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The Subpulmonary Infundibulum in Normal Heart. A Morphologic Study and Embryologic Considerations

El Infundíbulo Subpulmonar en el Corazón Normal. Estudio Morfológico y Consideraciones Embriológicas

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SUMMARY: A previous morphologic investigation by one of us on the septomarginal trabeculation of 81 normal fetal and neonatal human hearts showed that the outlet compartment of the right ventricle included the root of the supraventricular crest and the left cranial limb of the septomarginal trabeculation, the latter occupying an anterior ventricular septal position. This study showed also that the root of the supraventricular crest was parietally attached to the ventricular septum, a septal surface of this root (infundibular septum) being present only in very few cases. Furthermore, based only on anatomic observations, it was found that the root of the supraventricular crest and the left cranial limb of the septomarginal trabeculation corresponded, on the left ventricular side, to the subaortic right and left coronary leaflet districts respectively. These observations were confirmed very recently by dissections performed on normal pig hearts. This study emphasizes also the free-standing structure and position in normal conditions of the subpulmonary infundibulum, which is essentially the supraventricular crest, due to the interposition of extracavitatary fibro-adipose tissue between the aortic root and the subpulmonary infundibulum itself. In this regard it is emphasized that the pulmonary valve root is mostly supported by the free standing subpulmonary infundibulum, however a small portion of it, corresponding to the left pulmonary valve leaflet, is out of the confines of the subpulmonary infundibulum and in relation to the underlying anterior ventricular septum, representing then the point of anchorage of the pulmonary root to the ventricular septum itself.

KEY WORDS: Subpulmonary infundibulum; Supraventricular crest; Septomarginal trabeculation; Outlet septum; Aortic root.

INTRODUCTION

The subpulmonary infundibulum is one of the three components of the right ventricle. Indeed, developmental and morphologic studies in the past (Goor *et al*., 1970; Anderson & Becker, 1980) and in more recent years (Ho & Nihoyannopoulos, 2006; Mori *et al*.,2019) have promoted and emphasized the tripartite topography of the ventricles: inlet, apical trabecular – including most of the septomarginal trabeculation -, and outlet compartments. In the specific case of the right ventricle, most of the outlet component is made by the subpulmonary infundibulum.

The subpulmonary infundibulum is a sort of approximately cylindrical segment included, vertically and dorsally, between the pulmonary valve root and the leading edge of the supraventricular crest. The supraventricular crest is the essence of the subpulmonary infundibulum. The ventral anatomic borderline of the inferior edge of the subpulmonary infundibulum, along the anterior right ventricular wall, is unidentifiable. It must be pointed out that the left cranial limb of the septomarginal trabeculation or septal band, which occupies an anterior ventricular septal position and is considered an anterior ventricular septum, is not a subpulmonary infundibular component for embryologic and anatomic reasons, which will be touched upon in the discussion section.

The supraventricular crest is a prominent muscle band interposed between the pulmonary valve and the tricuspid valve. Its original name, crista supraventricularis, was introduced by Wolff in 1791, as cited by Grant *et al*. (1961).

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This anatomic structure represents the postnatal version of the embryonic conal infundibular septum which, in normal conditions, assumes an exteriorized parietal position between the aortic root and the right ventricle. This is due to the developmental remodeling of the outflow tract and consequently it has been often defined as parietal band (Van Praagh *et al*., 1964, 1979). The term supraventricular crest applies only to the normal heart since in some anomalous outflow tract conditions the embryonic infundibular septum does not exteriorize and the parietal crest does not develop. In these circumstances this muscle band assumes the position and identity of infundibular septum interposed between the subarterial valves outlets.

