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Anatomy Section

Comparative Analysis of Morphological and Morphometric Features of Human, Pig, Calf, and Sheep Aortic Valves: A Cross-sectional Study

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ABSTRACT

Introduction: The aortic valve plays a critical role in maintaining unidirectional blood flow from the left ventricle into the aorta, ensuring efficient circulation throughout the body. Comprising three cusps-the left coronary, right coronary, and non-coronary cusps-the intricate anatomy of the aortic valve is essential for its proper function. The scarcity of aortic valve homografts for transplantation has led to increased interest in studying readily available sources for suitable and durable xenografts.

Aim: To compare the morphological and morphometric characteristics of the aortic valves in humans with those in pigs, calves, and sheep.

Materials and Methods: The present cross-sectional study was conducted over a three-week period in July 2022. Aortic valves were collected from humans, pigs, calves, and sheep. Five human hearts were obtained from the Anatomy Department of Adichunchanagiri Institute of Medical Sciences, BG Nagar. Additionally, five hearts each from calves, pigs, and sheep were obtained from a nearby abattoir. The hearts were then fixed in a 10% formaldehyde solution for approximately 18 hours. All fat and muscle surrounding the aorta were removed, and the aorta with intact valves was dissected. An incision was made between the left coronary and non-coronary aortic cusps to measure the individual cusps. Morphological and morphometric measurements, including annulus diameter, cusp height, commissural distances, and length of the lunula, were taken using a vernier calliper. The obtained values were statistically compared using paired t-test.

Results: The mean values of various measurements of human aortic valves were found to be similar to those of pig aortic valves. Both humans and pigs have three aortic cusps, namely the left, right, and non-coronary cusps. The mean diameter of the aortic annulus in humans was 2.18 cm, while in pigs it was 2.28 cm. The height of the left and right cusps in both human and pig aortic valves was approximately 1.6 cm, whereas the height of the non-coronary cusp was 1.64 cm in humans and 1.38 cm in pigs. The external inter-commissural distance of the left cusp was 2.48 cm, and that of the right cusp was 2.58 cm in both humans and pigs. The external inter-commissural distance of the non-coronary cusp was 2.4 cm in humans and 2.36 cm in pigs. The length of the lunula and internal inter-commissural length of the aortic cusps in humans were relatively similar to those in pigs. However, when compared to measurements in cows and sheep, significant variations were observed.

Conclusion: The study findings provide valuable insights into the potential suitability of pig aortic valves for xenograft transplantation and their implications for cardiac surgical procedures.

Keywords: Cusps, Histology, Transplantation, Xenograft

INTRODUCTION

Heart valves are crucial components of the heart, responsible for ensuring the unidirectional flow of blood. Conditions like aortic stenosis or regurgitation, whether congenital or acquired, often necessitate valve replacement surgeries. An ideal replacement valve should possess attributes such as durability, easy availability, low immunogenicity, reduced thrombogenicity, and straightforward implantation. Aortic stenosis, a common valvular heart ailment, ranks as the third most prevalent cardiovascular condition in the Western world. Valve replacement surgeries stand as the primary mode of treatment for valvular heart diseases [1].

Homograft aortic valve replacement, while delivering excellent haemodynamic outcomes, is fraught with limitations like graft scarcity, limited durability, and challenges in implantation [2]. The prevailing preference for implantation revolves around mechanical bi-leaflet designs, with over 170,000 cases annually worldwide [3]. However, these mechanical valves entail the drawback of thrombo-embolic complications, necessitating long-term anticoagulant therapy [4].

Given the focus on biological grafts, scant literature exists on the distinct morphological variations between human and commonly accessible domestic animal valves. Addressing these concerns motivated the quest for a durable, conveniently available biological valve that minimises the need for prolonged anticoagulation [5]. This exploration is relevant both for refining reconstructed pericardial valves and assessing the feasibility of heterograft valve transplantation. A successful outcome could potentially provide a range of xenograft valves in varying sizes [6].

The novelty of the present research lies in its comprehensive approach, which involves precise measurements and observations to assess the potential for xenograft transplantation. This study fills a critical gap in the existing literature by providing a comprehensive evaluation of aortic valve attributes across different species.

The aim of the study is to measure and compare the dimensions of the aortic annulus, cusp height, lunula length, and intercommissural distance in human, pig, calf, and sheep aortic valves.

