




## REVIEW ARTICLE

# Revisiting the anatomy of the left ventricle in the light of knowledge of its development

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## Funding information

Rachel Charitable Trust

## Abstract

Despite centuries of investigation, certain aspects of left ventricular anatomy remain either controversial or uncertain. We make no claims to have resolved these issues, but our review, based on our current knowledge of development, hopefully identifies the issues requiring further investigation. When first formed, the left ventricle had only inlet and apical components. With the expansion of the atrioventricular canal, the developing ventricle cedes part of its inlet to the right ventricle whilst retaining the larger parts of the cushions dividing the atrioventricular canal. Further remodelling of the interventricular communication provides the ventricle with its outlet, with the aortic root being transferred to the left ventricle along with the newly formed myocardium supporting its leaflets. The definitive ventricle possesses inlet, apical and outlet parts. The inlet component is guarded by the mitral valve, with its leaflets, in the normal heart, supported by papillary muscles located infero-septally and supero-laterally. There is but a solitary zone of apposition between the leaflets, which we suggest are best described as being aortic and mural. The trabeculated component extends beyond the inlet to the apex and is confluent with the outlet part, which supports the aortic root. The leaflets of the aortic valve are supported in semilunar fashion within the root, with the ventricular cavity extending to the sinutubular junction. The myocardial-arterial junction, however, stops well short of the sinutubular junction, with myocardium found only at the bases of the sinuses, giving rise to the coronary arteries. We argue that the relationships between the various components should now be described using attitudinally appropriate terms rather than describing them as if the heart is removed from the body and positioned on its apex.

## KEYWORDS

aortic root, inferior pyramidal space, infero-septal recess, mitral valve, tripartite ventricular description, ventricular development

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## 1 | INTRODUCTION

Despite having been studied for centuries, certain aspects of left ventricular anatomy remain either controversial or uncertain. In the first instance, a major problem exists in determining the boundaries of the ventricle. The mural atrioventricular junction provides a clear-cut boundary for part of its proximal extent. The fibrous continuity between the leaflets of the mitral and aortic valves makes it much harder to define the proximal extent of the part of the junction in contiguity with the aortic root. The incorporation of the aortic root into the left ventricular outlet then creates further difficulties in defining its distal extent. This is because the distal extent of the myocardial border does not correlate with the proximal attachments of the leaflets of the aortic valve (Toh et al., 2020). Problems also remain when seeking to assess the anatomical basis of the findings produced by current techniques for clinical imaging. This is because the heart continues to be described as removed from the body and positioned on its apex rather than in an attitudinally appropriate fashion (Cook & Anderson, 2002). In a recent review of the anatomy of the right ventricle (Crucean et al., 2023), we showed how knowledge of cardiac development can now provide insights into the postnatal arrangement of the ventricular components. In this review, we show that a comparable situation is to be found when seeking to understand the nuances of left ventricular anatomy. When reviewing the developmental aspects, we take advantage of material demonstrating the changes observed in the human heart. We supplement this information, where appropriate, with images of murine development since the developmental changes are comparable in mice and men. With regard to the postnatal anatomy, however, we describe the arrangements only as seen in the human heart.

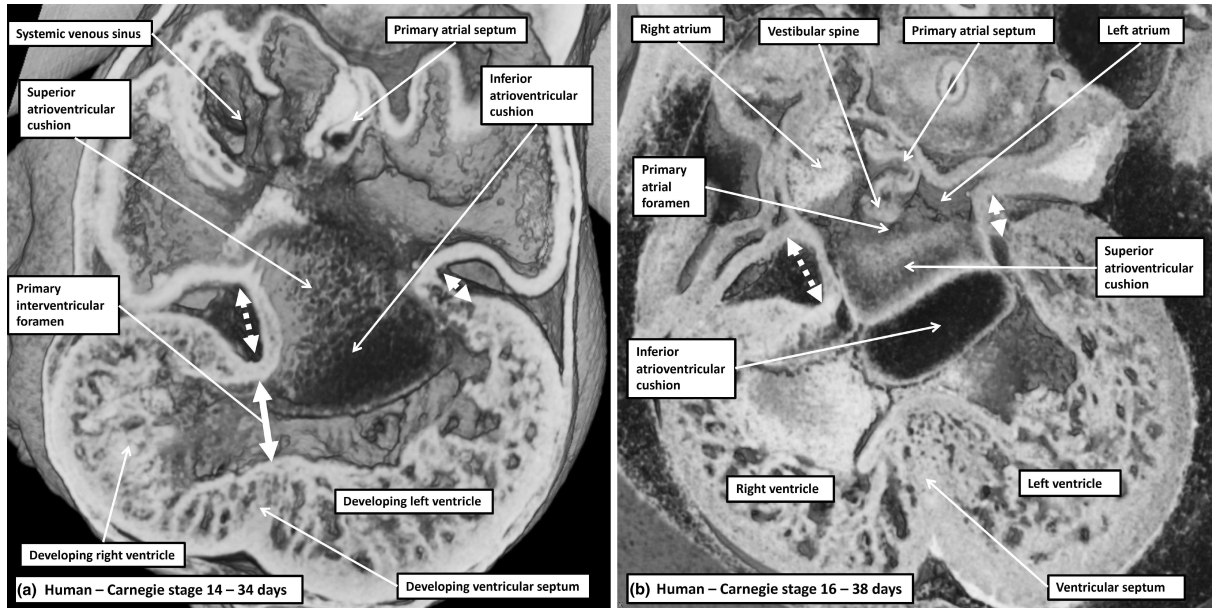
## 2 | DEVELOPMENT OF THE LEFT VENTRICLE

As we emphasised when describing the development of the right ventricle (Crucean et al., 2023), the relevance of interpretations depends very much on the quality of the material available for study. We have again based our interpretations on the examination of datasets from human hearts prepared using the three-dimensional technique of high-resolution episcopic microscopy (Mohun & Weninger, 2011). We have access, however, to only a limited number of human datasets. Where appropriate, therefore, we have also taken advantage of our access to a much greater number of murine datasets. We have then supplemented the three-dimensional material by interrogating additional datasets prepared by standard serial histological sectioning the material is now available via the Human Developmental Biology Resource (Gerrelli et al., 2015). We also have the advantage of the interactive pdf files created to show the development of the human heart throughout the embryonic period (Hikspoors et al., 2022). Many of the changes producing the final arrangement of the components of the left ventricle, however, do not become evident until after the end of embryonic development. We

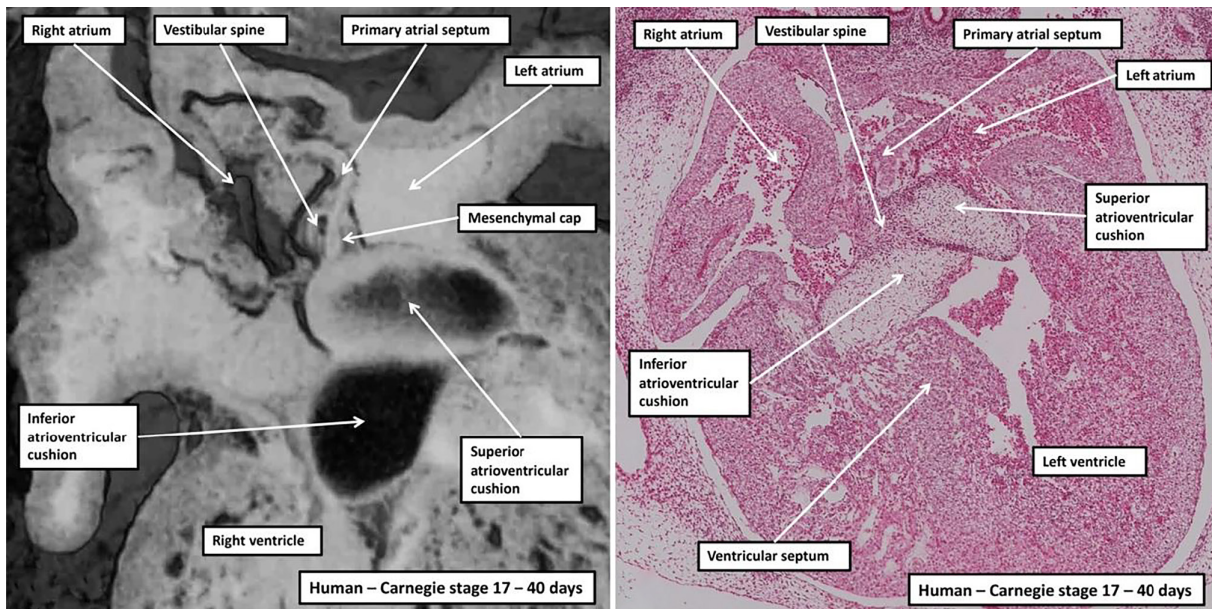
also assessed, therefore, the histological datasets prepared to show the changes occurring during the foetal period.

It is the looping of the primary heart tube that sets the scene for ventricular development (Hikspoors et al., 2022). This process occurs at the start of the fifth week of development, subsequent to fertilisation in humans. It coincides with the eleventh of the stages identified in the Carnegie series. In the mouse, the ventricular loop can be recognised on embryonic day 9.5. The primordiums of the ventricular apical components 'balloon' from the outer curvature of the loop. The apical part of the developing left ventricle, initially with thin walls and filled with trabeculations balloons from the inlet of the loop, with the apical part of the right developing from the outlet part. With the formation of the apical ventricular components, it becomes possible to recognise the primordium of the ventricular septum between them (Figure 1a). At the early stages of development, the atrioventricular canal, which provides communication with the developing atrial chambers, is supported exclusively by the developing left ventricle, while the outflow tract is supported exclusively by the developing right ventricle (Figure 1a). So as to produce the definitive chambers, therefore, it is necessary for the right ventricle to acquire its own inlet component, whilst part of the outflow tract must be transferred to the developing left ventricle to provide its subaortic outlet. At the initial stage, all the blood entering the loop and reaching the outflow tract must pass through the embryonic interventricular communication (Figure 1a). It follows that, with ongoing development, there needs to be significant remodelling of the boundaries of the primary foramen (Anderson et al., 2019).

