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Influence of leaflet geometry on hydrodynamic performance of transcatheter aortic valve prostheses

Abstract: The implantation of transcatheter aortic valve prostheses (TAVP) for therapy of aortic valve stenosis shows more and more clinically non-inferiority results compared to surgical valve replacement in intermediate and low risk patients. Commonly clinically used TAVP are manufactured from chemically fixed xenograft leaflet material, e.g. bovine or porcine pericardium. While the clinical use of TAVP currently extends, challenges concerning valve durability and leaflet calcification have to be addressed. In this regard, artificial leaflet materials represent a promising option for a next generation of TAVP.

As a first step for the development of TAVP from polymeric nonwoven, the aim of this study was to determine the influence of leaflet geometry on hydrodynamic performance of TAVP prototypes. Based on a parametric model of the valve leaflets, we varied the curvature of the belly line forming the leaflet coaptation area from an initial, quite concave, leaflet geometry with a value of 0.5° to an almost straight geometry for the leaflets with a value 0.15° .

Manufacturing of TAVP prototypes was conducted by means of electrospinning technique with a polycarbonate based silicone elastomer. Hydrodynamic characterization according to ISO 5840-3 standards was performed using a pulse duplicator system with a heart rate of 70 BPM, systolic duration of 35%, mean aortic pressure of 100 mmHg and a stroke volume of 96 ml. Cardiac output as well as mean transaortic pressure gradient, closing volume, leakage volume and regurgitation were measured to compare the different leaflet geometries.

To summarize, the curvature of the leaflets' belly has a

crucial impact on TAVP hydrodynamics under physiological test conditions. In particular, the opening and closing behavior is strongly influenced by a steeper curvature leading to larger closing volumes and higher regurgitant fractions. Further studies are planned to identify an optimum with respect to leaflet material selection, leaflet geometry and hydrodynamic properties of TAVP.

Keywords: transcatheter aortic valve, hydrodynamic testing, valve geometry.

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1 Introduction

Transcatheter aortic valve implantation (TAVI) has become the treatment of choice for inoperable or high-risk patients with symptomatic aortic valve stenosis [1]. Clinical performance of established TAVP increases constantly, leading to an extension of the therapy from high-risk over intermediate risk to low risk patients [2, 3]. However, challenges concerning valve durability and leaflet calcification have to be addressed when thinking about implanting TAVP into younger patient collectives [3].

Currently, all FDA- as well as CE-marked TAVP were manufactured from biologic material, e.g. bovine or porcine pericardium, although these materials are showing at least two major pathophysiological mechanisms leading to tissue degeneration in the long run [4]. Valve calcification, as well as non-calcific tissue degeneration, is synergistically leading to bioprosthetic failure, no matter if a surgical valve prosthesis (SVP) or TAVP was used for implantation [4].

In this regard, artificial leaflet materials such as polymers represent a promising option for a next generation of SVP or TAVP with extended durability [5]. Polymeric heart valve based on film material are being developed since the 1950s whereas no heart valve prototype was ever introduced into clinical practice [6]. The introduction of the electrospinning technique to fabricate polymeric nonwoven structures led to an upsurge in the field of polymeric heart valve development [7, 8].

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Therefore, this study aims to determine the influence of leaflet geometry of TAVP prototypes made from polymeric nonwoven on their hydrodynamic performance according to ISO 5840 standard experiments.

2 Materials and Methods

2.1 Valve leaflet geometry

The valve leaflet geometry was based on previous work and conducted as axially-symmetric trileaflet heart valve geometry developed in 3D computer-aided design (CAD) (Creo Parametric 5.0, Parametric Technology Corp., Needham, MA, USA) [9].

Based on this parametric model of the valve leaflets, the curvature of the belly line forming the leaflet coaptation area was varied from an initial, concave, leaflet geometry with a value of 0.5° to an almost straight geometry for the leaflets with a value 0.15° , see Fig. 1.

Figure 1: Schematic of leaflet geometries with different curvatures of the belly line forming the coaptation area of the valve leaflets.

2.2 Manufacturing of transcatheter aortic valve prostheses prototypes

The manufacturing of TAVP prototypes derived from the different geometries was performed by means of electrospinning. As a first step spinning molds were manufactured via stereolithography 3D-printing technique with black polymer (3D-printer: Form 2, polymer: black resin, Formlabs Inc. Somerville, MA, USA).