MATERIALS AND METHODS

A cross-sectional study was conducted at the Department of Anatomy, Adichuchangiri Institute of Medical Sciences, BG Nagar, over a period of three weeks in July 2022. A total of five hearts for each species were collected for the study of the aortic valve. Ethical clearance was obtained from the Institutional Ethical Committee

(AIMS/IEC/454L4/2022). Since the study primarily involved the post-mortem examination of animal hearts obtained from an abattoir after the animals were slaughtered for food production, an Animal Ethical Committee approval letter was not obtained. The study did not involve live animals or any procedures that would require animal ethical clearance. Therefore, the IEC, which focuses on human research ethics, was deemed sufficient for the ethical oversight of this research.

Sample size: The sample size was determined based on the availability of specimens within the study duration, so a convenient sampling method was adopted.

Inclusion criteria:

- Human hearts without congenital and structural abnormalities were included in the study.
- Hearts from pigs, calves, and sheep without any anomalies were included.

Exclusion criteria:

- Human hearts with congenital and acquired cardiac abnormalities were excluded.
- Specimens showing signs of decomposition or tissue damage were excluded.
- Specimens that were not properly fixed in 10% formaline solution for 18 hours were excluded.

Five human hearts were collected from the Department of Anatomy of Adichunchanagiri Institute of Medical Sciences, BG Nagar, and five hearts each from cows, pigs, and sheep were obtained from a nearby abattoir. These hearts were fixed in a 10% formaldehyde solution for approximately 18 hours [Table/Fig-1-4]. The fat and muscle surrounding the aorta were removed, and the aortae with intact valves were dissected. An incision was made between the left coronary and noncoronary aortic cusps to measure individual cusps [Table/Fig-5-8]. Morphological and morphometric measurements were taken for the annulus diameter, height of cusps, commissural distances, and length of lunula.

[Table/Fig-1-4]: The pictures of the heart of Human (1); Sheep (2); Cow (3); Pig (4). (Images from left to right)

[Table/Fig-5-8]: The pictures of the Aortic valves of Human (5); Sheep (6); Cow (7); Pig (8). (Images from left to right)

Annulus diameter: The annulus diameter was measured using a digital vernier calliper. The measurement was taken across the circular aortic annulus at its widest point, ensuring that the calliper jaws were aligned perpendicular to the plane of the annulus.

Height of cusps:

Left Coronary Cusp (LCC): The height of the left coronary cusp was measured from the base of the cusp, where it originates from the aortic annulus, to the tip of the cusp.

Right Coronary Cusp (RCC): Similarly, the height of the right coronary cusp was measured from its base to the tip.

Non-Coronary Cusp (NCC): The height of the noncoronary cusp was measured from its base to the tip.

Commissural Distances:

Right-right commissural distance: The distance between the two commissures of the right coronary and right coronary cusps was measured.

Left-left commissural distance: Similarly, the distance between the two commissures of the left coronary and left coronary cusps was measured.

Bottom-bottom commissural distance: The distance between the two commissures of the noncoronary and noncoronary cusps was measured.

Internal inter-commissural distance: This distance was measured between the inner edges of the left and right coronary cusps at the aortic annulus.

External inter-commissural distances: These distances were measured using a similar approach to the commissural distances. The external inter-commissural distance refers to the distance between the outer edges of the commissures.

Length of lunula: The length of the lunula, defined as the space between cusps, was measured by placing a thin cotton thread along the curved path between two adjacent cusps. The thread was then measured using a scale [7].

STATISTICAL ANALYSIS

The obtained values were statistically compared using the paired t-test with the help of Microsoft Excel software.

RESULTS

The mean morphological and morphometric measurements of each specimen are represented in [Table/Fig-9].

The comparison between pig and human aortic valves revealed significant differences in several key variables, indicating that these two species' valves have distinct morphological characteristics. The height of cusps and internal intercommissural distance were among the variables that highlighted the dissimilarity between pig and human aortic valves. However, it was observed that pig valves had higher similarity, suggesting that they were more morphologically nearer to human valves.

