

Anatomy of the pig heart: comparisons with normal human cardiac structure

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ABSTRACT

Transgenic technology has potentially solved many of the immunological difficulties of using pig organs to support life in the human recipient. Nevertheless, other problems still remain. Knowledge of cardiac anatomy of the pig (*Sus scrofa*) is limited despite the general acceptance in the literature that it is similar to that of man. A qualitative analysis of porcine and human cardiac anatomy was achieved by gross examination and dissection of hearts with macrophotography. The porcine organ had a classic ‘Valentine heart’ shape, reflecting its location within the thorax and to the orientation of the pig’s body (unguligrade stance). The human heart, in contrast, was trapezoidal in silhouette, reflecting man’s orthograde posture. The morphologically right atrium of the pig was characterised by the tubular shape of its appendage (a feature observed on the left in the human heart). The porcine superior and inferior caval veins opened into the atrium at right angles to one another, whereas in man the orifices were directly in line. A prominent left azygous vein (comparable to the much reduced left superior caval or oblique vein in man) entered on the left side of the pig heart and drained via the coronary sinus. The porcine left atrium received only 2 pulmonary veins, whereas 4 orifices were generally observed in man. The sweep between the inlet and outlet components of the porcine right ventricle was less marked than in man, and a prominent muscular moderator band was situated in a much higher position within the porcine right ventricle compared with that of man. The apical components of both porcine ventricles possessed very coarse trabeculations, much broader than those observed in the human ventricles. In general, aortic-mitral fibrous continuity was reduced in the outlet component of the porcine left ventricle, with approximately two-thirds of the aortic valve being supported by left ventricular musculature. Several potentially significant differences exist between porcine and human hearts. It is important that these differences are considered as the arguments continue concerning the use of transgenic pig hearts for xenotransplantation.

Key words: Cardiac anatomy; xenotransplantation.

INTRODUCTION

The prospect of transgenic pigs providing compatible organs for human xenotransplantation is becoming increasingly likely (Cooper et al. 1991; Chen & Michler, 1993; James, 1993; White & Wallwork, 1993; Cozzi & White, 1995), although arguments continue concerning the advisability of this procedure. The pig has nonetheless been widely used as a model in cardiovascular research (Guiney, 1965; Bustad &

McClellan, 1966; Douglas, 1972; Hughes, 1986). Currently, it may even rival the dog as the most frequently used animal model in experimental cardiology. One of the reasons for this was the recognition that dogs have some basic differences in cardiac anatomy, especially in their coronary arterial distribution. These differences, together with certain physiological characteristics, made difficult direct extrapolation to man (Hughes, 1986). In this context, it seems to be accepted in the literature that the

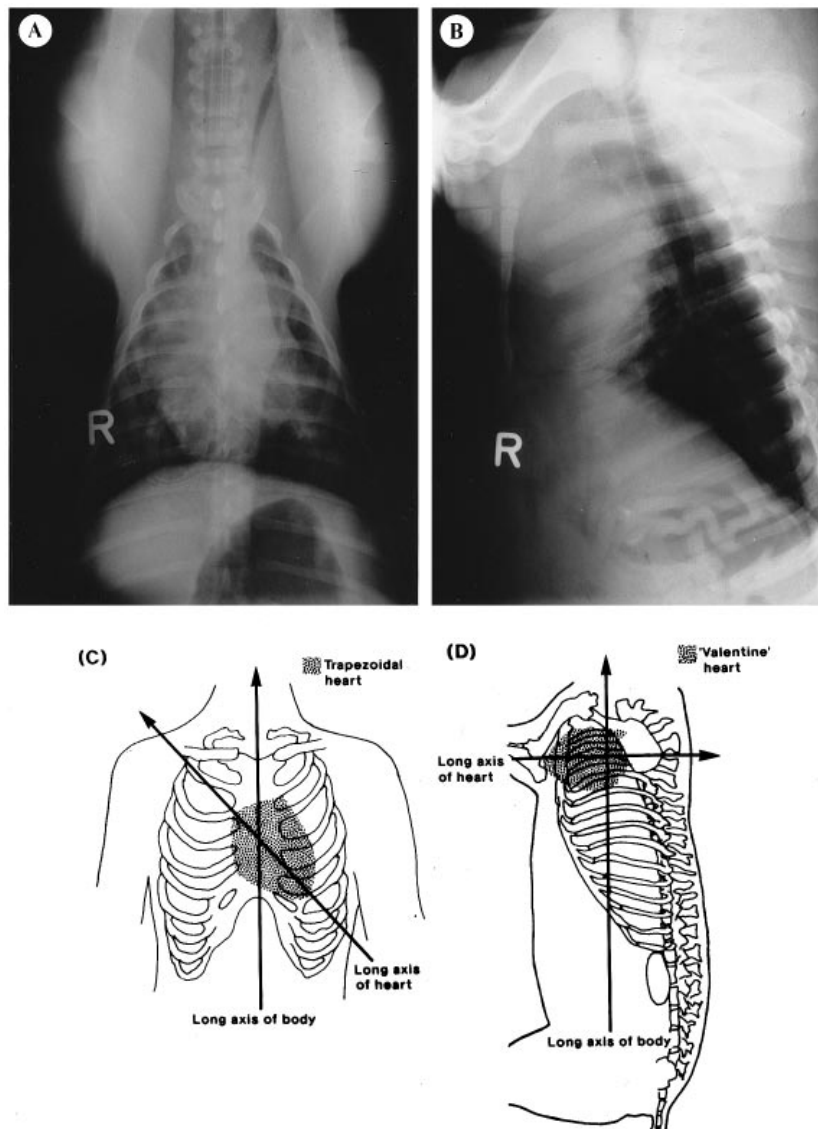


Fig. 1. Radiographs of the porcine thoracic cavity (*A, B*) together with comparative diagrammatic representations describing the different relationship of the cardiac silhouette to the surrounding rib cage in man (*C*) and in the pig (*D*). The pig has been x-rayed in the orthograde rather than unguigrade posture (*A, B*). R, right.

anatomy of the pig heart is almost identical to that of man (Lumb, 1966; Douglas, 1972; Hughes, 1986; Cooper et al. 1991; White & Wallwork, 1993). We were intrigued by this acceptance, the more so since knowledge of comparative porcine cardiac anatomy is limited. Previous studies have concerned themselves largely with comparisons of coronary vascular anatomy (Weaver et al. 1986; Bloor et al. 1992), postnatal development (Guerreiro et al. 1980; Gwathmey et al. 1989; Alvarez et al. 1993), or functional morphology (Hamlin, 1960; Bowman & Hughes, 1984*a, b*; Opthof et al. 1987). If transgenic pig hearts are to be used in cardiac transplantation, a detailed study of comparative cardiac anatomy between pig and man could hardly be less than relevant. In this study, therefore, we have compared hearts from domestic pigs of

various ages with our extensive collection of normal adult and neonatal human hearts.

