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# Development of an experimental setup for the *in vitro* investigation of mitral valve repair devices

**Abstract:** Mitral regurgitation (MR) occurs with a prevalence of approximately 10 % in patients aged 75 years or older and therefore is one of the most frequent indications for heart valve surgery. During the last decade surgical mitral valve repair (MVR) procedures emerged as the gold standard for the treatment of clinically relevant MR. However, for surgically inoperable or high-risk patients transcatheter-based MVR devices present a valuable treatment option. Within the current study, we developed an experimental setup to investigate the hydrodynamic performance of transcatheter-based MVR devices *in vitro*. The bicuspid mitral valve (MV) model employed in the experimental setup features a D-shaped MV annulus with $d_1 = 26.30$ mm, $d_2 = 30.05$ mm and chordae tendineae with a length of $l_1 = 25$ mm attached to two papillary muscle structures.

Pressure gradient – volumetric flow rate (Δp-Q) relations were investigated for steady state backward flow with transvalvular pressure gradients ranging from $0.75\ \text{mmHg} \leq \Delta p \leq 103.13\ \text{mmHg}$. Deionized water at 37 °C with a dynamic viscosity of 1.002 mPa·s and a density of 998 kg/m$^3$ was used. A test-chamber consisting of a press-fit MV holder and cylindrical in- and outflow tracts were developed. Different designs for the exchangeable press-fit MV holder were manufactured using additive manufacturing technologies providing an optimal fitting for variable MV sizes and pathologies. In- and outflow tracts featuring a diameter of $d = 50$ mm and a height of $h = 60$ mm were made from transparent polymethylmethacrylate to allow for easy optical access during measurements. The experimentally investigated $\Delta p$-$Q$ relation yields a quadratic correlation for the open MV and a linear correlation for the closed MV. A transvalvular closing pressure of $(4.94 \pm 0.04)$ mmHg was measured for the MV model.

**Keywords:** mitral regurgitation, mitral valve repair

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## 1 Introduction

The MV is a bicuspid valve located between the left atrium (LA) and the left ventricle (LV) consisting of four individual parts: (I) anterior and posterior leaflets, (II) papillary muscles, (III) chordae tendineae and (IV) mitral annulus [1]. In order to ensure mitral competence throughout the cardiac cycle, all parts of the MV and the LV need to be synchronized. [1, 2]. Any disturbance of the aforementioned structures can lead to MR and thereby to systolic retrograde blood flow from the LV to the LA, precipitating a decrease of both ventricular pressure and forward flow of oxygenated blood [1–3]. With a prevalence of approximately 10 % in patients older than 75 years, clinically significant MR is one of the most common valvular disorders [4–7].

MR is generally classified as either primary (structural) MR where the intrinsic anatomical structure of the MV apparatus is dysfunctional or secondary (functional) MR where the MV apparatus is structurally intact but the dysfunction is caused by LV remodeling [5, 8]. Of those two, primary MR is the most common entity of MR in the western world [9]. After the introduction of surgical MVR procedures, such as the edge-to-edge technique in 1991, surgical MVR evolved as the gold standard for the treatment of clinically significant MR [9, 10]. However, in inoperable patients or patients with high surgical risk suffering from severe MR, transcatheter-based MVR presents a viable treatment option [11, 12].

Although clinical data regarding the performance of transcatheter-based MVR devices are broadly available, the

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influence of these devices on the hemodynamics of the MV has not been fully understood yet. To address this problem, we developed an experimental setup which allows for the *in vitro* investigation of the hydrodynamic performance of different transcatheter-based MVR devices.

