Aortic regurgitation after transcatheter aortic valve replacement

Influence of valve prosthesis implantation depth inside the aortic annulus on paravalvular regurgitation in in vitro steady flow conditions

**Abstract:** The assessment of hydrodynamic performance of transcatheter aortic valve prostheses in vitro is essential for the development and approval of novel devices. Therefore, this study aims to investigate the correlation of target implantation depth and paravalvular regurgitation in a controlled in vitro test situation. We designed a test setup with retrograde steady flow conditions measuring paravalvular regurgitation as a function of increasing pressure on the closed valve ranging from 0 mmHg to 200 mmHg. Our future aim is to benchmark different valve prosthesis designs and describe the correlation between target implantation depth, paravalvular regurgitation and prosthesis design aspects.

The current study describes the developed test setup, validation experiments as well as first results for a self-expanding valve prosthesis. The highest regurgitation was measured at an implantation depth of 2 mm. In fact, regurgitation increases from 26.1 ± 8.2 ml/min at 0 mmHg to 1,490.7 ± 182.7 ml/min at 160 mmHg. The slightest regurgitation, however, was measured for an implantation depth of 6 mm ranging from 2.2 ± 0.6 ml/min at 0 mmHg to 605.8 ± 18.9 ml/min at 200 mmHg.

**Keywords:** transcatheter aortic valve, paravalvular regurgitation, hydrodynamic testing.
2 Materials and methods

2.1 Test bench for steady flow measurements

The schematic of the developed test setup for retrograde steady flow measurements is shown in Figure 1. The test setup consists of a tempered fluid reservoir including a pump (Julabo, Seelbach, Germany) (1, 2), an adjustable flow resistance (3, 4), a compliance chamber (5), two flow sensors parallel-connected, only one perfused at a time (LEVIFLOW LFS-008, LEVIFLOW LFS-08, Levitronix, Zürich, Switzerland) to cover a measuring range from 0 l/min to 8 l/min (6, 7), the test chamber with a silicone aortic annulus and the test valve prosthesis (8) and a pressure sensor (86A 3R-000000-005P G, Measurement Specialties, Hampton, VA, USA) (9).

Figure 1: Schematic of a steady flow test bench for measurement of aortic regurgitation of transcatheter aortic valve prostheses.

2.2 Validation of the steady flow test bench

Validation of the steady flow test bench was conducted according to ISO Standard 5840-2: 2015 [8]. The standard defines a nozzle geometry as seen in Figure 2 which we designed in CAD (Creo Parametric 3.0, Parametric Technology Corp., Needham, MA, USA) and build from polyoxymethylene. Furthermore, the standard gives a pressure-volume-characteristic curve for the defined nozzle, see equation 1.

\[ y = -0.0126 \times x^2 + 7.6499x + 306.13 \]  

The nozzle was placed at the outflow tract of the test chamber, at the same position where the tested heart valve prosthesis will be implanted (see Figure 1, no. 8).

Figure 2: Detail of nozzle geometry according to ISO 5840-2: 2015 (right) and nozzle build from polyoxymethylene used for validation experiments (left).

For validation, static pressure ranging from 40 mmHg to 200 mmHg in increments of 20 mmHg was applied with the help of pump and flow resistances (Figure 1, no. 2-4). Pressure as well as flow were measured and recorded at any step. The validation experiment was performed \( n = 2 \) times at 22°C ± 2°C with 0.9% saline, according to ISO 5840-2: 2015.

2.3 Aortic regurgitation as a function of valve prosthesis implantation depth

In order to investigate PVR as a function of implantation depth in the aortic annulus we implanted a TAVP (Evolut PRO, Medtronic, Minneapolis, MN, USA) in a silicone model of the aortic annulus with an inner diameter of 26 mm and circular geometry. The implantation process, i.e. valve prosthesis loading and release was performed according to the instructions for use (IFU) of the prosthesis.

To determine a correlation between PVR and target implantation depth the target implantation depth \( D \) was varied
between 0 mm, 2 mm, 4 mm and 6 mm, see Figure 3, in derogation to the IFU. According to the IFU target implantation depth for Medtronic’s Evolut PRO TAVP is between 3 mm to 5 mm and is hence considered in our experiments.

