Hemodynamic influence of design parameters of novel venous valve prostheses

Abstract: Venous ulcers of the lower limbs are one clinical manifestation of chronic venous insufficiency. Currently, there is no venous valve prosthesis available. This study presents novel venous valve prostheses made of three-dimensional electrospun fibrous nonwoven leaflets. The aim of this study was to prove the feasibility of the manufacturing process as well as to investigate design features of the venous valve prostheses from a hemodynamic point of view. An adapted pulse duplicator system (ViVitrolabs, Victoria, BC, CA) was used for characterization of the hydrodynamic performance. For eight different venous valve prototypes flow rate, effective orifice area and regurgitation fraction was investigated in vitro. In particular, tricuspid valve designs showed an up to 40% higher effective orifice area as well as 15% higher maximum flowrate compared to bicuspid valve designs. However, the regurgitation fraction of the bicuspid valve designs is up to 86% lower compared to tricuspid valve designs. Additionally, the hemodynamic performance of the tricuspid valves showed a high sensitivity regarding the leaflet length. Bicuspid valves are less sensitive to changes of design parameters, more sufficient and therefore highly reliable.

Keywords: Venous valve prostheses, electrospinning, hemodynamic, regurgitation fraction

1 Introduction

Venous ulcers of the lower limbs are one clinical manifestation of chronic venous insufficiency, which is associated with a high level of physical pain and physiological stress. It is caused by insufficiency of the venous valves, e.g. in the course of a post-thrombotic syndrome. As a result, the blood is not transported in a proper way from the lower extremities. Surgical procedures such as valve reconstruction or stripping are associated with high risk for elderly and multi-morbid patients.

Currently, there is no transcatheter-based venous valve prostheses available. Previously tested prototypes differ greatly in design, material of the leaflet and support structure as well as in functionality [1-4]. Venous valve prosthesis should be durable, non-thrombogenic, and functionally reliable to prevent reflux. The use of synthetic polymers for leaflet material, in particular for heart valve prostheses has been the subject of intensive research for years [5] and might be suitable also for venous valve prostheses. One approach, which is presented in this study, is the manufacture of polymer-based fibrous nonwovens by means of electrospinning.

2 Materials and methods

2.1 Manufacturing

The three-dimensional valve geometries were designed using the CAD software Creo Parametric 3.0 (PTC Inc. USA Needham). Two groups of venous valves were analyzed: bicuspid and tricuspid valves. Each valve had a diameter of 10.0 mm. Within each valve group a variety of design parameters such as the leaflet length and the coaptation radius were tested (see Table 1). Based on the valve designs, spinning molds were derived. The manufacturing of the spinning molds was performed with a commercial stereolithographic 3D printer (Formlabs Inc. Somerville, MA, USA).
Table 1: Design parameter describing the bicusp and tricuspid venous valve prostheses.

<table>
<thead>
<tr>
<th>Design</th>
<th>Coaptation radius [mm]</th>
<th>Leaflet length [mm]</th>
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<tbody>
<tr>
<td>Design 1</td>
<td>0</td>
<td>6</td>
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<tr>
<td>Design 2</td>
<td>0</td>
<td>3</td>
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<tr>
<td>Design 3</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Design 4</td>
<td>6</td>
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Figure 1: Basic models of the analyzed bicuspid and tricuspid venous valve designs

In preparation for the electrospinning process, a clear and homogenous polymer solution of 7.5 wt% commercial polycarbonate-based silicone elastomer was obtained by dissolving the polymer in a solvent mixture of chloroform, N,N-dimethylformamide and 2,2,2-trifluoroethanol (TFE) (1:8:8 v/v/v) at 37 °C. For the process of electrospinning, an in-house developed spinning device was used. Each spinning process was performed for about 10 minutes in three different emitter-to-collector positions in order to ensure a homogenous covering of the mold.

To assure high quality of the produced nonwoven structures scanning electron microscope imaging was conducted to control both the structure and the diameter of the fibers at different areas of the nonwovens. Afterwards, the electrosprun valve structures were attached to peripheral stents (Astron Pulsar, Biotronik AG, Bülach, CH) using silicone-based adhesive (RS 692-542, RS Components GmbH, Hessenring, Deutschland)(see Figure 2).

2.2 Testing

The influence of design parameters of venous valve prototypes, measurements of time dependent flow rate, effective orifice area (EOA) and regurgitation fraction were performed based on ISO 5840-3: 2013. The venous valve prototypes were implanted in a 10.0 mm silicon mock vessel. An adapted pulse duplicator system (ViVitrolabs, Victoria, BC, CA) was used for characterization of the hydrodynamic performance. Testing parameters were defined for beat rate (90 BPM), time-averaged flow rate (1.6 l/min), max distal pressure (100 mmHg), test solution (0.9 % NaCl) and temperature (37°C ± 2°C). Ten cycles were measured and averaged in order to obtain the presented results.

3 Results and discussion

The tricuspid valve prototypes showed a higher flow rate compared to bicuspid valves (see Figure 3). These results are in good accordance with the higher EOA of the tricuspid valves (see Figure 4).
When the tricuspid valve is open, the three leaflets are aligned with the stent structure. Due to both, the geometry and the disposition within the stent structure, the leaflets of the bicuspid valves induce a higher flow resistance due to a lower EOA. In particular, the bicuspid valve with design 4 showed a 34% lower EOA than the tricuspid valve. For a bicuspid valve, the EOA ranges from 0.238 cm$^2$ to 0.243 cm$^2$ depending on the leaflet length (3.0 mm vs. 10.0 mm).

The design parameters of tricuspid valves had a significant impact on the regurgitation fraction (see Figure 5). Compared to design 1, a tricuspid valve with design 4 leads to an increased regurgitation fraction by a factor of 2.6. Short leaflets and a coaptation radius of 6.0 mm seem to be preferable for bicuspid valve design. The regurgitation fraction of the bicuspid valve with design 4 is 6.2% and thus lower by a factor of 2.5 compared to the lowest regurgitation fraction of a tricuspid valve.

**4 Conclusion**

Eight venous valve prototypes made of three-dimensional electrospun valve leaflets were tested in vitro and analyzed by flow rate, EOA and regurgitation fraction. In particular, the hemodynamic performance of the tricuspid valves showed a high sensitivity with regard to leaflet length and coaptation radius. An adequate coaptation area is required to ensure a sufficient closure for tricuspid valves. Bicuspid valves are less sensitive to design parameters and with it highly reliable. Therefore, further investigations should focus on the development of transcatheter venous valves with two leaflets.

**Author Statement**

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**References**


