

Sex variations in the structure of human atrioventricular annuli

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[Received 1 December 2011; Accepted 10 January 2012]

Atrioventricular annuli are important in haemodynamic flexibility, competence, and support for tricuspid and mitral valves. The anatomical features of the annuli, such as circumference, organisation of connective tissue fibres, myocardium, and cellularity, may predispose to annular insufficiency and valvular incompetence. These pathologies occur more commonly in females, although the anatomical basis for this disparity is unclear. Sex variation in the structure of the annuli is important in providing a morphological basis for the patterns of these diseases. This study therefore aimed to determine the sex variations in the structure of human atrioventricular annuli. One hundred and one hearts (48 males, 53 females) obtained from the Department of Human Anatomy of the University of Nairobi were studied. Annular circumferences were measured using a flexible ruler and corrected for heart weight. Results were analysed using SPSS version 17.0 and sex differences determined using student’s t-test. A p-value of less than 0.05 was considered significant. For light microscopy, specimens were harvested within 48 hours post-mortem, processed, sectioned, and stained with Masson’s trichrome and Weigert’s elastic stain with van Gieson counterstaining. Females had significantly larger annular circumferences than males after correcting for heart weight ($p \leq 0.05$). Histologically, myocardium was consistently present in all male annuli while this was absent in females except in one specimen. The annuli were more elastic and cellular in males especially in the annulo-myocardial and annulo-valvular zones, respectively. The corrected larger annular circumference in females may limit heart valve coaptation during cardiac cycle and may be a risk factor for valvular insufficiency. The predominance of myocardium, annular cellularity, and elasticity may be more protective against heart valve incompetence in males than in females. (Folia Morphol 2012; 71: 1: 23–27)

Key words: atrioventricular annuli, sex variation, valve incompetence

INTRODUCTION

Atrioventricular annuli are part of the cardiac skeleton that supports and prevents over-distension of tricuspid and mitral valves [12]. They also confer haemodynamic stability to valves [14] and form a firm framework for myocardial attachment and placement of sutures during valve repair [11].

The circumference of the annulus is an important parameter in annular and valvular function. An increase in this parameter decreases valve coaptation during the cardiac cycle, and this may be a risk factor for valvular insufficiency [6, 14]. This parameter shows sex variation and differs between populations [20, 21]; however, it is undetermined for the Kenyan population.

Histologically, the annuli are endothelial-lined fibrous structures containing collagen, elastic fibres, and fibroblasts [22]. Extension of myocardium from atria to the annuli contributes to annular myocardium [15]. This structural organisation is important in valvular support and annular adaption to haemodynamic changes during the cardiac cycle [23]. Alteration in this structural organisation is associated with heart valve incompetence [1, 16]. This incompetence is more common in females [2, 9] although the structural basis for this disparity is unclear. Sex variation in atrioventricular annuli may be important in providing a morphological basis for the pattern of occurrence of this disease. This study, therefore, aimed to determine sex variations in the structure of human atrioventricular annuli.

MATERIAL AND METHODS

One hundred and one hearts (48 males, 53 females) of age range 18–45 years were studied. Eighty hearts (39 males, 41 females) were used for morphometric analysis while 21 (9 males, 12 females), used for histological study, were obtained within 48 hours of autopsy at the Nairobi city mortuary. All individuals had died suddenly either from gunshot wounds, strangulation, or road traffic accidents. Subjects with rheumatic and ischaemic heart diseases were excluded based on pre-morbid history. Hearts with obvious gross pathology of the leaflets, myocardium, or annuli were also excluded. Ethical approval was granted before commencement of the study. The mediastinum was opened by cutting bilaterally through the costal cartilages. Harvesting of the heart was done by dividing the great vessels 2 cm from the superior extent of their base. The hearts were weighed using a digital weighing balance, ABC Japan (accurate to 0.01 g). Harvesting of the annuli was done by making circular incisions around the bases of corresponding valve leaflets, and entire annuli with attached cusps were harvested intact. Annular circumferences were measured (in cm) using a flexible metric ruler and corrected for heart weight (circumference/heart weight [g]). For light microscopy, 5-mm thin sections were harvested from anterior and posterior parts of both annuli. Routine histological processing was done and 7-micron thick sections were obtained using a Lenz Wezlar (Germany) sledge microtome. Masson's trichrome stain and Weigert's elastic with van Gieson counterstaining were used to demonstrate collagen and elastic fibres, respectively.