# 2 Materials and methods

## 2.1 Experimental setup

The developed experimental setup (see **Figure 1**) consists of a fluid reservoir with temperature control, a pump (Corio CD, Julabo GmbH, GER), an adjustable flow resistance, a volumetric flow rate sensor (LFS-008, Levitronix GmbH, SUI), a test chamber holding the MV model and two pressure sensors (86A 3R–000000–005P G, Measurement Specialties Inc., USA) which are located proximally and distally to the MV model. The $\Delta p$-$Q$ relations were investigated for steady state backward flow applying physiological transvalvular pressure gradients ranging from 0.75 mmHg to 103.13 mmHg. Deionized water at 37 °C was used to perform three measurements of one MV model. The test-chamber is made of a press-fit mitral valve holder cassette and cylindrical in- and outflow tracts. Different designs for the exchangeable press-fit mitral valve holder were manufactured using additive manufacturing technologies, providing an optimal fitting for variable MV sizes and pathologies. In- and outflow tracts featuring a diameter of $d = 50$ mm and a height of $h = 60$ mm were made from transparent polymethylmethacrylate to allow for easy optical access during measurements.

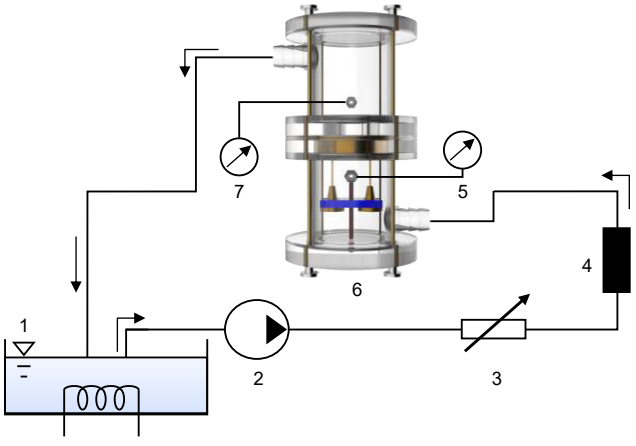


**Figure 1:** Experimental setup consisting of a fluid reservoir (1), a pump (2), an adjustable flow resistance (3), a flow sensor (4), distal and proximal pressure sensors (5,7) and the test chamber holding the MV model (6).

## 2.2 Mitral valve model

A MV model (LifeLike BioTissue Inc., CAN) featuring a D-shaped, lightly saddle-shaped annulus with an annulus area of 7.5 cm$^2$ and a circumference of 92 mm (see **Figure 2**) was used. The aorto-mural (AoM) distance $d_1$ is 26.30 mm and the intercommisural distance between the antero-lateral and postero-medial commissure $d_2$ is 30.05 mm. The anterior leaflet consists of a semi-circular structure with a thickness of 1.10 mm. The posterior leaflet is made up of three scallops and features a thickness of 1.10 mm. To allow for physiological valve opening and closure the MV model features two papillary muscle structures. From the tips of each of these structures, three chordae tendineae with a length of $l_1 = 25$ mm arise, inserting at the leading edges of the anterior and posterior MV leaflets.