Expansion of the atrioventricular canal provides the right ventricle with its inlet (Figure 1b; Kim et al., 2001; Lamers et al., 1992). The expansion is observed during the sixth week of development in the human heart, represented by Carnegie stages 15 and 16. The changes in the mouse hearts are seen during embryonic day 11.5. The expansion serves to take the atrioventricular endocardial cushions across the crest of the apical muscular septum (Figure 1b). During this process, the cushions themselves overlap and fuse. Subsequent to fusion, the greater part of the mass of the cushions remains above the cavity of the developing left ventricle. Having fused with one another and bridged the septal crest, the inferior parts of the cushion mass also fused with the septal crest, thus obliterating the inferior part of the primary interventricular communication. Over the same period, additional cushions have formed in the parietal walls of both the newly formed right and left atrioventricular orifices. The atrioventricular canal myocardium itself will eventually be sequestered on the atrial side of the area of atrioventricular insulation, becoming the vestibules of the developing atrial chambers. As part of these changes, the primary atrial septum, carrying on its leading edge a mesenchymal cap, grows towards the atrial surface of the fusing superior and inferior atrioventricular cushions. Eventual fusion of the cap with the superior cushion obliterates the primary interatrial foramen. The rightward side of the fused cushions and the mesenchymal cap is then reinforced by the growth into the cavity of the right atrium from the pharyngeal mesenchyme of the structure known as the vestibular spine, or the dorsal mesenchymal protrusion (Figure 2; His, 1880; Kim et al., 2001; Snarr et al., 2007).



**FIGURE 1** The images are taken from three-dimensional episodic datasets prepared from human embryos at (a) Carnegie stages 14 (SID1238) and (b) 16 (SID2100). Each image shows a 'four chamber' cut through the atrioventricular canal, as shown by the dashed double-headed arrows. At Carnegie stage 14, the canal is supported exclusively above the cavity of the developing left ventricle, such that all the blood from the atrial chambers must traverse the primary interventricular communication (double-headed solid white arrow) to reach the outflow tract, which is supported above the cavity of the developing right ventricle. By Carnegie stage 16, the canal has expanded to provide the right ventricle with its own inlet. The SID numbers indicate the dataset as prepared by Dr. Mohun.



**FIGURE 2** The left-hand panel is another 'four chamber' section from a three-dimensional episodic dataset, this time from a human embryo at Carnegie stage 17 (SID2096). It shows how the mesenchymal cap carried on the leading edge of the primary atrial septum has fused with the superior atrioventricular cushion to obliterate the primary atrial foramen. The right hand panel is a similar four chamber section, but from a histological dataset from an embryo again at Carnegie stage 17. It shows how the vestibular spine has reinforced the site of fusion of the atrioventricular cushions.

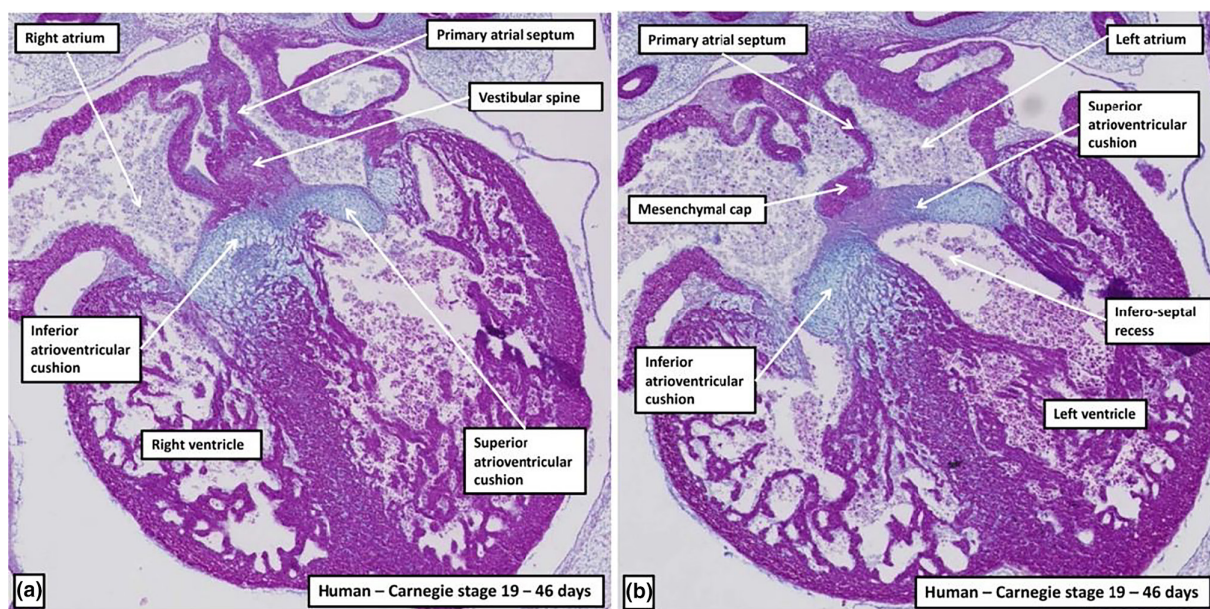
By the middle of the seventh week of development in the human heart, therefore, and during embryonic day 12.5 in the mouse, the right ventricle has acquired its own inlet. This is well seen at Carnegie stage 19, when the atrioventricular cushions have bound themselves

across the inferior part of the apical ventricular septum. By this time, the vestibular spine and mesenchymal cap have themselves muscularised to form the antero-inferior buttress of the atrial septum. This newly formed septal component is the true second atrial septum. It

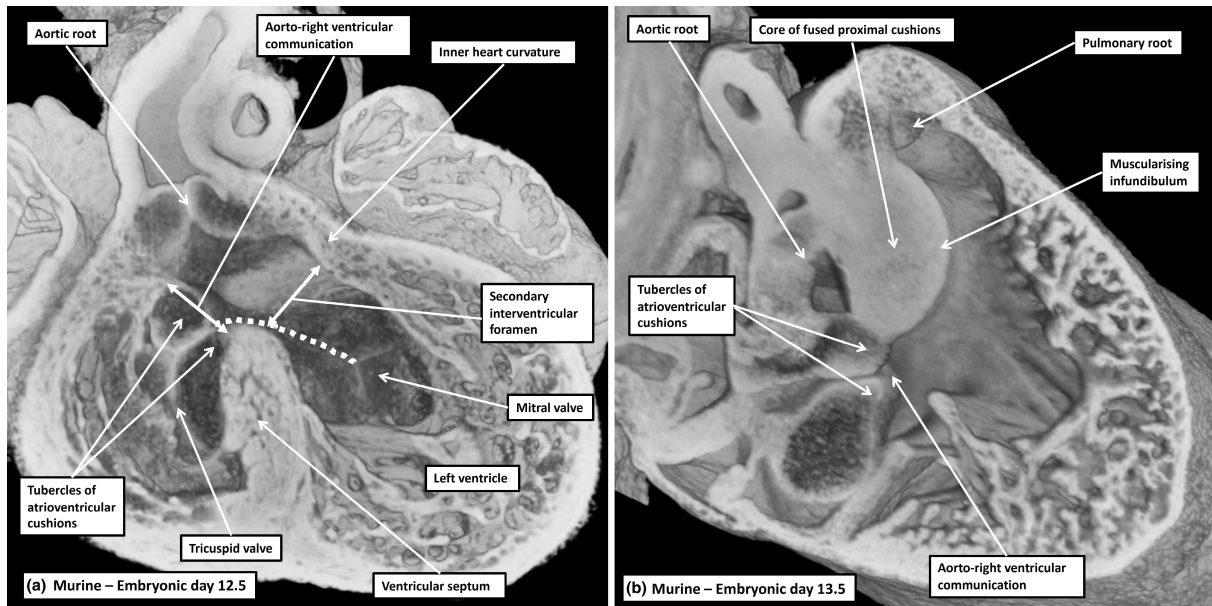
is off-set relative to the crest of the muscular ventricular septum. It is supported on the atrial aspect of the fused atrioventricular cushions, but specifically by the parts of the cushions that retain their relationship with the cavity of the left ventricle rather than the crest of the ventricular septum. This arrangement produces a significant space within the cavity of the left ventricle interposed between its septal surface and the leaflets of the developing mitral valve (Figure 3). This is the infero-septal recess (Tretter et al., 2022). With regard to the mitral valve itself, the initial trabeculations that formed the larger part of the ventricular wall are beginning to coalesce to form the papillary muscles, but with minimal formation as yet of the mural leaflet of the valve (Figure 3). At this stage, the developing right ventricle continues to support the entirety of the outflow tract.

The transfer of the separating aortic root to the developing left ventricle depends on the changes that have occurred during the same period within the outflow tract itself. The initial processes depend on the growth of the aortopulmonary septum from the dorsal wall of the aortic sac to separate the distal part of the outflow tract into the intrapericardial aortic and pulmonary trunks (Anderson et al., 2012). Over the same period, cushions have formed within the middle and proximal parts of the outflow tract (Anderson et al., 2024). The distal parts of these cushions fuse with each other and with the aortopulmonary septum to produce the primordiums of the developing aortic and pulmonary roots. The proximal parts of the cushions are initially attached to the septal and parietal walls of the right ventricle. As they fuse, they create a partition in the cavity of the right ventricle. At this stage, it is the secondary interventricular foramen that provides the outflow for the left ventricle itself (Figures 4a and 5a).