MATERIALS AND METHODS

A total of 27 pig hearts (*Sus scrofa*) were examined, 14 from neonates (age range newborn – 25 d; weight 1–5 kg) and 13 hearts from young adult animals (age range 3–6 mo; weight 20–50 kg). All hearts were normal (no congenital heart defects), and were obtained from healthy animals that had no recognisable cardiovascular disease, in accordance with the Home Office Guidance on the operation of the Animals (Scientific Procedures) Act 1986, published by HMSO, London (or the comparable guidelines for the state of Israel). After removal from the thoracic

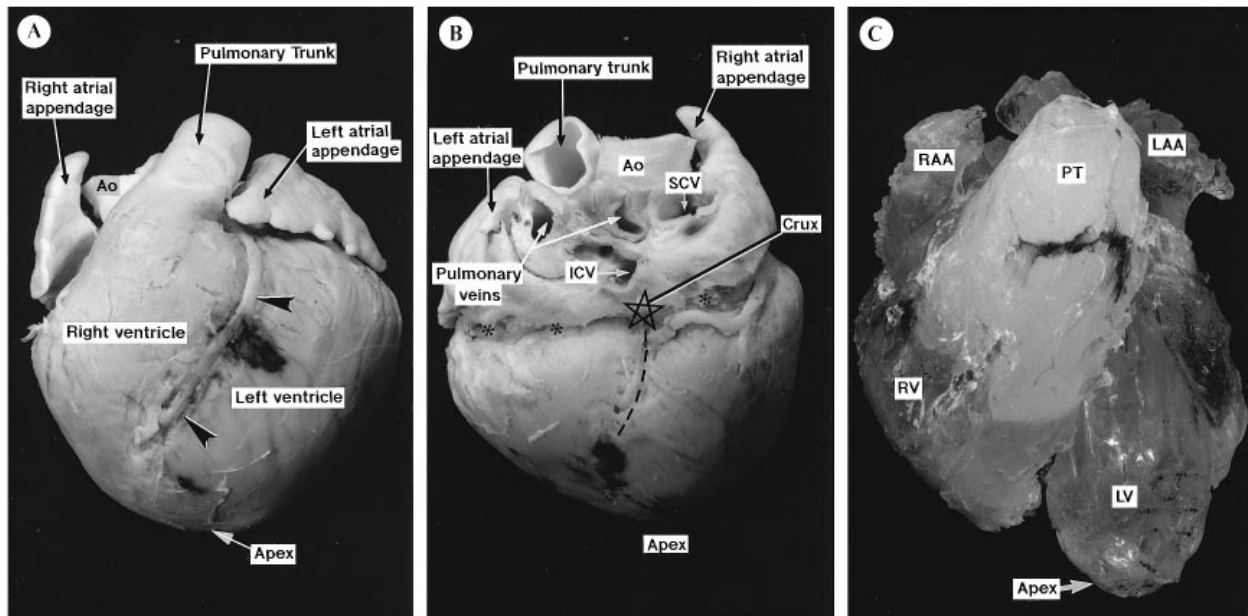


Fig. 2. External aspects of the porcine heart (*A, B*) showing both anterior (*A*) and posterior (*B*) surfaces (compare with Fig. 3). The heart has a characteristic Valentine shape. The anterior-posterior orientation of the porcine heart is reflected by the orientation of the atrial appendages (*A*). The anterior interventricular groove (closed arrowheads) is situated towards the sloping leftward margin of the ventricular mass (*A*). The posterior interventricular groove (broken line) runs along the mid-point of the posterior surface and bisects the atrioventricular groove (*) at the crux. Casts of both the left and right sides of a pig heart (*C*) illustrates that the apex is formed entirely of left ventricular musculature. Ao, aorta; SCV, superior caval vein; ICV, inferior caval vein; RAA, right atrial appendage; LAA, left atrial appendage; PT, pulmonary trunk; RV, right ventricle; LV, left ventricle.

cavity, the lungs were separated from the heart and the ascending components of the aorta and pulmonary trunk were cut well above the arterial valves. The atriums were opened from their posterior aspect. Blood clots, if present, were washed out from both the atrial and ventricular chambers. The hearts were then fixed by immersion in 10% formol saline (approximately 96 h). After fixation, the hearts were examined and dissected. The hearts were stripped of all external fat by sharp dissection, leaving the myocardium exposed in order to assess the arrangement of coronary blood vessels. During examination and dissection, comparisons were made with our extensive museum collection of normal neonatal and adult human hearts.

Method of dissection

Prior to dissection, we examined the overall morphology of each heart. Most hearts were dissected using the classical approach of opening each of the 4 chambers according to the flow of blood. In this dissection, the right atrium was opened from the inferior caval vein to the tip of the right atrial appendage. The right ventricle was opened along its attachment to the ventricular septum from the tricuspid orifice through to the pulmonary outflow

tract. An incision was then made along the acute (right) margin of the heart and was extended from the initial cut to the right ventricular apex. Another incision was made from the apex to the anterior papillary muscle creating a triangular flap, which remained attached to the septum by the moderator band. The left atrium was opened by an incision across its roof between the left and right pulmonary veins. The left ventricle was then opened laterally between the anterior and posterior papillary muscles, along the obtuse margin, to the apex. Another incision was then made along the anterior wall adjacent to the ventricular septum through the aortic outflow tract. The remaining hearts were prepared to demonstrate specific features, such as the interrelations of the cardiac valves in the short axis and the structure of individual chambers. For purposes of comparison with the human heart, all terms follow those used by Anderson & Becker (1992).

RESULTS

Gross morphology of the heart

Due to its location in the thorax, and the orientation of the body, the pig heart had a classic 'Valentine heart' shape (Fig. 1). This was quite unlike the human

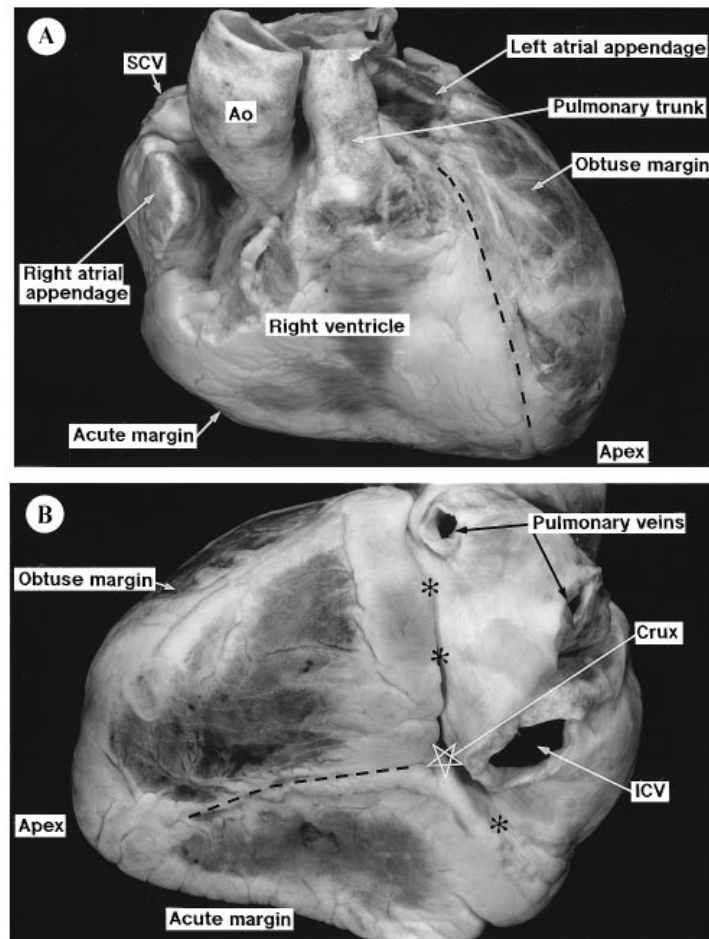


Fig. 3. External aspects of the human heart (*A, B*) showing both anterior (*A*) and posterior (*B*) surfaces. The human heart is trapezoidal in shape when observed in frontal projection. As in the porcine heart, the anterior interventricular groove (broken line) is situated towards the sloping leftward border, that is close to the obtuse margin (*A*). From the posterior viewpoint (*B*) the region between the acute and obtuse margins is the diaphragmatic surface, which is divided at its midpoint by the posterior interventricular groove (broken line). This also bisects the atrioventricular groove (*) at the crux. Ao, aorta; SCV, superior caval vein; ICV, inferior caval vein.

heart, which had a distinctly trapezoidal silhouette when seen in frontal projection (Fig. 1). The pig heart, nonetheless, retains an apex and a base, with upper and lower borders of dissimilar size, features comparable with those of the human heart. The ventricular mass of the pig was of basic conical morphology (Fig. 2), with the posterior (or caudal) surface adjacent to the diaphragm, and the anterior (or sternovertral) surface resting against the sternum. The locations of these external surfaces in the human heart were different (Fig. 3), this again being related to the difference in basic body orientation, with the pig having a unguigrade stance compared with the orthograde (upright) posture of man (Fig. 1). The basic anterior–posterior orientation of the pig heart was also clearly reflected by the anterior direction in which the atrial appendages face (Fig. 2). The apex of the pig heart was formed entirely by the left ventricle (Fig. 2). In keeping with the human arrangement, the

anterior interventricular groove was situated towards the sloping leftward margin of the ventricular mass, whereas the posterior interventricular groove was located along the midpoint of the diaphragmatic surface, and bisected the atrioventricular groove at the so-called crux (Figs 2, 3). The basal surface of the porcine heart revealed that the left and right atrial appendages were of approximately comparable size, whereas the extent of the human right atrial appendage was appreciably greater than the left (Fig. 4).

