Variation in ascending thoracic aorta position: an analysis by computed tomography

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ABSTRACT

Background: There is no evidence in current literature that demonstrates the prevalence of ascending thoracic aortic variation in relation to the sternum in the general, or diseased population. This measurement has become an important factor in decision-making for Trans-Catheter Aortic Valve Implantation (TAVI) and Minimally Invasive Cardiac Surgery (MICS).

Methods: We conducted a cross-sectional study in Cape Town, South Africa. We evaluated the Thoracic CT scans of pre-selected TAVI patients (n=25) and compared these to Thoracic CT scans from the same general population (n=100). Three parameters of ascending thoracic aorta variations were measured.

Results: Mean aorta distance from sternum was 28.01mm (95% CI: 24.56 - 31.48) in cases and 27.34mm (95% CI: 25.49 - 29.20) in controls (p<0.001). The mean position of the aorta relative to the sternum, favoured the aorta being less than 50% of its diameter to the right, in both groups. Aorto-ventricular angle showed a mean angle (degrees) of 47.92 (95% CI: 44.36 - 51.23) in cases and 37.06 (95% CI: 35.03 - 39.09) in controls. Subgroup analysis for age >60 years revealed no difference between groups (p=0.314). An overall linear relationship of aorto-ventricular angle, compared to age, was demonstrated.

Conclusion: Statistical analysis of ascending thoracic aorta position indicates that patients presenting for aortic valve surgery, especially older patients (>70 years), have favourable anatomy for MICS through a right thoracotomy. The aortic distance from the sternum was larger in the exposed group >60 years. Aortic valve disease does not cause variation in aorto-ventricular angle. The aorto-ventricular angle increases linearly with age, in both groups. SAHeart 2021;18:48-55

INTRODUCTION

Aortic stenosis affects the variation in thoracic aorta position and is a condition that affects 3% - 4% of the population over the age of 70 and 6% - 7% over the age of 80.[1] The gold standard in the management of symptomatic aortic stenosis is that of aortic valve replacement.[2] The procedure can be done with conventional open-heart surgery with cardiopulmonary bypass or via Transcatheter Aortic Valve Implantation (TAVI) if the risk for conventional surgery is too high. The open heart approach can be done via full sternotomy, ministernotomy or right mini-thoracotomy approach.[2] Minimally Invasive Cardiac Surgery (MICS) has been shown to have similar intra-operative safety as complete sternotomy. Moreover, it has been shown to decrease certain post-operative complications such as: post-operative bleeding,[3] mechanical ventilation time[3] and wound dehiscence.[4] It has also been shown to decrease the amount of in-hospital stay post-operatively.[5] With the advent of newer techniques such as TAVI and minimally invasive approaches, additional anatomical data is required for accurate placement of the prosthesis.[6] Access to the aortic valve through a minimally invasive 5cm right thoracotomy will be easier if the ascending aorta lies more to the right of the sternum and therefore closer to the incision.[7] If the take-off angle of the ascending aorta is more than 45 degrees in its annular plane, direct visualisation from the surgeon's perspective will be obscured. This most certainly results in a technically challenging operation.[8] Aorto-ventricular angle is the angle of the inclination of the valvular annulus and ascending aorta relative to the right of the midline (Figure 1).

MICS can be associated with longer aortic cross clamp, CBP and operating times.[9] Difficult access to the ascending aorta during MICS can thus increase CPB and cross clamp times. The following anatomical criteria are suggested by Glauber, et al. for minimally invasive aortic valve surgery through a right anterior thoracotomy as determined by CT scan.[8]

- More than half of the ascending aorta is to the right of the mid-sternal line.
- The distance from the ascending aorta to the sternum does not exceed 10cm.
- The inclination angle of the aorta should be more than 45 degrees.

The annular angulation is an important measurement when the TAVI approach is considered, as a more acute angle is associated with an increased risk of para-valvular leak.[10] This angle is measured between the horizontal plane and the plane of the aortic annulus.[11] The aorto-ventricular angle by CT measurement increases significantly in patients older than 80 years.[12] Bicuspid Aortic Valve Disease has an 80% incidence of ascending aorta dilatation,[13] which directly influences ascending thoracic aorta position.

