7</sup>. However, the reason for different mode of valve failure between aortic and pulmonary position remains elusive, while the potentially different hydrodynamic characteristics imposed by the different arterial systems would play a major role. Yet, no comprehensive evidence exists in that regard. Mock circulatory systems (MCS) is a popular method to gather hydrodynamic data in vitro to develop a new heart valve. They are made of tubing flow channels, compliance chambers, and a pump that mimics the arterial and/or venous circulatory system. Circulatory models simulate pressure/resistant changes in a physical system with flow and pressure monitoring. The real-time monitoring of flow in the loop gives hands-on feedback to manipulations of the cardiovascular system without a need to use animal subjects and allows investigation of the hemodynamics of various devices in the cardiovascular system, such as stents, artificial pumps, or heart valves<sup>8,9</sup>. In vitro hydrodynamic performance obtained by the MCS may mimic hemodynamic performance of the valves. We aimed to study in vitro hydrodynamic performance of the bovine pericardial and porcine valves in aortic and pulmonary settings. Pulmonary settings were further specified by varying pressures mimicking the clinical

scenario of patients with congenital heart disease requiring pulmonary valve replacement.

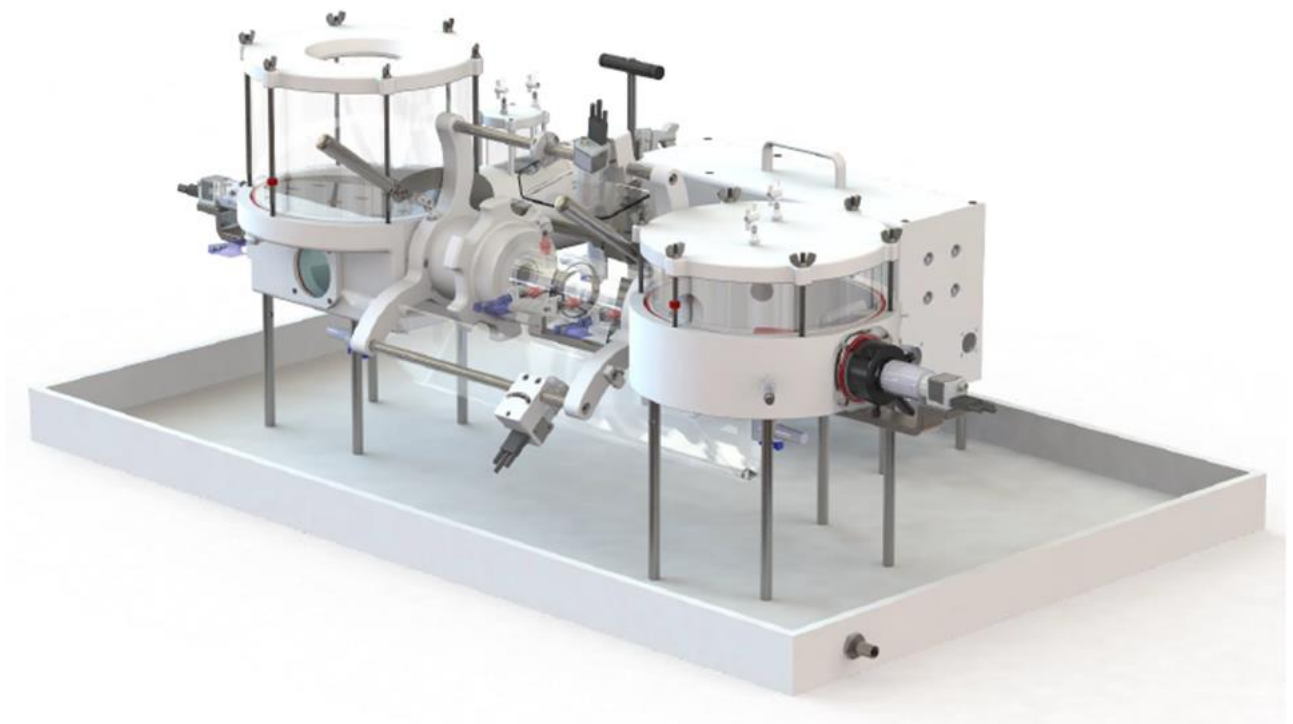
## II. Materials and Methods

### 1. Bioprosthetic Valves

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

### 2. Mock Circulatory System

- A. Aortic and pulmonary pressure systems were simulated with commercial pulse duplicator system (HDTi-6000 heart valve pulse duplicator, BDC Laboratories, Wheat Ridge, CO, USA) with a PD-1100 pulsatile pump (BDC Laboratories, Wheat Ridge, CO, USA) (Figure 1). Each chamber of pulse duplicator system was filled with distilled water. The flow and beat rate, as well as the driving waveform shape were controlled through the Statys® HDTi software (BDC Laboratories, Wheat Ridge, CO, USA) interface.
- B. A Transonic 9PXL perivascular ultrasound probe (Transonic Systems, Ithaca, NY) was used for flow measurements. The flow probe was connected to a Transonic TS410 tubing flow meter (Transonic Systems, Ithaca, NY). The pressure upstream and downstream from the valve was measured by a pressure transducer. Each test run was reported from a 10-cycle measurement average using Statys® HDTi software (BDC Laboratories) to determine the geometric orifice area and mean pressure gradient. Moving images were obtained using HDTi-6000 Vision Cameras at 600 frames per second.