Atria

As in man, each atrium had a venous component, an appendage and the vestibule of an atrioventricular valve, together with the septum separating the 2 atriums. The atrial appendages of the pig faced directly anteriorly towards the back, or posterior, of the anterior thoracic wall (sternum) (Figs 2, 4).

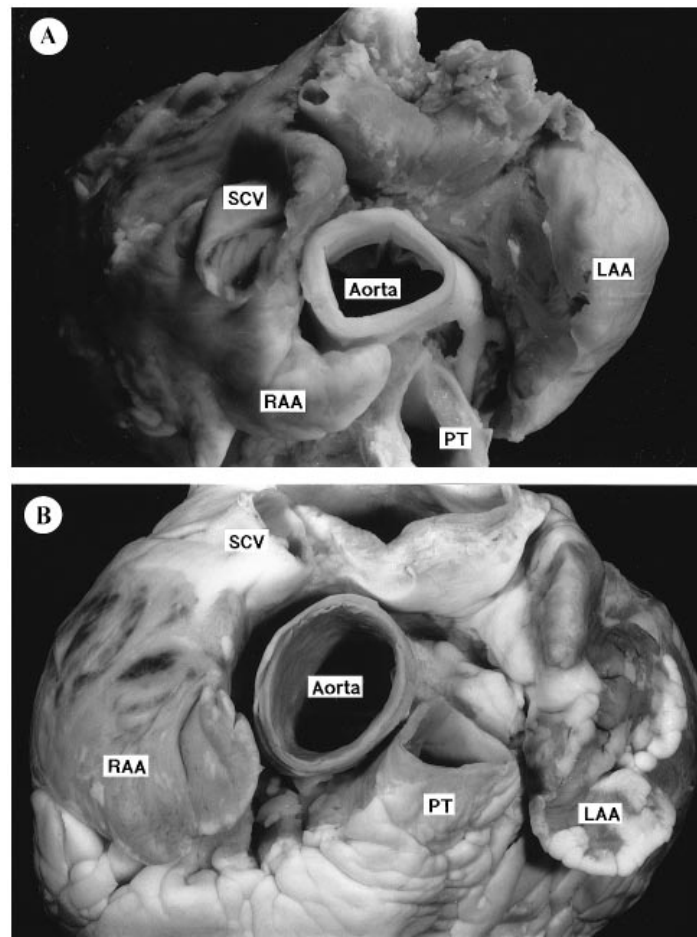


Fig. 4. External view of the basal surface of the porcine (A) and human heart (B). The contrasting size and morphology of the atrial appendages is apparent. The porcine left atrial appendage is of comparable size to its right counterpart whereas in the human heart the left atrial appendage is appreciably smaller than the right atrial appendage. The relative positions of the pulmonary trunk and the aorta are similar in both hearts, that is the pulmonary trunk is to the left of the aorta, and the aortic valve is very much the centre point of the heart in both species. RAA, right atrial appendage; LAA, left atrial appendage; SCV, superior caval vein; PT, pulmonary trunk.

In the morphologically right atrium of the pig (Fig. 5), the smooth-walled venous sinus received the superior and inferior caval veins and the orifice of the coronary sinus. The superior and inferior caval veins opened into the porcine atrium at right angles to one another (Fig. 5), whereas in man the orifices of the 2 caval veins were directly in line. A prominent left azygous vein then entered on the left side of the pig heart and drained into the coronary sinus, forming a third right angle relative to the other caval veins (Fig. 5). This vessel has been termed the left azygous vein in the pig, although we find this confusing since, in human anatomy, the azygous system drains the parietal structures. The comparable vessel was much reduced in the normal human heart, persisting only as the left atrial oblique vein (or left superior caval vein) so that, in the normal situation, it drains only venous return from a small part of the left atrial musculature. The morphologically right atrial appendage in the pig

had a narrow, tubular appearance (Fig. 5). This tubular morphology was more pronounced in the right atrial appendages of the juvenile pig hearts examined. In man, this structure had a characteristic triangular shape and joined the venous component over a broad area (Fig. 5). Nevertheless, as in man, the porcine right atrial appendage was lined internally by pectinate muscles that originated from the prominent muscle band, the terminal crest (Fig. 6). This structure separated the pectinate lining of the appendage from the smooth walls of the venous sinus. In both man and pig, these pectinate muscles then extended to surround entirely the parietal margins of the vestibule of the tricuspid valve. The vestibule itself was a smooth muscular structure that supported the leaflets of the tricuspid valve. The location of the true atrial septum in the pig was also different to that seen in man, although being marked by the characteristic landmarks of the oval fossa. In the pig, the fossa was

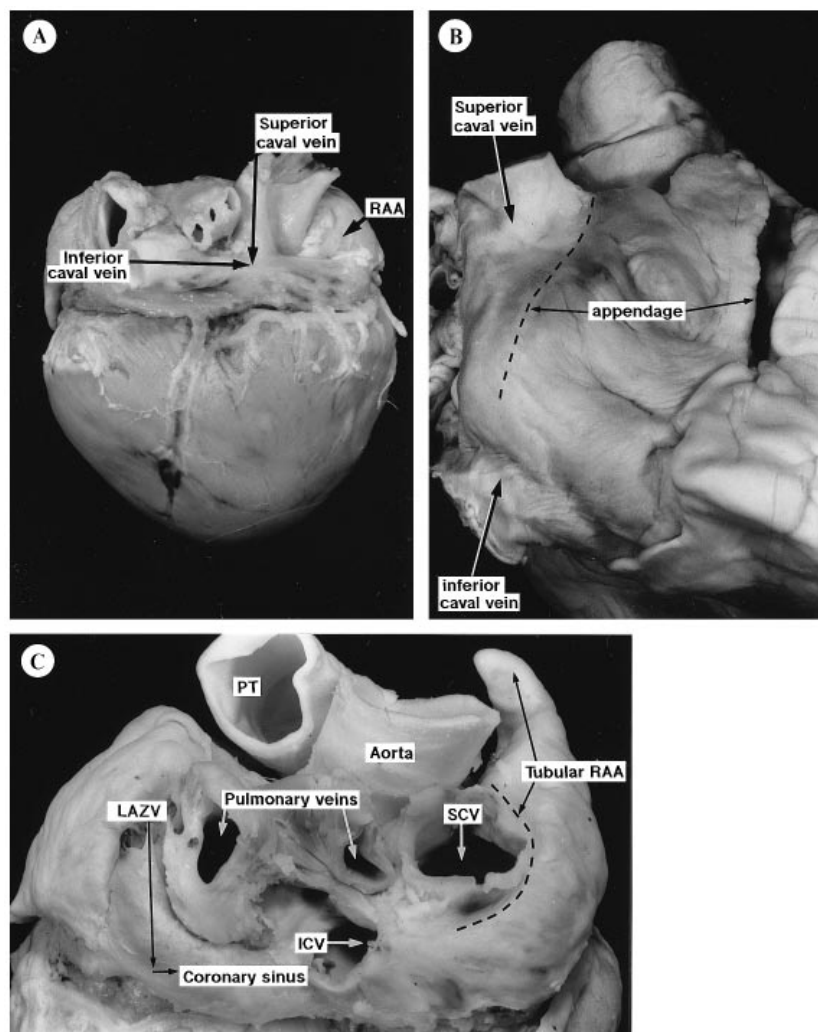


Fig. 5. External aspects of the porcine morphologically right atrium (*A*) in comparison with that of the human heart (*B*). The superior and inferior caval veins of the porcine right atrium are clearly observed to enter the chamber at right angles to one another. In the human right atrium the caval veins are almost perpendicular to one another (*B*). The external features of other venous components of the porcine heart are also shown (*C*). A prominent left azygous vein (LAZV) enters the left side of the porcine heart and drains via the coronary sinus. The terminal groove (broken line) marks the junction between the appendage and the venous sinus (*B*, *C*). The human appendage joins the venous component over a broader area than in the pig right atrium (*B*, *C*). RAA, right atrial appendage; SCV, superior caval vein; ICV, inferior caval vein; PT, pulmonary trunk.