The subpulmonary infundibulum, according to Goor *et al*. (1970), in addition to the supraventricular crest includes also the left cranial limb of the septomarginal trabeculation or anterior septum. We disagree with this opinion because the subpulmonary infundibulum is confined posteriorly only to the supraventricular crest, and indeed any time that the supraventricular crest is absent the subpulmonary infundibulum is also absent whereas the anterior ventricular septum persists. More specifically, more recent developmental investigations (Anderson *et al*., 2019; Crucean *et al*., 2024) have confirmed previous embryologic studies (Kramer, 1942; van Mierop *et al*., 1963; Goor *et al*., 1970) and shown unequivocally that the supraventricular crest and the left cranial limb of the septomarginal trabeculation are two totally independent developmental structures as will be discussed in more details. It is important to point out that the left cranial limb of the septomarginal trabeculation topographically occupies a septal position being located posteriorly to the anterior septo-parietal junction.

The supraventricular crest is a totally parietal structure anchored and attached to the ventricular septum and no exterior ventricular septal surface of this attachment is identifiable in most of the cases, as has been already emphasized in the past (Anderson & Becker, 1980).

The septal attachment of the supraventricular crest to the ventricular septum was subsequently described in more details (Restivo, 1988). This investigation found that in very few cases the root of the crest was attached to the ventricular septum showing a sort of triangular septal surface (Fig. 1) with a left margin fused to the left cranial limb of the septomarginal trabeculation and a right margin fused with the posterior inlet ventricular septum. This small septal structure can be considered the infundibular septum interposed between pulmonary and aortic outflow tracts. On the other hand, in the large majority of cases the root of the supraventricular crest showed no septal surface being directly attached to the ventricular septum as a parietal segment (Fig. 2). This showed however the same identical triangular configuration and the same lines of fusion with the septal ventricular structures as in the infrequent variety (Fig. 1). So, the septal root of the supraventricular crest (infundibular septum) present in Figure 1 disappears in Figure 2, as in this latter condition it seems to be buried into the parietal segment of the crest itself.

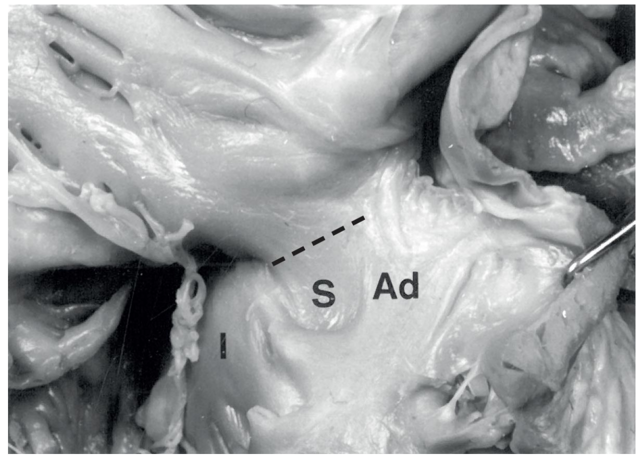

Fig. 1. This figure, reported from a previous study, shows the septal root (S) of the supraventricular crest. This septal portion of the crest is clasped between the left antero-superior limb (Ad) of the septomarginal trabeculation and the posterior inlet (I) ventricular septum. It shows an approximately triangular shape corresponding to the embryonic septal conal cushion. The dashed line, going from the posterior pulmonary valve commissure, between right and left leaflets, down to the leading edge of the supraventricular crest at its crossing point with the interventricular membranous septum corresponds to the embryonic conal cushions fusion line and it marks virtually the borderline between septal and parietal crest. Note that the septal root of the crest is not so small, indeed it looks approximately the same size as the left cranial limb of the septomarginal trabeculation. The junctional ridge ("bulbar raphe") between supraventricular crest septal root and left cranial limb of the septomarginal trabeculation is evident. Note also that the right posterior limb of the septomarginal trabeculation is absent and this area is occupied by the medial papillary muscle. The membranous septum is hidden by the proximal parietal segment of the supraventricular crest.

More anatomic details of Figure 1 are shown in Figure 3 by transillumination of the membranous septum.

Considering the lines of fusion of the supraventricular crest with the ventricular septal structures in the context of aortic dextroposition defects, in all Eisenmenger defects the left edge of the crest maintains its marginal fusion with the left cranial limb of the septomarginal trabeculation (Restivo *et al*., 2016). This sort of supraventricular crest/septomarginal trabeculation interconnection is also found in tetralogy of Fallot but only in a small percentage of cases. Most of the tetralogy of Fallot cases showed instead the crest attached in front of the septomarginal trabeculation (Restivo *et al*., 2017).