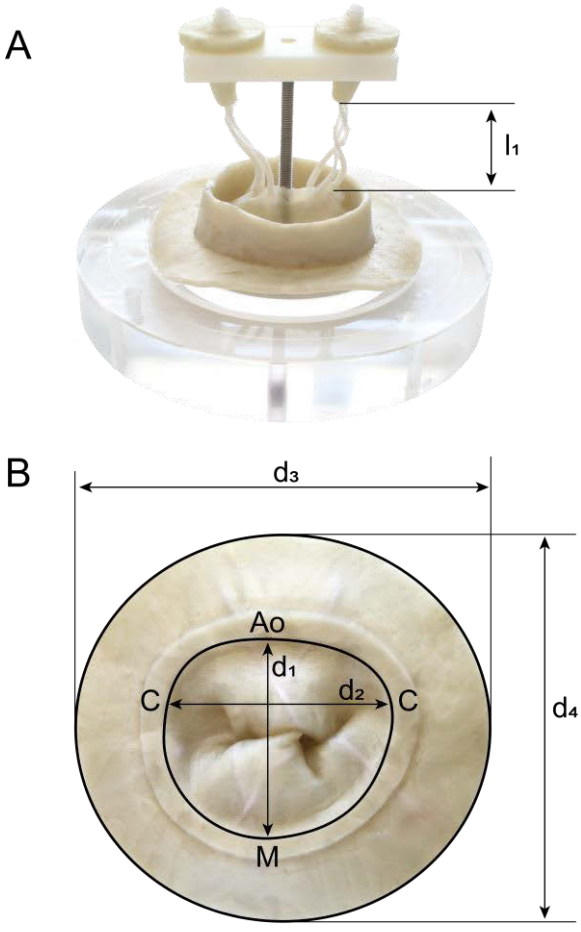


**Figure 2: A)** MV model with two papillary muscle structures and chordae tendineae with $l_1 = 25$ mm. **B)** MV model during the systole displayed from ventricular view. The aorto-mural (AoM) distance is $d_1 = 26.30$ mm, the intercommisural (CC) distance between antero-lateral and postero-medial commissure is $d_2 = 30.05$ mm and the diameters of the ovoid shaped MV are $d_3 = 62.90$ mm and $d_4 = 57.05$ mm.

# 3 Results and discussion

In accordance with Bernoulli's principle, the conducted measurements of the open MV configuration consistently show a quadratic correlation ($\Delta p \sim Q^2$) between $\Delta p$ and $Q$ (see **Figure 3**). The coefficients of the quadratic function calculated through quadratic regression and the coefficient of determination are presented in **Table 1**. In order to quantify the reproducibility of the experimental results of the open MV configuration, the maximum relative errors of the quadratic function coefficients were calculated. The maximum relative errors of the second, first and zeroth order for the open configuration are 2.1 %, 1.4 % and 0.8 %, respectively. Visual examination confirms coaptation and symmetrical overlap of the anterior and posterior MV leaflet at $\Delta p = (4.94 \pm 0.04)$ mmHg ($n = 3$). Since the normal left ventricular diastolic pressure ranges between 3 mmHg and 12 mmHg the measured closing pressure gradient lays within the physiological range of the human MV [13].

As a result of the MV closure, $\Delta p$ increases rapidly from 5 mmHg for the open MV configuration, to a transvalvular $\Delta p$ of 39 mmHg for the closed MV configuration. Unlike the open MV configuration, the investigation of the closed MV configuration yields a linear correlation between $\Delta p$ and $Q$ (see **Figure 4**). The coefficients of the linear function calculated by linear regression and the coefficient of determination are presented in **Table 2**. The maximum relative errors of first and zeroth order of the closed configuration are 3.2 % and 4.2 %, respectively.

As expected, the highest retrograde volumetric flow $Q_{max} = (0.54 \pm 0.01)$ l/min was measured at the highest transvalvular pressure gradient $\Delta p_{max} = (102.91 \pm 0.28)$ mmHg. The limited performance of the utilized pump impeded measurements for transvalvular pressure gradients physiologically ranging from 100 mmHg to 130 mmHg during the left ventricular systole [13]. The MV model, however, did not show any signs of mitral incompetence due to the applied transvalvular pressure gradient.