<table>
<tr><th>Particulars {Mean measurements in (cm)}</th><th colspan="6">Human aorta</th><th colspan="6">Pig aorta</th><th colspan="6">Sheep aorta</th><th colspan="6">Cow aorta</th></tr>
<tr><td>Diameter of aortic annulus</td><td colspan="6">2.18</td><td colspan="6">2.28</td><td colspan="6">2.02</td><td colspan="6">2.38</td></tr>
<tr><td rowspan="2">Height of cusps</td><td colspan="2">LC</td><td colspan="2">RC</td><td colspan="2">NC</td><td colspan="2">LC</td><td colspan="2">RC</td><td colspan="2">NC</td><td colspan="2">LC</td><td colspan="2">RC</td><td colspan="2">NC</td><td colspan="2">LC</td><td colspan="2">RC</td><td colspan="2">NC</td></tr>
<tr><td colspan="2">1.6</td><td colspan="2">1.6</td><td colspan="2">1.64</td><td colspan="2">1.62</td><td colspan="2">1.7</td><td colspan="2">1.38</td><td colspan="2">1.48</td><td colspan="2">1.44</td><td colspan="2">1.52</td><td colspan="2">1.88</td><td colspan="2">1.98</td><td colspan="2">2.0</td></tr>
<tr><td>Length of lunula</td><td colspan="2">3.06</td><td colspan="2">3.08</td><td colspan="2">2.94</td><td colspan="2">2.96</td><td colspan="2">2.98</td><td colspan="2">2.72</td><td colspan="2">2.7</td><td colspan="2">2.74</td><td colspan="2">2.68</td><td colspan="2">3.22</td><td colspan="2">3.3</td><td colspan="2">3.2</td></tr>
<tr><td>External inter-commisural distance</td><td colspan="2">2.48</td><td colspan="2">2.58</td><td colspan="2">2.4</td><td colspan="2">2.48</td><td colspan="2">2.58</td><td colspan="2">2.36</td><td colspan="2">2.26</td><td colspan="2">2.38</td><td colspan="2">2.16</td><td colspan="2">3.28</td><td colspan="2">3.36</td><td colspan="2">3.38</td></tr>
<tr><td>Internal inter-commisural distance</td><td colspan="2">2.0</td><td colspan="2">1.96</td><td colspan="2">1.82</td><td colspan="2">1.72</td><td colspan="2">1.78</td><td colspan="2">1.4</td><td colspan="2">1.48</td><td colspan="2">1.56</td><td colspan="2">1.44</td><td colspan="2">1.92</td><td colspan="2">2.1</td><td colspan="2">2.18</td></tr>
<tr><td rowspan="2">Left commissure of sinus of valsalva</td><td colspan="3">LC</td><td colspan="3">RC</td><td colspan="3">LC</td><td colspan="3">RC</td><td colspan="3">LC</td><td colspan="3">RC</td><td colspan="3">LC</td><td colspan="3">RC</td></tr>
<tr><td colspan="3">1.06</td><td colspan="3">1.16</td><td colspan="3">1.02</td><td colspan="3">1.08</td><td colspan="3">0.74</td><td colspan="3">0.9</td><td colspan="3">1.3</td><td colspan="3">1.38</td></tr>
<tr><td>Right commissure of sinus of valsalva</td><td colspan="3">1.2</td><td colspan="3">1.46</td><td colspan="3">0.92</td><td colspan="3">1.18</td><td colspan="3">0.74</td><td colspan="3">0.82</td><td colspan="3">0.74</td><td colspan="3">0.84</td></tr>
<tr><td>Bottom commissure of sinus of valsalva</td><td colspan="3">1.36</td><td colspan="3">1.5</td><td colspan="3">1.64</td><td colspan="3">1.7</td><td colspan="3">0.9</td><td colspan="3">0.9</td><td colspan="3">1.12</td><td colspan="3">1.24</td></tr>
</table>

[Table/Fig-9]: Mean morphological and morphometric measurements of each specimen.
LC: Left coronary cusp; RC: Right coronary cusp; NC: Non-coronary cusp

From the paired t-test with a confidence level of 99% (alpha=0.01), it is observed that pig valves had higher p-values, suggesting that pig valves have more morphological similarity with human valves [Table/Fig-10].

Variables	Human-pig			Human-sheep			Human-calf		
Diameter of Aortic annulus	0.2302			0.282135			0.141927		
Height of cusps	LC	RC	NC	LC	RC	NC	LC	RC	NC
	0.74	0.26	0.025	0.10	0.07	0.43	0.05	0.02	0.04
External intercommisural distance	1	1	0.64	0.18	0.23	0.20	0.002	0.001	0.004
Internal intercommisural distance	0.11	0.18	0.04	0.05	0.05	0.06	0.72	0.31	0.01
Right commissure of sinus of valsalva	LC	RC		LC	RC		LC	RC	
	0.23	0.71		0.01	0.008		0.009	0.023	
Left commissure of sinus of valsalva	0.37	0.24		0.06	0.018		0.05	0.062	
Bottom commissure of sinus of valsalva	0.051	0.14		0.0008	0.006		0.089	0.14	

[Table/Fig-10]: Showing the p-value of the paired t-test for the variables with a confidence level of 99%.
p-value was not determined for length of lunula as value itself was suggesting the relative similarities between human and pig

many patients, the present comparative analysis delves into broader anatomical considerations across species [10].