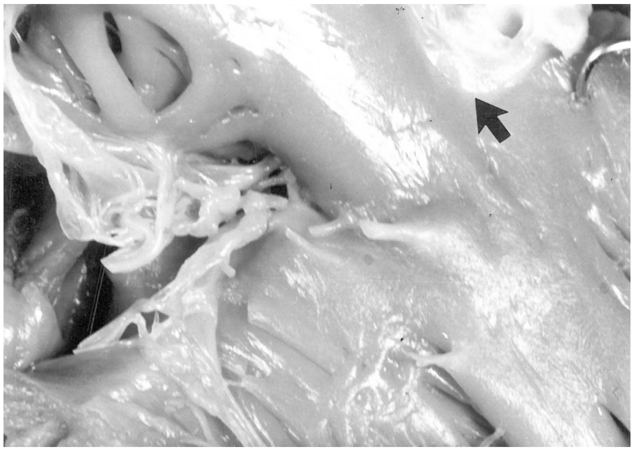

Fig. 2. This case, reported from the same previous study, shows absence of septal surface of the root of the supraventricular crest, all this muscle band appearing then parietal. The arrow shows the left superior limb of the septomarginal trabeculation under, as usually, the posterior left pulmonary valve leaflet. The junctional ridge ("bulbar raphe"), between supraventricular crest septal root and left cranial limb of the septomarginal trabeculation, is very tenuous or almost unidentifiable. Note that the right margin of the crest root is in line and fused with the posterior inlet ventricular septum the same as is its left margin with the edge of the left cranial limb of the septomarginal trabeculation. So, these lines of fusion are the same as in the variety reported in Figure 1, and indeed the root of the crest shows identical triangular configuration in both varieties.

More generally, the outlet segment of the ventricles deserves more detailed consideration. Indeed, the main aim of the present study is to make more clear the topographic correlation between the outlet compartments of the ventricles and the relationship of the subpulmonary infundibulum with the ventricular septum.

MATERIAL AND METHOD

A series of 81 cases of normal fetal and neonatal human hearts was reviewed in 1988 by one of us (AR) for a M.Sc. degree study submitted to the University of Liverpool, England. The more general purpose of the study, at that time, was the septomarginal trabeculation or septal band postnatal morphology and its related structures including the supraventricular crest. These observations allowed to identify the details of the attachment and lines of fusion of the supraventricular crest with the ventricular septal structures as has already been pointed out in the Introduction. Furthermore, a correlative anatomic assessment of the outlet septal surfaces of both ventricles was also approached at that time.

Very recently we performed dissections in two normal porcine hearts to reconsider the lines of anchorage of the supraventricular crest with the ventricular septum but also with the aim to correlate more precisely the outlet surfaces of both ventricles.