There is no published literature describing the statistical variation in ascending aortic anatomy such as position in relation to the sternum, inclination angle and aorto-ventricular angle for the general and diseased aortic valve population.

The aim of this study was to conduct a cross sectional study that compared the difference in variation of anatomy of the ascending aorta (aorto-ventricular angle, position relative to the sternum, and distance from the sternum) between a population with aortic valve stenosis, compared to a sample population without aortic valve stenosis from the same general population. The primary outcome was an epidemiological assessment and the statistical comparison of midline position and aorto-ventricular angle between selected cases and a demographically matched control population. The secondary outcome was to perform a subgroup analysis in order to obtain data that may be applied as a clinical aid to guide the assessment and decision-making process in minimally invasive and TAVI surgery compared to conventional open-heart surgery.

METHODS

Study design

This study was an analytical cross-sectional study. The study population were patients selected from online radiological registries in the Western Cape Province of South Africa.

Exposure/disease was defined as patients with clinically confirmed aortic valve stenosis.

Cases were patients with clinically confirmed aortic valve stenosis who underwent pre-operative planning Thoracic CT for TAVI. These patients had no other thoracic pathology that could influence mediastinal position. Controls were patients from the same population that produced the cases and who had no clinical aortic valve stenosis or other thoracic pathology influencing mediastinal position on thoracic CT. Primary outcome was the variation in ascending aorta position in patients with aortic valve stenosis between diseased and non-diseased patients from the same population.

For the Reporting of our Cross-sectional Study we used the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) statement. The statement may be found at http://equator-network.org.

Ethical approval was granted by Stellenbosch University's Health Research and Ethics Committee (HREC).

Study population and sample selection

Cases consisted of 25 (n=25) thoracic CT scans of adult patients who presented for TAVI and who fulfilled pre-selection inclusion criteria. Inclusion criteria for cases were those who underwent TAVI, who underwent pre-operative thoracic CT scanning, and that have clinically confirmed aortic valve stenosis with no other thoracic or spinal pathology influencing mediastinal position.

Controls consisted of 100 (n=100) thoracic CT scans that were randomly selected from Tygerberg Hospital's radiological registry by stratified randomisation technique. Inclusion criteria for controls were thoracic CT scans of adult patients (>14 years) that were radiologically reported, as having no thoracic pathology influencing mediastinal position. Exclusion criteria for cases and controls were thoracic CT scans that had other cardiac or thoracic disease influencing mediastinal position (diaphragmatic, pleural and mediastinal mass lesions, thoracic aortic disease, pleural and mediastinal fluid, atelectasis). Paediatric (<14 years) CT scans were also excluded due to the marked variability in the anatomy of these scans compared to adults.

Limitation of clinician access to the full archived database of CT scans at our institution, is limited. Thus, a manual search for all Thoracic CT scans conducted during 1 January - 31 December 2017 at Tygerberg Hospital, was performed with the assistance of the Tygerberg Hospital PACS/RIS archival team. Our search revealed a total of 4 023 thoracic CT scans performed during this period. A total of 100 controls that fulfilled inclusion criteria were selected by computer generated stratified random sampling (stratified for age 1:1 and sex 1:1).

Controls were matched for sex with a male to female ratio close to 1:1. Matching for age was done by categorising age groups into 4 age ranges to include an even distribution of age in cases and controls. The investigators were blinded to the identity of cases and controls.

Data measurement

Data measurement in the case and control groups was as raw data in the form of digital measurements. Measurements were performed with the aid of the online tool provided by the radiological registry software (Phillips Radiology iSite, 2006). This tool consists of protractor callipers and rulers that are able to measure angles and distances in a digital format, respectively.