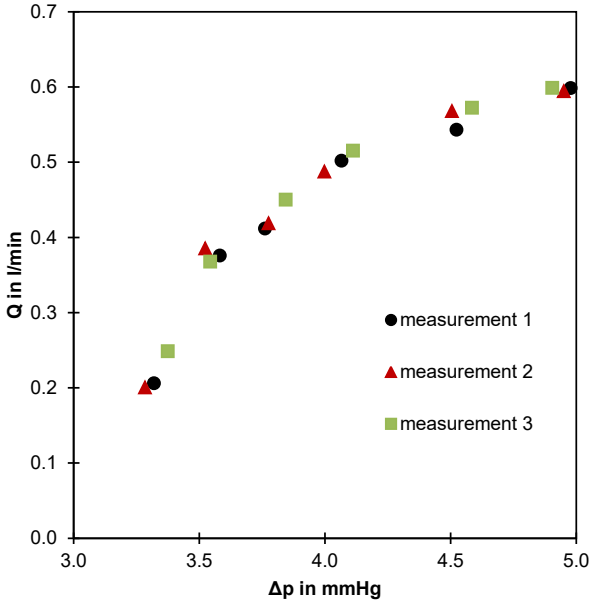


**Figure 3:** Experimentally investigated $\Delta p$-$Q$ relation for measurements 1-3 of the open MV configuration.

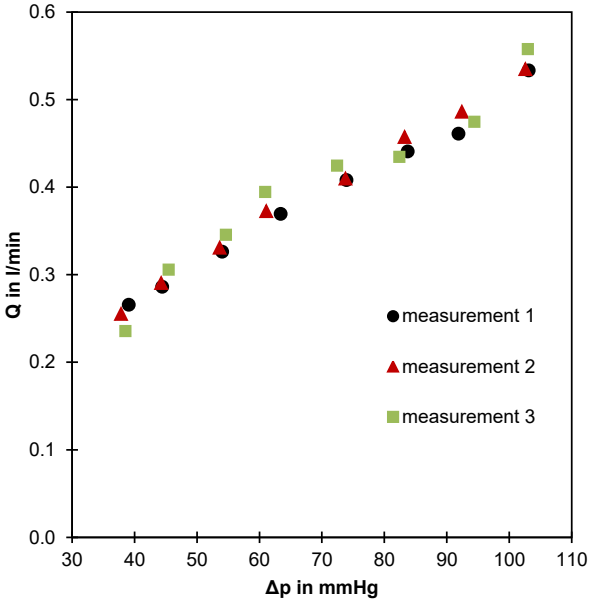


**Figure 4:** Experimentally investigated $\Delta p$-$Q$ relation for measurements 1-3 of the closed MV configuration.

**Table 1:** Results of the quadratic regression for the open MV configuration for measurements 1-3 are displayed as coefficients of a quadratic function of the form $Q = a \cdot \Delta p^2 + b \cdot \Delta p + c$ and the coefficient of determination $R^2$.

| | a | b | c | $R^2$ |
|---|---|---|---|---|
| **M1** | -0.1581 | 1.5264 | -3.0949 | 0.9721 |
| **M2** | -0.1639 | 1.5646 | -3.1420 | 0.9655 |
| **M3** | -0.1625 | 1.5555 | -3.1302 | 0.9846 |

**Table 2:** Results of the linear regression for the open MV configuration for measurements 1-3 are displayed as coefficients of a linear function of the form $Q = a \cdot \Delta p + b$ and the coefficient of determination $R^2$.

| | a | b | $R^2$ |
|---|---|---|---|
| **M1** | 0.0040 | 0.1101 | 0.9924 |
| **M2** | 0.0042 | 0.1137 | 0.9959 |
| **M3** | 0.0042 | 0.1046 | 0.9447 |

# 4 Conclusion

The current paper describes an experimental setup for the *in vitro* investigation of MVR devices under steady state flow conditions.

Reproducibility of the experimental results was evaluated by the calculation of maximum relative errors for linear and quadratic regression coefficients of the open and closed MV configuration. The maximum relative error is $\leq 4$ % and therefore sufficiently small for the investigation of the hydrodynamic performance of MVR devices.

On the one hand, anatomical dimensions of the MV model, such as the area of the D-shaped annulus, aorto-mural distance, intercommisural distance and thickness of the leaflets are in good accordance with the literature [1, 14]. On the other hand, chordae tendineae and papillary muscle are no anatomically and physiologically correct representations but rather simplifications to allow for *in vitro* valve opening and closing of the MV model. Moreover, the distinct parts of the MV model are supposed to dynamically vary in size and shape throughout the cardiac cycle. In order to change sizes and shapes of the MV model dynamically, a pump that is able to provide physiologic pulsatile flow conditions will be implemented in future investigations.

Furthermore, the experimental investigations were conducted without MVR devices implanted. Due to the optical access and the easy accessibility of the test chamber via catheter, however, the implantation and investigation of edge-to-edge MVR systems such as the MitralClip (Abbott, USA) and the Pascal (Edwards Lifesciences Corp., USA) transcatheter MVR systems can be performed *in vitro* in future studies.

### Author Statement

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