Quantitative image analysis for planning of aortic valve replacement
Elattar, M.A.
Chapter 6

Validation of a novel planning tool for minimally invasive aortic valve replacement: access angle and incision to aortic annulus distance for prediction of surgery difficulty

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In Preparation
6.1 Abstract

Background: Minimally invasive aortic valve replacement (mini-AVR) has proven its value over the last decade by its significant advancement of mortality, morbidity, and shorter admission time. However, mini-AVR is associated with some on-site difficulties such as limited aortic annulus exposure. Currently, computed tomography scans are used to evaluate the anatomic relationship among the intercostal spaces, ascending aorta, and aortic valve prior to surgery. We hypothesized that measurements such as access distance and access angle may have a relation with outcomes or aortic annulus access difficulty.

Methods: We introduce a novel mini-AVR planning prototype, which allows automatic measurements of access angle, access distance, and additional aortic annulus dimensions. The prototype visualizes these measurements on the chest cage as ISO-contours. The association of these measures with outcome parameters like extracorporeal circulation time (ECC), aortic cross-clamping time (AoX), and access difficulty score (easy and difficult groups) was assessed. We included 14 patients who received a new valve by ministernotomy.

Results: Access angle was strongly associated with aortic cross-clamping time (Pearson correlation coefficient = 0.60, p = 0.02) and access difficulty score (Spearman’s rank correlation coefficient = 0.57, p = 0.03). Access angles were significantly different between easy and difficult access groups (p = 0.03). There was no significant association between access distance and outcome parameters.

Conclusion: It was shown that access angle is strongly associated with procedure complexity. The automated presentation of this measure suggest added value of the prototype in clinical practice.
6.2 Introduction

Valve disease is a serious health problem as it carries a poor prognosis. Its prevalence is strongly linked to the population aging. Aortic stenosis (AS) is currently the most frequent native valve disease in Europe, which is most often seen in elderly patients. Valve replacement is the conventional therapy for patients with severe AS who have symptoms or observable consequences such as left ventricular (LV) dysfunction.

Traditional AVR is performed during an open surgical procedure with full sternotomy and with arterial cannulation in the ascendancy aorta and venous cannulation in the right atrium to enable extracorporeal circulation by means of a heart-lung machine [1]. Full sternotomy has the advantage of a direct view of and access to all the cardiac structures [2].

Operative mortality is quite low, even in elderly patients when properly selected and long-term results are satisfactory [3]. However, risk of surgery are higher in elderly patients with significant comorbidities [1]. During the past decade, surgical techniques improved creating an area for less and minimal invasive procedures. Moreover, a range of procedures classified as minimally invasive aortic valve replacement (mini-AVR) has been introduced (figure 1) [4]. Compared with conventional surgery, mini-AVR has shown to reduce postoperative mortality and morbidity. In addition, patients recover faster requiring less rehabilitations resources and shorter admission time [5].

The most common minimally invasive approach for valve replacement is partial upper ministernotomy (MS), followed by the right anterior minithoracotomy (RT) [6] (figure 1). MS is performed through a vertical incision through skin and sternum and completed by a transverse sternal incision [7]. RT is performed through a 5 to 6 cm skin incision at the level of the second or third intercostal space, starting from the border of the sternum toward the lateral right side [8].

Few studies researched the outcomes of each approach and compared the approaches in terms of life quality and duration, several studies reported only marginal benefits for MS compared to RT [9,10]. Although most surgeons that perform minimally invasive aortic valve surgery prefer the MS approach [11,12]. The right anterior minithoracotomy (RM) has the potential to be associated with improved outcomes [9,13,14]. Although, Patients undergoing mini-AVR via RM have longer operative times compared to MS [14–16] and operators may have difficulty seeing the right cusp annulus side (RC) using MS approach.