Primary Outcomes consisted of three assessed ascending thoracic aorta measurements, namely:

The position of the ascending aorta relative to the sternum (Figure 2)

- The relationship of the ascending aorta relative to the sternum (left or right) on Axial CT was measured.
- A digital line passing through the centre of the ascending aorta at the bifurcation of the main pulmonary artery on Axial CT was rendered. Another digitally rendered line passing through the centre of the sternum and vertebral column was rendered.
- The lateral distance of the ascending aorta from the sternum was compared to aortic diameter (at the level of the bifurcation of the main pulmonary artery). This was expressed as a ratio (%):
  - The diameter of the aorta, relative to the distance of the aorta from the midline, was expressed as a ratio in percentage (Figure 2).

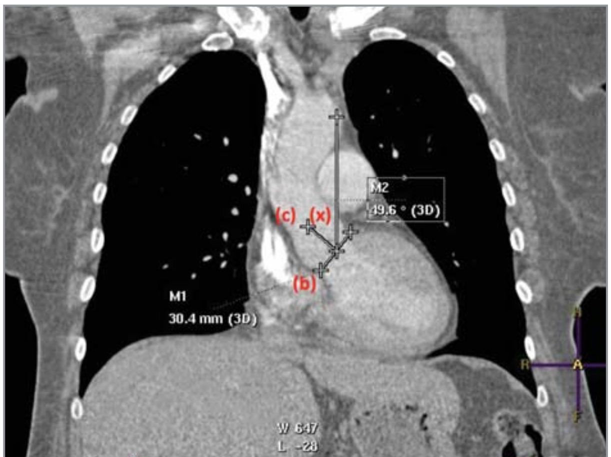

FIGURE 1: Aorto-ventricular angle.

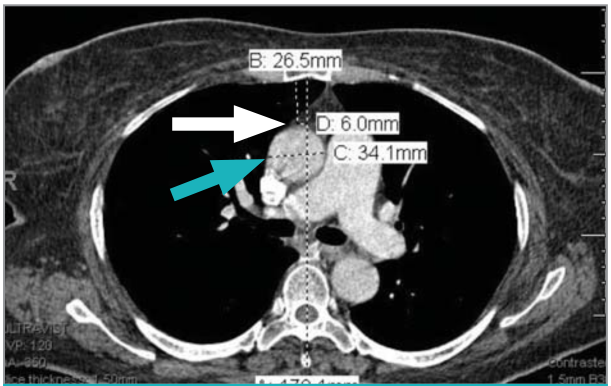

FIGURE 2: Distance of the Aorta from the midline expressed as a proportion (%) of its diameter.
Digitally rendered line measuring distance from the midline to the midpoint of the ascending aorta (D - white arrow).
Diameter of the ascending aorta at the level of the bifuration of the pulmonary artery (C - blue arrow).

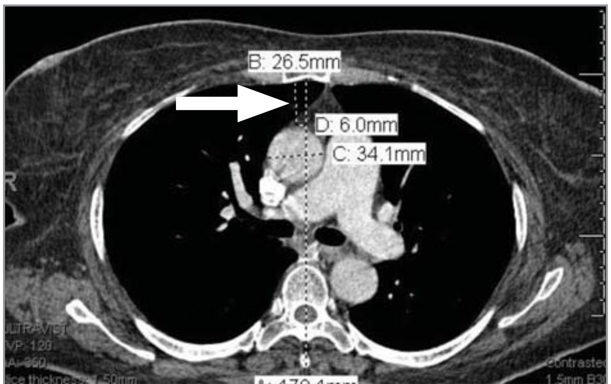

FIGURE 3: Distance of the ascending aorta from the posterior sternal table at the level of the pulmonary artery bifurcation.
Digitally rendered line from posterioe sternal table to the anterior wall of the aorta (B - white arrow).

The distance from the ascending aorta to the sternum (Figure 3)

- The distance of the posterior table of the sternum to the aorta at the level of the bifurcation of the main pulmonary artery.
- The measurement is a continuous variable (mm).