**Figure 1** Mock Circulatory System

### 3. Accelerated Wear Test

To investigate the durability of each valve in aortic and pulmonary settings in vitro, accelerated wear test (AWT) was used. AWT of prosthetic heart valves allows simulation of wear and fatigue sustained by the replaced heart valves, and to estimate the valves' life expectancy in human body<sup>10</sup>. Valves were cycled in speed of 20 Hz for 200 million cycles, which corresponds to 5 years of actual valve use.



**Figure 2** Accelerated Wear Test

#### 4. Test conditions

At first, both bovine pericardial and porcine valves were tested at aortic settings as a reference. Then, valves were tested for pulmonary settings. Because right ventricular pressure varies in congenital heart disease patients by pulmonary arterial development and resistance, various pressures settings were applied. As systolic and diastolic pressure was gradually increased from low (15/5 mmHg) pressure to high pressure (75/35 mmHg), hydrodynamic performance of the valves was recorded (Table 1). Ten consecutive cycles of pressure and flow recordings were performed in each test, and every test was repeated five times for validation. Aortic and pulmonary settings were based on ISO 5840-1 guideline<sup>11</sup>. The following variables were evaluated.

**Table 1** Testing pressure for each condition

|                               | Systolic pressure (mmHg) | Diastolic pressure (mmHg) |
|-------------------------------|--------------------------|---------------------------|
| Pulmonary hypotensive         | 15                       | 5                         |
| Pulmonary normotensive        | 30                       | 10                        |
| Pulmonary hypertensive        | 50                       | 20                        |
| Pulmonary severe-hypertensive | 75                       | 35                        |
| Aortic normotensive           | 110                      | 80                        |

- A. Transvalvular pressure difference: Pressure difference over the prosthetic valve during forward flow, mmHg
- B. Forward flow volume: Flow volume ejected through the prosthetic valve in a forward direction, mL
- C. Closing reverse flow: The volume that flows in reverse direction during the closing period, mL
- D. Leakage volume: The volume that flows in reverse direction after the end of the closing period until the beginning of the opening movement of the leaflets, mL
- E. Geometric orifice area: minimal cross-sectional area of the flow jet downstream of the aortic valve, cm<sup>2</sup>
- F. Regurgitant volume: fluid volume that flows through a prosthetic valve in the reverse direction during one cycle, mL
- G. Regurgitant fraction: Regurgitant volume expressed as a percentage of the forward flow volume, %



### Statistical Analysis

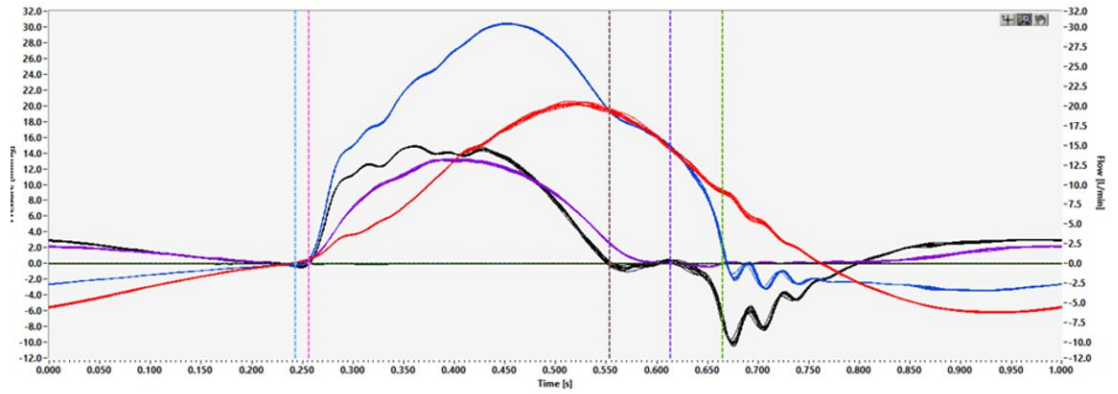
Continuous variables are presented as mean  $\pm$  standard deviation. Values were compared using independent t-test. All statistical analyses were performed using an SPSS Statistics version 26 (IBM Inc, Armonk, NY, USA).