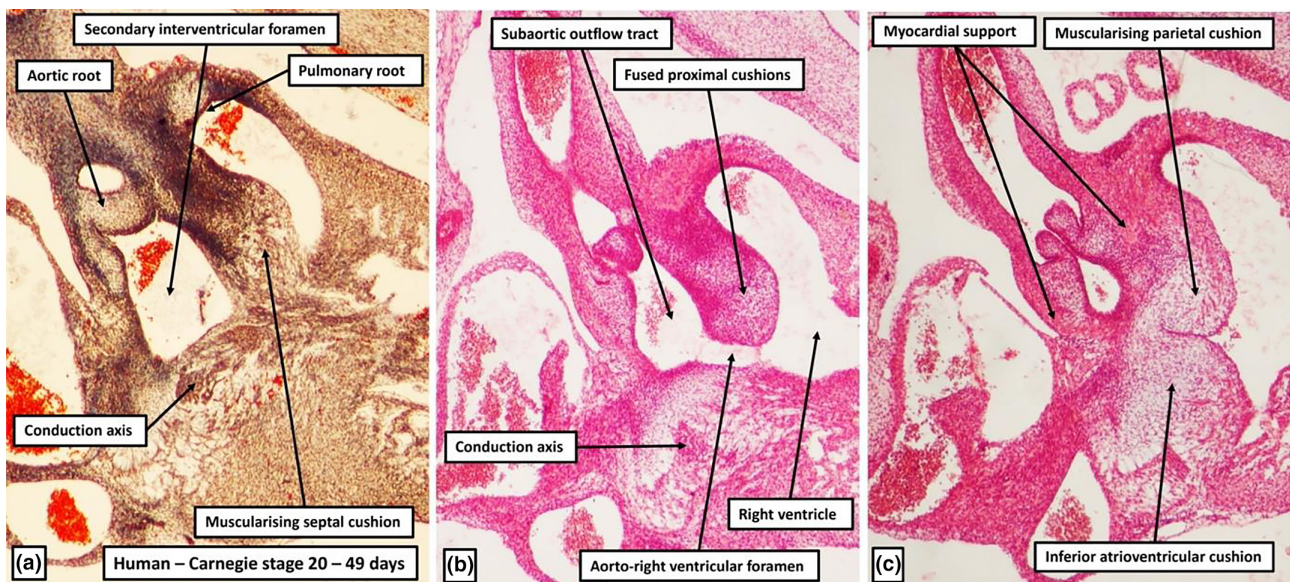
A communication remains with the developing aortic root, nonetheless, which is caudal to the partition formed within the right ventricle (Figures 4a and 5b). This aorto-right ventricular communication can also be considered to represent a tertiary interventricular foramen (Anderson et al., 2019). During the sixth week in the human heart and on embryonic day 13.5 in the murine heart, the outflow cushions begin to muscularise. Muscularisation distally provides myocardial support for the developing adjacent leaflets of the aortic and pulmonary valves. Muscularisation of the shell, as opposed to the core, of the proximal outflow cushions, in contrast, produces the myocardium that will become the free-standing infundibular sleeve of the right ventricle (Figure 4b). As the non-myocardial walls of the valvar sinuses begin to develop, there is a regression of the distal myocardial border towards the ventricular base. At the same time, the core of the fused proximal cushion mass is changed to become the fibro-adipose tissue that interposes between the myocardial wall of the subpulmonary infundibulum and the arterial walls of the adjacent sinuses of the aortic root (Figures 4b and 5a). The communication that was initially present between the developing aortic root and the cavity of the right ventricle, now forming the tertiary interventricular foramen, is closed by the rightward margins of the fused atrioventricular cushions (Figure 6). Odgers described these protuberances from the cushions in 1938 and named them the tubercles. These tissues then remodel to form the membranous part of the ventricular septum. The closure of the aorto-right ventricular communication completes the process of ventricular septation. At the stage at which septation is completed, which is during the eighth week of development in the human heart, in other words, at



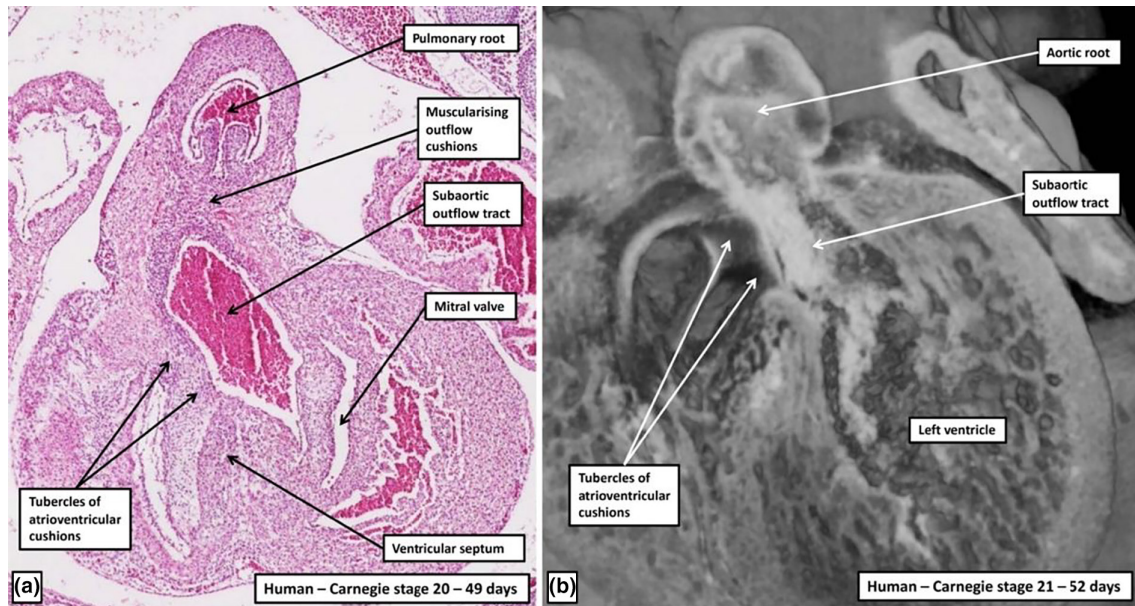
**FIGURE 3** The images show serial 'four chamber' sections from a histological dataset prepared from a human embryo at Carnegie stage 19. Panel (a) is dorsal to panel (b). The sections are stained using the Periodic Acid Schiff technique, which differentiates between the developing cushions and the myocardium. The images show how the larger parts of the fused atrioventricular cushions remain above the cavity of the left ventricle, forming the roof of an infero-septal recess of the left ventricular cavity. The images also show muscularisation of the vestibular spine and mesenchymal cap, producing the antero-inferior buttress of the atrial septum, which inserts on the atrial surface of the fused atrioventricular cushions.



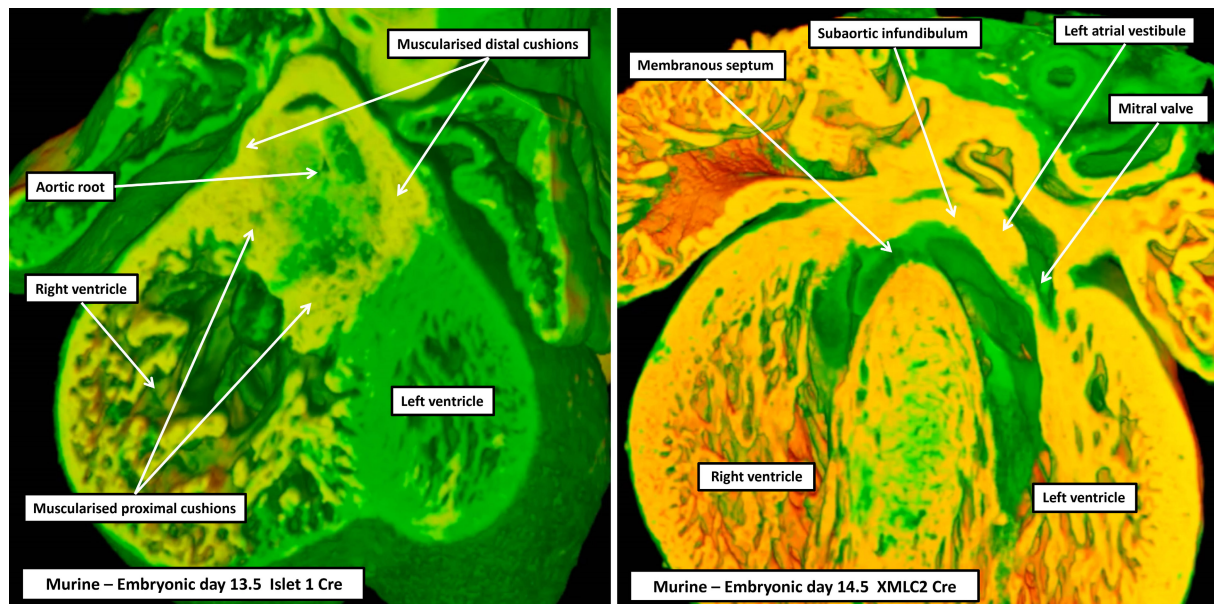
**FIGURE 4** The images are taken from episcopic datasets prepared from murine embryos sacrificed at (a) embryonic day 12.5 (SID1325) and (b) 13.5 (SID1327). The panel (a) is a four chamber section through the aortic root, showing the secondary interventricular foramen, which provides the outlet for the left ventricle, and the persisting communication between the aortic root and the right ventricle, bordered caudally by the so-called tubercles of the atrioventricular cushions. The white dashed line shows the line of fusion between the cushions. Panel (b) shows how, with ongoing development, the tubercles of the cushions have almost closed the aorto-right ventricular communication. The image also shows how the shell of the fused proximal cushions is muscularising. It will become the free-standing infundibular sleeve of the right ventricle, with the core of the fused cushions attenuating to produce the extracavitary tissues between the infundibular and the aortic root.



**FIGURE 5** The images show serial sagittal sections from a histological dataset prepared from a human embryo at Carnegie stage 20. The cuts replicate the so-called oblique subcostal plane used by echocardiographers to show the outflow tract of the right ventricle. Panel (a) was stained to show developing fibrous tissues, whereas panels (b, c) are stained with haematoxylin and eosin. The panels show how the fused outflow cushions build a partition within the cavity of the right ventricle, sequestering part of the cavity as the subaortic outflow tract. Closure of the aorto-right ventricular foramen will commit the aortic root to the left ventricle through the secondary interventricular foramen. Panel (c) shows how the inferior atrioventricular cushion, which will form the larger part of the septal leaflet of the tricuspid valve, overlaps the inferior part of the muscular ventricular septum.