The inclination angle of the ascending aorta (aorto-ventricular angle) (Figure 1)

- This is the angle of the plane of the aortic annulus relative to a vertical line through the middle of the sternum. A vertical line passing through the midline of the sternum (line a) and a line along the plane of the aortic annulus is created (line b). A third line is rendered (line c), which passes through the centre of the aortic annulus and perpendicular to the annular plane (line b). The angle of inclination of the ascending aorta is the angle between (line a) and (line c). Therefore it is the angle between the vertical midline of the sternum and the inclination of the ascending aorta (x).

- For optimal MICS criteria, this angle should be approximately 45 degrees.
- This will be a nominal ordinal variable measured in degrees.
- A secondary outcome was the number of subjects with angulation more than 45 degrees or less than 45 degrees, expressed as a binary variable.
- The secondary outcome was expressing the Aortic Inclination angle as a continuous variable for age and correlating this statistic in a linear model.

Blinding

Investigator blinding to the identity of cases and controls was by means of pooling and randomisation. Identification was exclusively based on patient file number. Investigators were blinded to age, sex and identity as these variables were excluded from analysis. Study demographics were retrospectively added after data capture. Results of blinding were not analysed, assessed or reported on.

Statistical considerations

Sample size and power

Evidence has shown that when comparing an exposed population with minimal study subjects (n<100) to an unexposed population where there is no pre-existing reference value, using an unexposed sample size 4 times the diseased population will demonstrate a significant p-value, effectively.[16] Furthermore, using an unexposed sample size more than 4 times the exposed population, has not shown any significant difference in the power of results.[17] Our ratio of cases to controls is therefore 1:4.

The prevalence of each parameter of ascending thoracic aorta variation in each group was calculated by using the 95% confidence interval aiming for a significance value of $p<0.05$. Cases were sampled based on available sample size, convenience, and no previous prevalence statistic available (hence an inability to calculate sample size).

Statistical analysis

Data Analysis was performed with Stata Statistical Package (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC). We calculated the mean for inclination angle (degrees) as a continuous variable between cases and controls and compared the results using a 2-tailed t-test as a measure of association.

We calculated proportions (as percentage) for our binary variables of >50% or <50% of the ratio of aortic diameter relative to the lateral sternal distance. We also used proportional calculation (as percentage) of our binary variable of "position of the aorta relative to the sternum (Left or Right)." We used chi-square testing for measure of association between categorical variables. We used student's t-test for measure of association between numerical variables.

Mean age was significantly higher in cases compared to controls. In order to correct for potential confounding, we conducted a subgroup analysis by only comparing controls older than 60 years, against cases.

Due to the multivariable results that were obtained from the cross-sectional study, measure of association was calculated by using the Prevalence Odds Ratio (POR) for each variable of the case and control populations. An overall odds ratio for binary outcomes was also calculated using logistic regression to demonstrate a significant POR between exposed and unexposed groups.

RESULTS

Subgroup analysis

The total combined subgroup analysis (n=59) consisted of patients >60 years from the diseased population (n=25) and the control population (n=34).

Table I shows the demographics of cases and controls in the study, and in the subgroup analysis.

Distance of ascending thoracic aorta from the sternum

The mean distance was 28.01mm (95% CI:24.56 - 31.48) in cases with aortic stenosis and 27.34mm (95% CI:25.49 - 29.20) in controls, which did not demonstrate a difference between groups (p=0.74). We conducted a subgroup analysis for patients >60 years. This analysis showed a difference (p<0.001), between cases (mean = 28.16mm [95% CI:24.56 - 31.48]) and controls (mean = 25.59 mm [95% CI:22.37 - 28.82]).

Ascending aorta position left/right of the sternum

Mean position left/right of the sternum favoured the right with a mean proportion of 96% (95% CI:90.64 - 98.34) in cases

TABLE I: Demographics for age during statistical analysis for ascending aorta position.

Analysis	Participant allocation	Number of participants (%)	Mean age (years)	Minimum age (years)	Maximum age (years)
Initial Analysis (n=125)	Case	25 (20%)	81.96	64	98
	Control	100 (80%)	45.3	15	82
Subgroup Analysis (Age >60 years) (n=59)	Case	25 (42.4%)	81.96	64	90
	Control	34 (57.6%)	68.29	60	82

TABLE II: Summarised statistical analysis for the variation of ascending aorta position in patients with aortic valve disease (cases) and the general population (controls).