found in a more deep-set and superior position, close to the orifice of the superior caval vein (Fig. 6). As in man, the inferior rim of the fossa was continuous with the sinus septum, this being the structure that separated the orifices of the coronary sinus and inferior caval vein. The tendon of Todaro coursed through this muscular region, forming the upper border of the triangle of Koch, which was similarly located as in the human heart, carrying the atrial surface of the atrioventricular muscular septum.

In the porcine morphologically left atrium (Fig. 7), the venous component received only 2 pulmonary veins. In the human left atrium, there were generally 4 orifices for the pulmonary veins. The left atrium of the pig was of a similar size to the right atrium,

whereas in the human heart, the right atrium, particularly its appendage, was appreciably larger than the left. The left appendage was a triangular structure, unlike the tubular appendage observed in man (Fig. 7). The pectinate muscles, nonetheless, were restricted to its internal walls, as in man (Fig. 8). The smooth-walled left atrial vestibule supported the leaflets of the mitral valve (Fig. 8). The atrial septal region of the pig appeared to be longer than in man when observed following removal of the atrial musculature to the level of the arterial valves (Fig. 8). This was a result of the different atrial morphology and also the apparent anterior displacement of the porcine aortic trunk compared to that of man (Fig. 8). This anterior aortic displacement was generally found

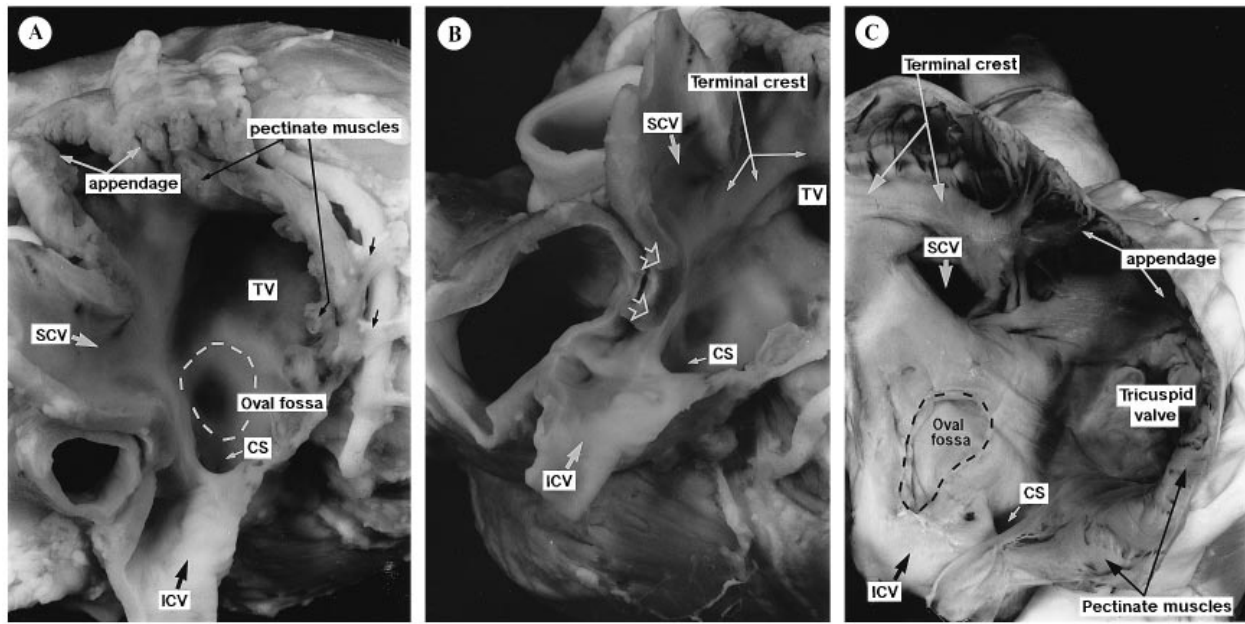


Fig. 6. Internal aspects of the porcine (*A, B*) and human (*C*) right atrium displayed through an incision made in the appendage. In both species the pectinate muscles (*A, C*), which are transected as a result of the incision, extend to surround the parietal margins of the vestibule of the tricuspid valve (TV). The borders of the oval fossa (broken line) are indicated (*A, C*). The rim of the oval fossa is formed by the infolded atrial walls (open arrows, *B*). In the porcine right atrium the fossa appears to be closer to the orifice of the superior caval vein than it does in the human right atrium. A prominent terminal crest is apparent in both species (*B, C*), and passes in front, and to the right, of the orifice of the superior caval vein. SCV, opening of superior caval vein; ICV, opening of inferior caval vein; CS, opening of coronary sinus.

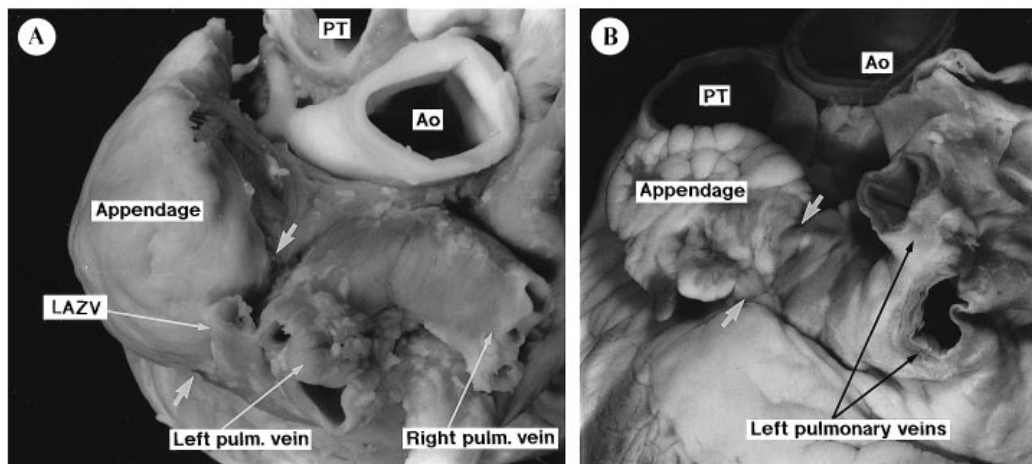


Fig. 7. External aspects of the porcine (*A*) and human (*B*) left atrium demonstrating their different appendage morphology. The porcine appendage is a triangular structure whereas in man it has a narrow tubular appearance. The porcine left atrial appendage has a broader junction (between arrows) to the pulmonary venous component than the left atrial appendage of man, which has a narrow appendage-venous junction (between arrows). The porcine venous component (*A*) receives only 2 pulmonary veins (left and right pulm. veins) whereas in man there are generally 4 orifices for the pulmonary veins (only 2 left veins are shown). Unlike man, the left atrium of the pig is of a similar size to its right-sided counterpart. A prominent left azygous vein (LAZV) enters on the left side of the pig heart (*A*) but is absent in the adult human heart. PT, pulmonary trunk; Ao, aorta.

to be a feature of adult porcine hearts, and was not observed in the neonatal hearts examined. As stated previously, the location of the true atrial septum was the floor of the oval fossa since the majority of the atrial septal region was composed of the infolded groove between the superior caval and right pulmonary veins in both species.

