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A Study on the Aortic Valves in Indian Population

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Abstract

The aortic valve, which is seen at the root of Aorta possess three semi lunar cusps namely the right coronary, the left coronary, and the noncoronary. Aortic valves**,** especially bicuspid and unicuspid valves, have generated considerable interest among clinicians, largely because the valves are frequently stenotic or incompetent and also because they may be corrected surgically [1]. Aortic valve malformations may also affect the wall of the aorta leading to pathological changes like calcification and plaque formation which may ultimately result in ischemia and cerebral infarction. The present study of Aortic valve in Indian subjects aims in discussing the findings according to the embryological, clinical and surgical implications. This study will also provide an anatomical basis to assist surgeons in performing safe vascular surgeries involving the aortic valve, in future.

Keywords: Aortic Valve; Unicuspid; Bicuspid; Ischemia; Infarction.

Review of Literature

Sir William Osler was one of the first to recognize the bicuspid aortic valve as a common congenital anomaly of the heart. Leonardo da Vinci recognized the superior engineering advantages of the normal trileaflet valve [2].

Anton E. Becker et al in 1970 studied 100 cadavers and reported that Bicuspid aortic valve was found in 31 of the 77 cases of group I (40%) and in 15 of the 23 cases of group II (65%), an overall incidence of 46%. In nine cases, this was the only associated anomaly, while in 37 cases of bicuspid aortic valve, additional malformations were found [3].

Clinical and necropsy observations are described by William C. Roberts in 1970 in 85 autopsy cases in which the subjects had congenially bicuspid aortic valves. Sixty-one subjects had aortic stenosis with or without aortic regurgitation; 11, pure aortic regurgitation; and 13 had a congenitally bicuspid aortic valve that apparently had functioned normally [4].

Clark RE, Finke EH in 1974 performed measurements of leaflet thickness in relaxed and stressed states. They showed that human leaflets thickness varied from 177 to 1.76 μm in relaxed state and from 150 to 1.75ìm in stressed state [5].

In 1977, J E Davia et al in their study noticed that three of the seven patients with quadricuspid aortic valves had aortic insufficiency, while the remaining four had no other clinical or pathologic evidence of congenital heart disease except for arteriosclerotic heart disease with varying degrees of left ventricular hypertrophy [6].

Aortic stenosis has been reported to occur in as many as 72 percent of adults with a congenital bicuspid aortic valve, with peak incidence occurring in the 5th and 6th decades of life in a study conducted by John J. Fenoglio Jr et al in 1977 [7].

Histologic examination of the ascending aorta frequently shows loss of smooth muscle cells and severe degeneration of the medial elastic fibres—so called "cystic medial necrosis". This has been attributed to the increased risk of dissection at least ninefold in bicuspid aortic valve according to a report

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by Edwards WD, et al in 1978 [8], and dissection tends to occur in younger patients than in those with tricuspid aortic valves according to Roberts CS et al's study in1991 [9].

34% of 35 Turner patients had isolated, nonstenotic bicuspid aortic valve in a study conducted by Martha J. Miller et al in 1983. These data indicate that bicuspid aortic valve may be the most common cardiac anomaly in Turner syndrome [10].

According to Clementi M et al in 1996 and Huntington K et al in 1997, Bicuspid aortic valve is the most common congenital cardiovascular anomaly, occurring in 1–2% of the population. They also suggest that it may have an autosomal dominant inheritance, perhaps with variable penetrance, for it has a male predominance and often occurs in multiple members of the same family [11,12].

Lin SL et al in 1997 reported that Patients with a thickened aortic valve had a greater incidence of Coronary Artery Disease (89 / 132, 67.4%) than those without (141 / 288, 49.0%) ($p < 0.05$) [13].

Stewart BF et al in 1997) and Otto CM et al in 1999 reported that the prevalence of calcific aortic stenosis increases with age, being present in 2% to 4% of adults over age 65 years [14,15].

Clouse WD et al in 1998 and Olsson C et al in 2006,by quoting The Society for Vascular Surgery, defined aneurysm as a vessel diameter 1.5[5.5 cm] times normal [3.7cm]. A lower threshold of >4.5 cm is considered to be more appropriate. Aortic dilatation is defined by a diameter >1.1 times normal on the basis of age, sex, and body surface area [16,17]. Bonderman D et al in 1999 defined the normal diameter of the ascending aorta as 20 to 37 mm [18].

