

Hemodynamic Factors Affecting the Functioning of the Aortic Valve

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Abstract: Early stages of aortic valve disease involve a subtle increase in leaflet stiffness which affects valve performance seen particularly in the opening and closing of the valve. In this study, a pulse duplicator which recreates physiologic flow waveforms was used to evaluate how changes in experimental conditions such as downstream resistance and flow rate affect the opening and closing patterns of valves with varying stiffness. A photographic technique which allowed for analysis of valve leaflet motion revealed various trends in relation to the flow, resistance, and stiffness of the valves. Increased flow and resistance lead towards shorter opening and closing times for the valves, while increased valve stiffness demonstrated an increase in the opening and closing times of the valves. Pressure drops across the aortic valves decreased during the closing cycles as the area decreased, and increased during the opening cycles as the area increased. These results indicate that hemodynamic factors influence the severity of the disease as demonstrated by the trends observed during the opening and closing cycles of the valve.

1. INTRODUCTION

The aortic valve, composed of three leaflets, permits the movement of blood from the left ventricle into the aorta as the ventricle contracts, and acts to prevent the backflow of blood from the aorta into the left ventricle as the heart relaxes [5]. In a normal valve the leaflets open and close completely and almost effortlessly. Aortic valve stenosis is defined as obstruction of the aortic valve. In a stenotic valve, leaflet opening areas are reduced (Figure 1) [4].

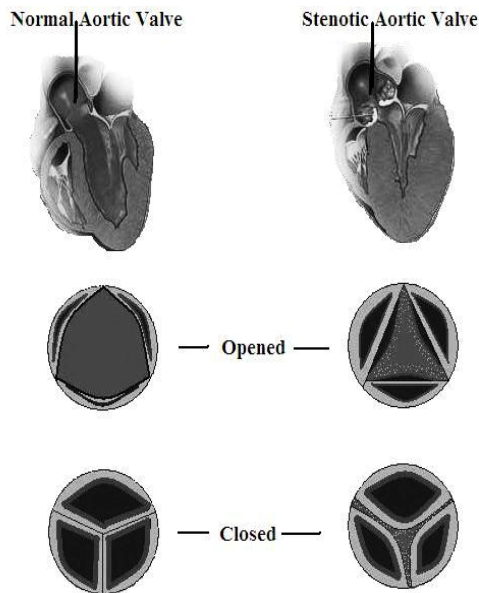


Figure 1 Image of a normal vs. a stenotic aortic valve.

Aortic stenosis may be caused by congenital defects or rheumatic fever, although in the United States, the degenerative form of the disease is seen in increasing frequency [1]. Degenerative valve disease affects approximately five of every ten thousand people in the United States [1]. In the early stages of the disease, left ventricular dilation occurs to compensate for the increased resistance allowing continued function of the heart [3]. The disease progresses in severity leading to ventricular hypertrophy, thickening of the heart muscle, which over time causes reduced cardiac output, thereby increasing the chances of heart failure [3,6,7]. Calcification, buildup of calcium on the leaflets of the valve renders the valve stiffer and obstructive [2]. At this advanced stage of the disease, symptoms develop indicating that surgery is required.

The rate of progression of degenerative valve disease is variable and nonlinear in an individual patient, making prediction of progression difficult [4,7]. Previous studies relating the rate of change of the aortic valve area within the cardiac cycle to the progression of aortic stenosis indicated that “in patients with aortic stenosis, the rate of change in aortic valve area as expressed by the aortic valve area ratio is a reliable predictor of an individual’s risk of rapid versus slow hemodynamic progression”[4]. The rationale for this measurement is based on the premise that stiffer valves will open and close at slower rates.

It is our hypothesis that the aortic valve area ratio is not solely determined by valve stiffness. Hemodynamic factors associated with increased afterload such as increased mean arterial pressure and increased vascular resistance, as well as the flow rate (cardiac output) through the valve could also affect valve mechanics as seen in the valve area calculations.