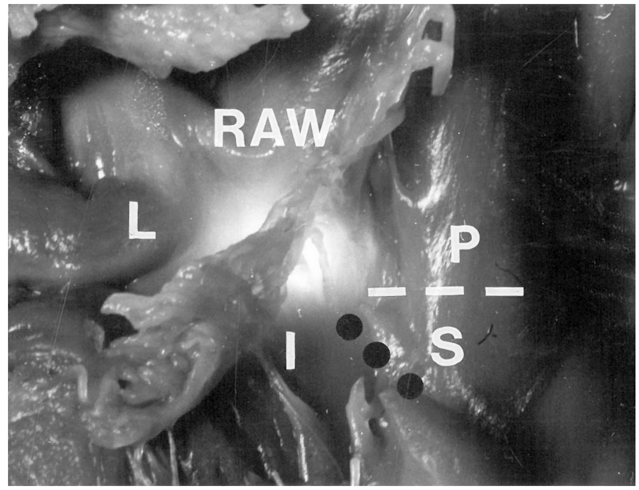

Fig. 3. In this case, which is the same as the one reported in Figure 1, transillumination of the entire membranous septum (atrio-ventricular and interventricular) is shown. The parietal portion of the crest was lifted vertically to show the membranous septum. As it can be seen, the interventricular membranous septum coincides exactly with the crossing point where the supraventricular crest takes off parietally (P) from its septal root (S). The oblique dotted line shows the junction between the crest septal root and the posterior inlet (I) ventricular septum. Antero-septal leaflets of the tricuspid valve, crossing the membranous septum and dividing it into atrio-ventricular and interventricular portions, can be seen. The limbic band (L) and right atrial wall (RAW), both above the atrio-ventricular membranous septum, are also shown. It is worth noting that the root of the supraventricular crest coincides with the embryonic septal conal cushion. The parietal segment of the crest corresponds to the parietal conal cushion, as found by previous developmental studies (Kramer 1942; van Mierop *et al*., 1963; Goor *et al*., 1970). This case shows that posteriorly the septal root of the supraventricular crest is primarily in line and fused with the posterior inlet ventricular septum. The right posterior limb of the septomarginal trabeculation is superimposed frequently, but only secondarily and not constantly, above it. Indeed, in this specific case the right posterior limb is absent and occupied by the root of the medial papillary muscle.

The hearts were opened in the conventional way, with special care while opening the left ventricle by performing a vertical incision parallel to the interventricular left anterior descending coronary artery. Indeed, the incision was performed not too close to this artery to preserve the left aortic coronary leaflet as much as possible.

In one heart, Figure 4 shows the right ventricular outlet portion before dissection and it is evident that the supraventricular crest does not show any septal surface being entirely parietal as occurring in the very large number of cases (Restivo, 1988).

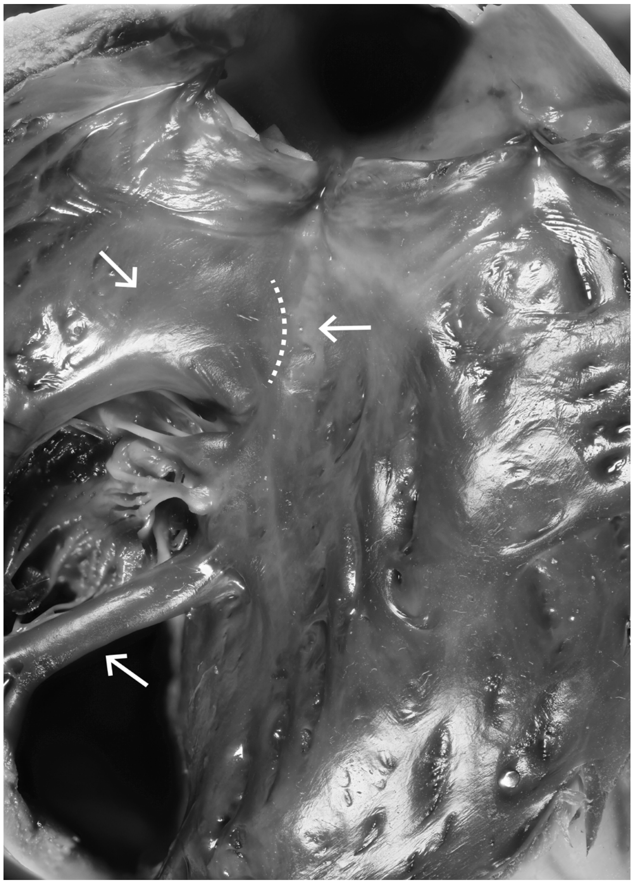

Fig. 4. One intact normal porcine heart is shown on its right ventricular side. The anatomy of this heart is very similar to the human heart. The only peculiarity in this specific specimen is the presence of high take off of the moderator band (lower arrow) crossing the right ventricular cavity, which however does not seem to produce a double chambered right ventricle. In any case the outflow tract anatomy is very similar to the normal human heart. The right upper arrow indicates the supraventricular crest (subpulmonary infundibulum) and the left upper arrow the left cranial limb of the septomarginal trabeculation (anterior ventricular septum). Note the dashed line (bulbar raphe) between these two structures, although such a raphe in this case is not as evident as in the case reported in Figure 1.

