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Software-automated multidetector computed tomography-based prosthesis-sizing in transcatheter aortic valve replacement: Inter-vendor comparison and relation to patient outcome

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ABSTRACT

Background: Correct sizing of the aortic annulus and determination of coronary height is crucial for the efficacy and safety of trans-catheter aortic valve replacement (TAVR). We aimed to compare 3 different software solutions and manual measurements with respect to MDCT-derived annulus sizing parameters, reproducibility and processing time for TAVR planning and to evaluate the impact on patients' outcome.
Methods: One-hundred-seventeen patients with severe aortic stenosis prior to TAVR were included. Prosthesis sizes were determined separately using 3 different platforms: i) 3mensio, ii) IntelliSpacePortal V7 (ISP7), and iii) ISP9. In addition, manual measurements were performed. Intra- and inter-observer reproducibility as well as systematic differences were assessed. Finally, hypothetical prosthesis sizing was related to patient outcome using 3mensio as the clinical reference standard.
Results: Intra- and inter-observer reproducibility were excellent for all annulus parameters (ICCs 0.787–0.994). Distances to coronary ostia showed excellent intra-observer reproducibility except for 3mensio (ICC LCO: 0.655; RCO: 0.020), while inter-observer reproducibility was poor except for ISP9. For annulus parameters, slightly larger values were observed for ISP9 when compared to the other platforms. ISP9 allowed for the fastest and most reproducible measurement of aortic annulus parameters (although it did result in slightly larger annulus sizing).
Conclusions: Reproducible measurement of aortic annulus parameters can be obtained by all investigated post-processing solutions. All post-processing platforms are likely to result in similar and reliable measurements and thus can be used interchangeably.

1. Introduction

Aortic stenosis (AS) is the most common valve disease requiring surgery in the western world with a constantly growing prevalence due to the ageing population [1]. In severe AS, transcatheter aortic valve replacement (TAVR) has become an established alternative treatment for patients with intermediate or high perioperative risk [2,3].

Accurate pre-procedural sizing of the prosthesis is of critical importance in order to limit peri- and post-procedural complications such as paravalvular leakage and annulus rupture [2], both representing important factors for patient outcome [4]. Accordingly, selection of a prosthesis which is too small for the native aortic annulus is considered the most important predisposing factor for postoperative paravalvular leakage [2]. In contrast, selection of a prosthesis which is too large might result in fatal annular rupture [2].

Multidetector computed tomography (MDCT) has emerged as the standard imaging modality for pre-procedural sizing of the aortic annulus [5]. However, accurate identification and sizing of the aortic annulus is a challenging procedure, involving the generation of an exact double-oblique view of the aortic annulus at the lowest insertion points of the three coronary cusps [6].

This has led to the introduction of a number of dedicated commercial software solutions for a (semi-) automated analysis of the aortic annulus and prosthesis sizing. These software tools might allow for a more reproducible and time-saving assessment of annular sizing parameters when compared to manual measurements on MDCT datasets. However, a direct comparison of different software solutions is lacking so far. Thus, it remains unclear whether different software solutions operated by cardiologists and radiologists deliver equally reproducible and reliable results without introducing systematic differences regarding

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annulus sizing parameters. Most importantly, it still has to be determined whether potential systematic differences in the derived annular sizing parameters might have an impact on peri-procedural complications as well as post-procedural patient outcome.

Thus, the aim of the present study was to compare three different commercial software solutions for (semi-)automated annulus sizing (3mensio, IntelliSpace Portal Version 7.0 [ISP7], and IntelliSpace Portal Version 9.0 [ISP9], in which the vendor performed a refinement and retraining of the landmark detection algorithm as compared to Version 7) based on MDCT datasets amongst each other as well as to manual prosthesis sizing with respect to intra- and inter-observer reproducibility. In addition, systematic differences of annulus sizing parameters between the different software solutions were assessed. Finally, we evaluated the impact of these systematic differences on patient outcome with a special focus of post-procedural paravalvular leakage, using the 3mensio platform as the clinical reference standard.