Variables	Cases	Controls	p-value*
	Mean (95% confidence interval)		
Sex (male)#	84%	52%	p=0.004
Aorta position relative to sternum†	96% (90.64 - 98.34)	96% (90.64 - 98.34)	p=1
Lateral position of aorta‡	72% (51.11 - 86.34)	92% (84.67 - 96.00)	p=0.006
Mean distance from sternum (mm)∞	28.01 (24.7 - 31.3)	27.34 (25.5 - 29.2)	p=0.7430
Aorto-ventricular angle (degrees)	47.79 (44.50 - 51.08)	37.06 (35.03 - 39.09)	p<0.001

**Subgroup analysis for age >60. #Number of males as a proportion (%). †The position of the ascending aorta to the right of the sternum. ‡The lateral distance of the ascending aorta from the sternum expressed as a proportion of its diameter (less than 50% of its diameter). ∞The distance of the anterior wall of the ascending aorta from the posterior sternal table in millimetres.*

and controls. POR = 1 (95% CI:0.93 - 51.26). No difference between groups was demonstrated (p=0.68) (Table II). Subgroup analysis for patients >60 years favoured the right position, with a mean proportion of 98.3% (95% CI:88.33 - 99.78) present in cases and controls. No difference was noted between groups in the subgroup analysis (p=0.424) (Table III).

Ascending aorta position lateral to sternum, expressed as a proportion of its diameter

The mean position of the aorta diameter, lateral to sternum, favoured the aorta being positioned less than 50% of its diameter (in mm), lateral to the sternum. A mean proportion of 72% (95% CI:51.11 - 86.34) in cases and 92% (95% CI:84.67 - 96.00) in controls was observed. A difference between groups was demonstrated (p=0.006). POR=0.22 (95% CI: 0.06 - 0.83). Subgroup analysis for patients >60 years favoured <50% position as well, with a mean proportion of 72% (95% CI:50.86 - 86.47) in cases and 88% (95% CI:71.78 - 95.67) in controls. No significant difference was noted between groups when adjusting for age in the subgroup analysis (p=0.114).

Aorto-ventricular angle

A difference (p<0.001) in mean aorto-ventricular angle was demonstrated, with a mean angle (degrees) of 47.92 (95% CI: 44.36 - 51.23) in cases compared to 37.06 (95% CI:35.03 - 39.09) in controls. This shows more than 10 degrees difference (23%) between groups. Subgroup analysis for age revealed no significant difference between groups (p=0.314).

An age related, linear relationship using linear regression modelling was calculated for aorto-ventricular angle (see Figure 4) and used to construct an angle estimate using "age" as the independent variable: aorto-ventricular angle = 0.31 × Age (years) + 22.92 (95% CI:0.25 - 0.40). The regression model for inclination angle as the dependant variable and age as the independent variable, demonstrated a coefficient of 0.31 (95% CI:0.25 - 0.37) with an adjusted R-squared value of 0.45.

Using this statistic, we calculated that the mean aorto-ventricular angle in patient's ≥71 years is approximately ≥45 degrees.

COMMENT

To the authors' knowledge, this is the first time that an outcome with p<0.05 and variation in ascending thoracic aorta variation has been shown in the general, and diseased population with aortic stenosis. It appears that the current acceptance of "ideal" position for MICS via right mini-thoracotomy approach

TABLE III: Subgroup analysis of patients >60 years: Summarised statistical analysis for the variation of ascending aorta position in patients with aortic valve disease (cases) and the general population (controls).

