Objective: The aim of this study was to test both in humans and using finite element (FE) aortic valve (AV) models whether the coaptation surface area (CoapSA) correlates with aortic insufficiency (AI) severity due to dilated aortic roots to determine the validity and utility of 3-dimensional transesophageal echocardiographic–measured CoapSA.

Design: Two-pronged, clinical and computational approach.

Setting: Single university hospital.

Participants: The study comprised 10 patients with known AI and 98 FE simulations of increasingly dilated human aortic roots.

Interventions: The CoapSA was calculated using intraoperative 3-dimensional transesophageal echocardiography data of patients with isolated AI and compared with established quantifiers of AI. In addition, the CoapSA and effective regurgitant orifice area (EROA) were determined using FE simulations.

Measurements and Main Results: In the 10 AI patients, regurgitant fraction (RF) increased with EROA ($R^2 = 0.77$, $p = 0.0008$); CoapSA decreased with RF ($R^2 = 0.72$, $p = 0.0020$); CoapSA decreased with EROA ($R^2 = 0.71$, $p = 0.0021$); and normalized CoapSA (CoapSA / [Ventriculo-Aortic Junction × Sinotubular Junction]) decreased with EROA ($R^2 = 0.60$, $p = 0.0088$). In the 98 FE simulations, normalized CoapSA decreased with EROA ($R^2 = 0.50$, $p = 0.0001$).

Conclusions: In both human and FE AV models, CoapSA was observed to be inversely correlated with AI severity, EROA, and RF, thereby supporting the validity and utility of 3D TEE–measured CoapSA. A clinical implication is the expectation that high values of CoapSA, measured intraoperatively after AV repairs, would correlate with better long-term outcomes of those repairs.

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Key Words: aortic valve; ventriculo-aortic junction; sinotubular junction; aortic insufficiency; cusp coaptation surface area; 3-dimensional transesophageal echocardiography; echocardiography
echocardiographic signs, such as the length of coaptation between the cusps after AV repair, have been described to evaluate the durability of AV repairs.4

The AV apparatus is a functional entity that consists of the left ventricular outflow tract (LVOT), the ventriculo-aortic junction (VAJ) (annular diameter measured in centimeters), the sinotubular junction (STJ) (diameter measured in centimeters), and the aortic cusps. To ensure unidirectional anterograde flow in the AV, diastolic collapse of the aortic cusps must occur. Upon collapse, each cusp must coapt with its adjacent cusp. With the exception of cusp perforation, any AI, by definition, is a result of insufficient cusp coaptation.5 For each cusp pair, studies have reported that the geometric shape of the leaflet coaptation surface can be approximated by a trapezoid, consisting of medial and lateral heights along with a distance between the 2 heights.6 The total leaflet coaptation surface area (CoapSA) can be obtained by adding the measurements for all 3 pairs of cusps (Fig 1, A and B), which represents a 3-dimensional (3D) approach to AV apparatus analysis and the understanding of its functionality. Using 3D transesophageal echocardiography (TEE), a reproducible and reliable technique to measure CoapSA has been described and shown to decrease cases of AI.7

Despite the fact that 3D TEE can be used to reliably measure CoapSA and that the anatomy and physiology of the aortic cusps logically support the concept of CoapSA, it is impossible to directly measure this surface area in a pressurized beating heart, and no gold standard exists that can be used for comparison. Instead, the authors introduce finite element (FE) modeling to independently evaluate the relationship between CoapSA and the effective orifice area (EROA), both obtained from computational simulations of increasingly dilated human aortic roots.

Indeed, in the last 5 decades, the FE method has become the prevalent computational approach used to analyze physical phenomena, not only in classic engineering processes, but also in cardiovascular mechanics simulations.8,9 In FE analysis, a complex physical structure is divided into a large number of smaller, simpler parts (finite elements), delimited by special points (nodes) that connect the elements to each other. The equations governing these FEs are assembled into a large system of equations that model the entire problem. Of

Fig 1. (A) Images of a normal AV from multiple plane reconstruction of the AV. (B) Trapezoidal shape of the AV CoapSA. AV, aortic valve; CoapSA, coaptation surface area.


