A practical set-up to create an adjustable insufficiency in a porcine aortic root.

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Chapter 1

Introduction

When the aortic root becomes dilated, it can cause aortic valve insufficiency. An insufficient aortic valve creates a live threatening situation. In this study a practical set-up is made in which it must be possible to simulate the physiological and insufficient situation of the aortic valve. It is an in vitro set-up with a porcine aortic root.

1.1 Cardiac anatomy and physiology

The heart has four chambers (right atrium, right ventricle, left atrium and left ventricle) and four valves (tricuspid, pulmonary, mitral and aortic valves) as shown in figure 1.1.

![Figure 1.1: Drawing of the heart showing its chambers and valves. Ra-right atrium, RV-right ventricle, LA-left atrium, LV-left ventricle, T- tricuspid valve, P-pulmonary valve, M- mitral valve, A- Aortic valve, PA- pulmonary artery, AO-aorta. Arrows indicate the path of the blood flow [1].](image)

The flow of the blood is achieved by the pumping action of the heart. During atrium filling, oxygen-depleted blood returns from the body via venae cavae to the right atrium, the oxygenated blood from the lungs returns via pulmonary veins to the left atrium. During ventricular filling, aortic and pulmonary valves remain closed and mitral and tricuspid valves remain open. The blood flows from the right atrium through the tricuspid valve into the right atrium and from the left atrium and through
the mitral valve to the left ventricle. During ventricular ejection, aortic and pulmonary valves remain open and mitral and tricuspid valves remain closed. The blood then flows from the left ventricle through the aortic valve to the aorta, and to the whole body. On the right side the blood flows from the right ventricle through the pulmonary valve to the pulmonary artery, and to the lungs [1]. The time course of pressure in the aorta, left atrium and left ventricle are given in figure 1.2.

![Figure 1.2. Pressure versus time plot of two cardiac cycles [1]](image)

1.2 Aortic valve anatomy and physiology

The aortic valve consists of three membranous leaflets and aortic sinuses. The valve is located between the left ventricle and the aorta and its function is to allow the blood to flow in one direction, from the ventricle to the aorta. The valve separates the ventricle from the aorta. The valve opens and closes approximately 103.00 times each day and approximately 3.7 billion times in its life span. This opening and closing of the aortic valve is achieved by the movement of its three leaflets. The aortic and pulmonary valves are called semilunar valves because their leaflets have the shape of a half moon. Semilunar valves function passively in response to blood flow [1]. When the left ventricle is in its systolic phase, it contracts to eject the blood from the heart into the aorta; the valve opens (as can be seen in figure 1.2). When in diastole the valve closes, the three cusps meet in the middle at a thickened area on each of the leaflets, called the nodes of Arantius. The node of Arantius is part of the surface where in diastole the leaflets make contact; the coaptation area. Behind the three cusps three cavities can be found, termed the sinuses of Valsalva. In two of these sinuses a coronary artery arises, hence the cusps are called the left coronary cusp, right coronary cusp and non-coronary cusp [2]. The crown-shaped fibrous line of attachment of the leaflets to the aortic wall is called the annulus fibrosus. The three areas where two adjacent leaflets are attached to the aortic root are the commissures as shown in figure 1.3.
1.3 Aortic valve insufficiency

Leakage and backflow of blood that is ejected from the left ventricle (LV) into the ascending aorta back into the left ventricle, is caused by aortic valve insufficiency (AI). As people become older, their heart and valve opening can enlarge. Due to this the leaflets can not close properly anymore. An increase in incidence of AI is predicted as a consequence of the advancing age of our population. More insight in AI through in vivo and in vitro studies is needed. A physiological representative in vitro AI model provides a numerous advantages over research in vivo AI. In an in vitro model it is possible to take exact pressure and flow measurements and visualize of the valve. Where in vitro models have also high reproducibility. An in vivo model will give interference of the auto regulation system and thus adaptation of the species.

Figure 1.3: Top: Schematic presentation of the aortic valve. Bottom: Drawing of the aortic valve showing left the side view and right the cross section of one leaflet. Rb-radius of the base, Rc-radius of the commissures, H-valve height, α-bottom surface angle of the leaflet, φ-free edge angle of the leaflet. Hs-height of the commissure, hs-sinus height, ds-radius of the outermost wall of the sinus. Cc-coaptation height[1].
1.4 Aim and outline of this study

In this study a practical set-up is made in which a porcine aortic root can be installed. In this set-up it must be possible to simulate the physiological and AI situation of a porcine aortic valve, to get a better insight in AI.