Variables	Cases	Controls	p-value[*]
	Mean (95% confidence interval)		
Sex (male)[#]	84%	47.06%	p=0.004
Aorta position relative to sternum[†]	96% (74.89 - 99.48)	100% (-)	p=0.240
Lateral position of aorta[‡]	72 (50.86 - 86.47)	88.24% (71.78 - 95.67)	p=0.114
Mean distance from sternum (mm)[∞]	28.016 (24.56 - 31.48)	25.59 (22.37 - 28.82)	p<0.001
Aorto-ventricular angle (degrees)	47.79 (44.36 - 51.23)	45.56 (42.65 - 48.47)	p=0.314

[*]Subgroup analysis for age >60. [#]Number of males as a proportion (%). [†]The position of the ascending aorta to the right of the sternum. [‡]The lateral distance of the ascending aorta from the sternum expressed as a proportion of its diameter (less than 50% of its diameter). [∞]The distance of the anterior wall of the ascending aorta from the posterior sternal table in millimetres.

only partially exists in the diseased and normal population and is significantly influenced by age.

Aortic variation in the diseased and exposed population

Aortic position of more than 50% of its diameter lateral to the sternum exists in only 18% of the diseased population with no significant difference present between the diseased and general population. In 96% of the diseased and general population, the ascending aorta lies to the right of the sternum, which anatomically, may favour a right mini thoracotomy approach. Mean distance of the aorta from the sternal table in the diseased and general population was >20mm across both populations, regardless of age or pre-existing disease. Aortic stenosis in participants >60 years caused a more marked distance from the sternum compared to the control group.

There was no difference in aorto-ventricular angle between the general and diseased population, which demonstrates that Aortic Stenosis does not cause variation in aorto-ventricular angle. The authors have also shown that the aorto-ventricular angle is more than 45 degrees in most patients presenting for surgery. This is most likely due to age-related unfolding of the aortic arch, causing distortion in the geometry of the ascending aorta, proximal to the fixed position of the aorta arch at the level of the ligamentum arteriosum. The mean aorto-ventricular angle was less than 45 degrees in patients <70 years old. The authors have shown a statistically significant age-related linear relationship in the aorto-ventricular angle that has not previously been described, and derived a statistic with which to predict the value of this angle according to age (provided no other factors exist that could influence mediastinal position). This statistic (aorto-ventricular angle = 0.31 x Age (years) + 22.92) may be used an aid for decision making in MICS, especially in younger patients (<70 years) presenting for surgery (Figure 4).

Study limitations

Analysis was done between cases and controls using age as a dependent variable in the subgroup analysis. Variation in the regression model exists. Increasing age and the related unfolding of the aorta, may perhaps not be the isolated cause of variation in distance of the aorta from the sternum and the aorto-ventricular angle. It may mask associated age-related cardiovascular diseases and connective tissue disorders that could potentially be causative factors for anatomical variation. Identifying these factors in order to adjust for confounding during regression analysis is difficult in a retrospective review of radiological data. The investigators only had access to radiological data and were therefore unable to exclude whether Aortic Stenosis had been excluded with prior investigation.

Evidence based limitations in the applicability of MICS criteria in clinical practise

As mentioned, MICS criteria for surgery, traditionally relies on specific measurements in the ascending thoracic aorta for prediction of favourable outcomes during surgery. Results from this analysis demonstrates that optimal anatomical criteria for MICS, appears to be lacking in the general and diseased population and is present in a very small sub-group of patients (Table IV). Whether suboptimal MICS criteria for: the distance of the aorta from the sternum, aorto-ventricular angle and position relative to the sternum, leads to poorer surgical outcomes, is yet to be shown. The recommendation for optimal MICS criteria has been based on "anticipated" outcomes and may be related to surgical experience amongst other confounders like pre-existing mediastinal and thoracic disease, influencing thoracic aorta position. Evidence is however still lacking to demonstrate whether