Ventricles

Both ventricles were well described in terms of inlet, apical trabecular and outlet components. The relative proportion of ventricular dimensions to the overall size of the heart was observed to be much smaller in neonatal porcine hearts compared with the adult. The

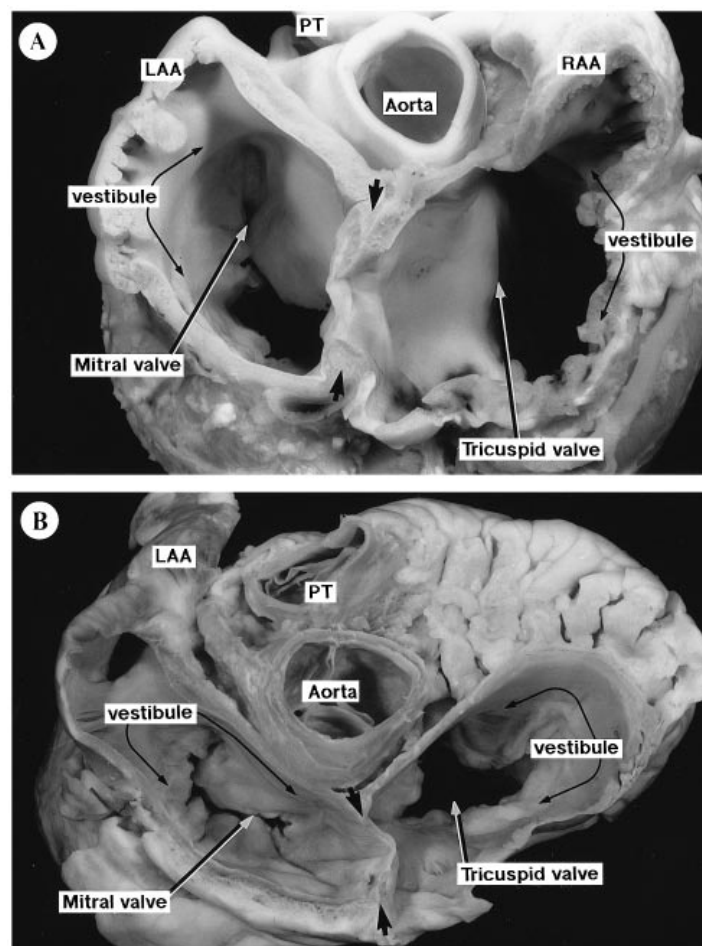


Fig. 8. Basal view of short axis sections through the atrioventricular junctions of the porcine (*A*) and human (*B*) heart following removal of the atrial musculature to the level of the arterial valves. This demonstrates that in both species the pectinate muscles of the left atrium are confined to the appendage, and the smooth-walled vestibule supports the leaflets of the mitral valve. In the right atrium of both species the pectinate muscles are found both in the appendage and surrounding the vestibule of the tricuspid valve. The length of the atrial septum (between closed arrows) appears to be longer in the pig than in man. LAA, left atrial appendage; RAA, right atrial appendage; PT, pulmonary trunk.

basic components of the morphologically right ventricle of the pig (Fig. 9) were structurally very similar to man. The inlet of the right ventricle extended from the atrioventricular junction to the distal attachments of the tension apparatus of the tricuspid valve. The 3 leaflets of the tricuspid valve were located septally, anterosuperiorly and inferiorly or murally, and their attachments were as found in the human right ventricle, including the characteristic feature of multiple cords running from the septal leaflet to the ventricular septum. As in man, the anterior papillary muscle, that supported the zone of apposition between the anterosuperior and inferior leaflets, was the largest of the muscular valvar attachments. A notable difference was seen, however, in the prominence of the muscular moderator band (Fig. 9). This was situated in a much higher position within the ventricle compared with man. In the pig, the band formed the direct continuation of the septomarginal trabeculation

to the parietal wall. In man, the moderator band was a much reduced structure, and was a continuation from the anterior papillary muscle, straddling the ventricular cavity at a much lower level than in man. The apical component of the pig right ventricle possessed very coarse trabeculations, much broader than those observed in the human right ventricle (Fig. 9). The most prominent of these muscular straps was the septomarginal trabeculation, which divided in the roof of the ventricle into 2 limbs which, in turn, clasped the infolding of the inner heart wall superiorly, this fold being the supraventricular crest or infundibulum (Fig. 9). The apical and septoparietal trabeculations were also much coarser in the right ventricle of the pig compared with man. As in man, the outlet of the right ventricle was a complete, free-standing muscular structure, the infundibulum, which supported the 3 leaflets of the pulmonary valve in semilunar fashion. Again as in man, the semilunar

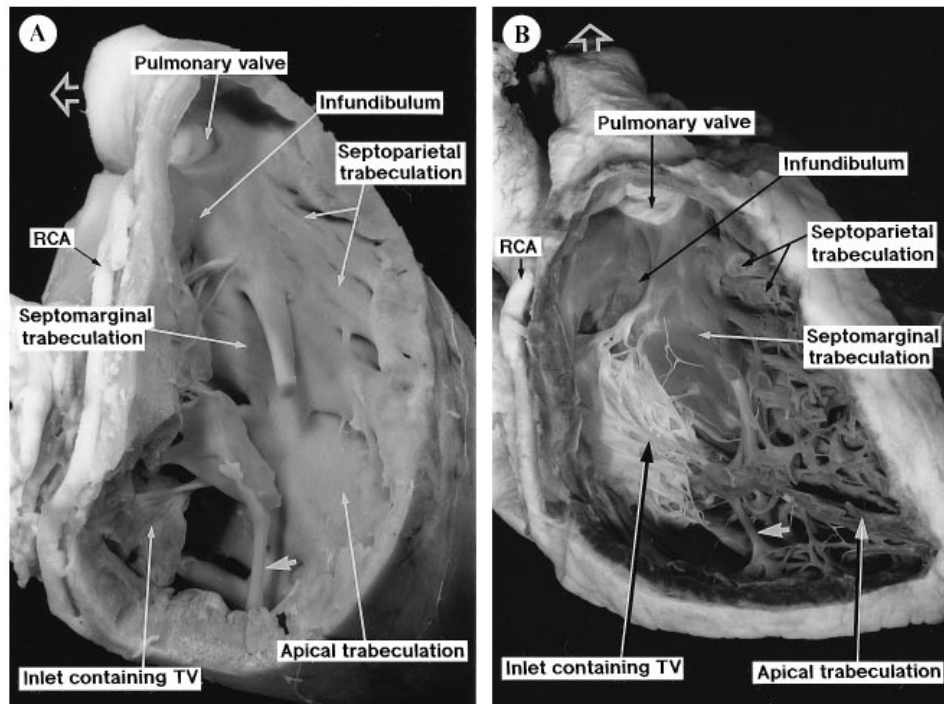


Fig. 9. Internal aspects of the morphologically right ventricle of pig (A) and man (B). A window has been made in the parietal wall to show the structure of the tricuspid valve and its attachments. The septomarginal, septoparietal and apical trabeculations are clearly much coarser in the pig than in man. The porcine right ventricle has a prominent muscular moderator band (closed arrow) which forms the direct continuation of the septomarginal trabeculation to the parietal wall. Compare this to the less prominent moderator band (closed arrow) in the human right ventricle. The orientation of the pulmonary valve and outlet component is indicated by open arrows. The porcine pulmonary valve is in parallel with the tricuspid valve. The human pulmonary valve is almost at right angles with the tricuspid valve. This anatomical adaptation is as a result of the contrasting postures between pig and man. RCA, right coronary artery.

hinge-points crossed the circular anatomical ventriculo-arterial junction. This arrangement incorporated crescents of infundibular musculature into the arterial sinuses, and triangles of arterial wall into the ventricular outflow tract (Fig. 8). In the pig, the outlet component was in direct alignment with the inlet component whereas in man these structures were almost at right angles with one another (Fig. 9). This may also be an adaptation to the different postures between pig and man.