Secondly, a clear and homogenous polymer solution of 7.5 wt% commercial polycarbonate-based polyurethane-silicone-copolymer and a solvent solution of chloroform, N,N-dimethylformamide and 2,2,2-trifluoroethanol (TFE) (1:8:8 v/v/v) was prepared at 37°C .

For the manufacturing of the polymeric valve prototypes an in-house developed electrospinning device was used. The spinning process contained three different steps, meaning three different emitter/collector positions in order to ensure homogenous covering of the spinning mold.

Finally, the polymeric nonwoven valve leaflets were adhered to a self-expanding TAVP-Stent prototype made from a nickel-titanium alloy (Nitinol) by means of silicone adhesive (RS Components, Hessenring, Germany), Fig. 2.

2.3 *In vitro* hydrodynamic testing

In order to investigate the influence leaflet geometry on hydrodynamic performance of the TAVP prototypes, measurements of effective orifice area (EOA) and regurgitation were performed according to ISO standard 5840-3:2013 by means of a commercial pulse duplicator system (ViVitrolabs, Victoria, BC, Canada).

For hydrodynamic testing, the following parameters were applied: heart rate: $70 \text{ BPM} \pm 5 \text{ BPM}$, mean aortic pressure: $100 \text{ mmHg} \pm 2 \text{ mmHg}$, systolic duration: $35\% \pm 5\%$, stroke volume: $96 \text{ ml} \pm 5 \text{ ml}$, test solution: 0.9% saline, temperature: $37^\circ\text{C} \pm 2^\circ\text{C}$. The hydrodynamic characterization was furthermore realized in an annulus model represented by a plain silicone ring with an inner diameter of 23 mm, see Fig. 2.

According to ISO standards $n = 10$ cycles were recorded for each measurement. To characterize opening and closing behavior of the TAVP prototypes, high-speed videos were performed using a frame rate of 500 fps (CR600x2, Optronis, Kehl, Germany).

Figure 2: Schematic of the annulus model (plain silicone ring) with an inner diameter of 23 mm (A) and a TAVP prototype manufactured from polymeric nonwoven (B).

3 Results and Discussion

With the described combination of 3D-CAD, 3D-printing, electrospinning and adherence it was possible to manufacture functional TAVP prototypes from polymeric nonwoven. The TAVP prototypes were implanted into silicone rings by hand without loading and release from a delivery catheter system and hydrodynamic *in vitro* testing according to ISO 5840-3:2103 was performed. In the following we describe the influence of valve geometry (belly curvature) on the opening

and closing behavior and the characteristic hydrodynamic properties of the TAVP prototypes.

3.1 Influence of belly curvature on opening and closing behavior

Opening and closing of the TAVP prototypes is strongly influenced by the valves' belly curvature. With a straight belly curvature, valve opening starts earlier during the cardiac cycle. With a belly curvature of 0.15° , valve opening starts at 70 ms when ventricular pressure (yellow lines) exceeds aortic pressure (red lines) a more concave shaped belly curvature leads to a delay of valve opening (100 ms with 0.25° and 107 ms with 0.5° , see Fig 3). Valve closing, when ventricular pressure drops beneath aortic pressure, is less affected by the geometry of the valves' belly curvature (0.15° : 382 ms, 0.25° : 398 ms, and 0.4° : 408 ms).

Figure 3: Mean aortic pressure, mean ventricular pressure and mean flow of $n = 10$ captured cycles of TAVP prototypes manufactured from polymeric nonwoven with different shapes of the belly curvature.

Fig. 4 shows exemplary pictures of the high speed videos derived from the hydrodynamic performance tests. Valve opening appears uniform, all three leaflets move the same way regardless of the belly curvature.

When looking at the moment of maximum forward flow it appears that the leaflets wrinkle up with increasing belly curvature leading to a non-uniform geometric opening area, see Fig. 3. Moreover, with increasing curvature of the belly line the valve leaflets are closing more unequally.