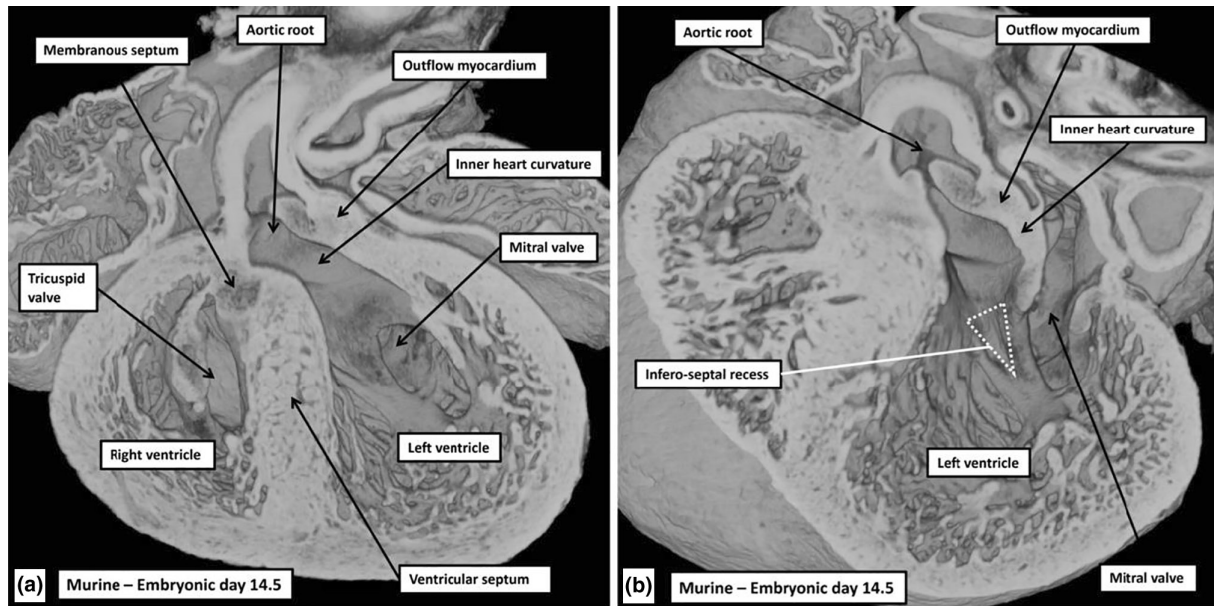
**FIGURE 6** The images are from human embryos at Carnegie stage 20 (a) and stage 21 (b). Panel (a) is from a histological dataset stained with haematoxylin and eosin, whereas panel (b), in the same frontal orientation, is from an episcopic dataset (SID1653). The images show how the tubercles of the atrioventricular cushions have closed the aorto-right ventricular communication. They will remodel to become the membranous septum. Panel (a) also shows how, at this stage, there has been minimal inferior expansion of the developing tricuspid valve, which is bifoliate at this stage of development.



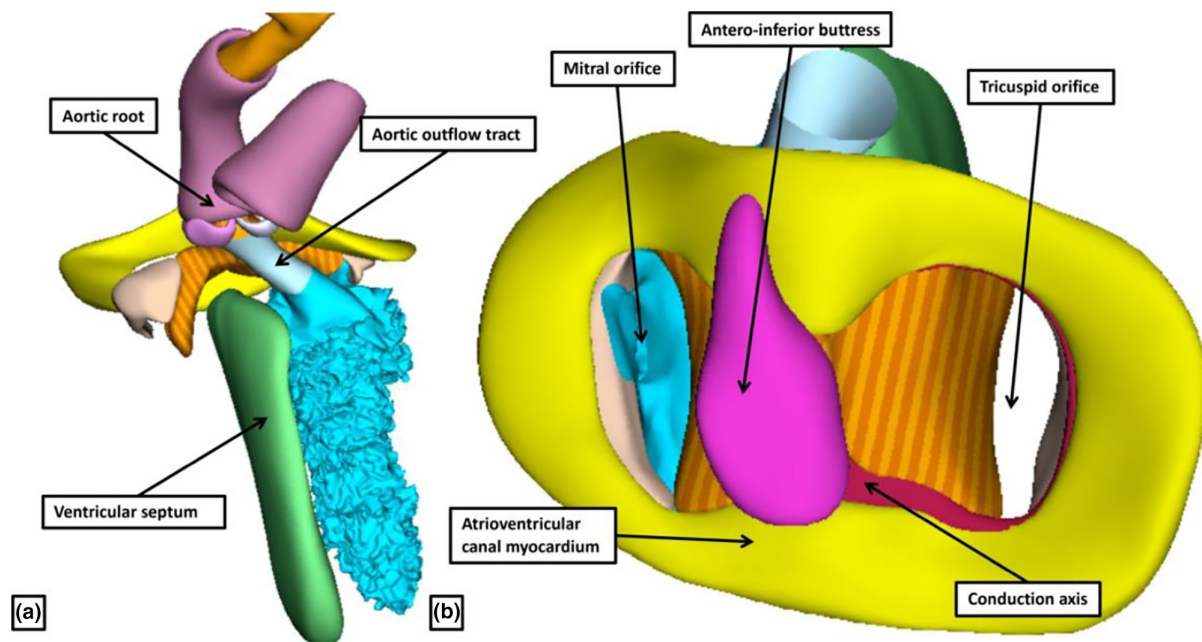
**FIGURE 7** The images are taken from murine embryos programmed to show the location of either Islet-1, a marker for the second heart field (left hand panel: SID3274) or myocardium (right hand panel: SID3556). The yellow tissues in the left hand panel show how the muscularised parts of the proximal outflow cushions are building the partition in the right ventricle to commit the aortic root to the left ventricle through the secondary interventricular communication, as shown in [Figure 6](#), with the muscularised distal cushions supporting the developing leaflets of the aortic root. The right hand panel shows how, subsequent to the transfer, and formation of the membranous septum, the aortic root is still supported by a muscular infundibulum. Note how the trabeculations are coalescing to produce the papillary muscles of the mitral valve.

the end of the embryonic period, and during embryonic day 14.5 in the murine heart, the aortic root, having been committed to the left ventricle, remains supported by a completely muscular infundibulum

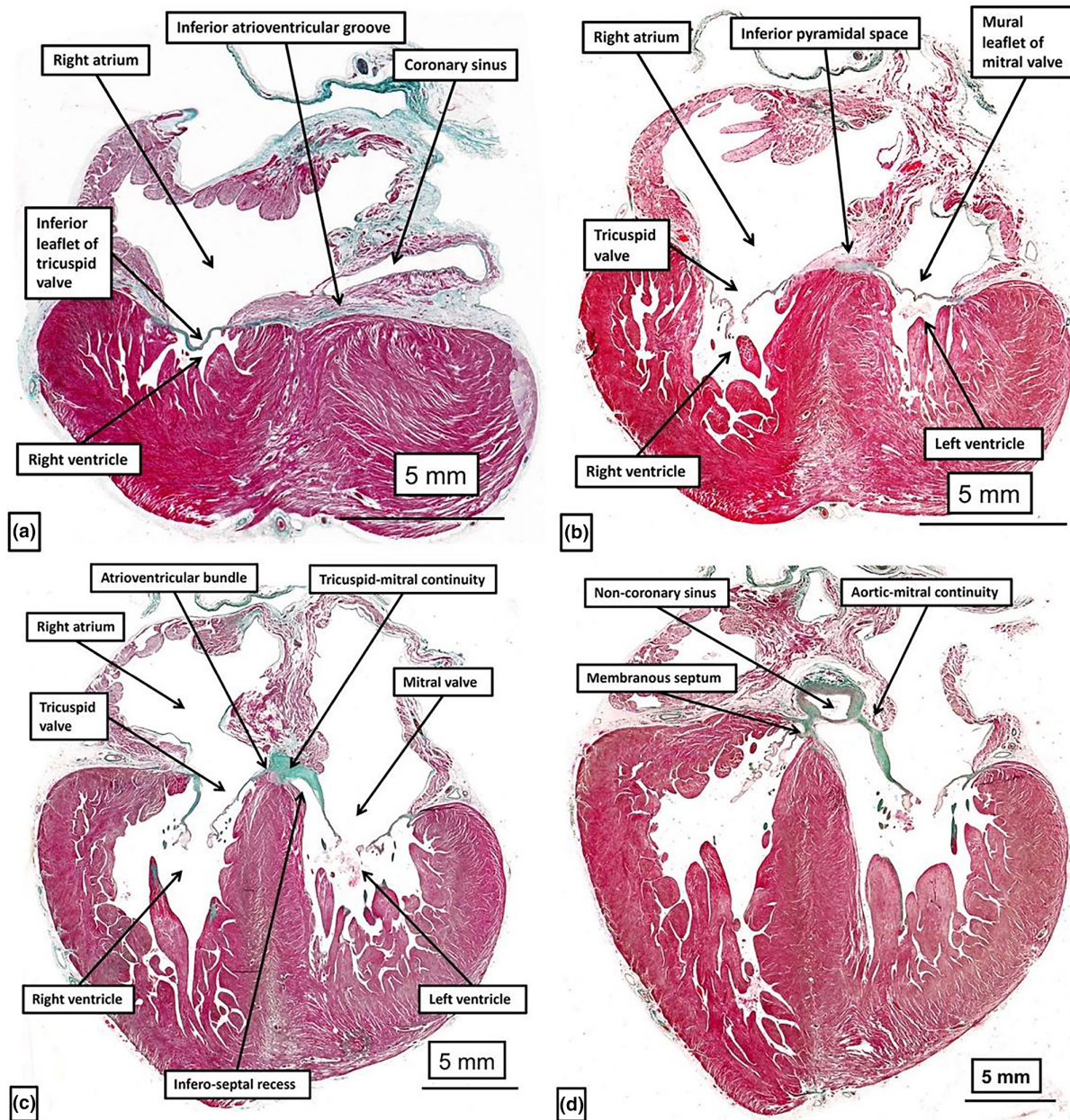
([Figure 7](#)). The part of the proximal outflow tract supporting the developing adjacent sinuses of the aortic root, which give rise to the coronary arteries, is formed by muscularisation of the distal extent



**FIGURE 8** The images, taken from the same episcopic dataset prepared from a murine embryo at embryonic day 14.5 (SID1361A), show the complete infundibulum that supports the aortic root immediately subsequent to its transfer to the left ventricle. Panel (a), a four-chamber section, shows how the infundibulum is formed parietally by the outflow myocardium derived by muscularisation of the distal outflow cushion supporting the left coronary aortic valvar sinus, and caudally by the inner heart curvature. Panel (b) is angled to show the persisting infero-septal recess formed between the aortic leaflet of the mitral valve and the septum.



**FIGURE 9** The panels are produced from an interactive pdf file prepared from a human embryo at Carnegie stage 23, which is the end of the embryonic period after 8 weeks of development. Although the aortic root has by now been transferred to the left ventricle, as shown in the frontal projection in panel (a), it remains supported above the cavity of the right ventricle and the crest of the muscular ventricular septum. And, as shown in panel (b) the atrioventricular junctions retain a common configuration, even though they are separated into mitral and tricuspid valvar orifices. The atrioventricular conduction axis emerges at the crux, and the atrioventricular orifices have yet to expand to form their definitive configurations.