Figure 5 of the same heart shows the dissected root of the supraventricular crest then penetrating into the left ventricle. Triangular configuration of the dissected crest root can then be seen.

A second heart showed intact outlet septum with, again, total parietal supraventricular crest. In this second heart (Fig. 6) the quadrangular left cranial limb of the septal band, underlying the left pulmonary valve leaflet, had been dissected and removed, then penetrating the left ventricle.

The anatomy of these porcine hearts was found to be very similar to the human heart. Nevertheless some differences exist (Crick *et al*., 1998; Macías *et al*., 2022). In the specific case of the ventricular anatomy, we first found moderate hypertrophy of the left ventricle and high take off of the moderator band in the right ventricle producing an anomalous muscle band without, however, evidence of a double chambered right ventricle. Finally, reduced extent of aortic-mitral fibrous continuity was found in these pig hearts. This latter specific aspect was particularly investigated by Crick *et al*. (1998) showing that, in contrast to the human heart where the non-coronary leaflet of the aortic valve is entirely fibrous supported by the membranous septum and aortic mitral leaflet, in a porcine heart instead almost half of the portion of the non-coronary leaflet is directly attached and supported by subaortic myocardium.

Fig. 5. In the heart shown in Figure 4 the septal root of the supraventricular crest was dissected and it shows the typical triangular configuration lined by the posterior inlet ventricular septum and the left cranial limb of the septomarginal trabeculation. Note also the left cranial limb of the septomarginal trabeculation under, as usual, the left pulmonary valve leaflet. The membranous septum is hidden by the parietal segment of the crest and it is posterior to the removed crest septal root. A tube was passed through the dissection into the left ventricle.

Nevertheless, these comparative anatomy differences did not interfere with our investigation concerning mainly the correlative positional assessment of the supraventricular crest root and of the left cranial limb of the septomarginal trabeculation position with the respective, corresponding subaortic surfaces of the left ventricle.

RESULTS

Both hearts were then repositioned on the left ventricular side. Figure 7, corresponding to Figure 5 on the right ventricular side, shows that the removed septal root of the supraventricular crest coincided specifically with the subaortic area under the right coronary leaflet anteriorly to the membranous septum. Moreover, the more posterior portion of this right coronary leaflet, crossing the membranous septum, assumed a parietal position following the parietal segment of the crest. Note the triangular configuration of the dissected supraventricular crest root (Figs. 5 and 7).

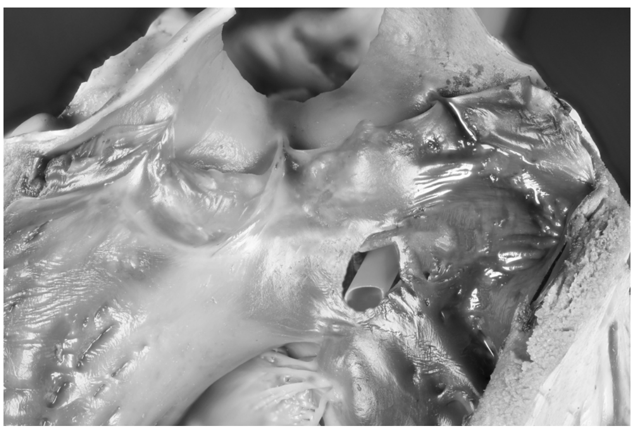

Fig. 6. A second intact and normal pig heart underwent dissection of the left cranial limb of the septomarginal trabeculation underlying the left pulmonary valve leaflet and the left ventricle was then penetrated.

Fig. 7. This figure shows the left ventricular side of the heart reported in Figure 5. A small tube was passed from the right to the left ventricle and the removed septal root of the supraventricular crest coincides with the triangular subaortic area under the right coronary leaflet anteriorly to the membranous septum.