Ward C in 2000, Edwards W.D et al in 1978 and Gersony W.M in 1993 studied Bicuspid aortic valve and opinioned that eventhough it is often considered a benign lesion early in life, complications of Bicuspid Aortic Valve, including aortic stenosis, aortic regurgitation, infective endocarditis, and aortic dilation and dissection, result in considerable morbidity and mortality later in life [19-21].

In 2002, Paladini D et al in their study demonstrated that aortic valve anatomy can be satisfactorily assessed in fetuses with and without left heart obstructive lesions by a detailed echocardiography [22]. According to Paul W.M. Fedak et al's work in 2002,Bicuspid aortic valves(BAV) develop when adjacent cusps fuse to form a single aberrant cusp, larger than its counterpart yet smaller than 2 normal cusps combined. It is likely the result of a complex developmental process, not simply the fusion of 2 normal cusps [23]. The conclusions of their study were: (1) The BAV is the most common congenital cardiac abnormality and may result from defects in genes that encode matrix elements; (2) BAV malformations are inherited, particularly in males, and echocardiographic screening of his children is appropriate; (3) the BAV is a disease of the entire aortic root and has a propensity for both valvular and aortic complications, often requiring surgery; (4) endocarditis is a devastating complication that can be prevented by antibiotic prophylaxis; (5) early referral to a cardiac surgeon can facilitate a plan for surgery that may prevent life-threatening complications [24].

In 2003, C A Warnes in their study quoted the strong association between bicuspid aortic valve and aortic medial abnormalities which have been proved in many reports decades ago [25].

J W Roos-Hesselink et al in 2003 reported that aortic valve [especially bicuspid] and aortic arch pathology are commonly encountered in patients with previous coarctation repair. In 60 patients (48%) they found aortic pathology. Dilatation of the ascending aorta was found in 35 patients (28%) and this was particularly prominent in patients with a bicuspid valve [26].

Linda Cripe et al in 2004 suggested the high heritability of Bicuspid aortic valve in their study population. The heritability of BAV plus other cardiovascular anomalies suggests that valve malformation can be primary to defective valvulogenesis or secondary to other elements of cardiogenesis [27]. Rosario V. Freeman and Catherine M in 2005 reported that calcific valve disease is an active disease process akin to atherosclerosis with lipoprotein deposition, chronic inflammation, and active leaflet calcification [28].

BAV has been identified at a prevalence of 4.6 cas-es per 1000 live births. The prevalence of BAV according to sex has been found to be 7.1 cases per 1000 among male neonates, and 1.9 per 1000 among female neonates according to a study by Tutar E et al in 2005 [29].

Bicuspid Aortic Valve has been recognized as a syndrome incorporating aortic valve disorders and aortic wall abnormalities by Shi-Min Yuan and Hua Jing's work in 2010. Congenital or hereditary dis-eases such as ventricular septal defect, patent ductus arteriosus, coarcta-tion of the aorta, Turner's syndrome, Marfan's syndrome etc. may fre-quently be associated with Bicuspid Aortic Valve [30].

Both pediatric [Beroukhim RS et al in 2006, Warren AE et al in 2006, Holmes KW in 2007] [31,32,33] and

adult [Davies RRet al in 2007, Yasuda H et al in 2003] [33] studies have demonstrated significantly faster aortic dilatation with BAV versus TAV. According to studies by La Canna G et al in 2006 and Davies RR et al in 2007, the age at presentation of aortic dilatation was significantly younger with BAV versus TAV (mean, 49 versus 61 to 64 years old) [33]. Beroukhim RS et al (2006),Warren AE et al (2006) and Holmes KW et al (2007) were of the opinion that the prevalence of ascending aortic dilatation among those with BAV increases with age, beginning in childhood and continuing throughout life [31-33].

Mohamed A in 2006 reviewed previous studies and reported that coarctation of aorta is associated with various cardiac and noncardiac abnormalities in up to 50 % of patients, the prevalence of bicuspid aortic valve being 50% [34].

According to Della Corte A in 2007, study of prevalence by age quintile showed dilatation in 56% of those aged <30 years old, up to 88% of those aged >80 years old [34]. Davies RR et al in 2007 studied the known association of bicuspid aortic valve with ascending aortic aneurysms which has been associated with a higher risk for aortic growth (0.19 cm / y versus 0.13 cm / y in nonbicuspid [34].

Himanshu J. Patel and G. Michael Deeb in 2008 opinioned that for those patients with aortic stenosis and bicuspid aortic valve disease, the risk for rupture, dissection, or death was higher than in those without aortic stenosis [35].