## III. Results

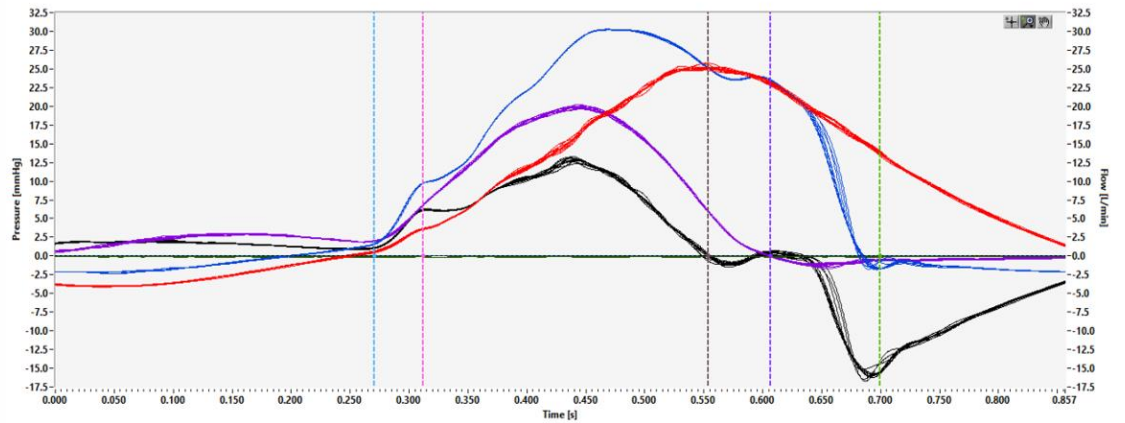
### 1. Flow and pressure curves

Figure 3 shows flow and pressure profiles of 21 mm valve generated under normotensive pulmonary condition. Some resonance was observed in pressure curves of Hancock valve. This finding was consistent with fluttering leaflet motion of the 21 mm Hancock valve.

A



B



**Figure 3** Pressure and flow output for pulmonary normotensive condition of 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

## 2. Valve leaflet motion by pressures and valve sizes

During testing under the normal pulmonary condition, all Hancock valves showed incomplete opening of the valve regardless of size. Restricted motion of one or two leaflets of the three cusps caused incomplete opening. Magna valves did not show incomplete opening but non-simultaneous, sequential opening of leaflets was observed. Geometric

orifice area (GOA) of the Hancock valve was smaller than the GOA of the Magna valve in all sizes ( $0.67 \pm 0.01$  vs  $1.41 \pm 0.01$  cm<sup>2</sup> for 21 mm valve;  $0.93 \pm 0.01$  vs  $1.70 \pm 0.01$  cm<sup>2</sup> for 23 mm valve;  $0.99 \pm 0.01$  vs  $1.75 \pm 0.01$  cm<sup>2</sup> for 25 mm valve;  $1.58 \pm 0.01$  vs  $2.25 \pm 0.02$  cm<sup>2</sup> for 27 mm valve, all  $p < 0.01$ ). Accordingly, transvalvular peak pressure gradient was higher and forward flow volume was smaller in Hancock valve in all sizes (Table 2).

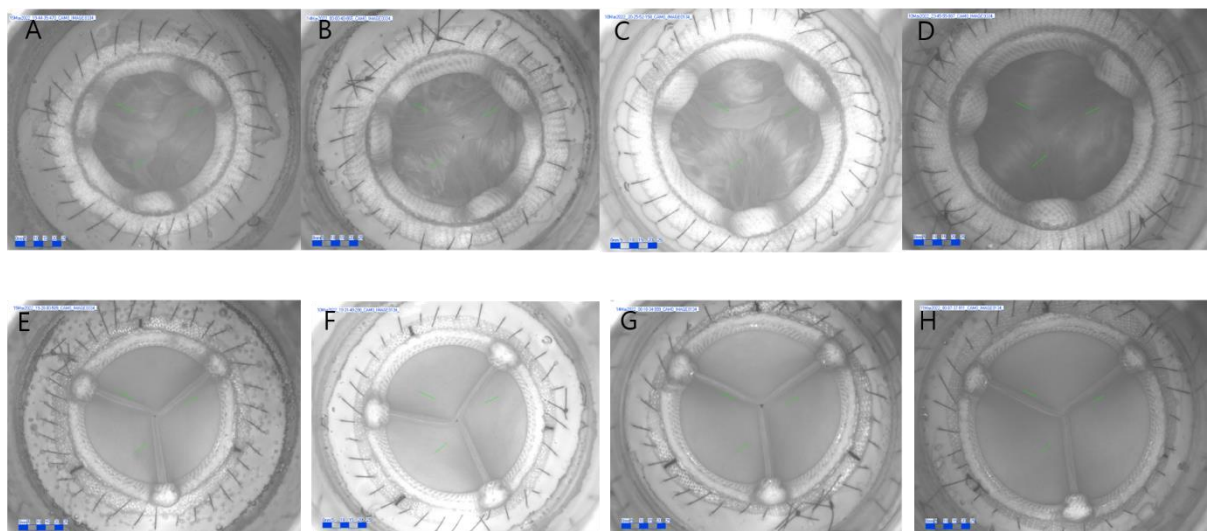
**Table 2** Hydrodynamic variables under normotensive pulmonary pressure condition (30/10 mmHg)

|  | 21 mm          |                | 23 mm          |                | 25 mm          |                | 27 mm          |                |
|--|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|  | Hancock        | Magna          | Hancock        | Magna          | Hancock        | Magna          | Hancock        | Magna          |
| Transvalvular peak pressure gradient, mmHg | 20.78±0.3<br>8 | 18.36±0.3<br>4 | 15.75±0.1<br>4 | 12.57±0.4<br>7 | 14.85±0.0<br>5 | 12.87±0.2<br>8 | 15.72±0.3<br>2 | 7.91±0.03      |
| Forward flow volume, ml                    | 35.27±0.0<br>5 | 64.67±0.1<br>2 | 42.27±0.0<br>5 | 64.79±0.1<br>4 | 46.41±0.0<br>6 | 64.28±0.1<br>8 | 72.64±0.1<br>7 | 73.25±0.0<br>7 |
| 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±5.4<br>4 |
| GOA, cm <sup>2</sup>                       | 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      |