Figure 8, referring to the left ventricle and corresponding to Figure 6 of the right ventricle, shows the dissected and removed quadrangular left cranial limb of the septomarginal trabeculation occupying the area under the left coronary leaflet of the aortic valve. It is important to note that the left coronary leaflet makes a bridge between septal and parietal surfaces of the left ventricle. Furthermore, anteriorly such a leaflet occupies the septal subaortic position where the left cranial limb of the septomarginal trabeculation projects itself to the left ventricular septal surface, whereas posteriorly this aortic leaflet becomes parietal being related and attached to the aortic leaflet of the mitral valve.

Fig. 8. The left ventricular side of the heart reported in Figure 6 is shown. The dissected and removed left cranial limb of the septomarginal trabeculation coincides on the left (see the small tube passing from right to the left) with the subaortic area under the anterior half of the left coronary leaflet. It is worth noting that the left coronary leaflet more posteriorly is related to the aortic leaflet of the mitral valve becoming then parietal. The dissection inevitably divided the left coronary leaflet in two (septal and parietal) portions. A fraction of the parietal portion of this coronary leaflet overlying the aortic mitral leaflet can be seen, although the aortic mitral valve leaflet in this case results damaged somehow by the dissection.

DISCUSSION

The anatomy of the subpulmonary infundibulum in the normal human heart is complex and it deserves detailed consideration.

Most of the supraventricular crest, which is interposed between the pulmonary valve and the tricuspid valve, occupies a parietal position in the normal heart.

Considering the parietal predominance of the supraventricular crest, first we thought important to clarify its septal attachment to the ventricular septum. Indeed, in light of a previous investigation (Restivo, 1988), in most cases the root of the supraventricular crest did not show an identifiable endocardial septal surface and it appeared entirely as a parietal muscle band attached directly to the ventricular septum (Fig. 2). In this study it was found that only in very few cases a septal surface of the crest was present as shown in Figure 1, and regrettably no exact percentage of incidence of such a condition was recorded at that time.

Often a junctional ridge, "bulbar raphe" according to the original definition of Van Mierop *et al*. (1963), is evident between the crest septal root and the left cranial limb of the septomarginal trabeculation, as Figure 1 shows.

The left cranial limb of the septomarginal trabeculation was defined as the anterior infundibulo-ventricular septum by Goor *et al*. (1970) since it was emphasized that this anterior septum, in their own opinion, is septally interposed between the subpulmonary infundibulum and the left ventricle. Moreover, Goor *et al*. (1970) considered the left cranial limb of the septomarginal trabeculation as part of the subpulmonary infundibulum. As already mentioned in the Introduction, we disagree with this view for embryologic and morphologic reasons. Indeed, morphologically, moving from the normal heart to a ventricular septal defect (VSD) with absent infundibular septum, for instance, there is no sign of existing subpulmonary infundibulum. So, the cranial extension of the septomarginal trabeculation does not represent, in our opinion, a residual fraction of subpulmonary infundibulum. More significantly, previous embryological studies (Kramer, 1942, van Mierop *et al*., 1963, Goor *et al*., 1970) and the most recent developmental investigations (Anderson *et al*., 2019; Crucean *et al*., 2024) showed and confirmed unequivocally that the supraventricular crest is a primordial embryonic mesenchymal structure due to the development and fusion of the proximal outflow cushions (Anderson *et al*., 2003) well known as conal cushions. These conal cushions, underlying the distal truncal cushions according to the previous cited embryologic studies (Kramer, 1942; van Mierop *et al*., 1963; Goor *et al*., 1970), once fused undergo myocardialization. Quite interestingly these most recent cited investigations (Anderson *et al*., 2019; Crucean *et al*., 2024) found some new aspects concerning specifically the failure of some small portions of the fused conal or proximal outflow cushions to muscularize. So, according to these studies, these small portions of the fused conal cushions do not undergo myoblastic commitment and differentiation molecular genetic program. As a consequence of this, ultimately various quantities of extracavitary fibro-fatty tissue infiltrated the myocardium interposed between the subpulmonary infundibulum and its dorsal subaortic region. According to these recent findings, the subpulmonary infundibulum results myocardially detached from its dorsal subaortic region. On the other hand, the left cranial limb of the septomarginal trabeculation, although belonging to the outlet segment and underlying the left pulmonary valve leaflet, is not a mesenchymal septal structure and has no relationship with the embryonic conal cushions. Indeed, it was found that this cranial extension of the septomarginal trabeculation is a myocardial structure since the very beginning due to the invasion of precursor myocardial cells colonizing from the secondary heart field (SHF) (Kelly *et al*., 2001; Waldo *et al*., 2001).