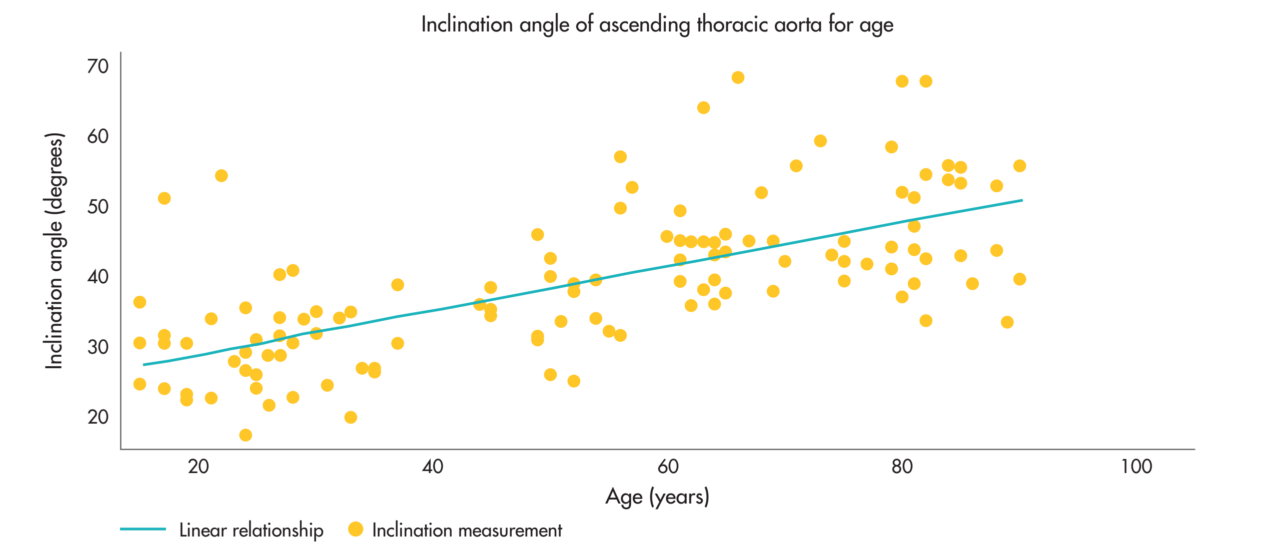

FIGURE 4: Linear correlation of aorto-ventricular angle for age.

TABLE 1V: Patients in the subgroup analysis for age >60 years, who have optimal anatomical criteria for MICS.

Participant allocation (Age >60 years)	>50% diameter# (95% CI)	Right of sternum† (95% CI)	>45 degrees‡ (95% CI)	Distance from sternum <10cm∞ (95% CI)
Cases (n=25)	28% (12.07 - 49.38)	96% (74.89 - 99.48)	48% (27.80 - 68.69)	4% (10.12 - 20.35)
Controls (n=34)	11.76% (03.30 - 27.45)	100% (-)	50% (32.43 - 67.57)	8% (01.85 - 23.67)

#The lateral distance of the ascending aorta from the sternum expressed as a proportion of its diameter (more than 50% of its diameter). †The position of the ascending aorta to the right of the sternum. ‡The aorto-ventricular angle being >45°. ∞The distance of the anterior wall of the ascending aorta from the sternum.

variation and anatomical differences may lead to difficult access and longer aortic cross-clamp time which may precipitate prolonged cardiopulmonary bypass and result in poor post-operative outcomes. This study may potentially initiate further research into the avenue of clinical outcomes in MICS, based on pre-selection and assessment of optimal anatomical criteria in patients undergoing aortic valve surgery.

CONCLUSION

The results obtained in this statistical analysis of ascending thoracic aorta position, indicates significant difference in anatomical parameters between exposed and unexposed individuals with aortic valve disease. Patients presenting for aortic valve surgery, especially older patients (>70 years) have favourable anatomy for MICS through a right thoracotomy. The aortic distance from the sternum was larger in the Aortic Valve Disease Group >60 years. Aortic valve disease does not cause variation in aorto-ventricular angle. The aorto-ventricular angle increases linearly with age in both groups. Optimal anatomical criteria for MICS is present in a small subgroup of the diseased and general population.

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Conflict of interest: none declared.

MULTIPLE CHOICE QUESTIONS

1. In what context did the need arise to perform this study?

A. The variability of ascending thoracic aorta variability is unknown in the general and diseased populations and is of epidemiological importance.

B. Minimally invasive Cardiac Surgery (MICS) and Transcatheter Aortic Valve Implantation (TAVI) requires the use of this measurement in clinical decision making.