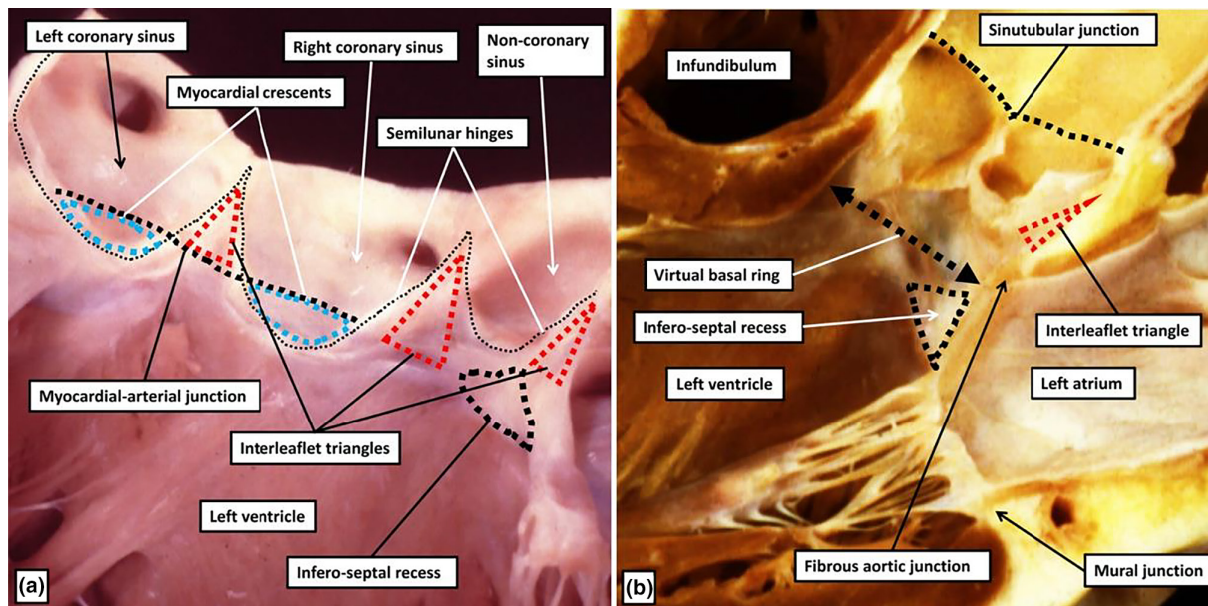
**FIGURE 10** The images show serial frontal histological sections taken from a dataset prepared from a human foetus at 21 weeks of gestation. The sections are stained using Masson's trichrome technique, which differentiates the myocardial and fibrous tissues. Panel (a) is taken through the inferior part of the ventricular, with the sections extending superiorly from (b) through (d). They show how, subsequent to the end of the embryonic period, there have been inferior expansions of both the tricuspid valvar orifice, producing its inferior leaflet, as shown in panel (a), and the mural leaflet of the mitral valve, as shown in panel (b). The expansion of the atrioventricular junctions encloses the inferior pyramidal space between the vestibules of the atrioventricular valves (b). Panel (c) shows the area of fibrous continuity between the leaflets of the tricuspid and mitral valves, formed from the fused atrioventricular cushions, which provides the roof of the infraseptal recess. Panel (d) shows the non-coronary sinus and the area of aortic-to-mitral valvar fibrous continuity. The fibrous tissue, stained green, now replaces the initially muscular infundibulum that supported the aortic root subsequent to its initial transfer to the left ventricle (see Figures 6 and 7).

of the major outflow cushions. The part supporting the non-adjacent sinus, in contrast, is part of the wall of the distal part of the outflow tract that retained its myocardial phenotype during the maturation of the arterial roots (Figure 8).

At the end of the embryonic period of development in humans, although ventricular septation has been completed and the cavity

of the aortic root has been incorporated as part of the left ventricle, the anatomical relationships are far from definitive. This is because the aortic root, although now part of the left ventricle, is positioned above the crest of the ventricular septum and the cavity of the right ventricle. And the atrioventricular junctions, although separated from each other, retain a common configuration (Figure 9). The





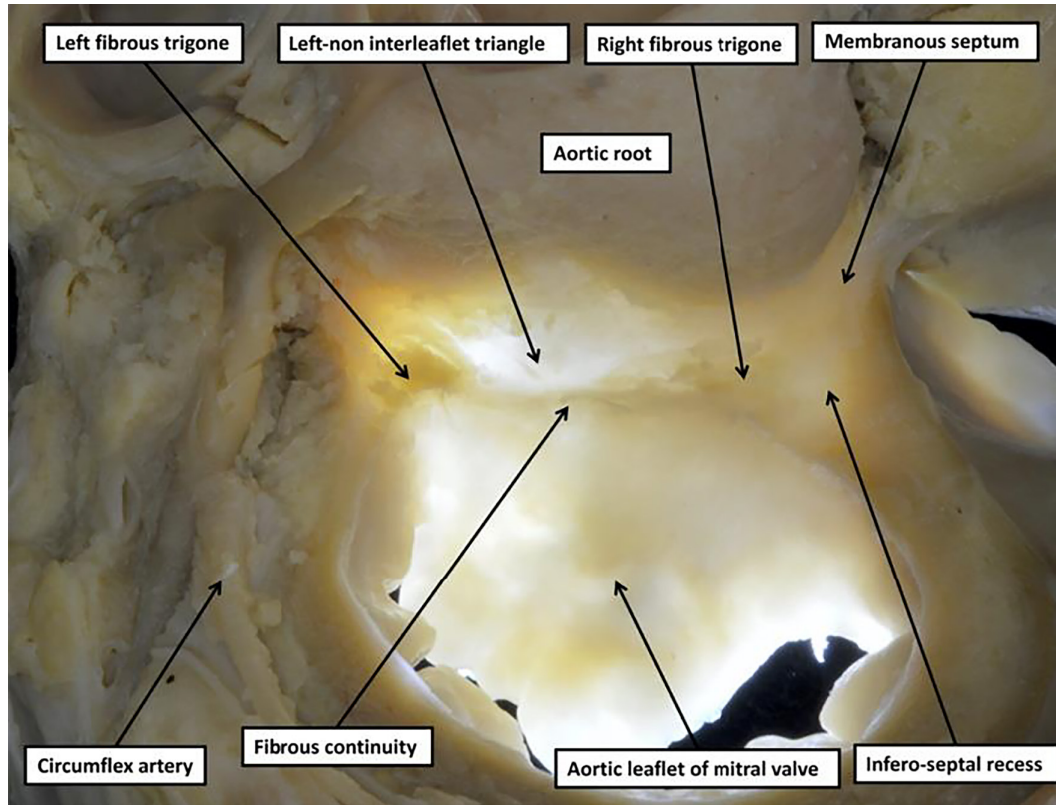
**FIGURE 11** The images show the boundaries of the adult human left ventricle in greater detail. Panel (a) shows the arrangement at the myocardial-arterial junction, having divided the aortic root from the intrapericardial aorta at the level of the sinutubular junction and removed the aortic valvar leaflets to show their semilunar hinges. All three interleaflet triangles can be seen to extend to the sinutubular junction. A myocardial-arterial junction is found only at the bases of the sinuses, giving rise to the coronary arteries, with the myocardium forming small crescents within the walls of the sinuses. Panel (b) is a simulation of the echocardiographic parasternal long axis section, showing the continuity between the atrioventricular junction and the aortic root in the inner heart curvature. The cavity of the outflow tract extends inferiorly as the infero-septal recess, and superiorly as the interleaflet triangle between the non-coronary and left coronary aortic valvar sinuses.

additional changes that take place subsequent to Carnegie stage 23, during the early weeks of foetal development, involve expansion of the atrioventricular orifices and attenuation of the muscular subaortic infundibulum. The details of these changes have yet to be investigated. By 21 weeks of gestation, nonetheless, it is possible to recognise the inferior leaflet of the tricuspid valve (Figure 10a), with the mural leaflet of the mitral valve also having been remodelled such that it now guards two-thirds of the orifice of the mitral valve (Figure 10b). The inferior expansion of the junctions has resulted in part of the inferior atrioventricular groove becoming incorporated into the atrioventricular junctions as the space initially described by Sealy and colleagues and named by them as the inferior pyramidal space (Sealy & Gallagher, 1980; Tretter et al., 2022). The atrioventricular conduction axis now penetrates into the ventricular mass in the midportion of the atrioventricular junctions (Figure 10c) rather than at the crux, as was the situation at the end of the embryonic period (Figure 9b). The aortic root is now further wedged between the aortic leaflet of the mitral valve and the septum by virtue of the remodelling of the inner heart curvature and the aortic root. This process has now produced the fibrous continuity between the leaflets of the aortic and mitral valves (Figure 10d). With all these changes, the tissues of the initial atrioventricular cushions have produced the so-called central fibrous body, which is made up of the roof of the infero-septal recess, the membranous septum and the right fibrous trigone, with the right trigone defined as the rightward end of the area of continuity between the leaflets of the mitral and aortic valves. The initial myocardial walls that surrounded the aortic

root during its development also attenuate. Subsequent to these changes, the non-myocardial interleaflet triangles, which interpose between the non-coronary sinus and the sinuses giving rise to the coronary arteries, separate the extensions of the left ventricular outflow tract from the pericardial space (Sutton et al., 1995). The triangle formed between the coronary aortic sinuses themselves, in contrast, separates the cavity of the left ventricle from the fibroadipose tissues now formed between the free-standing infundibular sleeve of the right ventricle and the aortic root. The newly formed myocardium that supported these sinuses during the transfer of the root to the left ventricle nonetheless persists at their base as part of the crest of the muscular ventricular septum (Anderson et al., 2024; Toh et al., 2020).