P < 0.01 for all parameters. GOA, geometric orifice area

In terms of valve closing, the result was contrary. All of the Hancock valves closed

completely under the normal pulmonary pressure condition, whereas Magna valves showed incomplete closing at the center except the 27 mm valve (Figure 4). For valves sizing from 23 mm to 27 mm, closing reverse flow was greater in Magna valve ( $0.20 \pm 0.02$  vs  $0.65 \pm 0.29$  for 23 mm valve;  $0.17 \pm 0.01$  vs  $0.66 \pm 0.07$  for 25 mm valve;  $0.83 \pm 0.09$  vs  $3.56 \pm 2.27$  for 27 mm valve, all  $p < 0.01$ ). Leakage volume was larger in Magna valves in all sizes, therefore regurgitant fraction was higher in Magna valves (Table 2).



**Figure 4** Closing of the bioprosthetic valves under normal pulmonary pressure condition (30/15 mmHg). (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

Under pulmonary hypotensive condition, opening motion of the Hancock valve was more reduced. For 21 mm valve, one leaflet was fixed and the other leaflet partly opened so that only single leaflet was moving properly. From 23 mm to 27 mm valve, a single leaflet did not open and other leaflets opened sequentially, not simultaneously. Altered movements were noted for these 3 sizes of Hancock valve by each beat. Magna valves showed different

motions under pulmonary hypotensive pressure. Leaflets were opened sequentially but eventually all of the leaflets were completely opened (Table 3). Forward flow was greater in Magna valve of any size and Hancock valve had reduced GOA in all sizes. During the pulmonary hypotensive testing, all Magna valves did not close completely at the center. As a result, leakage volume and regurgitant fraction was higher in Magna valves (Table 4).

**Table 3** Completeness of opening and closure of 25 mm valves

| Pressure,<br>mmHg | Hancock |         | Magna   |         |
|-------------------|---------|---------|---------|---------|
|                   | Opening | Closing | Opening | Closing |
| 15                | -       | -       | +       | --      |
| 30                | -       | +       | +       | --      |
| 50                | +       | +       | +       | -       |
| 75                | +       | +       | +       | +       |
| 110               | +       | +       | +       | +       |

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

**Table 4** Hydrodynamic variables under hypotensive pulmonary pressure condition (15/5 mmHg)

|  | 21 mm     |           | 23 mm     |           | 25 mm     |           | 27 mm     |           |
|--|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|  | Hancock   | Magna     | Hancock   | Magna     | Hancock   | Magna     | Hancock   | Magna     |
| Transvalvular peak pressure gradient, mmHg | 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±0.0 | 39.01±0.1 | 24.20±0.0 | 36.64±0.0 | 23.19±0.0 | 34.97±0.0 | 34.88±0.0 | 43.76±0.1 |
|  | 5         | 0         | 6         | 6         | 3         | 6         | 8         | 3         |

|                          |                |                |           |           |           |           |           |           |
|--------------------------|----------------|----------------|-----------|-----------|-----------|-----------|-----------|-----------|
| Closing reverse flow, ml | 0.44±0.02<br>* | 0.41±0.06<br>* | 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 <sup>2</sup>     | 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 |

P < 0.01 for all parameters except noted. GOA, geometric orifice area. \* P=0.01

With pulmonary hypertensive pressure (50/20 mmHg and 75/35 mmHg), Magna valves showed simultaneous opening of the leaflets and complete closing. On the other hand, Hancock valves showed different motions by size. One leaflet of 21 mm Hancock valve did not open in 50 mm Hg pressure and every leaflet opened under 75 mmHg pressure. Fluttering motion of the leaflets was noted under pressure of 75 mmHg. For 23 mm to 27 mm Hancock valve, simultaneous but asymmetric opening of the leaflets were observed during pulmonary hypertensive testing. For valves sizing 21 and 23 mm, forward flow volume was larger in Hancock valve (Table 5). For 25 and 27 mm valves, forward flow volume was larger in Magna valves. GOA was larger in any size of Magna valve. Incomplete closing of Magna valve noted under hypotensive condition was not apparent in hypertensive setting. However, higher regurgitant fraction was still noted for Magna valves compared to Hancock valves.