Table 1

<table>
<thead>
<tr>
<th>Step</th>
<th>What</th>
<th>How</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Obtain 3D dataset of AV</td>
<td>Start AV short axis (45 degrees) Minimize depth to AV only Multiple beat gated acquisition</td>
</tr>
<tr>
<td>2</td>
<td>Launch data analysis software</td>
<td>Using AV short axis at the midlevel of the sinus of Valsalva, align the long axis slice plane at the medial aspect of the RCC and NCC scroll from the LVOT in a cephalad direction into the AV apparatus into the AV apparatus toward the STJ. When the cusps split apart, the inferior level of coaptation height medially has been identified.</td>
</tr>
<tr>
<td>3</td>
<td>Align 2D slice plane at the lateral aspect of the NCC-RCC coaptation (see Fig 1, step 1)</td>
<td>Measure distance between inferior and superior borders of coaptation</td>
</tr>
<tr>
<td>4</td>
<td>Identify the inferior point of coaptation</td>
<td>When the cusps split apart, the inferior level of coaptation height medially has been identified</td>
</tr>
<tr>
<td>5</td>
<td>Identify the superior point of coaptation</td>
<td>Continue to scroll in a cephalad direction through the AV apparatus toward the STJ</td>
</tr>
<tr>
<td>6</td>
<td>Measure coaptation height (Fig 2, step 1 [A])</td>
<td>Measure distance between inferior and superior borders of coaptation</td>
</tr>
<tr>
<td>7</td>
<td>Align 2D slice planes at the lateral aspect of the NCC-RCC coaptation (see Fig 2, step 2)</td>
<td>Using AV short axis at the midlevel of the sinus of Valsalva, align the long axis slice plane at the lateral aspect of the RCC and NCC</td>
</tr>
<tr>
<td>8</td>
<td>Identify and measure lateral coaptation height (Fig 2, step 2 [B])</td>
<td>Repeat steps 4-6</td>
</tr>
<tr>
<td>9</td>
<td>Measure coaptation length (Fig 2, step 3 [C])</td>
<td>Measure the distance between the lateral and medial aspects of the cusps along the coaptation line</td>
</tr>
<tr>
<td>10</td>
<td>Calculate CoapSA</td>
<td>Medial height + Lateral height)/2 \times \text{length}</td>
</tr>
<tr>
<td>11</td>
<td>Repeat steps 3-10 for RCC-LCC coaptation</td>
<td>Add CoapSA of the 3 cusps</td>
</tr>
<tr>
<td>12</td>
<td>Repeat steps 3-10 for RCC-LCC coaptation</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Calculate total CoapSA</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AV, aortic valve; CoapSA, coaptation surface area; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, non coronary cusp; RCC, right coronary cusp; STJ, sinotubular junction; TEE, transesophageal echocardiography

Analysis of Intraoperative 3D TEE Data of Patients With AI

A Philips iE33 ultrasound (Philips Ultrasound, Bothell, WA) 3D transesophageal X7-2t probe and QLab platform were used to image and analyze the AV in 10 consecutive patients with AI ranging from mild to severe as a result of dilated aortic roots. Patients with signs of AV calcification were excluded. The regurgitant fraction (RF) and the EROA obtained using 3D planimetry were used to quantify the severity of AI, as described in the widely accepted guidelines on the evaluation of valvular disease. The RF was determined using the continuity equation:

$$RF = \frac{VTI_{LVOT} \times LVOT \text{ CSA} - VTI_{MV} \times MV \text{ Annular CSA}}{VTI_{LVOT} \times LVOT \text{ CSA}}$$

where the velocity time integrals for the LVOT and the mitral valve (VTI_{LVOT} and VTI_{MV}, respectively) were obtained using spectral Doppler display with continuous-wave Doppler and the cross-sectional areas (LVOT CSA) and MV annular CSA were determined using 3D planimetry. Details for calculating these parameters are specified elsewhere, along with their associated standard ranges for RF and EROA to grade among mild, moderate, and severe cases of aortic regurgitation. The CoapSA was calculated using a previously published technique, briefly summarized as follows. The trapezoid coaptation area for each coapting cusp pair was first determined as the half-sum of the medial and lateral coaptation heights multiplied by the distance between the medial and lateral coaptation heights (see Fig 1, A and B). Then, CoapSA was finally obtained by adding the 3 results together. Step-by-step calculation of CoapSA is detailed in Table 1. The

particular interest herein, structural FE analysis can be used to study the relationship between AV shape (eg, normal or dilated) and its ability to close properly in end diastole. FE analysis requires the reconstruction of the valve geometry, modeling of the tissue properties, and the definition of the loading and boundary conditions (here, time-wise applied pressures and anchor points for the valve). Given that the various input parameters can be changed easily to investigate their effects on the simulations, FE studies provide information that experiments can hardly deliver.