1.5 Approach

First a practical set-up is made in which a porcine aortic root can be installed, then the set-up is tuned to generate a physiological situation (70 ml stroke volume, aortic pressure 120 over 80 mmHg). After this, the aortic valve will be made insufficient. All the other conditions will stay the same.

Various dimensions of the aortic valve have been measured using different techniques in several mammalian species. An overview of the outcome of these studies is given in table 1.1:

<table>
<thead>
<tr>
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<th>Man</th>
<th>Pig</th>
<th>Pig</th>
</tr>
</thead>
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<tr>
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<td>2,48</td>
<td>4,28</td>
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<td>1,71</td>
</tr>
</tbody>
</table>

Table 1.1: Dimensions of the Aortic Valve as shown in figure (1.3) in various species, scaled with respect to Rb=1

Variations in the dimensions appear to be in the range of natural variations expected in any given species. This observation suggests that the aortic valve in all mammalian species is very similar [1]. In this study a porcine aortic root is use, to simulate a human aorta. As shown in table 1.1, the porcine heart valve is similar to the human.
Chapter 2

Material and Methods

2.1 Experimental set-up

In this section the experimental set-up used in this study is described. In the set-up as shown in figure 2.1, physiologically representative pressure and flow boundary conditions of the aortic valve can be created, in which an adjustable AI can be made.

![Figure 2.1: Experimental setup; the servo pump creates in combination with the windkessel model a physiological flow and pressure, over the porcine aortic root. Measured with: PressureWire, pressure sensor and the flow meter.](image)

Physiological representative *in vitro* aortic model

The model used to create the physiological representative aortic pressure and flow is developed and described by Stijnen *et al* [9] and remodeled as shown in figure 2.1. Here, a short description will be given supplemented with the extra elements to make it suitable for AI experiments. The model consists of three parts: the heart, the systemic circulation and the stretch cylinders. The heart consists of the left ventricle (LV) and its two valves: the mitral and aortic valve.

The heart is modeled as a rigid chamber with a piston pump attached to it. The piston is driven by a computer controlled linear servo motor (ETB32, Parker, Houston, TX). The mitral valve is an artificial valve homemade from a silicone material, the aortic valve is a fresh aortic root of a 100 kg pig. The preparation of the aorta is done as shown in the Hemolab aorta root preparation protocol [11].

The systemic circulation consists of the pig aorta, connected to a windkessel, which represents the distal systemic compliance. The resistances of the windkessel are located at the in and out flow of the windkessel. These resistances model the aortic and peripheral resistance respectively.
The AI is created by pulling the commissure points in radial direction this is done by the stretch cylinders. The stretch cylinders are two handmade cylinders, of stainless steel, which fit perfectly together. The cylinders can rotate in each other as shown in figure 2.2.

On the outside of the cylinder there are ribs, the rib on the first cylinder guides the suture and the suture is connected to the rib on the second cylinder. The suture is stitched in to the aortic root at the commissure point, as shown in figure 2.3.

Figure 2.2: The stretch cylinders, two concentric cylinders with each 3 ribs to connect the suture on.

Figure 2.3: The suture has to be stitched at the commissure points, the suture will be connected to the stretch cylinders.
Moving the cylinders will make the distance between the ribs larger and will stretch up the aorta in radial direction, as shown in figure 2.4. This will make the \( R_c \) as shown in figure 1.3 larger. This simulates a dilated aortic root creating an insufficiency aortic valve.

![Diagram](image)

**Figure 2.4**: Aortic root placed in the stretch cylinders, the suture is guided over the first rib and connected to the second rib. Turning the second cylinder will enlarge the distance between the ribs and will stretch up the aortic root. In the stretched situation the aortic valve can not close properly.

### 2.2 Data acquisition and processing

#### 2.2.1 Acquisition

**Software/hardware**

A standard PC is used with the following software: National Instruments, Labview and Matlab. All the data is measured at a sample frequency of 1000 Hz.

**Aortic pressure**

Aortic pressure was measured directly distal to the aortic valve using a pressure transducer (P10EZ, Becton Dickinson, Franklin Lakes, NJ) and a bridge amplifier (Picas, Peekel Industries, Rotterdam, The Netherlands).