For both techniques, the selection of the optimal location of the incision is one of the most important aspects of a successful valve replacement [17,18]. Preoperative planning of patients eligible for mini-AVR is performed using computed tomography angiography (CTA) (Figure 1). A previous study proposed a visualization system for surgical planning of mini-AVR candidate patients using CTA images. This tool renders the chest cage with the ascending aorta which visually supports the decision for the type of procedure [19]. Current planning tools do not yet provide quantitative measurements.
In another study [18], Glauber et al. stated that patients are suitable for RT only if the following criteria are met: (1) the distance from the ascending aorta to the sternum does not exceed 10 cm; (2) the angle between the sternum midline and the inclination of ascending aorta should be larger than 45 degrees. It has also been suggested that it is important to measure aortic valve dimensions such as the diameter of the aortic valve annulus, the length of the ascending aorta, and the calcifications of the aortic valve and the ascending aorta in the pre-procedural planning process because it is strongly recommended to remove all the eccentric calcifications and create a complete decalcification of the aortic annulus [18,20].

We developed a mini-AVR planning tool that combines 3D visualization of the access with addition of quantitative assessment of important planning measures. In this tool we provide the access angle and distance from the incision location on the chest cage quantitatively and visually using 3D rendering methods. This tool gives an impression of the difficulty of the access by measuring how far and how aligned the access with the aortic root.

We validated our planning tool by assessment of the association of the provided quantitative measures with outcome parameters surgery time, clamping time, and annulus access difficulty score.

6.3 Methods

6.3.1 Planning Tool

6.3.1.1 Automated measures

Since access distance and access angle are interesting parameters to measure for mini-AVR patients. The tool provides those quantitative measurements based on the geometrical location of the aortic root landmarks and the incision location. The measurements are calculated as follow. Access distance is defined as the distance between incision location and the aortic sinotubular junction where the surgeon make the aortic incision. Access angle is defined as the angle between the aortic root center axis and incision-annulus line. The aortic root center axis is the vector that connects annulus and sinotubular junction centers. The incision–annulus center axis is the vector that connects the incision with the annulus center (Figure 6.1). Other annulus dimensions such as minimum, maximum diameters, area, perimeter, and calcium volume are calculated based on a previously presented automated method, which automatically detected aortic root landmarks and calculated sizing parameters [21].
The introduced mini-AVR planning tool has a specific workflow to detect the aortic annulus, sinotubular junction, and segment the ribcage then produce the final measurements. This workflow consists of set of interactive steps. Subsequently, the chest ribs are segmented from the full body scan automatically. The intercostal spaces are represented as gaps between the segmented ribs.

Access distance and angle are reported in a form of ISO contour maps. To calculate the distance and angle maps, a mesh that represents the ribs is reconstructed as shown in Figure 6.2. To ease analysis, distance and angle measurements are visualized with ISO contours. An ISO contour connects points of equal value. Each two ISO contours define a range of values between them as shown in Error! Reference source not found..

Figure 6.1: schematic drawing showing the methodology of calculating the access distance and angle based on the location of three landmarks; aortic annulus center, sinotubular junction, and incision point.

Figure 6.2: Segmented chest rib cage shown after applying morphological closing and superior-inferior blurring (Left). Sample matrix showing ISO-contours based on the values inside matrix cells (Right).

6.3.1.2 Usage

The developed prototype works as follows: First, the user loads 3D CT Angiography (CTA) images. After choosing the mini-AVR workflow from the main User Interface (UI),
the software automatically segments the aortic root and then detects the annulus. Next, the sinotubular junction is detected.

After the automatic detection, tools are made available for the user to perform some corrections to the detected landmarks if needed. Another developed tool which helps the user to select interactively a specific location on the 3D rendered chest cage to make local measurements such as access distance and angle measurements, we call this tool the 3D probe (Figure 6.3).

Distance and angle measurements are evaluated per point (vertex) of the reconstructed chest cage mesh by measuring distance from each vertex point to the STJ and angle difference in the same manner.

The ISO contours of distance and angle were rendered on the 3D volume using a blue and green palette, respectively. The difference between each two successive ISO contours of the distance and angle measurements scale were 5 mm and 10 degrees. The tool allows different rendering modes combined with the ISO contours such as full body volume rendering, chest cage with segmented aorta, skin with segmented aorta, and the segmented aorta with calcification.