The morphologically left ventricle of the pig (Fig. 10) had features in common with man, but also possessed some notable differences. The inlet component supported the mitral valve and its tension apparatus, the latter formed of paired papillary muscles located obliquely within the ventricular cavity. As in man, the mitral valve had 2 leaflets, mural and aortic, with the mural (posterior) leaflet guarding two-thirds of the circumference of the valve, and with the aortic (anterior) leaflet in fibrous continuity with the leaflets of the aortic valve (see below). Both in pig and man, the paired papillary muscles attached to the mitral leaflets were located anterolaterally and posteromedially within the ventricular mass. As in the right ventricle, nonetheless,

these muscles are coarser in the pig. The apical trabeculations of the left ventricle were coarse, and were not obviously finer than their counterparts in the right ventricle. The fine criss-crossing left ventricular trabeculations were the characteristic feature in differentiating the human ventricles. The left ventricular wall of the adult pig was much thicker than that of a size-matched human heart (Fig. 10), however, this difference was more subtle in the neonatal pig hearts examined. A subtle difference was also observed in the outlet component with regard both to its relationship to the mitral valve and to the muscle mass supporting it. The aortic leaflet of the mitral valve was in fibrous continuity with the leaflets of the aortic valve (Fig. 11), but the extent of this continuity was reduced in the pig compared with man. In the pig, approximately two-thirds of the circumference of the aortic valve (or the hinge-points of one and a half aortic leaflets) was supported by left ventricular musculature (Fig. 11). This influenced the location of the membranous septum within the subaortic outflow tract (Fig. 11). The pig possessed a separate and discrete right fibrous trigone which, together with the membranous septum, formed the posterior extension of the subaortic outflow tract, supporting one end of

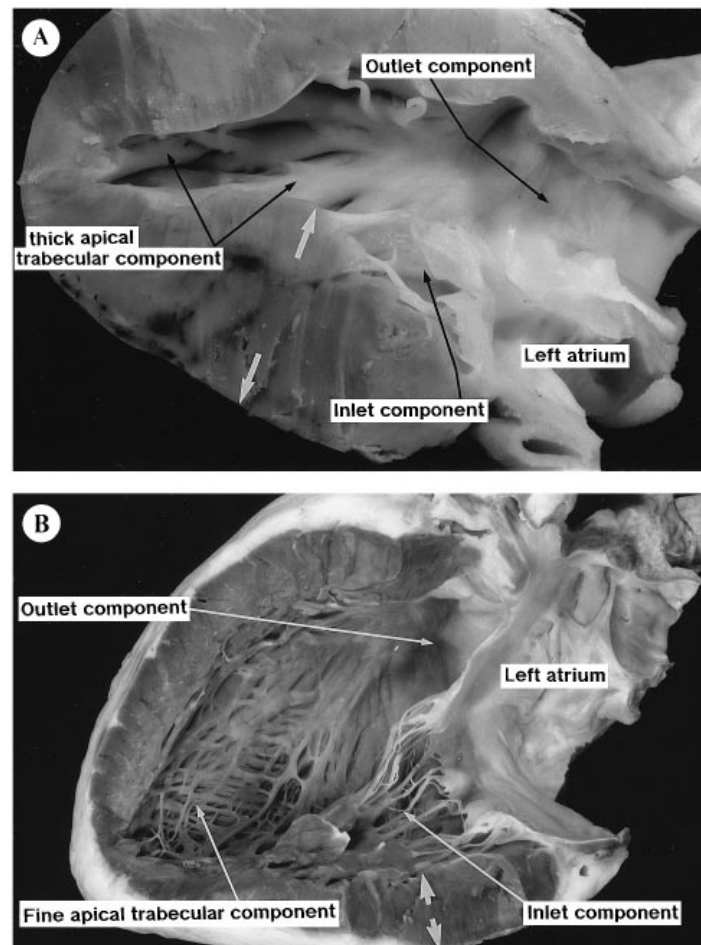


Fig. 10. Internal view of the porcine (*A*) and human (*B*) left ventricle, showing its inlet, outlet and apical trabecular component parts. The fine criss-crossing left ventricular trabeculations of the human heart are replaced by much coarser muscles in the pig. The greater thickness of the porcine left ventricular free wall compared with that of man is indicated (between closed arrows). The mitral valve and its paired papillary muscle attachments are structurally very similar in man and pig.

the area of aortic-mitral continuity. The other end was the prominent left fibrous trigone. A region of pale tissue, representing the left bundle of the atrio-ventricular conduction axis, fanned out beneath the aortic valve, but originated within the muscular septum (Fig. 11).

An overall view of comparative morphology of both left and right chambers was achieved by the examination of a 4-chamber section (Fig. 12). This section in the porcine heart demonstrated that the left chambers represented approximately two-thirds of the section, with the interventricular septum displaced towards the right. As mentioned previously, this dominance was also reflected in the fact that the apex was composed entirely of left ventricular musculature. An equivalent section of the human heart (Fig. 12) showed that both left and right chambers represented approximately equal proportions of the section, with the interventricular septum occupying an almost central position.

Coronary circulation

Even though the study by Weaver et al. (1986) provided a detailed quantitative description of coronary arterial anatomy and distribution, a brief overview is justified in a report of this nature. As in the human heart, the coronary arteries arose from their respective aortic sinuses. The right coronary artery, therefore, emerged from the right facing (or adjacent) sinus while the left coronary artery arose from the left facing (or adjacent) sinus. The right coronary artery passed directly into the right coronary groove (Fig. 13). As in man, the left coronary artery coursed only a short distance before dividing into the anterior interventricular and the circumflex branches (Fig. 13). Like man, these 3 coronary arterial branches formed 2 circuits, one in the atrioventricular and the other in the interventricular grooves. In most of the pig hearts examined (80%), the right coronary artery was dominant, encircling the tricuspid valvar orifice

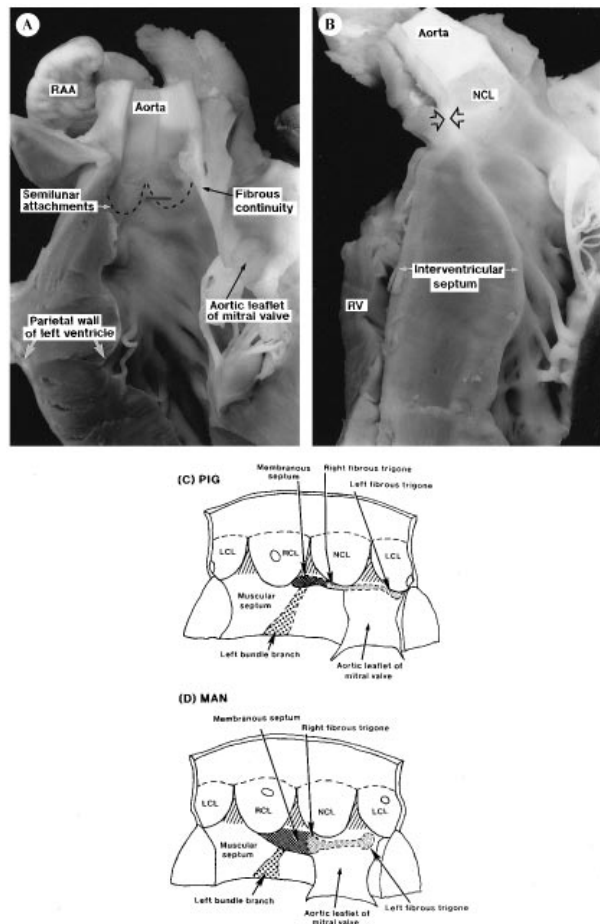


Fig. 11. Internal view (A) and transverse section (B) of the porcine subaortic outflow tract. A pin marks the position of the membranous septum (A) which is also shown in transverse section, indicated between the open arrows (B). Diagrammatic representations of the porcine (C) and human (D) subaortic outflow tracts showing the extent of fibrous continuity between the aortic and mitral valves, and the extent to which the aortic valve is supported by ventricular musculature. In the pig, three-quarters of the circumference of the aortic valve is supported by the muscular ventricular septum. RAA, right atrial appendage; RV, right ventricle; LCL, left coronary leaflet; NCL, noncoronary leaflet; RCL, right coronary leaflet.