**Aortic flow**

The aortic flow is measured with an ultrasonic flow probe (ME 25 PXM, Transonic Systems Inc, Ithaca, NY). The flow probe is placed at approximately 500 mm distal to the aortic valve.

**Left ventricle pressure**

A Radi PressureWire® is used to measure the LV pressure. The PressureWire consists of a 0.355 mm diameter guidewire with a working length of 1750 mm. The sensor is
located 300m proximal to the tip. The PressureWire is introduced into the system through the LV in front of the descending aorta at 20 mm of the aortic valve.

Visualization of the aortic valve

To make video footage of the valves an endoscope (Olympus endoscope, series 5), an internal light source (Olympus ILH-2A) and external lighting (dedo cool light) are used. The endoscope was introduced into the system through the windkessel aortic resistance.

2.2.2 Processing
Visualization pressure and flow data

Characteristic pressure and flow signals obtained with this set-up are stored on a hard disk and visualized in Matlab shown in figure 2.5.

![Pressure and flow data](image)

**Figure 2.5:** Pressure and flow data, received form the setup in physiological situation.

Quantification flow differences

To compare the flow signal in the AI situation \(q_{AI}\) with the physiological situation \(q_{phys}\) ten strokes of both signals are integrated. This will give the total flow of ten strokes. Then the difference is calculated and the regurgitation is expressed as a percentage of the flow in the physiological situation. As shown in the formulas 2.1, 2.2 and 2.3
\[ q_{AI} = \frac{1}{10} \int_0^{10} q_{AI} \, dt \] [2.1]

\[ q_{phys} = \frac{1}{10} \int_0^{10} q_{phys} \, dt \] [2.2]

\[ \frac{(q_{phys} - q_{AI})}{q_{phys}} \times 100\% = \text{regurgitation} \] [2.3]

2.3 Protocol

In this section the experiments are described and explained.

2.3.1 Experiments in aortic model

With the aortic model the intention is to create pressure and flow which is representative for that of the human aorta. The aortic flow created by the piston pump, is similar to the stroke volume of the human heart (round about 70 ml/s). The aortic pressure is set to approximately 120-80 mmHg. The aortic flow peak was about 25 l/min. This was accomplished by fine tuning the volume in the windkessel compliance chamber, the two resistances and the stroke volume of the pump. The video footage was taken after about 20 cycles, in order for the system to balance itself.

2.3.2 Experiments in the insufficient aortic model

This experiment is identical to the experiment in the aortic model; the only thing that is added is the insufficiency. When the physiological pressure and flow are reached, we measure the pressure and flow at different stretch levels as imposed by the stretch cylinders. At a certain stretch level the insufficiency will occur. The video footage was taken about 20 cycles after the insufficiency occurred.
Chapter 3

Results

3.1 Physiological situation

3.1.1 Physiological pressure and flow

Figure 3.1 shows the pressure and flow data measured in the experiment with physiological aortic pressure and flow. The aortic pressure is 130-80 mmHg, which is considered physiological. The left ventricle pressure is 130-0 mmHg, which is considered physiological. The flow peak is 25 l/min and the minimum flow is -7 l/min. The flow data contains an unwanted reflection oscillation. Also in the left ventricular pressure curve is a high frequent distortion.

As shown in figure 3.2, the video footage shows that the valve is opening and closing properly.

Figure 3.1: Top left: aortic pressure, top right: left ventricular pressure, bottom left aortic flow, bottom right: aortic and left ventricle pressure.

Figure 3.2: Movement of the aortic valve at physiological pressure and flow, in the first and the last snapshot the valve is fully closed.
Chapter 3. Results

3.2 Insufficient situation

3.2.1 Pressure and flow with insufficient aortic valve

Figure 3.3 shows the pressure and flow data measured in the experiment of physiological aortic pressure and flow in the AI situation. The aortic pressure is 110-60 mmHg. This is lower than the physiological aortic pressure. The left ventricle pressure is 0-110 mmHg. The peak is lower than the physiological left ventricle pressure peak. The peak flow is 25 l/min and the minimum flow is -10 l/min.

![Figure 3.3: Top left: aortic pressure, top right: left ventricular pressure, bottom left aortic flow, bottom right: aortic and left ventricle pressure.](image)

As shown in figure 3.4, the video footage shows that the valve is not closing properly in the AI situation.