**Table 5** Hydrodynamic variables under hypertensive pulmonary pressure condition (50/20 mmHg)

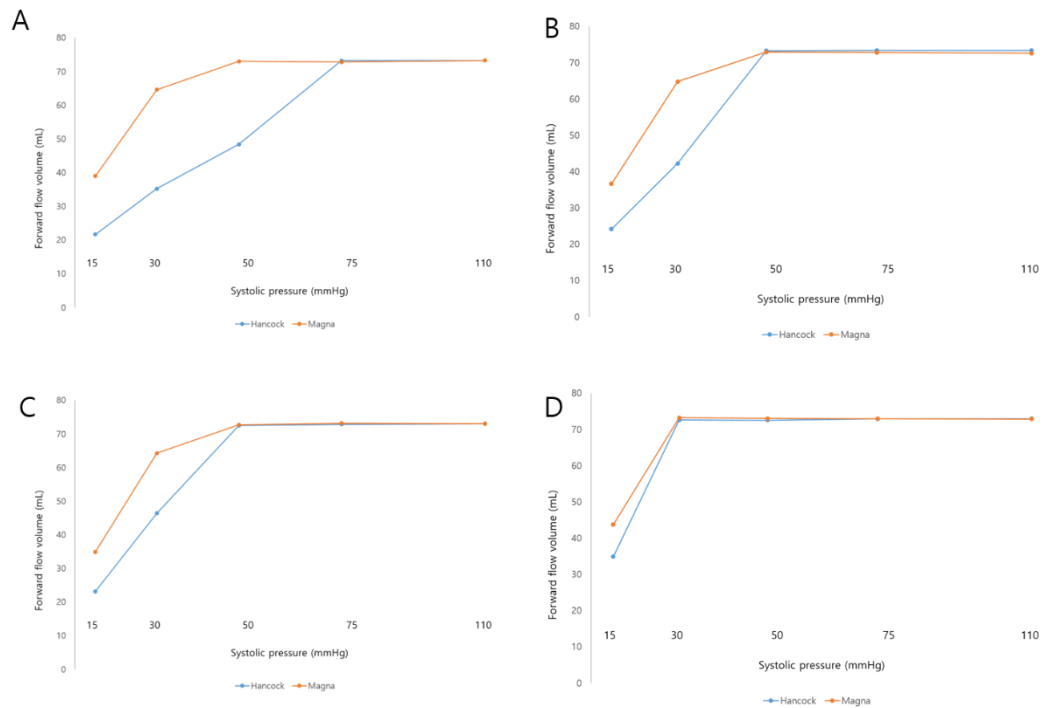
|                    | 21 mm          |                | 23 mm          |                | 25 mm          |                | 27 mm          |           |
|--------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|-----------|
|                    | Hancock        | Magna          | Hancock        | Magna          | Hancock        | Magna          | Hancock        | Magna     |
| Transvalvular peak | 35.77±0.2<br>3 | 24.15±0.6<br>4 | 33.71±0.3<br>1 | 16.31±0.4<br>8 | 29.04±0.3<br>2 | 13.77±0.3<br>5 | 15.81±0.1<br>4 | 7.39±0.14 |

|                                |                |                |                |                |                |                |                |                |
|--------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| pressure<br>gradient,<br>mmHg  |                |                |                |                |                |                |                |                |
| Forward<br>flow<br>volume, ml  | 48.43±0.0<br>5 | 73.06±0.0<br>9 | 73.31±0.1<br>2 | 72.95±0.0<br>6 | 72.55±0.1<br>0 | 72.75±0.1<br>0 | 72.64±0.1<br>7 | 73.25±0.0<br>7 |
| Closing<br>reverse<br>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<br>volume, ml          | 0.12±0.05      | 5.31±0.14      | 1.69±0.36      | 12.42±0.3<br>7 | 2.64±0.25      | 11.58±0.3<br>6 | 1.11±0.43      | 8.18±1.74      |
| Regurgitant<br>fraction, %     | 0.89±0.14      | 8.05±0.24      | 2.83±0.49      | 13.81±0.4<br>4 | 4.42±0.35      | 17.17±0.4<br>8 | 2.67±0.64      | 16.02±5.4<br>4 |
| GOA, cm <sup>2</sup>           | 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      |

P < 0.01 for all parameters. GOA, geometric orifice area.

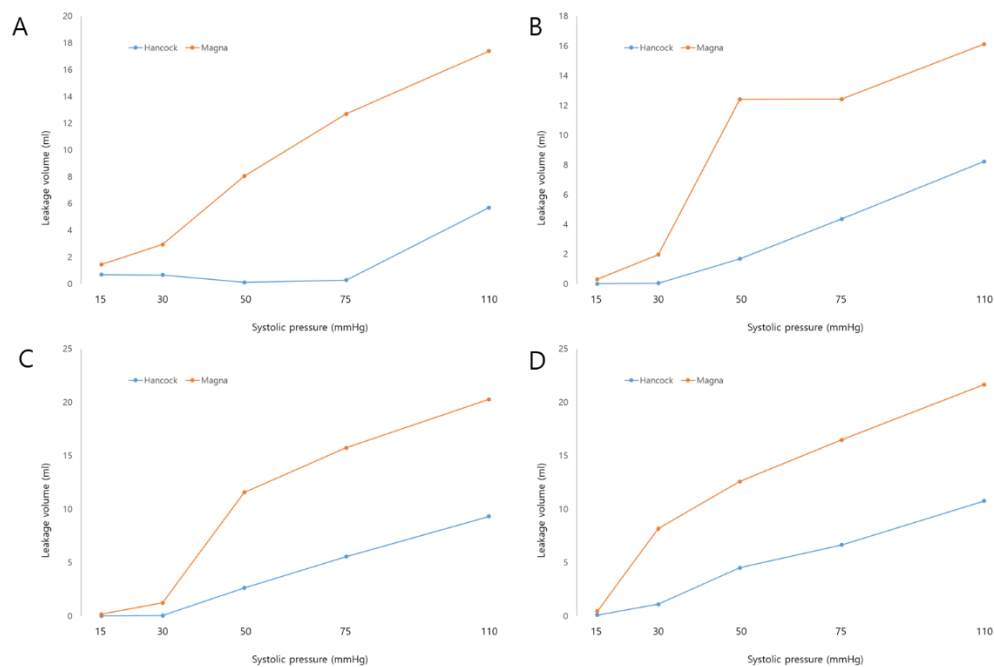
### 3. Valve performance by pressure elevation