2. MATERIALS AND METHODS

Six aortic valves obtained from pigs were fixed in sets of three for 96 h in ethanol or glutaraldehyde. An additional set of three valves not fixed with ethanol or glutaraldehyde were maintained as controls. After fixation, the valves were preserved in phosphate buffered saline (PBS), which has a pH of 7.4, close to the pH value of human blood. Valve diameters and root diameters are given in Table 1.

	Valve Diameter (mm)	Root Diameter (mm)
ETHANOL		
Valve 1	12.9	14.8
Valve 2	11.6	16.6
Valve 3	10.2	8.9
GLUTARALDEHYDE		
Valve 1	8.3	12
Valve 2	8.8	13.8
Valve 3	10.5	7.8
PBS		
Valve 1	10.6	8.8
Valve 2	13.7	11.6
Valve 3	10.2	14.4

Table 1. Valve and root diameters for valves tested. Variations in size did not reach statistical significance at a level of $p > 0.05$.

The pulse duplicator used in this study (Figure 2) consists of an atrial tank that supplies the ventricular chamber by gravity. In between the atrial tank and the ventricular chamber a check valve simulates the activity of the mitral valve. The ventricular chamber contains two solenoid valves to allow compressed air in and out of the system. As compressed air enters the

system it generates systole, and as the air exits the system it in generates diastole. The pulse duplicator system also contains an aortic valve-testing chamber, where the valves are tested.

Downstream, a compliance chamber consists of flexible tubing. Increasing the external pressure, or “backpressure,” reduces the effective compliance by making the tubing stiffer. Through manipulation of the compliance and resistance, increased afterload was acquired. A control and data acquisition system is used to set parameters such as the heart rate and systolic ejection time and to acquire and display hemodynamic data.

Clinical markers of stenosis severity include pressure drop across the valve and orifice area of the valve. In the aortic valve chamber, pressure transducers were placed upstream (P1), and downstream the valve (P2).

Flow rates were measured using an ultrasonic flow meter. Valve opening area was measured throughout the cardiac cycle using a photographic system consisting of a camera and stroboscope. The timing of the images was controlled and recorded by the computer.

A mixture of water and glycerin was prepared to circulate through the system, imitating the properties (e.g., density, viscosity) of human blood. Blood has a density and viscosity of 1.06g/cm^3 and 0.04 Poise, respectively. Backpressures at 60mmHg and 90mmHg with flow measurements ranging from 3 to 5 liters per min were used for evaluation.

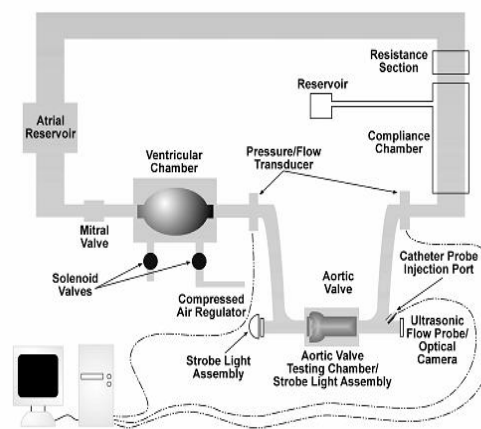


Figure 2 Pulse Duplicator System.

3. RESULTS

In Figure 3, trends for the maximum areas of each of the treated valves can be observed. A one tailed t-test with unequal variances suggests that the areas for the valves treated with glutaraldehyde and ethanol are statistically ($p < 0.05$) lower than the areas of valves stored in the phosphate saline buffered solution. The differences between valves

treated in ethanol and glutaraldehyde were not statistically significant.

Figure 4 illustrates the pressure gradient trends for each group of valves. A one tailed t-test with unequal variances suggests that the pressure gradients for the valves treated with both glutaraldehyde and ethanol are statistically ($p < 0.05$) greater than that for valves in PBS.