In Literature influence of leaflet geometry on the performance of TAVP is mainly investigated by means of computational frameworks, e.g. finite element analysis, simulating leaflet stress distribution, aiming at optimizing TAVP leaflet design to reduce peak stress in the leaflets. Parametric analysis of Gunning et al. or Li et al. revealed that e.g. increasing the free edge width of the leaflet had the highest overall impact on decreasing the peak stress by 5%

when simulating the implantation of generic TAVP in a circular or elliptical aortic annulus configuration [10-11].

Nevertheless, the influence of leaflet geometry on the hydrodynamic properties of the TAVP is not described. Here investigation by means of fluid structure interaction could describe the interplay between structural mechanics and fluids.

3.2 Influence of belly curvature on hydrodynamic properties

The hydrodynamic properties derived from the tests according to ISO 5840-3: 2013 were listed in Tab. 1. To summarize, we see values increasing with increasing straightness of the TAVP belly curvature especially if looking at transaortic mean pressure, leakage volume and regurgitant fraction. The effective orifice area (EOA) is not influenced by the belly curvature. For the other hydrodynamic parameter there is no systematic trend discernible.

Figure 4: Opening and Closing of TAVP prototypes manufactured from polymeric nonwoven with different shapes of the belly curvature during a cardiac cycle, 1 – valve fully closed, 2 – valve during opening, 3 – valve at maximum forward flow, 4 – valve during closing.

In detail, a transaortic mean pressure from 7.6 ± 0.1 mmHg to 9.6 ± 0.2 mmHg, a closing volume of 5.4 ± 0.3 mmHg to 6.8 ± 0.3 mmHg and an EOA of 2.2 ± 0.02 cm² to 2.4 ± 0.02 cm² was measured ($n = 10$).

When comparing these values to literature, e.g. a pericardium TAVP-prototype or a TAVP-prototype manufactured from polymeric film material, it is recognizable that the results are promising. In earlier studies, we measured a transaortic mean pressure of 15.4 mmHg ± 0.1 mmHg, a closing volume of 2.7 ml ± 0.2 ml and an EOA of 1.2 cm² ± 0.0 cm² for a TAVP-prototype from porcine pericardium [10]. Rotman et al. presented a transvalvular pressure gradient ranging from

13.85 mmHg to 24.64 mmHg and an EOA of 1.65 cm² to 1.83 cm² for a TAVP-prototype from polymeric film material manufactured with compression molding [11]. Future investigations especially regarding valve and leaflet durability need to show if polymeric nonwoven is a suitable option for a new generation of TAVP.

Table 1: Hydrodynamic properties of TAVP-prototypes manufactured from polymeric nonwoven with different geometries of belly curvature ($n = 10$).

characteristic hydrodynamic parameter	belly curvature of TAVP-prototype		
	0.5	0.25	0.15
transaortic mean pressure [mmHg]	7.6 ± 0.1	8.2 ± 0.1	9.6 ± 0.2
cardiac output [l/min]	3.4 ± 0.1	3.3 ± 0.1	2.5 ± 0.1
closing volume [ml]	5.4 ± 0.3	17.0 ± 3.5	6.8 ± 0.3
leakage volume [ml]	19.2 ± 1.0	14.6 ± 3.4	53.3 ± 0.7
regurge fraction [%]	33.7 ± 1.6	40.1 ± 1.0	62.4 ± 1.0
Effective orifice area [cm ²]	2.2 ± 0.02	2.2 ± 0.02	2.4 ± 0.02

4 Conclusion

Commonly clinically used TAVP are manufactured from chemically fixed xenograft leaflet material, e.g. bovine or porcine pericardium. While the clinical use of TAVP extends, challenges concerning valve durability and leaflet calcification have to be addressed. In this regard, artificial leaflet materials represent a promising option for a next generation of TAVP. Therefore, in this work we characterized the influence of leaflet geometry on hydrodynamic properties of TAVP-prototypes manufactured from polymeric nonwoven. We varied the curvature of the belly line forming the leaflet coaptation area from an initial, concave, leaflet geometry to a nearly straight line.

The achieved results were promising; the belly curvature has a crucial impact on the hydrodynamic properties of TAVP. Future studies need to identify the optimal leaflet geometry with respect to material choice, hydrodynamic properties and especially valve durability.

Author Statement

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