Forward flow volume of valves increased by testing pressure and reached plateau at some point (Figure 5). Magna valve showed maximum forward flow volume under pressure of more than 50 mmHg (30 mmHg for 27 mm valve). Hancock valve reached plateau forward flow volume at 75 mmHg for 21 mm valve. Hancock valve had decreased forward flow volume than Magna valve when the valve was tested under normo- and hypotensive conditions. Closing reverse flow of valves did not increase by elevation of pressure but leakage volume and regurgitant fraction differed. For Hancock valve, leakage volume did not increase under normo- and hypotensive pressures. Leakage volume increased by elevation of pressure for Magna valve (Figure 6).



**Figure 5** Forward flow volume of each valve by testing systolic pressure. (A) 21 mm (B) 23 mm (C) 25 mm (D) 27 mm

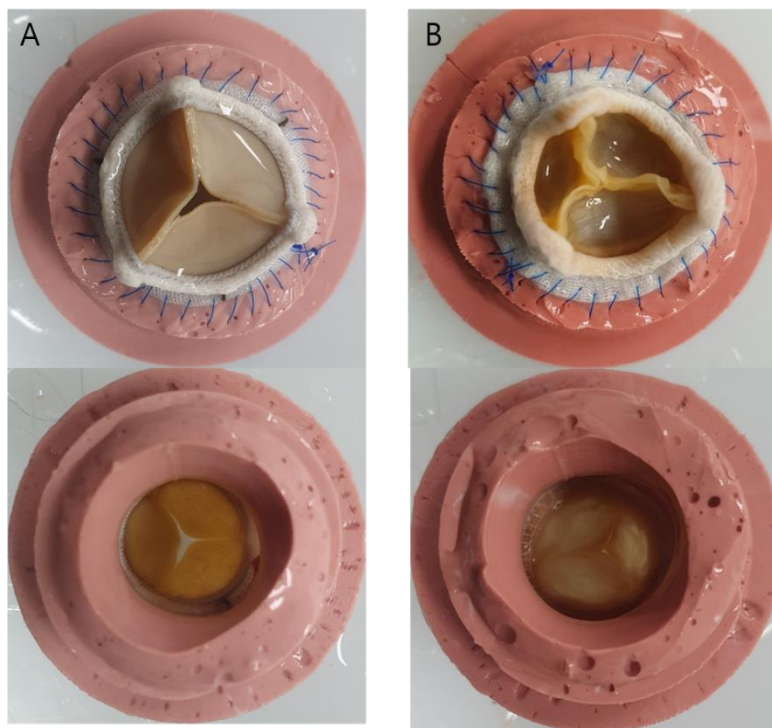




**Figure 6** Leakage volume of each valve by testing pressure. (A) 21 mm (B) 23 mm (C) 25 mm (D) 27 mm

#### 4. Accelerated Wear Test

25 mm valves were not able to be tested in the accelerated wear test circuit. One leaflet of the Magna valve did not move under speed of 20 Hz whereas motion of the Hancock valve worked normally. Therefore we changed the size of the valve to 21 mm which worked normally during the testing. After 200 million cycles, there was no damage or deformation of the valves (Figure 7).



**Figure 7** Pulmonary arterial side (upper panel) and ventricular side (lower panel) of 21 mm Magna valve (A) and Hancock (B) valve after completion of 200 million cycles of accelerated wear test.

#### IV. Discussion

Bovine pericardial and porcine valves are the most frequently used bioprosthetic valves. Off-label use of these bioprosthetic valves designed for aortic valve surgery in pulmonary valve position is a common practice in congenital heart surgery. However, the outcome and failure mode of the bioprostheses is different in the pulmonary valve position. Hemodynamic performance of the prostheses in the pulmonary setting is not well discovered. To investigate the difference in the hydrodynamic performance of bovine pericardial and porcine valves between the aortic and pulmonary positions, we used a Mock

Circulatory System. Unfavorable hemodynamic parameters of prosthetic valve such as high transvalvular pressure gradient and valve regurgitation is known risk factor for hemodynamic valve deterioration, valve reintervention, and poor survival<sup>12</sup>. In vitro hydrodynamic performance obtained by the MCS may mimic hemodynamic performance of the valve as a part of mechanical components of the valve degeneration mechanism.