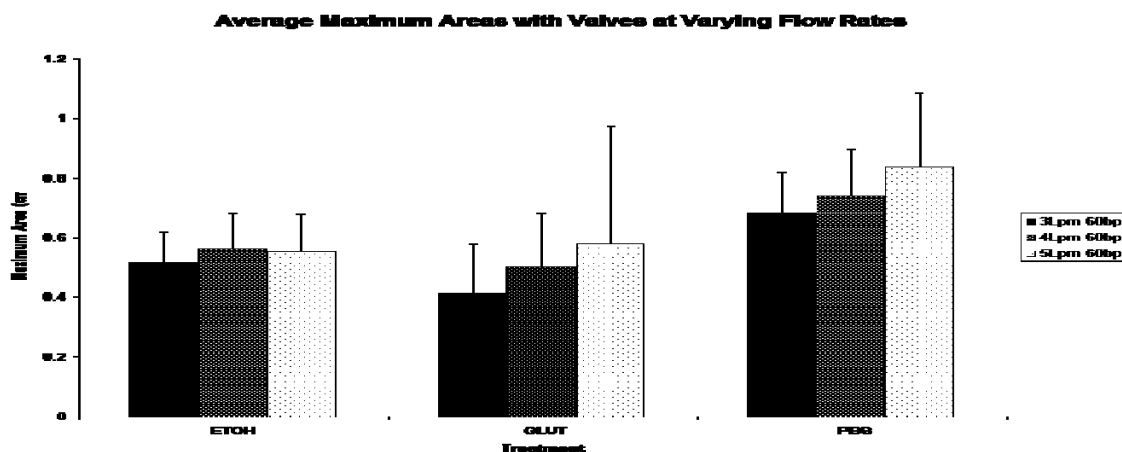


Figure 3 Area trends for valves in PBS, ethanol, and glutaraldehyde. Error bars indicate standard error of the mean.

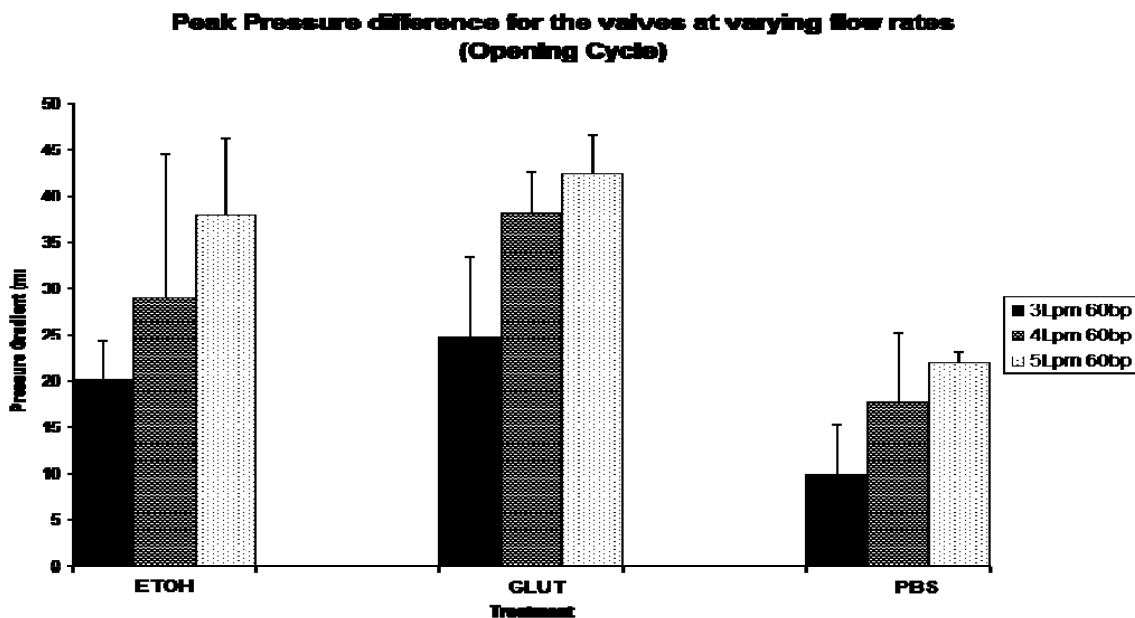


Figure 4 Pressure gradient trends for valves in PBS, ethanol, and glutaraldehyde. Error bars indicate standard error of the mean.