Table 1. Sex difference in annular circumferences (uncorrected values)

| Parameter | Sex | Mean \pm SD | P |
|------------------------------|--------|---------------|------|
| Tricuspid circumference [cm] | Male | 9.1 \pm 1.9 | 0.12 |
| | Female | 8.4 \pm 1.8 | |
| Mitral circumference [cm] | Male | 7.1 \pm 1.3 | 0.57 |
| | Female | 6.9 \pm 1.5 | |

Table 2. Corrected sex differences in annular circumference

| Parameter | Sex | Corrected mean value | P |
|-------------------------|--------|----------------------|-------|
| Tricuspid circumference | Male | 0.35 | 0.025 |
| | Female | 0.44 | |
| Mitral circumference | Male | 0.27 | 0.007 |
| | Female | 0.36 | |

Samples were viewed using a bright-field light microscope (Leica model BME, Germany). A Fujifilm A235 digital camera was used to take photomicrographs. The data obtained was analysed using SPSS version 17.0, and sex differences were determined using independent student's t-test. A p-value of less than 0.05 was taken as significant.

RESULTS

Morphometric analysis

A total of 80 hearts were used (39 males, 41 females). The average heart weight was 286 \pm 84 g in males and 222 \pm 76 g in females ($p = 0.001$). The uncorrected tricuspid and mitral circumferences were greater in males than in females although the differences were statistically insignificant ($p = 0.12$ and 0.57 for tricuspid and mitral annulus, respectively) (Table 1).

After correcting circumferences for heart weights, females had significantly larger circumference than males (Table 2).

Histological analysis

A total of 21 hearts (9 males, 12 females) were available for microscopic analysis.

General histological structure of the annuli

The annuli in both sexes were endothelial lined fibrous structures made up of three zones: central zone, valvular zone, and myocardial zone (Fig. 1A). These zones contained collagen and elastic fibres, and in males myocardium was also present (Fig. 1B).

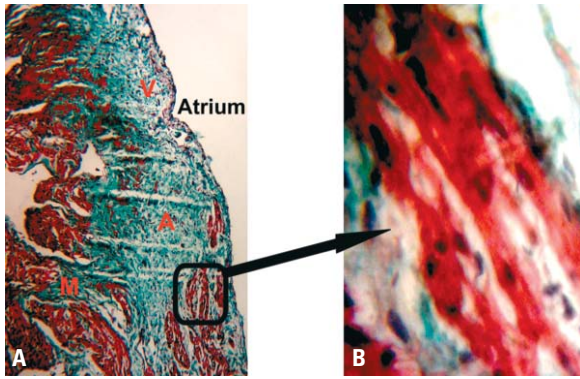


Figure 1. General histological structure of the annulus (30 year-old male); note the three zones: valvular (V), annular core (A), and myocardial (M) zones (Masson's Trichrome stain) (A). Note also the predominance of myocardium in this male sample; B. An enlarged segment of the specimen in (A) to demonstrate the cardiac muscle fibres at a higher power. A. Magnification $\times 100$; B. Magnification $\times 1000$.

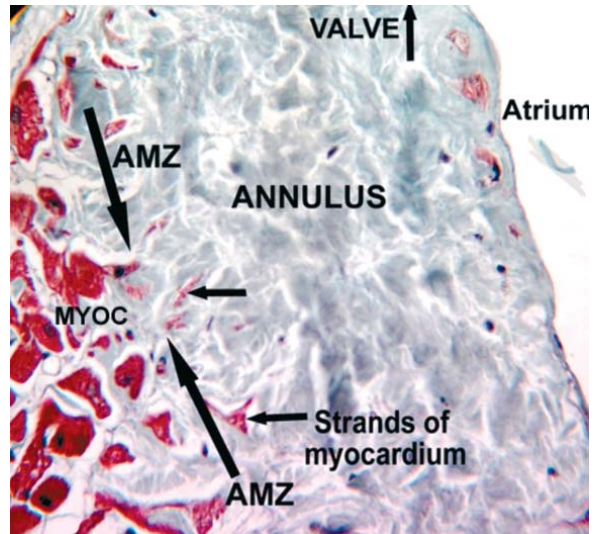


Figure 3. A 35-year-old female annulus. Note the strands of myocardium at the annulo-myocardial zone (AMZ). This was demonstrated only in this specimen; MYOC — atrial myocardium (Masson's Trichrome stain; magnification $\times 400$).