Thomas M. Tadros et al in 2009 reported that ascending aortic dilatation occurs more frequently and at a younger age in patients with bicuspid aortic valves (BAV) than it does in patients with normal trileaflet aortic valves (TAV). The clinical significance of this correlation is based on the following- First; BAV is the most common congenital cardiac abnormality, occurring in 0.46% to 1.37% of the population. Second, aortic dilatation has a propensity for dissection and rupture, making it a potentially lethal disease. For these reasons they warrant frequent monitoring in cases of ascending aorta dilatation with bicuspid aortic valve, with possible early prophylactic surgical intervention to prevent dissection or rupture [35].

The first detectable macroscopic changes in the leaflets, according to Nalini M. Rajamannan's work in 2011, is seen as calcification, or focal leaflet thickening with normal valve function, which is termed as aortic valve sclerosis. Disease progression is characterized by a process of thickening of the valve leaflets and the formation of calcium nodules which are concentrated near the aortic surface.

Materials and Methods

Study Design

The present study was done as a cross sectional study

Study Setting

The study was conducted in the Department Of Anatomy, Govt.Medical College Thrissur , Department Of Forensic Medicine, Govt.Medical College Thrissur,Department Of Obstetrics and Gynaecology,Govt.Medical College Thrissur

Study Duration

The total duration of the present study was one and a half years.

12 months were allotted for data collection starting from April 2012 –March 2013

Sample Size

Sample size was calculated using the formula

P = prevalence of variation

Q =100-P

d = allowable error[20% of P]

Here P is taken as 50 from a study by Mohamed A (2006) .The study was on coarctation of aorta and associated cardiac and noncardiac abnormalities and the prevalence of bicuspid aortic valve,one of the determinants of present study was found to be 50%.[34]

So, applying to the above formula

$$\frac{4 \times 50 \times (100 - 50)}{(\frac{20}{100} \times 50)^2} = 100$$

Hence the sample size was taken as 100.

Sampling Technique

The sampling was done based on the Non-probability technique

3 months were allotted for each department

April 2012 – June 2012 → Department Of Forensic medicine

July 2012 – September 2012 → Department of Anatomy

October 2012 – December 2012 → Department of O & G

January 2013 – March 2013 → Department of

Anatomy (for histological study).

Selection of Study Subjects

All cadavers available in the Department of Anatomy during the study period [n = 25]

Foetuses collected from labour room during the study period [n = 25]

Postmortem specimen collected from Forensic Department during the period of study [n = 50]

The specimens were of different age groups ranging from 14 weeks of intrauterine life to 85 years

Inclusion Criteria

Cadaver, autopsy specimen and Foetus with intact thoracic cage.

Exclusion Criteria

Any surgeries done on the arch of aorta,aortic valve and its branches

Tumours or growths hindering the view of aortic arch, aortic valve and the arch of aorta

Analysis

The continuous variables are expressed in mean with standard deviation

The qualitative variables are expressed in frequency & proportions

Correlation of various factors are done using appropriate statistical tests.

Study Methodology-Method of Collection of Data

In the autopsy room ,after opening the thoracic cavity,the arch of aorta along with the aortic valve and ascending aorta was dissected out.Similarly the specimens were collected from the cadavers and foetuses.The specimens were fixed in 10% Formaline.

Results

A. Anomalous Valve

A total of 5 cases of anomalous bicuspid Aortic valves were noted in the study subjects.2 of the 5 cases belonged to foetal group [14-39wks], 2 were from 21-40 yr age group and the remaining 1 from 41-60 yrs.

B. Thickness of Aortic Valves

The thickness of the three Aortic valves, anterior, right posterior and left posterior were studied and the mean ranged from 0.54-0.69mm [anterior], 0.54-0.67mm [right posterior] and 0.51-0.80mm [left posterior] respectively. The minimum thickness was found to be the same in all the three types and was 0.43mm.The maximum thickness of the anterior valve was 3.83mm [41-60 yrs] Right posterior vale had a maximum thickness of 3.4mm [41-60yrs] and left posterior had a maximum thickness of 3.4mm [0-20yrs].