C. Complications with minimally invasive techniques post-procedurally could potentially be predicted with knowledge of the underlying aortic anatomy.

D. All of the above.

2. With regard to the sub-group analysis in the study:

A. Patients were <60 years and all 59 patients were evaluated as a whole.

B. Patients were <60 years and sub-divided into diseased (n=25) and controls (n=34).

C. Patients were >60 years and sub-divided into diseased (n=25) and controls (n=34).

D. Patients were <60 years and sub-divided into diseased (n=34) and controls (n=25).

3. With regard to the Thoracic Aorta:

A. The aorta was situated more than 50% of its diameter, lateral to the sternum, in 72% of the population.

B. The aorta was situated more than 50% of its diameter, lateral to the sternum, in 18% of the population

C. Mean distance from the sternum was <20mm in both populations

D. Aortic stenosis causes variation in the angle of the ascending aorta.

REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: A population-based study. Lancet (London, England) 2006;368:1005-11.
2. Brown JM, O'Brien SM, Wu C, et al. Isolated aortic valve replacement in North America comprising 108 687 patients in 10 years: Changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. J Thorac Cardiovasc Surg 2009;137:82-90.
3. Murtuza B, Pepper JR, DeL Stanbridge R, et al. Minimal access aortic valve replacement: Is It Worth It? Ann Thorac Surg 2008;85:1121-31.
4. Bonacchi M, Prifti E, Giunti G, et al. Does ministernotomy improve postoperative outcome in aortic valve operation? A prospective randomised study. Ann Thorac Surg 2002;73:460-5.
5. Khoshbin E, Prayaga S, Kinsella J, et al. Mini-sternotomy for aortic valve replacement reduces the length of stay in the cardiac intensive care unit: Meta-analysis of randomised controlled trials. BMJ Open 2011;1
6. Piazza N, de Jaegere P, Schultz C, et al. Anatomy of the aortic valvar complex and its implications for transcatheter implantation of the aortic valve. Circ Cardiovasc Interv 2008;1:74-81.
7. Malaisrie SC, Barnhart GR, Farivar RS, et al. Current era minimally invasive aortic valve replacement: Techniques and practice. J Thorac Cardiovasc Surg 2014;147:6-14.
8. Glauber M, Ferrarini M, Miceli A. Minimally invasive aortic valve surgery: State of the art and future directions. Ann Cardiothorac Surg 2015;4:26-32.
9. Lucà F, van Garsse L, Rao CM, et al. Minimally invasive mitral valve surgery: A systematic review. Minim Invasive Surg 2013;2013:179569.
10. Généreux P, Head SJ, Hahn R, et al. Paravalvular leak after transcatheter aortic valve replacement: The New Achilles' Heel? A comprehensive review of the literature. J Am Coll Cardiol 2013;61:1125-36.
11. Popma JJ, Reardon MJ, Yakubov SJ, et al. Safety and efficacy of self-expanding TAVR in patients with aortoventricular angulation. JACC Cardiovasc Imaging 2016;9:973-81.
12. Leipsic J, Gurvitch R, LaBounty TM, et al. Multidetector computed tomography in transcatheter aortic valve implantation. JACC Cardiovasc Imaging 2011;4:416-29.
13. Roberts WC. The congenitally bicuspid aortic valve: A study of 85 autopsy cases. Am J Cardiol 1970;26:72-83.
14. Bissell MM, Hess AT, Biasiolli L, et al. Aortic dilation in bicuspid aortic valve disease: Flow pattern is a major contributor and differs with valve fusion type. Circ Cardiovasc Imaging 2013;6:499-507.
15. Yammine K. Evidence-Based Anatomy. Clin Anat 2014;27:847-52.
16. Malhotra RK, Indrayan A. A simple nomogram for sample size for estimating sensitivity and specificity of medical tests. Indian J Ophthalmol 2010;58:519-22.
17. Cohen J. Statistical power analysis for the behavioral sciences. L. Erlbaum Associates 1988.