2. Methods

This study had institutional review board and local ethics committee approval. All MDCT studies were clinically indicated. Written informed consent requirement was waived because of the retrospective nature of the study.

2.1. Study population

A total of 120 consecutive patients with symptomatic severe AS not eligible for surgery or at high operative risk underwent TAVR between March 2015 and May 2016. Patients with bicuspid valve, patients with valve in valve procedure and patients with external MDCT for prosthesis sizing were not included.

2.2. Multidetector computed tomography

Prior to TAVR, a contrast-enhanced MDCT was performed in all patients. All examinations were performed on a 384-slice dual source CT system (Somatom Force, Siemens Healthcare, Erlangen, Germany) in single-energy mode. CT scans were performed with the following standard technical parameters: collimation 0.6 mm, 80–100 kV, 123–448 mAs, effective slice thickness 0.75 mm, reconstruction increment 0.5 mm, field of view 255 mm. A bolus of 50–60 ml of nonionic iodinated contrast agent (Accupaque 350, GE Healthcare, Chalfont St Giles, Great Britain) was administered at an injection rate of 4–6 ml/s using an automatic injector (Accutron CT-D, Medtron, Saarbrücken, Germany). Mean radiation dose was 190.7 ± 57.0 mGycm (weight-adapted radiation dose modulation). Data were reconstructed in the enddiastolic phase (65–80% of the RR interval).

2.3. MDCT image analysis

All MDCT examinations were reviewed by two experienced cardiac CT readers (one cardiologist and one radiologist) (blinded). Each examination was reviewed on three different post-processing platforms dedicated to MDCT based TAVR sizing: i) 3mensio (3mensio Version 8.0, Pie Medical Imaging BV, Maastricht, The Netherlands), operated by an expert cardiologist, ii) ISP7 (IntelliSpace Portal Version 7.0, Philips Healthcare, Best, The Netherlands), and iii) ISP9 (IntelliSpace Portal Version 9.0, Philips Healthcare, Best, The Netherlands), both operated by an expert radiologist. Since the vendor performed a refinement and retraining of the landmark detection algorithm in the ISP9 version, we decided to compare both software versions in the present study. In addition, manual multiplanar reformation and sizing of the aortic annulus was performed on a standard clinical PACS workstation (AGFA IMPAX EE R20, AGFA Healthcare, Mortsel, Belgium) according to current recommendations [7].

Intra- and inter-observer reproducibility was tested in a randomly selected subgroup of 20 patients. MDCT images of selected patients were reviewed twice by the abovementioned experienced readers for intra-observer analysis with a pause of 3 weeks between the two readings and blinded to the results of the first reading. For inter-observer analysis, two additional expert reviewers (blinded) (a cardiologist for 3mensio and a radiologist for the other two platforms as well as manual measurements) reviewed the 20 cases separately and blinded to the results of the first readers.

Each reader recorded the time for performing the entire analysis of each patient, starting at the first working step (i.e. excluding the time it took the system to open the images).

2.4. Prosthesis sizing based on MDCT images using different software solutions

While using different post-processing platforms for semiautomatic prosthesis sizing in the present study, all platforms required a very similar step-by-step user interaction. After loading the case, each software automatically selected the plane of the virtual aortic annulus. The points on the virtual plane had to be checked and modified when appropriate. Once the annular plane was defined, ISP7 as well as ISP9 software automatically delineated area, perimeter as well as minimum and maximum diameters of the aortic annulus. All measurements were adjusted manually when necessary. With 3mensio these measures needed to be determined manually. All measurements were recorded. In addition, ISP7 and ISP9 highlighted the ostium of the left and right coronary artery. These points also had to be checked and appropriately modified by the user. With 3mensio the ostia need to be set manually. The distance between the annular plane and the left and right coronary ostium (LCO, RCO) were also recorded.

Besides the three different approaches to semiautomatic prosthesis sizing, additional manual measurements of all abovementioned annulus parameters were performed after manual reconstruction of the aortic annulus plane in line with the SCCT consensus recommendations on CT imaging before TAVR [7].