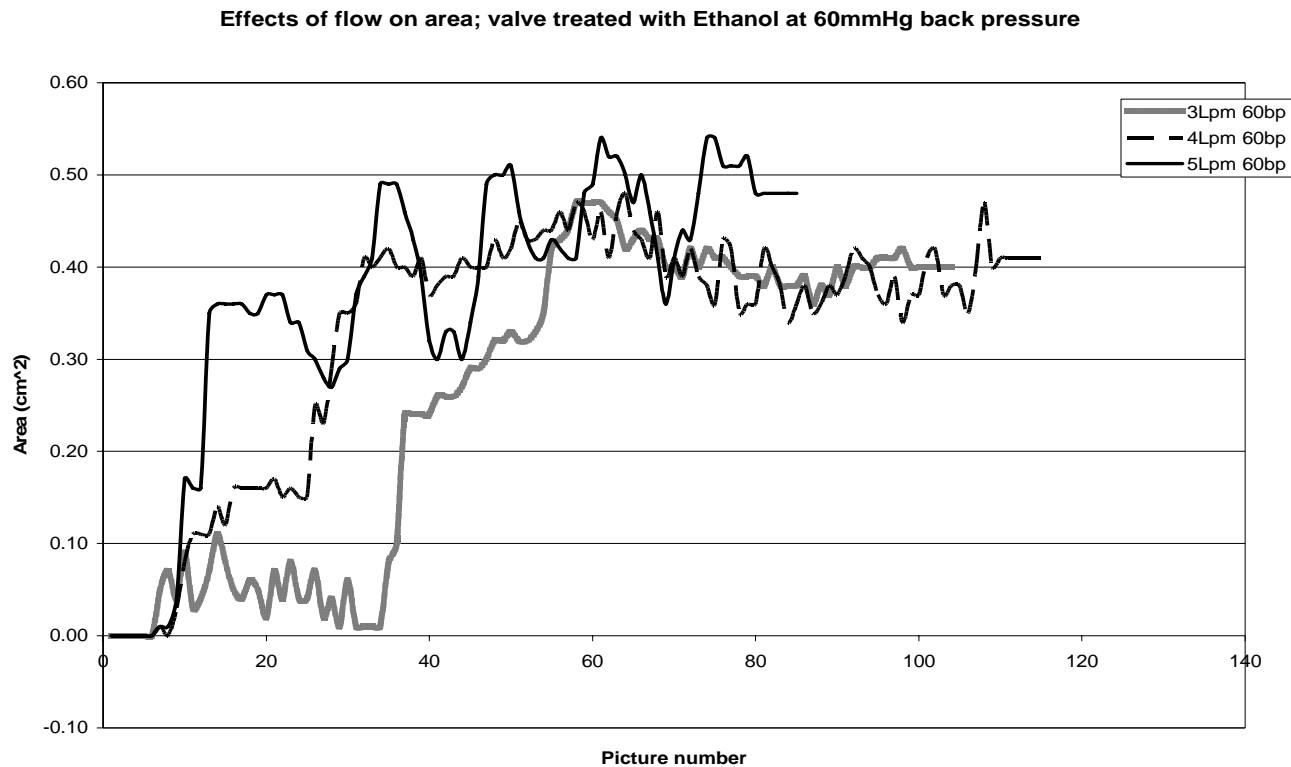


Figure 5 Flow rate dependency.