6.3.2 Clinical Validation

6.3.2.1 Study Population

We collected preprocedural 3D volume image data of fourteen patients eligible for mini-AVR with three CT and eleven CTA acquisitions from our institute (Academic Medical Center, The Netherlands). All CT-scans were performed on a Philips Brilliance 64 slice CT scanner; imaging parameters were 120 kV, and convolution kernel B.
chest, abdomen, and pelvis were scanned using one bolus of 120 ml contrast Iomeron 400, intravenously infused at a rate of 5 ml/s.

In case of dynamic scans, which included ten cardiac phases, we selected images acquired at 70% of the cardiac cycle. This specific phase mimics the non-beating heart and extracorporeal circulation settings during surgery [22] Also, at this phase the aortic valve is closed [23]. All image volumes contained about 500–800 slices. Each slice in a volume contains 512 × 512 isotropic pixels with a 16 bit depth. The in-plane image resolution varies from 0.44 mm to 0.68 mm. The slice thickness for all data sets is 0.9 mm and the overlap between each two successive slices is 0.45 mm.

All patients included in this study were operated using the MS approach by the same operator (Dr. Kaya). This approach is done through an incision with the shape of the character J starting from the sternal angle (manubriosternal joint) moving caudally for 4 cm in the sternum body.

6.3.2.2  Image based Parameters

Access distance and access angle measurements were successful for both CT and CTA scans of all patients. Annulus measurements such as minimum, maximum diameter, area, perimeter, and calcium volume were assessed only in CTA. To collect the prementioned measurements at the same incision location used during the surgery, 3D probe was placed at the center of the manubriosternal joint which was also used by surgeon to mark the incision before surgery.

6.3.2.3  Outcome Parameters

Extracorporeal circulation time (ECC), aortic cross-clamping time (AoX), and access difficulty score were collected as the outcome parameters. Access difficulty score was subjectively assessed by the operator and it reflects the complexity of the annulus access performing the stitches to implant the new valve. The score has four grades (very easy, easy, moderate, and difficult) and we dichotomized this score to easy (very easy and easy) and difficult (moderate and difficult). Assuring independent scoring, raters were blinded to additional information.

6.3.2.4  Statistical Analysis

Normally distributed and continuous values were expressed as mean ± standard deviation (SD) and median and interquartile range otherwise. Significance of associations between outcome parameters and image based parameters were tested using spearman’s rank correlation coefficient (rho). Significant associated parameters were also evaluated using Pearson product-moment correlation coefficient. Aortic annulus measurements were compared between groups of easy and difficult access.

The distribution of access angles and aortic cross-clamping time for dichotomized access difficulty categories was visualized with box-and-whisker plots. Scatter plots were used to illustrate the association between access angle and access difficulty score. Significant difference of access angle between easy and difficult access groups was determined by paired t-tests.
To predict procedure difficulty, we selected an optimal access angle threshold, using the receiver operating characteristic (ROC), which illustrates classification performance of a binary classifier system. Statistical analyses were performed using SPSS (version 19.0, SPSS Inc., and Chicago, IL) and MATLAB (Version R2013b, The Mathworks Inc., and Natick, MA). Associations with p-values of 0.05 or smaller were considered statistically significant.

### 6.4 Results

Aortic valve stenosis was present in all patients included in the study and bicuspid aortic valve stenosis was present in 2 patients (14%). Two patients were scanned using CT and the rest were scanned using CTA. Four scans were excluded from annulus dimension measurements. For two patients only non-contrast CT was available which makes annulus measurements less accurate to assess because of poor contrast between blood and aortic root wall. The other two scans were excluded because they were scanned after surgery, which hinders annulus measurements due to the strong blooming effect of the stent at annulus level.