The authors hypothesized that in both human and FE AV models, CoapSA would correlate with AI severity, thereby supporting the validity and utility of 3D TEE–measured CoapSA.

Methods

This study was approved by the University of Ottawa Heart Institute Human Research Ethics Board, which waived the requirement for written, informed consent. The manuscript adheres to the Statistical Analyses and Methods in the Published Literature guideline of the Enhancing the Quality and Transparency Of health Research network. The following 2-pronged, clinical and computational approach was used: (1) CoapSA was calculated using intraoperative 3D TEE data of patients with isolated AI and compared with established quantifiers of AI, and (2) CoapSA and EROA were determined in FE computer simulations of increasingly dilated human AV annuli.
FE Modeling of Normal and Increasingly Dilated Human Aortic Roots

Recently, the authors’ group presented the first integrated framework to process subject-specific 3D TEE AV data, determine age-matched material properties for the aortic and cusp tissues, build an FE model of the unpressurized AV, and simulate the AV opening and closing throughout a whole cardiac cycle. This framework, which was validated with 10 normal AVs, is briefly described in the following sections.

Normal aortic valve geometry

The AV geometry was estimated from 3D TEE datasets of normal valves in late diastole using 21 AV anatomic landmarks including the nadirs of the cusps, the apices of the sinuses, and the proximal and cephalad ends of the central coaptation heights. The landmarks were manually extracted from the images using a semi-automated graphical-user interface implemented in MATLAB (MathWorks, Natick, MA). The AV model consisted of the LVOT, 3 cusps, 3 sinuses of Valsalva, and the proximal portion of the ascending aorta (Fig 2).

Material properties of aorta and cusps

The elastic properties of the human aorta were previously measured from pressurization experiments in 14 fresh, excised human aortas. It was observed that the average stretch ratios in both circumferential and longitudinal directions for pressures between 0 and 160 mmHg varied linearly with age. Using the data reported by Labrosse et al, the circumferential and longitudinal stretch ratios at any given age were determined using linear interpolation for the present study, and the thickness of the unpressurized ascending aorta was set at 1.86 mm. The material properties of the aortic sinuses were assumed to be identical to those of the ascending aorta.

The elastic properties of the aortic cusps were estimated using planar equibiaxial data from porcine and human aortic valves (average age = 80.6 yr). It was assumed that the porcine data were valid to describe the behavior of aortic cusps in 18-year-old humans, as suggested by Martin et al. The thickness and the circumferential and radial stretch ratios for the cusps were assumed to vary linearly with age.

FE model

The AV model was divided into approximately 10,000 8-noded hexahedral FEs (see Fig 2). Three elements were used through the aortic thickness, whereas 2 were used through the cusp thickness. Each simulation of 1 cardiac cycle started from the unpressurized AV apparatus. To estimate the unpressurized geometry of the AV model, an iterative approach was applied to minimize the error between the 3D TEE-measured dimensions of the VAJ, STJ, cusp free edge lengths and heights, and their simulated counterparts, all which were measured in late diastole.

All the nodes on the proximal cross-section of the LVOT in the AV model were fixed. The opening and closing of normal and dilated AVs were analyzed in dynamics by applying aortic and left ventricular pressure pulses to the aortic and the left ventricular sides of the AV components. However, because the analysis started from the unpressurized geometry, the pressure was ramped from 0 to 80 mmHg before the cardiac cycle started in early systole. Simulations were performed in the commercial FE software LS-Dyna 971 (LSTC, Livermore, CA).