Table 1: Thickness of Aortic Valves in the Study Subjects

Age Group (yrs)	Anterior Aortic Valve Mean ± SD(mm) (min-max)	Right posterior Aortic Valve Mean ± SD(mm) (min-max)	Left Posterior Aortic Valve Mean ± SD(mm) (min-max)
0-20	0.69 ± 0.74(0.43-2.55)	0.58 ± 0.44(0.43-1.7)	0.80 ± 1.05(0.43-3.4)
21-40	0.43*	0.43*	0.43*
41-60	0.57 ± 0.60(0.43-3.83)	0.67 ± 0.67(0.43-3.4)	0.59 ± 0.57(0.43-2.98)
61-80	0.54 ± 0.33(0.43-1.7)	0.54 ± 0.33(0.43-1.7)	0.51 ± 0.32(0.43-1.7)
>80	0.43**	0.43**	0.43**

*****SD = 0, min=max.
**** ***single observation, hence mean, SD, min, max cannot be calculated

C. Relation between Anomalous Valve and Diameter of Aorta

Table 2: Relation between Anomalous valve and Diameter of Aorta in the study subjects

	ANV	N	Mean	Std. Deviation
DOA	Yes	3	2.0533	.28919
	No	72	2.0276	.52914

DOA-Diameter of Aorta, ANV-Anomalous Valve

The diameter of Aorta in subjects with anomalous valve was compared with those having normal valve. The mean diameter of Aorta was found to be 2.05 (SD ±0.29) in the subjects with anomalous valve compared to the normal group (2.02±0.53). This was statistically analysed using T-test. t = 0.144; p = 0.89. Hence the relation was found to be not significant.

Discussion

A total of 5 cases of anomalous bicuspid Aortic valves were noted in the studied samples. 2 of the 5 cases belonged to foetus group (14-39weeks) ,2 were from 21-40yrs and the remaining 1 from 41-60yr age group. 2 cases of bicuspid Aortic valves from foetus had associated congenital malformations. A 40yr old female had bicuspid aortic valve and variation of the arch , and she died of cardiac tamponade following aortic dissection. A 35yr old male also had a similar history. Ward C, Edwards W.D et al and Gersony W.M in 1993 studied Bicuspid aortic valve and opinioned that eventhough it is often considered a benign lesion early in life, complications of Bicuspid Aortic Valve, including aortic stenosis, aortic regurgitation, infective endocarditis, and aortic dilation and dissection, result in considerable morbidity and mortality later in life . This proved to be true in the present study.

Anton E. Becker et al studied 100 cadavers and reported that Bicuspid aortic valve had an overall incidence of 46% and in 37 cases of bicuspid aortic valve, additional malformations were found. According to Clementi M et al in 1996 and Huntington, K et al, Bicuspid aortic valve is the most common congenital cardiovascular anomaly, occurring in 1–2% of the population.These two studies contradicts the present findings where the incidence is only 5%. According to Paul W.M. Fedak et al 's work, Bicuspid aortic valves (BAV) develop when adjacent cusps fuse to form a single aberrant cusp, larger than its counterpart yet smaller than 2 normal cusps combined. This is found to be true in the present case.

The diameter of Aorta in subjects with anomalous valve was compared with those having normal valve. The mean diameter of Aorta was found to be 2.05 ± 0.29cm in the subjects with anomalous valve compared to normal group (2.02±0.53cm). But the relation was found to be not significant.

The thickness of the Aortic valves was studied. The thickness of the anterior valve ranged between 0.43-3.83mm, the maximum thickness of 3.83mm noted in 41-60yr age group. The thickness of the right posterior Aortic valve was noted and ranged between 0.43-3.4mm, the maximum thickness of 3.4mm was noted in 41-60yr age group. The thickness of left posterior Aortic valve ranged between 0.43-3.4mm, the maximum thickness of 3.4mm was noted in 0-20yr age group. Clark RE, Finke EH performed measurements of leaflet thickness in relaxed and stressed states. They showed that human leaflets thickness varied from 177 to 1.76ìm in relaxed state and from 150 to 1.75μm in stressed state.This study shows a little disparity with the present study where the minimum thickness was 0.43mm and the reasons may be due to the hardening effects of formalin or the technique used. 13 cases out of 100 samples had atheromatous plaques over the interior of Aorta. Among them majority (27.8%) belonged to 21-40yr age group. This may be because of the fact that most of the post-mortem cases were from road traffic accidents where younger age groups are involved and often the elderly and diseased were not taken into consideration. So this fact cannot be taken as an extrapolation of the whole population.

Summary and Conclusion

- The thickness of the Aortic valves was: the anterior valve ranged between 0.43-3.83mm, the right posterior Aortic valve ranged between 0.43-3.4mm and the left posterior Aortic valve ranged between 0.43-3.4mm.
- The diameter of Aorta in subjects with anomalous valve was compared with those having normal valve and the relation was found to be not significant.
- A case of valvular anomaly which can be detected easily should undergo a thorough cardiology workup to prevent complications like Aortic dissection, Cardiac tamponade which may prove fatal later in life.

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