and continuing beyond the crux having given rise to the posterior interventricular branch. The extension of the right coronary artery into the left atrioventricular groove supplied the majority of the posterior (diaphragmatic) wall of the heart. Most human hearts (approximately 90%) also displayed right coronary arterial dominance (Anderson & Becker, 1992). In the pig, the sinus and atrioventricular node were supplied by branches of the right coronary artery. In man, the sinus node was supplied in only 55–66% of cases by an atrial branch of the right coronary artery. Two other coronary arterial arrangements were observed, left dominance and a balanced supply. Only one of the pig hearts we examined had a left dominant supply, with the

circumflex arterial branch encircling the entirety of the mural leaflet of the mitral valve and giving rise to the posterior interventricular branch at the crux. Three hearts, however, possessed a balanced arrangement, where both the right coronary artery and circumflex arterial branch supplied the area of the crux, giving rise to paired posterior descending arterial branches. Such an arrangement was rare in human hearts. The coronary venous system was dominated by the coronary sinus situated within the left atrioventricular groove. The great cardiac vein ascended in the anterior interventricular groove and turned into the groove to join with the descending left azygous vein, at this point becoming the coronary sinus. In the pig, it is the left azygous vein and coronary sinus that were the dominant vessels, whereas in man the left superior caval vein (oblique vein) was much reduced or even absent, as previously mentioned. As the coronary sinus passed round the mural leaflet of the mitral valve, it received the marginal veins, and then received the middle cardiac vein at the crux, together with the small cardiac vein (drains blood from the posterior surface of the right ventricle). This arrangement was similar to coronary venous drainage in the human heart, with the anterior (minor) veins from the right ventricle draining directly into the right atrium. As in man, there were also a series of thebesian veins draining the atrial musculature directly to the atrial cavities.

DISCUSSION

The purpose of our study was to compare the anatomy of the porcine heart to that of man, identifying any differences that might prove of significance during xenotransplantation. With this in mind, we observed several important and notable anatomical differences between the hearts of pig and man, and were indeed surprised at the accepted convention that the pig heart is virtually identical, anatomically, to the human heart. Many of the gross morphological differences between the porcine and human hearts, nonetheless, can simply be explained by the contrasting stances of the 2 species, ungradigrade versus orthograde, or alternatively, quadrupedal versus bipedal, with gravity surely being an important factor in the evolution of their respective cardiovascular systems. It can also be considered that some of the differences between porcine and human hearts could have resulted from the more laterally compressed form of the thorax of pigs compared with the unusually dorsoventrally flattened human chest.

The more classic Valentine shape of the porcine

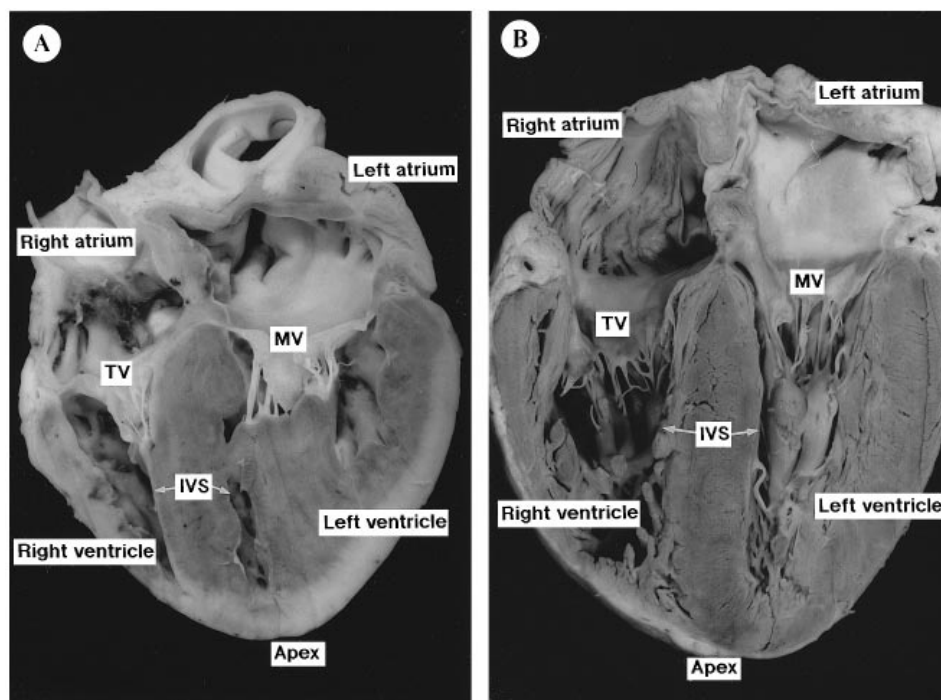


Fig. 12. Four chamber sections of the porcine (*A*) and human (*B*) heart illustrating the differences in the morphological proportions of atrial and ventricular chambers. In the porcine heart the greater proportion of the section is taken up by the left chambers, especially the left ventricle, which means that the interventricular septum is situated more to the right of the heart. This also means the apex is composed entirely of left ventricular musculature, unlike the apex of the human heart. In the human heart the left chambers are less dominant and as a result, the interventricular septum occupies a more central position within the section. TV, leaflets of tricuspid valve; MV, leaflets of mitral valve; IVS, interventricular septum.

heart reflects this markedly different location within the thoracic cavity compared with the human heart. The porcine heart is essentially suspended in the thoracic cavity by its major blood vessels, with its anterior surface resting near to the sternum, and the majority of the posterior surface adjacent to the diaphragm. The human heart, in contrast, has a trapezoidal silhouette, with a markedly eccentric apex. The porcine heart 'rests' on its apex, which is formed by only the left ventricular mass. These facts may have implications for the positioning of the cardiac xenograft within the thoracic cavity during transplantation (Cabrol et al. 1989). They may also affect the postoperative performance of the transplanted heart, in that it would need to adapt rapidly to the influence of gravitational changes on blood pressures required by the human body.

As might be expected the shape of the pig heart, and its position within the thoracic cavity, have important implications for internal anatomy (Anderson & Becker, 1992). It is this fact, along with the postural effect, which accounts for the right angles between the orifices of the superior and inferior caval veins as they enter the right atrium. In physiological terms, this adaptation allows for an adequate venous return in the pig and in other quadrupedal mammals. The

orifices of the human caval veins, in contrast, are vertically in line with one another, reflecting the upright stance of the human body. The only other species to have adapted completely to an upright (orthograde) posture are other 'bipedal' animals such as kangaroos and primates (Hammer, 1991). The problem of adaptation of the transplanted pig cardiac xenograft to differing venous and arterial pressures within the human body is unknown, and is not likely to become known until clinical trials are performed. Some physiological data on blood pressures in the pig have been collected (Stone & Sawyer, 1966; Swan & Meagler, 1971; Lucke, 1976; Tranquilli et al. 1982), and differences in central venous, pulmonary arterial and pulmonary wedge pressures are apparent. These need to be taken into account when planning clinical trials, should they become acceptable.