Functional aortic annulus dilation

Building from the validated models of the same 10 normal AVs as studied by Labrosse et al, the authors of the present study investigated the effect of VAJ and STJ dilation on EROA by considering the following 2 categories of functional aortic annulus (FAA) dilations:

1. STJ dilation: The initial STJ size was increased in 2 mm increments
2. Combined STJ and VAJ dilations: The original VAJ size was increased by 4 mm and STJ was dilated in 2 mm increments

The dilation amount was applied to the unpressurized geometry and was incrementally increased until the cusps became too small for their underlying roots (ie, the valves were fully open in end diastole, an unrealistic scenario). This resulted in 98 simulated AVs (including the original normal valves). The AV geometric parameters including VAJ, STJ, valve height, effective height, average cusp height, and average cusp free edge length, were recorded in end diastole (Table A1).
CoapSA and EROA were determined in end diastole after each simulation. CoapSA was defined as the total surface area under contact pressures > 0.1 mmHg (13.3 Pa) between adjacent cusps. This threshold pressure value was selected because it provided an excellent correlation between 3D TEE–measured and simulated CoapSA values in normal valves.12 To calculate EROA, 3 nodes defining the corners of the end diastolic orifice (shown by white points in Fig 3, A) were identified as the first nodes having a contact pressure > 13.3 Pa when scanning the nodes on the cusp free edges from the center toward the commissures. The EROA perimeter was outlined by the nodes on the cusp free edges between the corner nodes. EROA was measured as the area outlined by the projection of all the perimeter nodes onto the plane fitted through the 3 corner nodes (Fig 3, B).

Statistical Analysis

The relationships among different parameters were determined using linear regressions. The coefficient of determination ($R^2$) and probability (p) of the regressions are given in all plots. Box-and-whisker plots also were used to graphically compare the EROA (measured from simulations) in all AV groups. In each group, the plot depicts minimum EROA values, lower quartile (25th percentile), median, upper quartile (75 percentile), and maximum EROA values. Statistical significance was set at p < 0.05. The analysis was performed using the statistical analysis program MedCalc (MedCalc Software, Ostend, Belgium).

Results

Analysis of Intraoperative 3D TEE Data of Patients With AI

The 10 AI patients presented with a continuum of values for RF and EROA that spanned AI grades from mild to severe and therefore provided meaningful data outside the normal range. Detailed data are presented in the Appendix. Figure 4 illustrates the important conclusions gleaned from linear regression analysis of the established AI metrics (RF and EROA), CoapSA, and the normalized CoapSA. Specifically, RF increased with EROA ($R^2 = 0.77$, p = 0.0008 [Fig 4, A]); CoapSA decreased with RF ($R^2 = 0.72$, p = 0.0020 [Fig 4, B]); CoapSA decreased with EROA ($R^2 = 0.71$, p = 0.0021 [Fig 4, C]); and normalized CoapSA decreased with EROA ($R^2 = 0.60$, p = 0.0088 [Fig 4, D]).

FE Models of Normal and Increasingly Dilated Human Aortic Roots

Detailed simulation data are presented in Table A2 in the Appendix. Box-and-whisker plots of EROA for different FAA dilation groups are shown in Figure 5, A. Increasing the size of the STJ or VAJ caused the cusps to stretch in diastole, leading to an increase in free edge length (see Table A1). If the dilation were small (up to 4 mm), the cusps still were able to properly coapt with no statistically significant change in the EROA (see Fig 5, A). However in both categories of dilations, increasing the size of the FAA > 4 mm significantly increased the EROA compared with that of the control patients (see Fig 5, A). Figure 5, B shows that normalized CoapSA significantly decreased with increasing EROA (p < 0.0001). This reflects the mechanism of AI in dilated aortic roots—dilation of the FAA causes a reduction in the cusps’ central coaptation, which progressively leads to an increase in the EROA.

Discussion

For an AV to be competent and prevent backflow during diastole, there must be coaptation of the cusps, thereby sealing the aortic outflow tract. When the cusps abut one another, they define a coaptation surface, whose area can be measured. 3D TEE using multiplanar reconstruction analysis has allowed for measurement of CoapSA.7 Although intuitive and highly reproducible, this technique and concept have been limited in more widespread use by the lack of a gold standard for which to compare it (ie, none exists). This study sought to reinforce the concept by comparing CoapSA values to known quantifiers of AI. It also sought to verify the concept by evaluating CoapSA in computer simulations with FAA
dilation. The results show that both approaches resulted in the same conclusion.