![Figure 3.4: Movement of the aortic valve at physiological pressure and flow in the AI situation, in the first and the last snapshot the valve is not fully closed, see the back spot in the middle.](image)
3.3 Quantification of insufficiency

3.3.1 Pressure drop

Figure 3.5 shows the difference between left ventricular and aortic pressure in the AI situation and physiological situation. The pressure in the AI situation is overall lower than in the physiological situation. The mean aortic pressure difference is approximately 19 mmHg.

![Figure 3.5](image-url)
3.3.2 Regurgitation

Figure 3.6 shows the flow patterns of the AI and the physiological situation in a representative heart cycle. There is a total flow difference of 15% in each stroke. This difference is due to geometrical transformation of the aortic valve. The aortic valve can not close properly and regurgitation occurs.

![Figure 3.6](image)

**Figure 3.6**: Flow pattern of one stroke, the physiological situation compared with the AI situation.

3.3.3 Movement

Figure 3.2 and figure 3.4 are compared in figure 3.7, the AI is clearly visible in first and last pictures of figure 3.7.

![Figure 3.7](image)

**Figure 3.7**: Movement compared in the physiological situation (top) with the AI situation (bottom).
Chapter 4

Discussion and Conclusion

The goal of this study was to design a set-up to create an adjustable AI in vitro, in a porcine aortic root, at physiological pressure and flow.

The designed set-up with a properly closing aortic valve produces an aortic pressure of 130-80 mmHg, a left ventricular pressure is 130-80 mmHg a flow peak of 25 l/min and a minimum of -7 l/min. In the AI situation: the aortic pressure is 110-60 mmHg, a left ventricular pressure of 110-0 mmHg, a flow peak is 25 l/min and the minimum is -10 l/min.

We can conclude from the pressure and flow data that there is a 15% less netto forward flow and that there is a 19 mmHg mean pressure drop, in the AI situation. The pressure and flow drop indicates that there could be an AI. The video footage supports this conclusion; there is a clear example of the AI.

The preload and afterload system that is used creates physiological pressures and flow is functioning very well. The stretch system stretches the aortic root and makes the aortic valve insufficient, at physiological pressure and flow. Although the stretch system creates an adjustable AI, it may be possible that more accurate stretch system will improve the adjustability of the AI. It could be valuable to quantify the stretch level. Instead of three ribs per cylinder there it would be better to used six ribs per cylinder, this will give a more homogeneous distribution of the stretch forces.

It is unclear what the high frequent distortion in the left ventricular pressure signal is, it could be caused by a spindle of the Servo pump.

The aortic flow is measured at the end of the polyurethane tube (qa); this is a reasonable indication about the leakage of the aortic valve. It would be better to measure the aortic flow directly behind the valves (qav) at the same point as the aortic pressure is measured. Because qa is the sum of qav and qat and it would be more precise to just have qav. As shown in figure 4.1.

\[
q_a = q_{av} + q_{at}
\]

Figure 4.1: In this study is measured the flow at qa, this is the sum of qav and qat. This is reasonable a indication of the qav, to have accurate flow measurement, flow probe should be placed right behind the porcine aortic root.
As is described in ISO standards for non-active heart valve substitutes [10], the regurgitation volume is the sum of the closing volume and the leakage volume, as is depicted in figure 4.2. Leakage volume is associated with leakage through the closed valve.

\[ \text{regurgitant volume} = \text{closing volume (cv)} + \text{leakage volume (lv)} \]

**Figure 4.2**: Schematic flow versus time plot of an aortic valve showing regurgitated volume (closing volume plus leakage volume) for one cardiac cycle[10].

It was not possible to analyze the flow data of this study with the ISO standard because of the reflections in the flow signal. If the reflections can be filtered out, the ISO standard could be a valuable method to compare the closing volume of the AI situation with the physiological situation.

Nonetheless, this set-up creates an adjustable AI in vitro in a porcine aortic root. Which makes it possible to simulate the physiological and AI situation of a porcine aortic valve. It is shown that only a little insufficiency as shown in figure 3.3, will cause 15% of regurgitation.
Bibliography

[9] Stijnen, J.M.A. / Interaction between the mitral and aortic heart valve
[10] ISO 5840: *Cardiovascular implants -- Cardiac valve prostheses*
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