### 3 | THE ANATOMY OF THE DEFINITIVE LEFT VENTRICLE

When considering the anatomy, we concentrate exclusively on the arrangement as found in the human heart. As we discussed in our introduction, problems exist in defining the extent of the left ventricle. Not all of its walls are myocardial. Parts of the walls of its outlet component, which incorporates the aortic root, are made up of fibrous tissues (Figure 11a). These are the triangles that interpose between the arterial valvar sinuses that support the semilunar leaflets of the aortic valve (Anderson, 2000; Sutton et al., 1995). These triangles extend to reach the sinutubular junction. The overall walls



**FIGURE 12** The myocardial walls of the left atrium of an infant human heart have been removed to show the continuity between the aortic root and the left atrioventricular junction in the inner curvature of the heart. The dissection has then been transilluminated from the cavity of the left ventricle to show the arrangement of the fibrous tissues formed by the continuity between the leaflets of the aortic and mitral valves. The area of fibrous continuity is thickened at its ends to form the left and right fibrous trigones. The right trigone is then continuous with the fibrous roof of the infero-septal recess, which is bounded on its right side by the fibrous membranous septum.

enclosing the cavity of the left ventricle, therefore, extend from the atrioventricular to the sinutubular junctions (Figure 11b). The myocardial walls of the left ventricle, in contrast, do not reach the sinutubular junction. The myocardium of the ventricular septum, however, is found only at the bases of the aortic valvar sinuses that give rise to the coronary arteries and also at the base of the intervening interleaflet triangle (Figure 11a). A major feature of the left ventricle, therefore, distinguishing it from its morphologically right counterpart, is that hardly ever does the chamber possess a completely myocardial infundibulum. Instead, the leaflet supported by the non-coronary sinus of the aortic root, along with part of the left coronary aortic leaflet, is in fibrous continuity in the inner heart curvature with one of the leaflets of the mitral valve (Figures 11b and 12). The chamber thus formed, nonetheless, can still be described in terms of possessing inlet, apical, and outlet components, with the outlet component supporting the aortic root (Figure 13). Because of the contiguity between the inlet and outlet components in the inner heart curvature (Figure 12), it is also the case that only part of the atrioventricular junction has myocardial support (Figure 11b). Within this mural atrioventricular junction, the vestibule of the left atrium is separated by the fibro-adipose tissues of the inferior atrioventricular groove from the summit of the ventricular myocardial cone

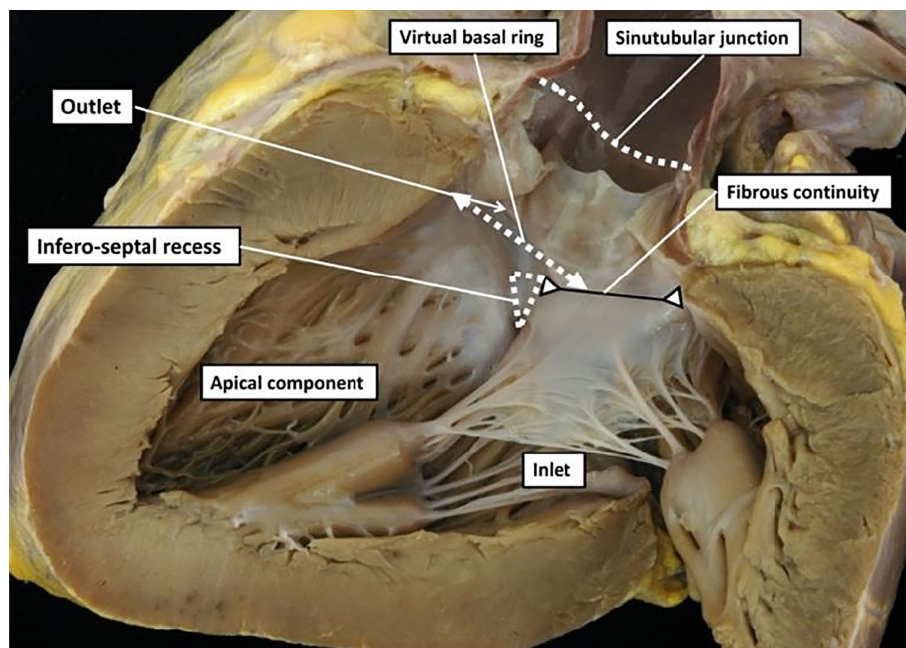
(Figure 11b). When the ventricular cavity is viewed from the apex looking towards the base, the fibrous continuity between the leaflets of its inlet and outlet valves can be seen to form its roof (Figure 14). The orifices of the two valves overlap within the roof. The extensive infero-septal recess of the outflow tract then interposes between the aortic, or anterior, leaflet of the mitral valve and the inferior extension of the muscular ventricular septum (Figure 15). The fibrous roof of the recess is itself continuous with the rightward end of the area of fibrous continuity between the leaflets of the mitral and aortic valves, which we defined as the right fibrous trigone (Figure 12). The atrioventricular component of the fibrous membranous septum forms the right wall of the recess (Figure 15). When traced inferiorly, the apex of the recess overlaps the superiorly directed apex of the inferior pyramidal space. This space is the area on the atrial side of the atrioventricular junctions, enclosed by the diverging vestibules of the right and left atrial chambers. By virtue of the overlap, the atrioventricular conduction axis is able to penetrate the fibrous insulating tissues to reach its position on the crest of the muscular ventricular septum, where it branches to give rise to its right and left fascicles (Figure 16).

The mitral valve guards the ventricular inlet (Figure 13). Its leaflets are attached within the atrioventricular junction, albeit

with no continuous fibrous 'annulus' supporting their hinges. One of the leaflets is tethered within the mural part of the atrioventricular junction (Figure 17a). In some places, the hinge of the leaflet is provided by a fibrous cord, which also provides the atrioventricular insulation. Within other parts of the junction in the same heart, the leaflet can be tethered by a fibrous sheet, which separates the leading edge of the left atrial vestibule from the crest of the parietal wall of the ventricle. This is the arrangement described as a mitral annular disjunction. As was shown by Henle in the 19th century, such support by a fibrous sheet is part of the normal arrangement (1888). In other parts of the same junction, the leaflet is hinged directly to the ventricular wall. It is the fibro-adipose tissue of the junction that then provides the atrioventricular insulation (Angelini et al., 1988). These variations are to be found to different degrees in all hearts. Their presence as a normal finding calls into question the emphasis currently placed on such disjunction as a pathological feature (Anderson et al., 2023). The leaflets themselves close together along a solitary zone of apposition. They guard unequal parts of the valvar orifice. The mural leaflet guards approximately two-thirds of the circumference, wrapping around the second leaflet at the ends of the zone of apposition (Figure 17a). The second leaflet is the one that is in fibrous continuity with the non-coronary and left coronary leaflets of the aortic valve (Figure 12). It guards only one-third of the valvar circumference. In the normal human heart, by virtue of its relation to the aortic root, it is well described as the aortic leaflet, although,

as indicated above, it is usually described as being 'anterior', with the mural leaflet then described as being 'posterior'. When viewed attitudinally, the mural leaflet wraps around the aortic leaflet at the ends of the zone of apposition between them (Figures 14 and 17a). Not all parts of the leaflet, therefore, are strictly 'anterior'. Although the leaflet is well described as being 'aortic' in the setting of concordant atrioventricular connections, in hearts with discordant ventriculo-arterial connections, the leaflet would be described as being 'pulmonary', and it would be 'truncal' in the setting of common arterial trunk. It is only when there are bilateral infundibulums, as is often the case in the double outlet right ventricle, that it is more accurate to describe the leaflet as being 'anterior'.

With regard to the mural leaflet, it has now become conventional to describe it as having three 'scallops' (Carpentier, 1983). There is, however, marked variation in the arrangement of these individual parts. It is the presence of multiple slits in the overall skirt of leaflet tissue that permits the two leaflets to fit snugly when closed (Victor & Nayak, 1994). The ends of the solitary zone of apposition do not reach the atrioventricular junction. Additional components of the skirt guard the so-called commissural areas (Figure 17a; Kumar et al., 1995). When the atrioventricular junction is opened, and the skirt of leaflet tissue spreads, it becomes obvious that, although the two leaflets guard dissimilar proportions of the valvar orifice, they have comparable areas. This is because the aortic leaflet is deep, whereas the components of the mural leaflet, including the

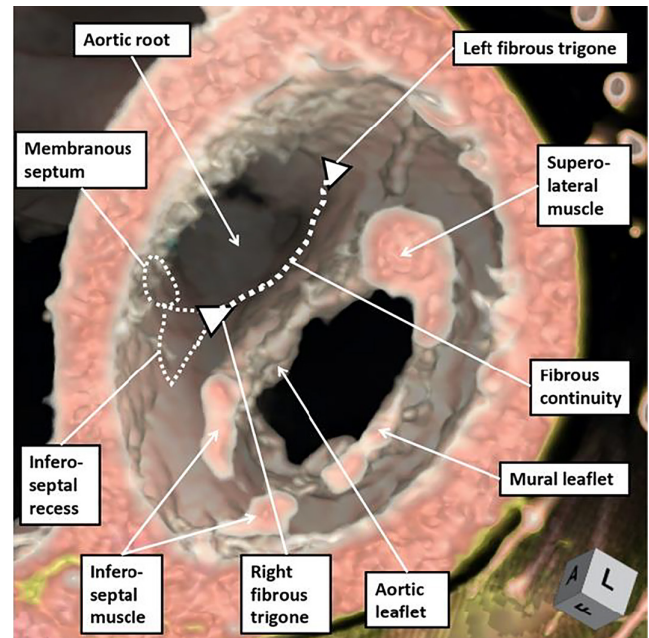


**FIGURE 13** The image shows how the left ventricle of the human heart can be assessed in terms of its inlet, apical and outlet components. The ventricle has been opened through a superior incision parallel to the anterior interventricular groove. The roof of the ventricle is formed by the area of fibrous continuity between the leaflets of the aortic and mitral valves, which is thickened at its ends to form the right and left fibrous trigones (white triangles with black borders). The outlet component is complex, extending beyond the so-called echocardiographic 'annulus', which in reality is no more than a virtual basal ring, to reach the level of the sinutubular junction. Note the infero-septal recess of the outflow tract, which interposes between the leaflets of the mitral valve and the septum.

commissural zones, are shallow (Figure 17b). The leaflets are supported by tendinous cords along the entirety of their free edges. The free-edge cords tether the leaflets to the papillary muscles, which are located infero-septally and supero-laterally within the short axis of the ventricular cone. Additional strut cords extend from the papillary muscles to reinforce the support provided to the aortic leaflet on its ventricular surface, while multiple basal cords extend from the parietal wall of the ventricle to the ventricular surfaces of the components of the mural leaflet. Some observers have created exceedingly complex systems when seeking to categorise the tendinous cords (Lam et al., 1970). We find it sufficient simply to account for the free-edge, strut and basal cords. The free-edge cords from each of the leaflets attach to the same papillary muscle (Figure 17b). The papillary muscles themselves are anchored to the parietal ventricular walls, often with trabeculations interposed at the junction of the muscles with the compact ventricular wall (Axel, 2004).