Sex differences in structure of the annuli

Myocardium was consistently present at the annulo-myocardial zone in all male annuli while this was absent in females (Fig. 2). Only one female specimen had strands of cardiac muscle at the annulo-myocardial zone (Fig. 3).

The annuli in males consisted of dense elastic fibres surrounding the annular myocardium while females had interrupted and less dense elastic fibres (Fig. 4). Collagen fibres were, however, more regularly arranged in female specimens (Fig. 5).

Generally, male annuli had densely populated cells, probably fibroblasts, while females had relatively scattered cells within the collagen matrix (Fig. 5).

DISCUSSION

The present study provides morphological adaptations of atrioventricular annuli to haemodynamic stresses in different sexes to explain the pattern of diseases affecting them.

Gross measurements

The larger circumference in males before correction may be due to heavier hearts and, probably, body mass index as previous reports have shown an association between these parameters [19]. Thus, when corrected, females had significantly larger circumferences. Clinically, wider annular circumferences

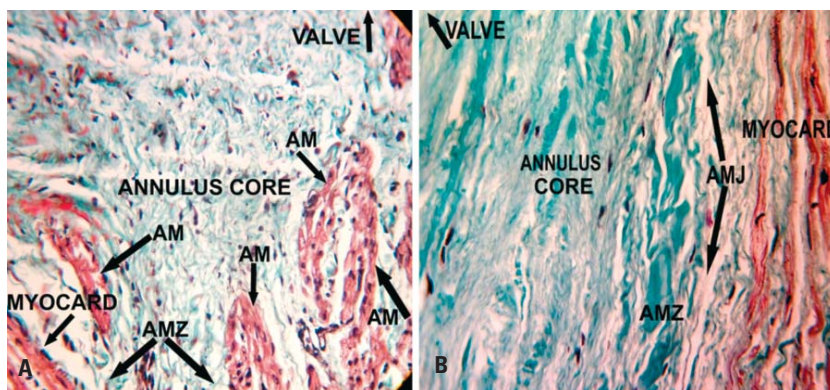


Figure 2. Sex difference in the occurrence of annular myocardium. Note the prominent cardiac muscle bundles at the annulo-myocardial zone (AMZ) in the male annulus and the absence of this in the female specimen; A. 20-year-old male; tricuspid; B. 22-year-old female; tricuspid; AM — annular myocardium; AMJ — annulo-myocardial junction (Masson's Trichrome stain; magnification $\times 400$).

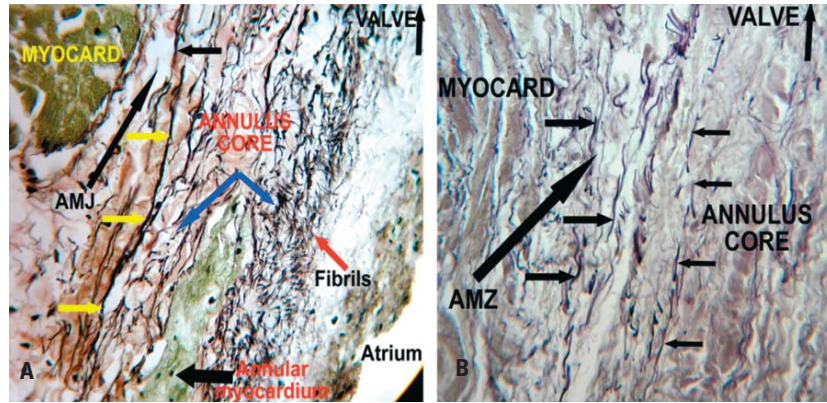


Figure 4. Sex difference in the distribution of elastic fibres (arrows). Note the dense elastic fibres surrounding the annular myocardium in the male annulus. Compare with the interrupted elastic fibres in the female annulus; **A.** 37-year-old male; mitral; **B.** 39-year-old female; mitral; AMJ — annulo-myocardial junction; AMZ — annulo-myocardial zone (Weigert's elastic with van Gieson counterstaining; magnification $\times 400$).