The morphologically right atrium of the pig differs markedly from that of the human heart, notably having an obviously tubular atrial appendage. A functional reason for this is unclear, but it may help to explain the different electrophysiological characteristics of the porcine atrial appendage P wave (6.1–25.3 ms) (Bowman & Hughes, 1984*a*), compared with that of man (60–100 ms). The different morphology of the porcine right atrial appendage (and

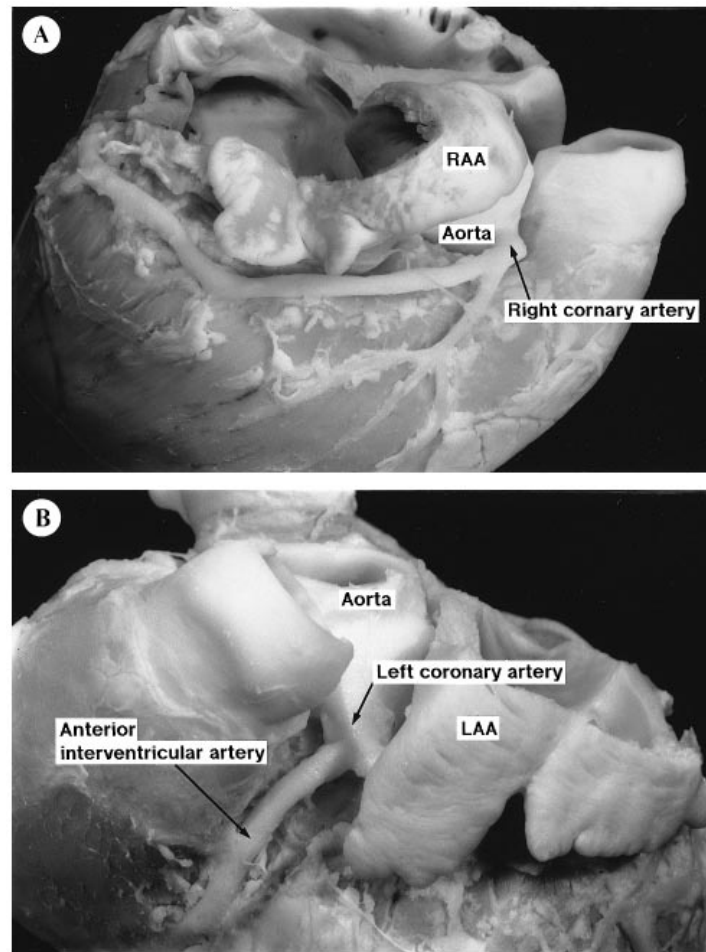


Fig. 13. External aspect of the porcine heart showing the course of the left (A) and right (B) coronary arterial system. As in man, the left coronary artery runs only a short course before dividing into the anterior interventricular and circumflex (hidden by left atrial appendage) arteries. RAA, right atrial appendage; LAA, left atrial appendage.

right atrium) must also affect the architecture of muscle bundles within the atrial wall, but does not change the overall arrangement of a 'bag full of holes'. As reported for the human atriums, this arrangement has important implications for overall atrial contraction, providing a suitable medium for preferential conduction (Wang et al. 1995). The more superior location of the oval fossa within the porcine right atrium, together with the tubular appendage, and the different location of the caval venous orifices, almost certainly account for the different morphology of the porcine atrial electrocardiogram when compared with man (Bowman & Hughes, 1984*a, b*; Hughes, 1986).

The right ventricle of the pig possesses structural similarities to that of the human heart such as similar tricuspid and pulmonary valvar arrangements. Nevertheless, there are some important differences, the most notable being the orientation of the pulmonary valve and hence the entire outlet component. This structure is more directly aligned with the orientation of the

inlet component and this, once more, is an adaptation to the unguligrade stance of the pig. In man, the pulmonary trunk is more at right angles with the inlet component of the right ventricle, reflecting the upright stance of man. The difference in orientation of the pulmonary outflow tract may create surgical problems for xenotransplantation. Another characteristic difference, however, is the prominence of the muscular moderator band and its higher position within the porcine right ventricle. The moderator band, as in the human heart (Anderson & Becker, 1992), carries a division of the right bundle branch and is, therefore, responsible for the conduction of the impulse to the parietal wall through the Purkinje fibre network. The high position of the moderator band might explain the faster activation of the right ventricle in the pig heart. This is reflected in the considerably shorter PR-interval of the pig, 70–113 ms (Larks et al. 1971), compared with 120–200 ms in man (Timmis, 1988). It is also known that the pig has a different activation sequence of its ventricles (Hughes, 1986). Further-

more, as the pig ages, other changes in the form and electrical force of the QRS complex occur, these being indicative of work overload (Hamlin, 1960). Swine, in particular, are known to be easily excitable, with marked and rapid increases of systemic and especially pulmonary arterial pressures (Engelhardt, 1966). They are also markedly susceptible to ventricular fibrillation (Verdouw et al. 1983). All these features have important implications for xenotransplantation, since a high proportion of early mortality in heterogenic cardiac transplant patients are a result of right-sided cardiac failure (Pennington, 1989; Mann, 1992).

The left ventricle of the pig also possesses some notable structural differences compared with that of the human heart. The most striking of these is the much thicker porcine left ventricular wall of the pig. Two-thirds of the hinge-points of the aortic valve of the pig are supported by left ventricular musculature. This means that there is a lesser degree of aortic to mitral fibrous continuity, which has important consequences for the location of the membranous septum and also for the atrioventricular conduction system. In man, the axis of the compact atrioventricular node gathers at the apex of the triangle of Koch and then courses into the central fibrous body to become the penetrating atrioventricular bundle. After penetration of the fibrous body, the axis of conduction tissue reaches the crest of the muscular ventricular septum beneath the membranous septum, and begins to branch. In the pig, the penetrating atrioventricular bundle reaches the crest of the ventricular septum in a more proximal position. The anterior displacement of the porcine aortic trunk compared with that of man is significant, although its general orientation appears to be compatible with that of man.

In the human heart, the fine criss-crossing left ventricular trabeculations are the characteristic feature for differentiating the left and right ventricles (Anderson & Becker, 1992). The trabeculations of both porcine ventricles are extremely coarse, and do not permit us, using this feature alone, to differentiate between the 2 chambers. A functional role for the thickness of the papillary muscles and the trabeculations is speculative, but could be associated with either mitral or tricuspid valvar function, and could influence ventricular contractility (Sarris & Miller, 1988; Uemura et al. 1995). The thick trabeculations may also have an effect on blood flow within the ventricular chamber. The thickness of the trabeculations could also explain further the efficiency of ventricular activation in the pig heart.

As already emphasised by Weaver et al. (1986), the coronary arterial circulation of the pig is remarkably

similar to man. The anatomy of coronary venous return, however, is very different from that of the human heart, but mainly because of the presence of a prominent left azygous vein. Recognition of this anatomical difference is important for the surgeon. The pig does not possess a (right) azygous vein, unlike carnivores, ruminants, horses, and indeed man, where this vessel drains into the (right) superior (or cranial) caval vein. The left azygous vein is also found in ruminants which possess paired azygous veins. During the (xeno)transplantation procedure the left azygous vein of the donor pig heart would have to be tied presumably at a point above its insertion into the coronary sinus. Also, the azygous vein of the human recipient would be anastomosed to the (right) superior caval vein of the donor pig heart. In studies using the pig as an experimental model, the presence of this vein also creates a problem for the collection of uncontaminated samples of cardiac venous blood from the whole heart for metabolic analysis (Liedtke et al. 1975).

The rapid advances in transgenic technology have potentially solved many of the immunological difficulties of using pig organs to support life in a human being. Nevertheless, other difficulties still remain. Of great significance, are the reservations concerning the possibility of transfer of porcine viral pathogens to the immunosuppressed human recipient (Cozzi & White, 1995). This is particularly important in view of the reputed link between the human equivalent of bovine spongiform encephalopathy, and the consumption of beef infected with the pathogen responsible for this disease. This problem has resulted in the prohibition of clinical trials of transplantation using transgenic porcine organs until this matter is researched further, and ultimately resolved. Also, the shorter pig life span of 2 decades has implications for the effect of ageing changes on the survival of the xenograft, such as ischaemia and fibrosis. Our observations, nonetheless, have demonstrated several potentially significant anatomical differences between porcine and human hearts that might affect the success of the cardiac xenograft within the human recipient. It is important that we are aware of them as arguments continue concerning the advisability of using the porcine organ for human xenotransplantation.

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