VIRTUAL COHORT GENERATION FOR *IN SILICO* TRIALS OF TRANSCATHETER AORTIC VALVE IMPLANTATION

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Introduction

After transcatheter aortic valve implantation (TAVI), patients can suffer from several procedural complications such as paravalvular leakage, and conduction problems. Two aortic valve morphologies that influence the occurrence of those complications are: (1) the shape of the left ventricular outflow tract (LVOT), either convergent or divergent, and (2) the angle between the LVOT and the ascending aorta ($\angle \mathrm{LVOT} - \mathrm{AA}$) (Fig. 1). TAVI manufacturers are still developing their devices to prevent these procedural complications in the future. *In silico* clinical trials are a promising method to increase the efficiency of the development of transcatheter aortic valve implantation (TAVI) devices. With an *in silico* trial, devices can be tested on virtual patients which are computer models that realistically mimic the physiological response induced by TAVI implantation. The domain of interest of each patient of the virtual cohort for TAVI evaluations is represented by a synthetic aortic valve geometry. The aim of this research is to develop a framework to generate synthetic aortic valve geometries, that (1) are anatomically plausible, and (2) allow for selection of the aforementioned morphologies.

Methods

Non-parametric statistical shape modeling (SSM) [1] was used to extract the mean shape and shape variance (shape modes) from a set of 97 stenotic aortic valve geometries. Each geometry within or outside this data set was approximated by adding a weighted combination of 24 shape modes to the mean shape. With the SSM 500 synthetic geometries were generated by sampling new weight combinations from an inferred distribution [2]. Logistic regression and linear regression models were used to filter synthetic geometries on LVOT morphology and ∠LVOT-AA respectively.

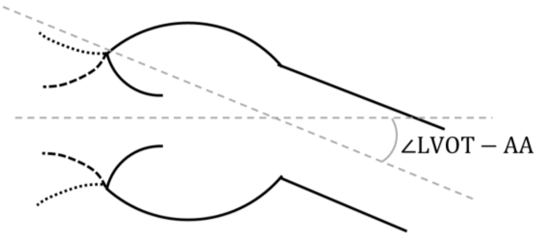

Figure 1: Schematic overview of important morphologies: convergent (dashed line), and divergent (dotted line) LVOT, and angle between LVOT and ascending aorta.

Results

Eight shape features, characteristic for aortic valve geometries, were compared between the real and synthetic geometries. The correlations between the eight features were similar for both groups (Fig. 2). A non-parametric multivariate ANOVA test revealed that the 8-dimensional distributions of both groups did not differ significantly ($p = 0.47 > 0.05$). Furthermore, the filters were able to successfully filter convergent or divergent geometries with a sensitivity of 98% and 99% respectively, and to filter small, medium and large angles with a sensitivity of 86%, 85%, and 97% respectively.

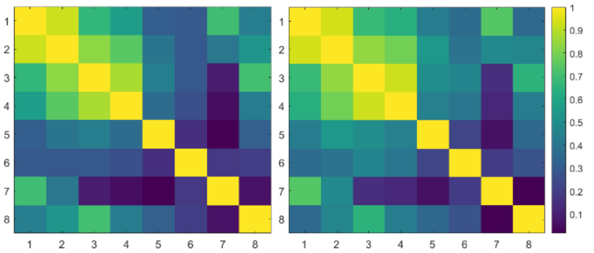

Figure 2: *correlations between LVOT (1), annulus (2), sinus (3), and sinotubular junction diameters (4), aortic valve area (5), ∠LVOT-AA (6), the ratio between LVOT and annulus diameter (7), and sinus height (8), for real (left), and synthetic geometries (right).*

Discussion

These results demonstrate that the framework developed in this study, (1) succeeded in generating synthetic geometries that are anatomically plausible, and (2) makes it possible to select geometries with certain morphologies. Consequently, this framework has the potential to generate synthetic data sets for *in silico* TAVI trials. The next steps towards *in silico* TAVI trials is to integrate calcifications in synthetic geometries, and to simulate the hemodynamic and structural behavior of these valves before and after TAVI.

References

1. Bône et al., LNCS: 3-13, 2018
2. Niederer et al., Philos. Trans. Royal Soc. A, 378, 2020

Acknowledgements

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