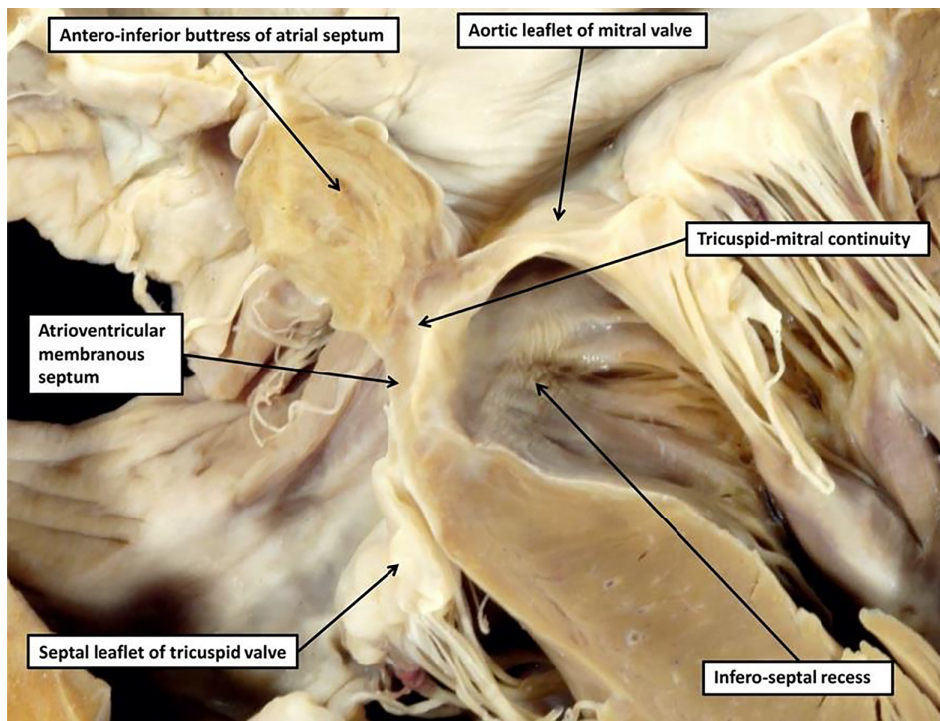
The apical part of the ventricle, as the name suggests, extends beyond the ventricular inlet to the apex of the ventricular myocardial cone. Its wall is very thin at the apical point. It has characteristic fine criss-crossing trabeculations but a smooth septal surface. The branches of the conduction axis cascade down the septal surface, with the superior and inferior fascicles running from the branching part of the central conduction axis and extending towards the papillary muscles. Branches of the fascicles cross the ventricular cavity from the septum to the papillary muscles as the false tendons (Luetmer et al., 1986). The apical part continues without any obvious anatomical boundary to become the ventricular outlet, which is limited inferiorly by the aortic leaflet of the mitral valve. As we have already shown, an extensive recess extends inferiorly between the aortic leaflet of the mitral valve and the septum (Figure 15). The presence of the fibrous triangles interposing between the semilunar leaflets of the aortic valve means that the ventricular cavity extends to the level of the sinutubular junction (Figures 11a and 18). The semilunar nature of the hinges of the valvar leaflets has created great confusion with regard to the description of a valvar 'annulus' (Sievers et al., 2012). Echocardiographers define the 'annulus' in terms of the level that can be constructed by joining together the nadirs of attachment of the semilunar leaflets. This is no more than a virtual plane (Figure 11b). In contrast, many cardiac surgeons define the semilunar remnants used for the anchorage of sutures subsequent to the removal of the leaflets during valve replacement as the 'annulus'. At the least, these remaining structures are real anatomical entities. Further confusion exists with the use of 'cusp'. Although initially used to describe the valvar leaflets, the word is increasingly used by electrophysiologists to account for the valvar sinuses. The solution to this problem is simply to avoid using 'cusp', and to describe separately the leaflets and the sinuses (Anderson et al., 2022).

It is less easy to adjudicate on which entity should be defined as the 'annulus', the more so since the most obvious ring within the aortic root is the sinutubular junction (Anderson, 2000). It is probably the dimensions of the virtual basal ring that are of most overall clinical significance. During diastole, when the valve aims to

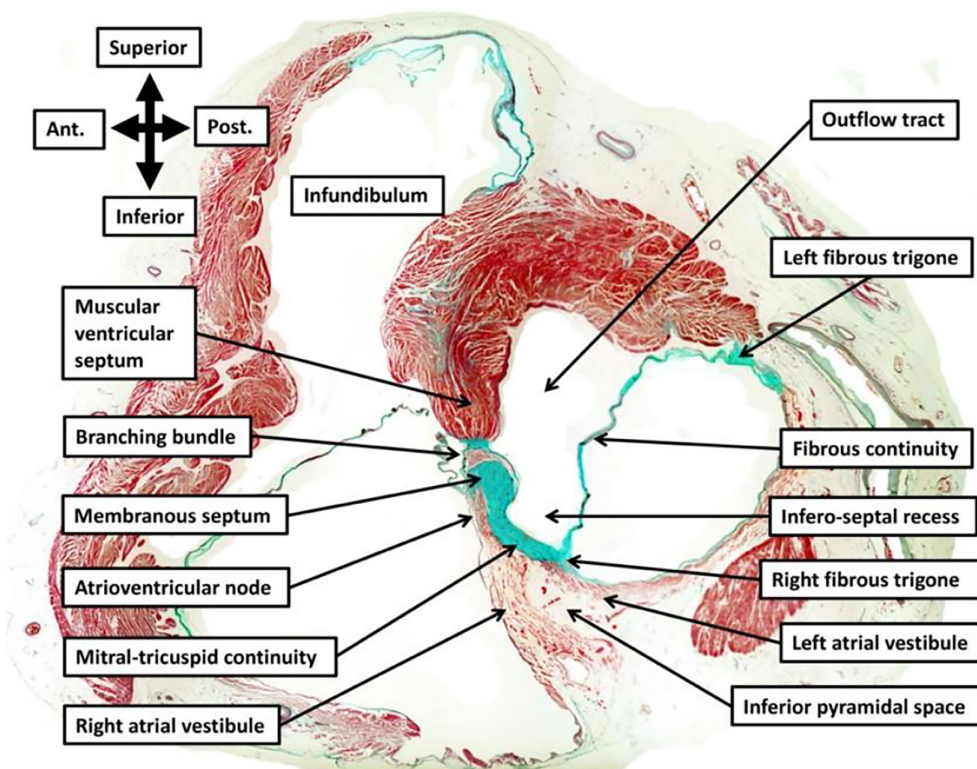


**FIGURE 14** The image is a virtual dissection from a computed tomographic dataset prepared from a normal individual. The pink colour shows the cut surfaces. The box in the bottom right hand corner shows the bodily coordinates, with A showing anterior, L left and F the feet. The image shows how the inlet and outlet components overlap when viewed within the short axis of the cone. The papillary muscles supporting the leaflets are located infero-septally and supero-laterally. It is a mistake to describe them as being 'postero-septal' and 'antero-lateral'. There is an area of fibrous continuity between the leaflets of the aortic and mitral valves. It is thickened at its ends to produce the right and left fibrous trigones, which anchor the area of fibrous continuity within the ventricular base. The right trigone is itself continuous with the infero-septal recess, which interposes between the aortic leaflet of the mitral valve and the inferior extent of the muscular ventricular septum.

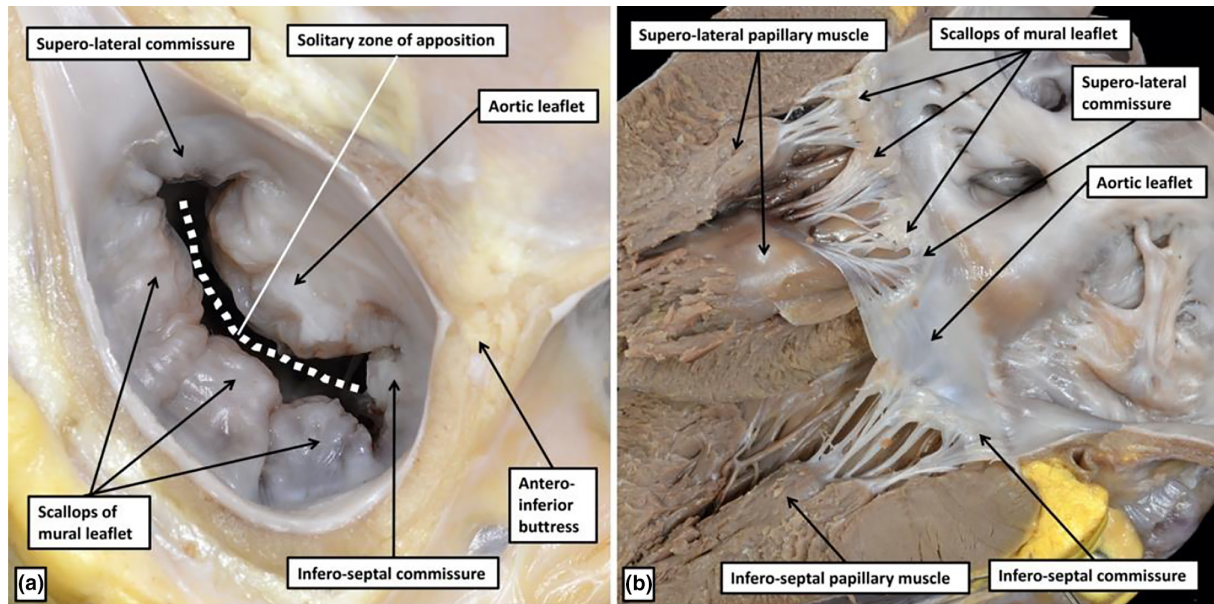
achieve competency, this plane is oval rather than circular (Tretter et al., 2023). The semilunar hinges permit the leaflets themselves to close in perfect fashion to achieve valvar competence during ventricular diastole. It is at this stage of the cardiac cycle that the leaflets come together under the influence of the arterial pressure exceeding the ventricular pressure. So as to achieve this competency, the leaflets of the aortic valve do not require the extensive tension apparatus that retains the leaflets of the atrioventricular valves in their closed position during ventricular systole. The interaction between the leaflets, the walls of the sinuses and the ventricular support is just as complex, nonetheless, as the arrangement to be found in the ventricular inlet. When the leaflets are in their closed position, the centroid of the valvar complex lies well below the level of the sinutubular junction (Figure 18a). The cavity itself, however, extends to the level of the sinutubular junction (Figure 18b). The line of closure of the leaflets is itself away from their free edge, meaning that the fenestrations often found within the lunules of the leaflets towards their edges do not produce any valvar incompetence.