Access angle and distance measurements using the 3D probe tool was successful for all patients. Average access angle was 40.3 ± 5.1° and the distance from incision to the sinotubular junction was 94.9 ± 11.1 mm. The remaining measurements are reported in Table 6.1.

| Table 6.1: Average, standard deviation, median, interquartile range (IQR) of the Access angle, distance from incision, annulus minimum diameter, maximum diameter, area, and perimeter. |
|---------------------------------|-----------------|-----------------|-----------------|
|                                  | Mean            | Standard Deviation | Median          |
| Access Angle (degrees)          | 40.3            | 5.1              | 40.0            |
| Distance from Incision (mm)     | 94.9            | 11.1             | 94.7            |
| Annulus Minimum Diameter (mm)   | 26.2            | 3.1              | 26.6            |
| Annulus Maximum Diameter (mm)   | 32.4            | 2.9              | 32.1            |
| Annulus Area (mm²)              | 687.1           | 122.5            | 678.7           |
| Annulus Perimeter (mm)          | 94.3            | 8.1              | 93.6            |

The access angle was significantly associated with aortic cross-clamping time (AoX), four graded, and two graded access difficulty scores with Spearman Correlation Coefficient (rho) of 0.55 (p = 0.042), 0.59 (p = 0.028), and 0.60 (p = 0.025). The other image based measurements were not significantly associated with the outcome parameters (see Table 6.2). Linear correlation between access angle and all outcome parameters was found to be significantly good and all Pearson product-moment correlation coefficients are reported in Table 6.3.

Access angle measurements were significantly different (p = 0.03) between both easy and difficult groups based on the 2-point access difficulty score.
Validation of a novel planning tool for mini-AVR

Table 6.2: Spearman correlation coefficient and its significance between image based measurements (access angle, distance from incision, annulus minimum diameter, maximum diameter, area, perimeter, and age) and the outcome parameters (Extracorporeal Circulation Time (ECC), Aortic Cross-clamping Time (AoX), Access Difficulty Score (four grades), and Access Difficulty Score (two grades)). Significant correlation coefficients are bold.

<table>
<thead>
<tr>
<th>Spearman Correlation Coefficient (rho) / Significance P-value</th>
<th>Extracorporeal Circulation Time (ECC)</th>
<th>Aortic Cross-clamping Time (AoX)</th>
<th>Access Difficulty Score (four grades)</th>
<th>Access Difficulty Score (two grades)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rho</td>
<td>p-value</td>
<td>rho</td>
<td>p-value</td>
</tr>
<tr>
<td>Access Angle</td>
<td>0.42</td>
<td>0.13</td>
<td>0.55</td>
<td>0.04</td>
</tr>
<tr>
<td>Distance from Incision</td>
<td>-0.04</td>
<td>0.9</td>
<td>-0.07</td>
<td>0.81</td>
</tr>
<tr>
<td>Annulus Minimum Diameter</td>
<td>-0.22</td>
<td>0.44</td>
<td>-0.45</td>
<td>0.11</td>
</tr>
<tr>
<td>Annulus Maximum Diameter</td>
<td>-0.29</td>
<td>0.31</td>
<td>-0.39</td>
<td>0.17</td>
</tr>
<tr>
<td>Annulus Area</td>
<td>-0.21</td>
<td>0.48</td>
<td>-0.36</td>
<td>0.21</td>
</tr>
<tr>
<td>Annulus Perimeter</td>
<td>-0.17</td>
<td>0.57</td>
<td>-0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Age</td>
<td>-0.19</td>
<td>0.51</td>
<td>-0.26</td>
<td>0.37</td>
</tr>
</tbody>
</table>

The strongest association was between access angle and AoX. (See the scatter plot in Figure 6.4). In Figure 6.5, the box-plot shows a clear separation in the access angle between easy and difficult categories. On the other hand, there was an overlap in access angle between very easy and moderate categories on the four grades difficulty score.

Table 6.3: Pearson correlation between access angle and the outcome parameters (Extracorporeal Circulation Time (ECC), Aortic Cross-clamping Time (AoX), Access Difficulty Score (four grades), and Access Difficulty Score (two grades)).

<table>
<thead>
<tr>
<th>Access Angle</th>
<th>Pearson Correlation</th>
<th>Extracorporeal Circulation Time (ECC)</th>
<th>Aortic Cross-clamping Time (AoX)</th>
<th>Access Difficulty Score (four grades)</th>
<th>Access Difficulty Score (two grades)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P-value (2-tailed)</td>
<td>0.56</td>
<td>0.60</td>
<td>0.55</td>
<td>0.57</td>
</tr>
<tr>
<td>Access Angle</td>
<td>P-value (2-tailed)</td>
<td>0.04</td>
<td>0.02</td>
<td>0.04</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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Figure 6.4: Scatter plot of access angle versus aortic cross-clamping time (AoX) showing the fitting line and the confidence interval.