Leaflet motion during the cardiac cycle showed that bovine pericardial valves do not close completely during diastole under normo- and hypotensive pulmonary pressure condition in contrast to high pulmonary pressure or aortic pressure condition where full closure is always attained. In a study describing in vitro behavior of bileaflet mechanical valve in a low-pressure system, low impedance produced incomplete closure of the prosthesis, which does not become an issue in the high-pressure system<sup>13</sup>. Similar phenomenon was observed for bovine pericardial valve in pulmonary pressure system. Incomplete closing of the valve occurred in the pulmonary system in contrast to the aortic pressure system<sup>14</sup>. High leakage volume and regurgitant fraction was associated with bovine pericardial valve. Incomplete closure of the valve accelerates reduced motion of the leaflets, which could possibly influence the fixation of valve leaflets<sup>14</sup>. Incomplete closure may contribute to leaflet calcification and fibrosis which was suggested as a main mechanism causing stenosis of bovine pericardial valve<sup>7</sup>. Thus this finding may provide mechanistic insight for understanding the mechanism of valve degeneration. However, the effect of incomplete opening observed in porcine valve mock circulation need to be elucidated. Incomplete opening, low forward flow volume, and small orifice area may lead to higher heart rate requirement to obtain optimal cardiac output which may accelerate prosthetic valve degeneration.

On the other hand, porcine valve showed incomplete opening and had smaller geometric orifice area. Leaflet tearing has been suggested as a mechanism for porcine valve degeneration in aortic valve position<sup>7,8</sup>. Transvalvular pressure gradient was higher in porcine valve compared to the bovine pericardial valve under the same pressure condition and the difference of transvalvular pressure gradient between two valves was increased by

systolic pressure. High transvalvular pressure gradient of porcine valve under aortic pressure may associate with leaflet tearing, therefore, the leaflet tearing may not be a problem in usual pulmonary pressure condition with acceptable transvalvular pressure gradient.

Bovine pericardial valve demonstrated greater forward flow volume under normal pulmonary pressure condition which is a consistent finding with previous reports for aortic valve position<sup>15,16</sup>. The Magna valve has been reported to have the best hydrodynamic properties in terms of effective orifice area and pressure gradient compared with porcine valves under aortic conditions<sup>17</sup>. This can be an advantage of bovine pericardial valve in pulmonary position. Small porcine valve demonstrated sub-maximum forward flow in pulmonary normo- and hypotensive condition and the forward flow volume difference between porcine and bovine pericardial valve was greater for 21 mm valve. Moreover, small sized-porcine valves showed the worse hydrodynamic performance in terms of opening motion and area during systole. In contrast, bovine pericardial valve required lower systolic pressure to reach maximum forward flow. Therefore, small sized-porcine valve should be avoided for pulmonary prosthesis in normotensive condition in terms of hydrodynamic performance. Not only the various pressure environment, i.e. the degree of pulmonary hypertension, but also the size of the valve itself may affect the behavior of the bioprosthesis in pulmonary position.

Under pulmonary normotensive condition, high forward flow volume and low transvalvular pressure gradient of bovine pericardial valve is advantageous. High leakage volume may play a deleterious role in hemodynamic performance and incomplete closure may contribute to leaflet fixation which may affect durability of the bovine pericardial valve. Porcine valve showed low forward flow volume and low transvalvular pressure gradient which may prevent leaflet tearing in long-term. This hydrodynamic phenomenon may partly explain the better durability of the porcine valve in pulmonary position<sup>5</sup>. In pulmonary hypertensive condition, on the other hand, bovine pericardial valve showed complete closure eliminating the concern in leaflet fixation and higher forward flow

volume than the porcine valve. For porcine valve, low forward flow volume is unfavorable for hemodynamic efficacy and high transvalvular pressure gradient may be related to leaflet tearing similar to the aortic valve position. Thus, bovine pericardial valve may be the choice for pulmonary prosthesis under pulmonary hypertensive condition in terms of hydrodynamic data.

After 200 million cycles of accelerated wear test under pulmonary pressure condition, there was no damage or deformation of the valve leaflets. This finding suggests that various etiologies other than hydrodynamic wearing play a major role in valve degeneration. Further studies with longer test cycles equivalent to ten or twenty years of life span is required to reveal hydrodynamic influence to the prosthesis.

Valves designed for the left heart showed aberrant behavior as pulmonary valves by alterations of pulmonary vascular resistance in vitro<sup>1</sup>. In vitro testing of bovine and porcine valve in different pressure system may investigate the effect of valve type to valve performance and longevity in each pressure system by regulating other confounding factors. However, extreme caution is warranted to apply our in vitro hydrodynamic testing results to the clinical practice. Other components such as calcification and thrombosis may play a much more important role in valve degeneration process and needs to be considered. Further research is needed to evaluate whether or not these results are associated with potential increased risk of prosthetic valve degeneration in the pulmonary condition.

The study has some limitations. All tests were performed using distilled water. Because the density of the water is thinner than blood, obtained hydrodynamic data may differ from the real hemodynamic data. The testing was performed in a linear, cylindrical tube which is different from natural right ventricular outflow tract anatomy. The influence of anatomical factors such as sinus of Valsalva and pulmonary artery bifurcation on hydrodynamic performance could not be demonstrated in the present study.