2.5. TAVR procedures and device positioning

TAVR procedure was performed under general anesthesia. Three different prostheses types were implanted: i) self-expandable prostheses Symetis ACURATE Neo TF (Symetis SA, Ecublens, Switzerland) size 23, 25, or 27 mm, ii) Balloon-Expandable prostheses Edwards SAPIEN3 (Edwards Lifesciences, Irvine, CA, USA) size 23, 26, or 29 mm and iii) Medtronic CoreValve Evolut R (Medtronic, Minneapolis, MN, USA) size 23, 26, or 29 mm. Balloon valvuloplasty was performed with a balloon of 20–26 mm in diameter during simultaneous rapid pacing before placing the device at the operators discretion. Post-dilatation was performed when clinically indicated (paravalvular leakage > mild or elevated transvalvular gradient). The access was trans-femoral when possible or trans-apical, and the device was deployed under fluoroscopic guidance. The size of the valve was chosen according to the MDCT basal ring area or perimeter as analyzed by 3mensio, following current recommendations [8].

2.6. Assessment of patient outcome

During and within the first seven days following TAVR procedure, the following adverse events were recorded: i) need of pacemaker implantation, ii) annulus rupture, iii) conversion to open valve surgery, iv) ischemic stroke, and v) death. Before discharge, transthoracic echocardiography was performed to evaluate paravalvular leakage.

2.7. Relation of prosthesis sizing to patient outcome

Prosthesis sizes were determined separately using all three software algorithms and manual measurements. Since all TAVR prostheses were sized using the 3mensio sizing algorithm operated by an expert cardiologist during clinical routine, 3mensio was used as the in-house references standard for prosthesis sizing. In order to evaluate whether a smaller or larger prosthesis size would have been selected using the other sizing methods (manual, ISP7, ISP9), measurements derived from these alternative sizing algorithms were compared to the reference standard. A decision was made if the patient would have received a smaller or lager prosthesis as compared to the 3mensio-based selection of the TAVR prosthesis. Finally, the decision whether resizing would have been necessary was related to patient outcomes as described above. A workflow for the entire prosthesis sizing process with correlation to patient outcome is shown in Supplemental Fig. 1.

2.8. Statistical analysis

Statistical analysis was performed in R 3.4.0 [9] with RStudio 1.0.136 [10], using the packages ggplot2 [11] for graphical visualization, pastecs [12] for descriptive statistics, multcomp [13] for analyses of variance (ANOVA), irr [14] for calculation of intra-class correlation coefficients (ICCs), randomForest [15] for random forest models, and epade [16] for Bland-Altman analyses.

All continuous data are given as mean ± standard deviation. A p-value of <0.05 was considered statistically significant. Testing for significant differences between the four post-processing algorithms was performed using repeated measures ANOVA design with Tukey-type post-hoc comparisons.

Intra- and inter-observer reproducibility was tested in a randomly selected subgroup of 20 patients using Bland-Altman analyses, ICCs and coefficients of variation (CV). The CV was computed as the SD of the differences divided by the mean of the parameter under consideration [17]. ICCs were defined as excellent (ICC ≥ 0.75), good (ICC = 0.60–0.74), moderate (ICC = 0.40–0.59) and poor (ICC ≤ 0.39) as previously proposed [18].

Analysis of the relation of prosthesis resizing to patient outcome was performed using mosaic plots, cross tables including chi squared tests, logistic regression analyses and random forest models, where the most important influencing factor for patient outcome was assessed using the Gini-index.

3. Results

3.1. Study population

Of 120 patients, 3 had to be excluded due to incomplete follow-up data. Finally, a total of 117 patients (mean age 82 ± 6 years, 58 [50%] females) with severe AS were included into the study. On echocardiographic evaluation mean calculated aortic valve area was 0.7 ± 0.2 cm^2 and mean gradient across the aortic valve was 44 ± 16 mmHg. The mean logistic EuroSCORE of the study population was

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