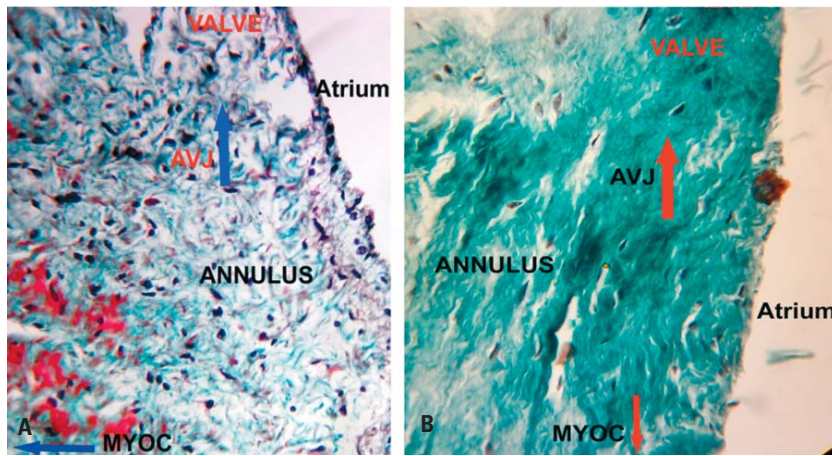


Figure 5. Sex difference in annular cellularity. Note the densely populated cells in the male annulus and relatively scattered cells in females. Note, however, the more regular arrangement of collagen fibres in females; **A.** 24-year-old male; tricuspid; **B.** 23-year-old female; tricuspid; AVJ — annulo-valvular junction; MYOC — myocardium (Masson's Trichrome stain; magnification $\times 400$).

may decrease heart valve coaptation during the cardiac cycle [14], and this may be a risk for valvular insufficiency and annular incompetence [13, 18].

Microscopic structure

The presence of cardiac muscle in male annuli is a unique finding. Dudziak et al. [5] found no myocardium in male or female tricuspid annulus. Racker et al. [17] demonstrated myofibres in the tricuspid annulus of a canine model. The current results demonstrate the existence of myocardium in all male annuli and in one female specimen. Furthermore, comparative animal [3] and human studies [8] have also demonstrated the presence of myocardium in other valvular apparatus. This therefore raises the question as to the function of myocardium in the annulus.

Atrio-ventricular annuli are considered passive structures moving in response to haemodynamic forc-

es generated by cardiac contractions [10]. Current findings indicate that the annuli are capable of independent contractions, which may influence the timing and effectiveness of atrio-ventricular valve closure [23]. Myocardium in the annuli may therefore serve to regulate annular contraction and relaxation during the cardiac cycle. The myocardium may also enhance haemodynamic pliability of the valves where they attach to the annulus. Contraction of this muscle may also aid in the closure of corresponding valve orifices during ventricular systole [23]. Thus the myocardial composition in males may serve to provide better haemodynamic flexibility and pliability to the valves during the cardiac cycle, making them less predisposed to valvular insufficiency.

The interruption and density of elastic fibres in females in the current study may be functionally significant. Elastic fibres are usually found in

areas subjected to stretch and have the unique feature of being extensible [4]. Relating these facts to our present findings suggests that the interruption of these fibres may make female annuli less adapted to withstanding stretching and extension. Hence, when subjected to varying biomechanical forces in the cardiac cycle, they may have a higher probability of insufficiency. On the other hand, the more regular arrangement of collagen fibres in this sex may be protective against this valvular anomaly.

The dense cellular profile in males in the current study could be fibroblastic in nature [5]. This author showed that fibroblasts are widely distributed in human annular tissue, and studies done on these cells in culture have shown that they are contractile and have smooth muscle properties [7]. This feature may, therefore, add pliability to male annuli making them better adapted haemodynamically.

CONCLUSIONS

The corrected larger annular circumference in females may limit heart valve coaptation during the cardiac cycle, and this may be a risk factor for valvular insufficiency. The predominance of myocardium, annular cellularity, and elasticity in males may make them less predisposed to valvular incompetence than females are.

ACKNOWLEDGEMENTS

We are grateful to the staff of the microscopic anatomy laboratory for their technical assistance.

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