Figure 6.5: Box-whisker plots representing access angle values per group for the 4-points access difficulty scale (Left) and 2-points difficulty scale (Right).

Age was negatively associated with the access difficulty score where access was judged to be easier for older patients. Also AoX time was reduced with increasing age (Figure 6.6). The ROC curve for access angle predicting access difficulty has an area under the curve of 0.86 (Figure 6.6). The optimal access angle to distinguish access difficulty for the annulus stitching was 38° with a sensitivity of 78% and a specificity of 80%.
6.5 Discussion

We here have presented a novel mini-AVR tool that combines 3D imaging with quantitative planning measures. This study shows significant association between access angle and extracorporeal circulation time, aortic cross-clamping time, and access difficulty. Against our expectation, access distance was not associated with the complexity of the procedure. In our study, it was also shown that older patients were easier to operate and having shorter operation time. In our study, the optimal access angle threshold to distinguish difficult form easy procedures is $38^\circ$.

Image based quantitative preoperative planning of minimally invasive aortic valve replacement was proposed by multiple studies [17,24]. To the best of our knowledge, this is the first study that presents a tool for automated quantitative measurements to assess the difficulty of mini-AVR procedures.

Loor et al. proposed a visualization system using CTA images that utilizes multi-planar reconstruction, maximum intensity projections, volume rendering reconstructions and 3D rendering. In their system, image post-processing was performed on a dedicated stand-alone workstation. Similar to our solution, their tool renders the chest cage with the ascending aorta [19]. However, this tool does not provide quantitative measurements to support the planning and as a consequence, they have not evaluated the added value of this system in clinical practice.

In another study [18], Glauber et al. proposed the usage of distance from ascending aorta to the sternum and the angle between the sternum midline and the inclination of the ascending aorta as parameters for planning the prospective approach. However, in this approach, analysis was proposed to be performed manually on 2d axial and coronal CT images instead of 3D as proposed in our study.
Surprisingly, access distance was not associated significantly with the outcome parameters, which contradicts with previous studies [18,24]. The reason for this discrepancy with previous literature could be due to the treatment selection performed for the patients in this study. Only patients that were considered suitable for ministernotomy were included in this study. This may have resulted in the exclusion of patients with extensive distances.

This study showed that procedures were considered easier to perform for older patients. The negative association found between age and access difficulty score may be explained by the fact that older patients have a larger aortic annulus [25] and smaller access angle probably due to an increased vessel tortuosity, which is common in the elderly [26,27].

The reported association and strong relation of access angle and procedure complexity suggest that the access angle could be used to support the choice of type of mini-AVR approach and estimating the onsite complications. In this study, we showed that an access angle of 38° was a good threshold to distinguish easy from difficult Ministernotomy procedures. For access angle larger than 38°, right anterior mini-thoracotomy could be a more suitable alternative. However, the comparison of different mini-AVR approaches was beyond the scope of this study.

Our design suffers from a number of limitations. This is a single center retrospective patient study including only a relatively small number of patients, which may not be a representative sample of the wider population, and mainly shows the proof of concept of this tool. Only a single rater performed the measurements. The robustness of these measures and its association with the outcome measures need to be validated by more raters. In only 9 patients, calcium at the level of the annulus could be measured. This is insufficient to perform reliable statistical analysis which is the reason that it was not reported in our study.

We have introduced a mini-AVR planning tool, which combines 3D rendering of the patient’s anatomy with quantitative measures. With this tool, the access distance and angle are automatically determined. We have shown that this access angle is strongly associated with procedure complexity. This study also suggests that older patients are easier to operate than younger patients.

Informed consent The Institutional Review Board granted approval of the study design and waived informed consent since solely data obtained in the context of clinical care is utilized.
6.6 References


Chapter 6