**FIGURE 15** The adult heart has been sectioned to simulate the four-chamber image as produced by echocardiographers. The image shows the infero-septal recess, formed by the area of fibrous continuity between the leaflets of the tricuspid and mitral valves. It supports the antero-inferior buttress of the atrial septum. It is limited on its right side by the atrioventricular component of the membranous septum.



**FIGURE 16** The histological section, from an adult human heart, stained using Masson's trichrome technique to differentiate myocardial and fibrous tissues, and replicating the image shown in Figure 14, shows how the apex of the inferior pyramidal space overlaps the apex of the infero-septal recess. The conduction axis penetrates through the central fibrous body at the site of intersection, then branches on the crest of the muscular septum.

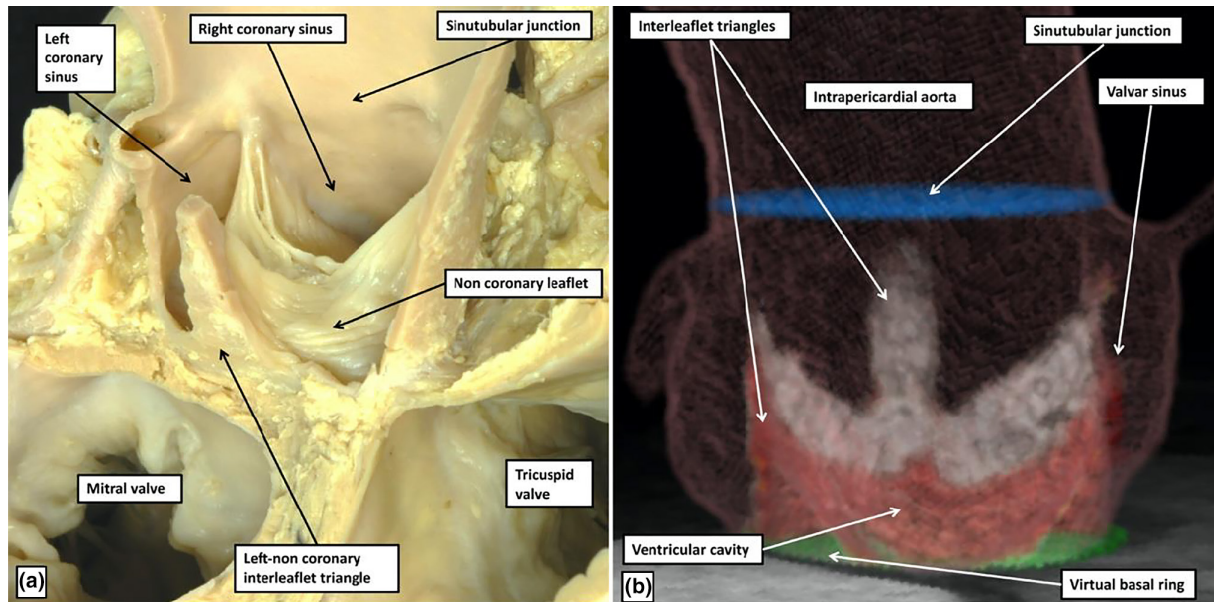


**FIGURE 17** The images show the features of the mitral valve in a heart from an infant. In panel (a), the intact junction is shown from the atrial aspect, have removed the myocardium of the left atrium. There is a solitary zone of apposition between the aortic and mural leaflets of the valve. The mural leaflet is divided by slits into its so-called scallops, but additional components of leaflet tissue are found at the commissural regions, which are the ends of the solitary zone of apposition. In panel (b), the left ventricle has been opened through the infero-septal commissure, and the mural part of the junction is reflected superiorly.

#### 4 | DISCUSSION

It is surprising that, after centuries of investigation, so many features of the left ventricle should remain potentially contentious. Some of these disagreements amongst anatomists have been self-inflicted. One of the first rules of anatomy taught to medical students is that all structures within the body should be described as viewed with the subject in anatomical position. It is a mystery, therefore, why anatomists should have chosen to describe the components of the heart as seen when it is removed from the body and positioned on its apex. Only when viewed in this unnatural position are the papillary muscles of the mitral valve located posteromedially and anterolaterally. Reverting to attitudinally appropriate descriptions is now more important, since it is arguable that the components of the left ventricle can now be displayed with just as much clarity using virtual dissection of clinically obtained datasets as when the heart is in the hands of the prosector in the dissecting room (Mori et al., 2019). The beauty of virtual dissections is that the features of the left ventricle can be revealed as they are seen in the living patient without having to distort their relationships by opening the heart. The same features can now be obtained when using Hip-CT interrogation of autopsied hearts. It is assessment in this fashion that clarifies the structure of features such as the so-called central fibrous body. The insights to be gained from current knowledge of cardiac development also contribute to clarifying the make-up of this structure. Its basis is the roof of the infero-septal recess, which can be seen from developmental evidence to be a major part of the endocardial cushions that fuse to separate the atrioventricular canal into its right and

left components. It is the tubercles of these cushions that eventually serve to close the embryonic interventricular communication. It is no surprise, therefore, that these structures, which form the membranous septum, are also part of the central body. The contributions made by the fused cushions were emphasised by Keith and Flack when they clarified their own understanding of the atrioventricular conduction axis subsequent to the publication of the stellar monograph of Tawara (1906). In their extensive letter, they also noted the presence of the myocardium supporting the aortic valvar sinuses that give rise to the coronary arteries, although at the time they admitted to being unaware of its potential significance. We now know that the myocardium is formed by the muscularisation of the distal parts of the cushions that separate the outflow tract into its aortic and pulmonary parts. We also now know that the myocardium is derived from the second heart field and is subsequently incorporated into the crest of the muscular ventricular septum (Anderson et al., 2024). Prior to the closure of the embryonic interventricular foramen, the muscularising cushion mass functions as an embryonic outlet septum, separating as it does the developing outlets of the right and left ventricles. With closure of the foramen by the tubercles of the atrioventricular cushions, the formation of fibro-adipose tissue in the core of the mass results in the shell of the mass becoming the free-standing subpulmonary infundibulum. We can appreciate the changes on the basis of the observed anatomy. As of yet, the mechanisms of formation of the fibro-adipose tissues remain to be determined. The anatomical observations also serve to show the marked variation in the formation of the hinge of the mural leaflet of the mitral valve. Again, the mechanisms of the



**FIGURE 18** Panel (a) shows a dissection of an infant heart in which the aortic root is viewed from posteriorly and to the right. The wall of the non-coronary aortic valvar sinus and half of the left coronary sinus, have been resected to show the arrangement when the leaflets of the aortic valve are in closed position. The peripheral ends of the zones of apposition between the leaflets are tethered at the sinutubular junction. When the leaflets are closed, the area distal to them is part of the cavity of the ascending aorta, whereas the cavity proximal to the closed leaflets belongs to the left ventricle. Panel (b) illustrates how this cavity, coloured pink, extends to the level of the sinutubular junction, which therefore forms the distal extent of the left ventricular cavity. The image is a virtual dissection of a computed tomographic dataset prepared from a normal individual.

formation of the hinge and, indeed the separation of the atrioventricular canal myocardium to form the vestibules of the atrial chambers have still to be clarified. At least we are now able to describe, with accuracy, the anatomical changes.

## 5 | CONCLUSIONS

Our purpose in producing our review was to provide a counterpart to our similar recent assessment of the morphologically right ventricle (Crucean et al., 2023). In so doing, we have concentrated exclusively on the anatomical changes taking place during development. Knowledge of these changes now provides the basis for understanding the subtleties of features such as the location of the infero-septal recess and the discrepancies to be found between the myocardial-arterial and haemodynamic ventriculo-arterial junctions within the aortic root. We hope that our review has clarified these issues, although, as we have emphasised, there are many aspects still to be learned.

### AUTHOR CONTRIBUTIONS

All authors discussed in advance the topics to be discussed and how best to address them. Dr. Crucean took the lead in determining the material to be presented. Mrs. Spicer prepared the anatomical dissections, which were then supplemented by the virtual dissections of clinical datasets by Dr. Tretter and Professor Cook. Dr. Mohun prepared all the epicopic datasets. Dr. Hikspoors and

Professor Lamers produced and interrogated the interactive pdf files, revealing the details of ventricular development. Professor Anderson was responsible for analysing the histological datasets available from human and murine embryos. All authors were involved in writing the manuscript and agreeing on the draft prepared for submission.

### ACKNOWLEDGEMENTS

Our co-author, Dr. Tim Mohun, from the Crick Institute in London, prepared all the epicopic datasets we used for the purposes of this review. The numbers are those given to them during their preparation by Dr. Mohun. The datasets are now available for interrogation in the files of the Human Developmental Biology Resource.

### FUNDING INFORMATION

Prof Cook's research takes place in the Noé Heart Centre Laboratories which are supported by the Rachel Charitable Trust via Great Ormond Street Hospital Children's Charity (GOSH Charity). The Noé Heart Centre Laboratories are based in The Zayed Centre for Research into Rare Disease in Children, which was made possible thanks to Her Highness Sheikha Fatima bint Mubarak, wife of the late Sheikh Zayed bin Sultan Al Nahyan, founding father of the United Arab Emirates, as well as other generous funders.

### CONFLICT OF INTEREST STATEMENT

None of the authors have interests to declare.

## DATA AVAILABILITY STATEMENT

Not applicable.

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**How to cite this article:** Crucean, A., Spicer, D.E., Tretter, J.T., Mohun, T.J., Cook, A.C., Sanchez-Quintana, D. et al. (2024) Revisiting the anatomy of the left ventricle in the light of knowledge of its development. *Journal of Anatomy*, 00, 1–16. Available from: <https://doi.org/10.1111/joa.14048>