Al-Atassi et al.\textsuperscript{16} using a combined experimental and FE study of normal and dilated porcine aortic roots, reported reduced leaflet CoapSA (measured using 3D TEE) and higher EROA as the STJ diameter was increased. Laboratory experiments already had shown that dilation of the STJ alone can lead to deformation of the AV and consecutive AI in stentless AV substitutes\textsuperscript{17} and canine hearts.\textsuperscript{18}

Using computational simulations, Grande et al.\textsuperscript{19} evaluated the impact of dilation of the aortic root by 5%, 15%, 30%, and 50% compared with a control FE model established from magnetic resonance imaging of 1 normal, unpressurized human AV. The models were loaded to peak physiologic transvalvular pressure. They reported decreases in CoapSA of 3%, 8%, and 18% for dilations of the aortic root of 5% to 15%, 30%, and 50%, respectively.

Diseases of the AV historically have been treated surgically with AV replacement. Even though effective, mechanical and bioprosthetic valves both have their drawbacks.\textsuperscript{20–23} Repair techniques for the AV have been implemented for over 20 years and boast advantages over replacement techniques, including lower incidence of thromboembolic events, the avoidance of long-term anticoagulation, and a reduced risk of endocarditis.\textsuperscript{23–25} Mid- and long-term data on repair technique outcomes are becoming more available, which has led to the refinement and evolution of the surgical approach to AV repair.\textsuperscript{26} As the surgical skillset is growing, so too is the need to provide intraoperative imaging analysis to assist the surgeon to optimally reconstruct an AV apparatus.

The growth and development of intraoperative AV imaging follow a similar path to that of mitral valve (MV) repair 2 decades ago. As MV repair became more prevalent, intraoperative TEE developed into a tool to accurately define the MV structure and function in the operating room (OR). That detailed structure and function knowledge is what the surgeon needs to know in real time. Lambert et al.\textsuperscript{27} showed that TEE can precisely identify MV anatomy in the OR, and Savage and Cosgrove’s accompanying editorial explained why obtaining this information in the OR is beneficial for the surgeon. The same now holds true with AV repair.

TEE has provided excellent high-quality images of the AV apparatus, and unlike other imaging modalities, does so in the pressurized dynamic heart in the OR. 2D TEE predictors of
recurrent aortic regurgitation after AV repair have been demonstrated and include coaptation length, level of coaptation, residual AI, and effective height of coaptation. However, these predictors are significantly limited because of the location of the TEE probe within the thoracic cavity. Due to this physical limitation, it not possible with 2D TEE technology to obtain a true 3D assessment of the AV apparatus, in particular regarding the relationship of the noncoronary to the left coronary cusps. It was only with the introduction of 3D TEE technology that a more thorough 3D assessment of the AV apparatus was made possible. This more complete analysis has the potential to empower anesthesiologists and surgeons with a better understanding of the structure and function of the valve intraoperatively and help guide the approach to repair in relative real time.28,29

Because a larger coaptation length has been shown to translate into more durable AI repairs,4 one would expect that the same would be true for higher values of normalized CoapSA. Therefore, one clinical implication of this study is to apply the intraoperative measurement of normalized CoapSA to the evaluation of the durability of AV repair.

Study Limitations

Although this study involved only 10 patients with AI, each patient’s case was analyzed through the lenses of multiple established quantifiers of AI. The AI grades ranged from mild to severe and therefore provided meaningful data outside the normal spectrum.

Due to poor 3D TEE image quality of AVs after surgery, it was not possible to compare CoapSA and EROA in AVs before and after surgery. This motivated the use of FE modeling to evaluate these parameters for AVs with different STJ and VAJ dimensions. Considering the lack of experimental data on the material properties of dilated AVs, normal and dilated valves were given the same age-varying elastic properties. This did not reflect possible histologic and structural changes to the tissues as they dilate over time but appropriately described acute dilations.

More work still is warranted to establish a robust, quantitative scale between normalized CoapSA and AI severity. In addition, desirable cutoff values of normalized CoapSA that correlate with durable repair need to be determined. This includes cases of billowing aortic cusps and bicuspid AVs.30,31

Conclusions

The authors observed that in both human and FE AV models, CoapSA inversely correlated with AI severity, thereby supporting the validity and utility of 3D TEE–measured CoapSA. A clinical implication is the expectation that high values of CoapSA, measured intraoperatively after AV repairs, would correlate with better long-term outcomes of those repairs.

Acknowledgments

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Appendix A. Supplementary Material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1053/j.jvca.2017.08.043.

References