Finally, in clinical in vivo setting, the hemodynamic performance of prosthetic valves is not only affected by pulmonary artery pressure but also by various other factors such as

ventricular function, heart rates, other underlying patients' conditions, and it may not reflect the exact situation occurring in human body.

## V. Conclusion

Bovine pericardial and porcine bioprosthetic valves has different hydrodynamic characteristics under various pulmonary pressure conditions. Porcine valves were associated with incomplete opening and smaller forward flow volume and geometric orifice area whereas bovine pericardial valves were associated with incomplete closure and higher regurgitant fraction.

Although the patients requiring pulmonic valve replacements are much smaller than patients requiring aortic valve, understanding the hydrodynamic characteristics of each valves and selection of proper type of prosthetic valves in each cardiac position can be a paramount importance to obtain best clinical results in these population.

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ABSTRACT (IN KOREAN)

모의 순환 시스템을 이용한 폐동맥 판막 위치에서의 소심장막 인공 판막과 돼지 인공 판막의 유체역학적 특성의 비교

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신유림

배경: 폐동맥 판막 치환술을 시행할 때 대동맥 판막 위치를 위해 고안된 조직 판막이 주로 사용되나 폐동맥 판막 환경에서 대동맥 인공 판막의 혈역학적 분석은 미비하다. 본 연구에서는 주로 사용하는 대동맥 인공 판막인 소심장막 인공 판막과 돼지 인공 판막의 유체 역학적 특성을 폐동맥 판막 환경에서 알아보고자 하였다.

방법: 모의 순환 시스템을 이용하여 21, 23, 25, 27 mm 크기의 소심장막 인공 판막과 돼지 인공 판막의 유체역학적 특성을 실험하였다. 다양한 폐동맥 판막 환경과 대동맥 판막 환경에서 각각의 판막의 개구면적, 역류혈액량, 역류분율, 경판막압력차, 순방향혈류를 구하고, 고속 카메라를 이용하여 판막의 운동을 분석하였다. 가속 마모 실험을 통해 두

개의 판막의 변화를 관찰하였다.

결과: 정상 및 저혈압 폐동맥 환경에서는 소심장막 인공 판막이 불완전한 폐쇄를 보였으며 고혈압 폐동맥 환경 및 대동맥 환경에서는 완전 폐쇄가 관찰되었다. 소심장막 인공판막은 돼지 인공 판막에 비해 넓은 개구면적 (21 mm 판막에서  $0.67 \pm 0.01$  vs  $1.41 \pm 0.01$  cm<sup>2</sup>; 23 mm 판막에서  $0.93 \pm 0.01$  vs  $1.70 \pm 0.01$  cm<sup>2</sup>; 25 mm 판막에서  $0.99 \pm 0.01$  vs  $1.75 \pm 0.01$  cm<sup>2</sup>; 27 mm 판막에서  $1.58 \pm 0.01$  vs  $2.25 \pm 0.02$  cm<sup>2</sup>, 모두  $p < 0.01$ )과 큰 순방향혈류를 보였다 (21 mm 판막에서  $35.27 \pm 0.05$  vs  $64.7 \pm 0.12$  mL; 23 mm 판막에서  $42.27 \pm 0.05$  vs  $64.79 \pm 0.14$  mL; 25 mm 판막에서  $46.41 \pm 0.06$  vs  $64.28 \pm 0.18$  mL; 27 mm 판막에서  $72.64 \pm 0.17$  vs  $73.25 \pm 0.07$  mL, 모두  $p < 0.01$ ). 돼지 인공 판막에서는 불완전한 열림 및 작은 개구면적, 적은 역류 분율이 관찰되었다. 경판막압력차는 소심장막 인공판막에서 낮게 나타났다. (21 mm 판막에서  $20.78 \pm 0.38$  vs  $18.36 \pm 0.34$ ; 23 mm 판막에서  $15.75 \pm 0.14$  vs  $12.57 \pm 0.47$ ; 25 mm 판막에서  $14.85 \pm 0.05$  vs  $12.87 \pm 0.28$ ; 27 mm 판막에서  $15.72 \pm 0.32$  vs  $7.91 \pm 0.03$ ). 가속마모실험 후의 유체역학적 특성은 두 가지 판막 모두에서 변화를 보이지 않았다.

결론: 소심장막 인공 판막 및 돼지 인공 판막은 다양한 폐동맥 압력 환경에서 유체 역학 결과에 차이를 보였다. 소심장막 인공 판막은 불완전 폐쇄 및 넓은 개구 면적과 높은 순방향 혈류와 연관되었고, 돼지 인공 판막은 불완전한 열림 및 작은 개구 면적, 적은 역류 분율을 보였다. 이러한 유체 역학 결과의 차이가 폐동맥판막 위치에서 인공 판막의 내구성 및 기능 악화에 영향을 미치는지 추후 연구가 필요하다.

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핵심되는 말: 모의 순환 시스템, 폐동맥 판막, 인공 조직 판막, 유체 역학