For the investigation the fluid reservoir was filled with distilled water and tempered to 37°C ± 2°C. With the help of a pump and flow resistances (Figure 1, no. 2-4) a static pressure was applied to the TAVP leading to full valve closure. As a result, the measured regurgitation is assumed as solely paravalvular between prosthesis skirt and annulus model.

The static pressure on the valve was increased from 0 mmHg to 200 mmHg in 10 mmHg increments. Pressure as well as flow was recorded at every step. One measurement cycle consisted of valve loading and release and the measurement of the four different implantation depths. Overall \( n = 3 \) measurement cycles were performed.

### 3 Results and Discussion

#### 3.1 Validation of the steady flow test bench

The validation of the test bench was successful as seen in Figure 4. The data measured with the self-made standard nozzle shows an average deviation of +3.4% compared to the characteristic curve according to the ISO standard [8]. The maximum deviation is +8.3% representing 61.8 ml/min.

The deviation might be a result of the manufacturing process. In fact the normative requested tolerance values for the different surfaces and measures could not be fulfilled by the available manufacturing facilities and vary from 12.8%

on the inflow side of the nozzle to 3.5% on its outflow side. Nevertheless, we assume the test bench as precise and therefore continued with the experiments.

#### 3.2 Aortic regurgitation as a function of valve prosthesis implantation depth

In general, we determined a uniform trend between an increasing target implantation depth from 2 mm to 6 mm and a decreasing PVR, see Figure 5. At an implantation depth of 0 mm the whole skirt of the TAVP seals with the model of the silicone annulus and therefore PVR is mild and comparable to an implantation depth of 6 mm.

The slope of the different pressure-flow curves increases nonlinear. Due to the increased PVR at target implantation depths of 2 mm and 4 mm the pressure on the closed valve could only be increased up to 160 mmHg. We assume a more powerful pump would lead to higher applicable pressure on the closed valve. A future adaption of the test bench might be necessary.

In comparison, Sherif et al. developed in vivo procedural predictors of PVR for CoreValve bioprosthesis, a predecessor of the examined and presented TAVP. The cardiologist determined an optimal implantation depth of 10 mm which correlates to a minimal chance of PVR [9]. Nevertheless, this implantation depth was measured from the plane of noncoronary and right coronary cusp (valve leaflets) and not from the plane of the aortic annulus. Therefore the results might on the one hand not be directly comparable to the target implantation depth investigated in our experiments. On the other hand the study shows that a lower implantation depth can also result in milder PVR. However, as mentioned, further investigations probably with even lower target implantation
depths and a larger number of TAVP specimen need to show if the described trend is consistent.

The highest PVR was measured at an implantation depth of 2 mm. In fact, PVR increases from 26.1 ± 8.2 ml/min at 0 mmHg to 1,490.7 ± 182.7 ml/min at 160 mmHg. The slightest regurgitation, however, was measured for an implantation depth of 6 mm ranging from 2.2 ± 0.6 ml/min at 0 mmHg to 605.8 ± 18.9 ml/min at 200 mmHg.

4 Conclusion

PVR remains one of the major threatening complications of TAVI in clinical practice, due to its association with increased 1-year mortality [3]. Therefore, within the presented work, we developed an in vitro test setup measuring a correlation between the clinical parameter target implantation depth of TAVP and the resulting PVR.

The developed test bench was validated according to ISO standard 5840-2 by means of a normative nozzle. Validation of the test bench was successful showing an average deviation of only +3.4% in comparison to the nozzle’s characteristic curve according to the ISO standard.

Furthermore, a current generation TAVP was analysed in four different target implantation depths in retrograde steady flow. The resulting PVR as a function of increasing pressure ranging from 0 mmHg to 200 mmHg was measured. As a result, we determined a uniform trend between an increasing target implantation depth from 0 mm to 4 mm and an increasing PVR. To further verify the presented results more TAVP specimen need to be investigated.

Our future aim is to benchmark different valve prosthesis designs and describe the correlation between target implantation depth, PVR and prosthesis design aspects.

Author Statement

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References