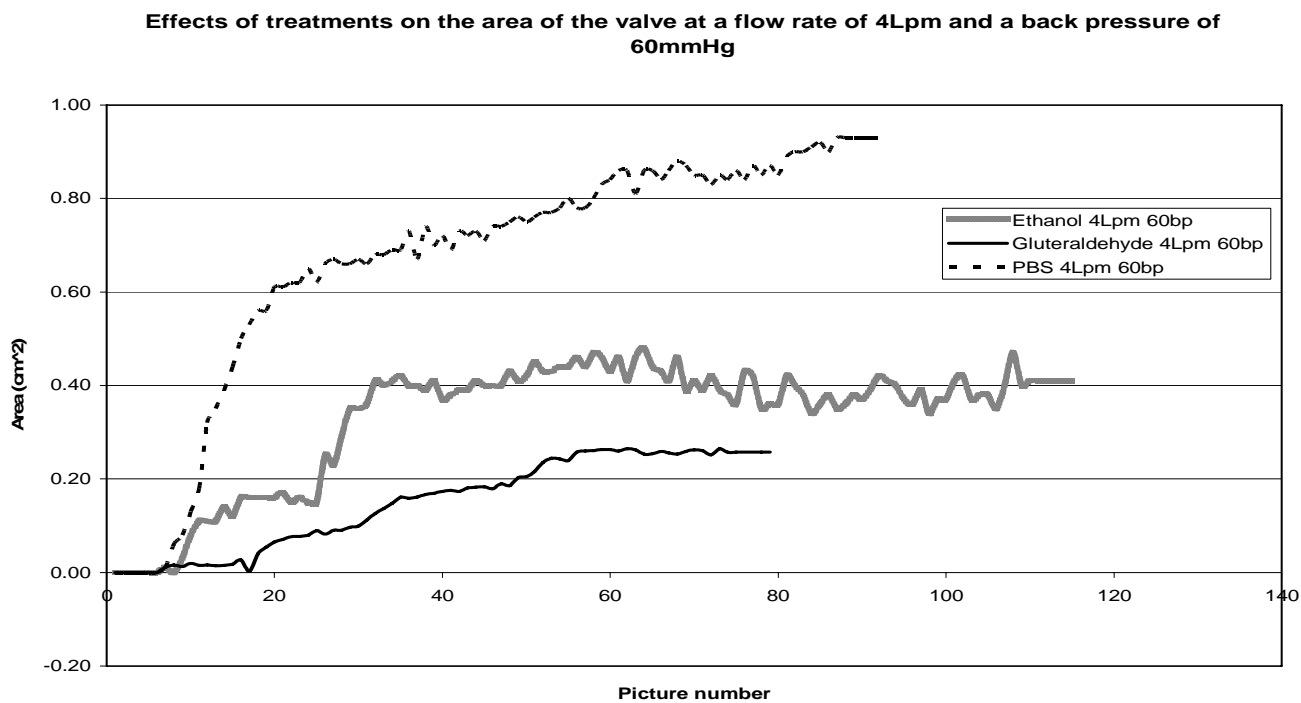


Figure 6 Effect of valve treatment.

4. DISCUSSION

Trends observed corresponded to age-related changes as hypothesized. Backpressure and flow readings were varied throughout the experiments to determine their influence on valve mechanics.

Increased valve stiffness leads toward smaller orifice areas (Figure 3) as well as greater pressure drops across the valves (Figure 4). As the degree of stenosis increased, a pressure difference was established across the valve, higher pressure differences. This would indicate more severe stenosis [3,4,7]. Therefore we should be able to measure valve orifice areas as well as pressure differences across a valve as well, and correlate the values obtained to the level of stenosis expressed on a valve.

Trends were still evident with increased flow and backpressure as seen in the graphs. Although, valves fixed with ethanol tended to show less flow dependency compared to valves fixed with glutaraldehyde or PBS (Figure 3).

Factors that affected the opening times for the valves were evident when considering flow rate (Figure 5) and valve stiffness (Figure 6).

Increased flow rate as well as valve stiffness tended to show decreased opening times for the valves. As previously stated, when the valve becomes more stenotic, a pressure difference is established across the valve [3,6,7]. The higher the pressure differences, the faster the valve would open or close in order to relieve stress. As is shown in Figure 6, increased stiffness caused shorter opening times for the valves.

5. CONCLUSION

These data suggest that changes in valve mechanics can be correlated to age.

By measuring the degree of changes in area and pressure differences for the valves fixed in glutaraldehyde and ethanol compared to those left in PBS buffer, and knowing the level of stenosis that each treatment expresses on the valve proper markers for predicting the progression of aortic stenosis can be developed.

We could also evaluate how progression of the disease depends on flow rate by seeing if the progression either increases or decreases based on increased flow rate.

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