Supadevi SK et al., found similarities in the morphology of human and porcine atrioventricular valves, suggesting their utility as substitutes.

DISCUSSION

The study's comprehensive comparative analysis of aortic valves from humans, pigs, calves, and sheep provides valuable insights. Notably, the remarkable morphometric similarity between human and pig aortic valves suggests that pig aortic valves could be promising xenografts for aortic valve replacement surgeries in humans. However, variations in the morphology of calf and sheep aortic valves emphasise the need for careful donor selection in xenotransplantation procedures.

Sands MP et al., provided insights into the structural variances among pig, calf, sheep, and human heart valves. Their observation of increased muscular support at the annulus in animal valves is noteworthy. Importantly, the authors highlighted variations in the attachment of non-coronary leaflets, favouring fibrous attachment in human and pig valves over muscular attachment, which might render pig aortic valves more suitable for heterograft use [5].

Jatene MB et al., highlighted variations in aortic annulus measurements linked to factors such as sex, age, and race. While they demonstrated differences in inter-commissural distances between genders, their study did not encompass interspecies comparisons [7].

An in-depth understanding of the anatomical intricacies of the aortic valvar complex holds paramount significance in the context of valve replacement surgeries. This comprehension is pivotal not only for ensuring the precise positioning of prostheses to mitigate rejection risks but also to avert potential hazards such as coronary ischaemia [8]. Given the limitations in accurately measuring the aortic annulus through methods like echocardiography, angiography, or MRI, a comprehensive grasp of aortic valve anatomy becomes crucial in minimising the likelihood of size mismatches.

Sim EK et al., research suggested differences in geometrical size between porcine and human aortic valves. Contrarily, our study demonstrates a remarkable similarity in the geometrical size of human and pig valves, supporting the potential viability of pig aortic valves for xenotransplantation [9].

The remarkable similarity in geometrical size between human and pig aortic valves observed in our study may be attributed to genetic factors and evolutionary similarities between the two species. These findings suggest that pigs, due to their comparable valve dimensions, could serve as suitable donors for xenotransplantation, potentially mitigating size-related compatibility concerns in organ transplantation.

Ionescu MI et al., presented an innovative technique involving a semi-rigid teflon ring and dacron-covered titanium frame for valve replacement. Although, their study yielded positive outcomes for the study extended this insight by exploring comprehensive morphological and morphometric aspects to ascertain optimal heterograft options [11].

Incorporating these comparative analyses with our results enhances our understanding of aortic valve compatibility across species. This comprehensive approach underscores the potential of genetically engineered pig aortic valves as suitable xenografts, offering a solution to organ shortage while considering anatomical nuances and interspecies variations.

These findings have profound clinical implications, potentially mitigating the shortage of suitable human homografts for transplantation and improving patient outcomes.

While further research is warranted to address limitations and delve deeper into functional aspects, this study offers a foundation for understanding the structural nuances of aortic valves and their potential applications in medical interventions. Incorporating these insights, clinicians can make informed decisions regarding valve replacement strategies, and researchers can focus on refining xenotransplantation techniques. Ultimately, this study contributes to the ongoing pursuit of effective treatments for valvular heart diseases, fostering the advancement of cardiovascular medicine.

Limitation(s)

The study relies on a relatively small sample size of human and pig hearts. This limited sample might not fully represent the broader population, leading to potential biases or inaccuracies in the conclusions drawn. Aortic valve morphology can vary not only between species but also within individual hearts due to factors such as age, health status, and genetics. The study might not capture the full spectrum of natural variation within each species.

The measurements taken from dissected hearts might not fully capture the dynamic aspects of valve function within a living cardiovascular system. The study does not account for factors such as valve motion, blood flow dynamics, and tissue elasticity, which could impact the overall performance of the valve.

CONCLUSION(S)

Overall, the morphological data suggested that pig aortic valves possess dimensions that are generally compatible with human valves, indicating their potential as xenograft donor candidates. These findings hold implications for cardiac surgeons seeking suitable valve replacements and advancements in xenotransplantation.

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