Furthermore, it was also previously hypothesized (Goor *et al*., 1970) that this cranial extension of the septomarginal trabeculation coincided, in terms of developmental anatomy, with the left anterior end of the embryonic conoventricular flange which fuses with the main central body of the septomarginal trabeculation itself. In contrast, this left cranial limb of the septomarginal trabeculation occupying an anterior outlet ventricular septal position was considered by Bartelings & Gittenberger-de Groot (1989) derivative of the primordial ventricular septum extending up to the anterior outlet compartment. Despite these different developmental interpretations, in any case it is unequivocally established that left limb of the septomarginal trabeculation and supraventricular crest are two totally different embryonic derivatives. Nevertheless, it might be a matter of controversial debate that, although an extra infundibular structure, the left limb of the septomarginal trabeculation underlies constantly the posterior left pulmonary valve leaflet contributing then, even if more marginally, to the subpulmonary outlet segment. So, controversial questions might arise from this specific aspect concerning the extra infundibular identity of such a structure. However, strictly speaking, the infundibular and the outlet are not in fact synonymous. So, we are inclined to consider that the left limb of the septomarginal trabeculation is an extra infundibular component of the whole outlet segment of the right ventricle. More generally, as far as this potential controversial aspect is concerned, in our opinion the pulmonary valve root is mostly supported and related to the subpulmonary infundibulum but not entirely since its left pulmonary valve leaflet overlies and is related with the anterior outlet ventricular septum.

The totally parietal supraventricular crest root, occurring in the large majority of cases (Figs. 2 and 4), shows a left ventricular septal counterpart under the anterior portion of the aortic right coronary leaflet anteriorly to the membranous septum. As shown by our dissection (Fig. 7), this however, in our opinion, does not allow to state that a true anatomic septation occurs between the posterior outlet regions of the ventricles. Indeed, effective septation implies in strict anatomic terms myocardial septal continuity and presence of two identifiable right and left corresponding septal endocardial surfaces. This is not the case occurring in most normal hearts. Rather, a sort of dissociation occurs. This potentially septal outlet portion of the left ventricular side results totally parietal on the right ventricular side.

The existence of a free and myocardially detached subpulmonary infundibulum, due to the interposition of fibro-adipose extracavitary tissue (Anderson *et al*.,2019; Crucean *et al* 2024), allows for the Ross surgical procedure (Ross, 1967), performed in early previous years, which mobilizes the subpulmonary infundibulum. This procedure removes the pulmonary valve as an autograft for aortic valve replacement and leaves the dorsal subaortic area totally undisturbed and intact (Merrick *et al*., 2000). We presume that special care should be given by dissecting the left pulmonary valve component of the pulmonary root to preserve the first septal perforating branch of the interventricular left anterior descending coronary artery.

It is also worth noting that since the parietal segment of the supraventricular crest is normally interposed between the aortic root and the subpulmonary infundibulum, in the total absence of the supraventricular crest the aortic root results in direct continuity with the anterior right ventricular free wall, simulating then a most severe aortic dextroposition defect.

Furthermore, although the parietal crest is lateralized and out of the plane of the ventricular septum, and considering such a normal supraventricular crest barrier between aortic root and subpulmonary infundibulum, any developmental deficiency in different portions, proximal or distal, of the parietal crest produces inevitably a communication between the ventricles. This is due to the fact that the aortic root, more specifically the right coronary leaflet, in the normal heart overrides spatially the right ventricle through the membranous septum and through the parietal crest.

It is quite important and interesting to note that while the right ventricular view of the left cranial limb of the septomarginal trabeculation occupies the outlet septal surface of the right ventricle, if projected to the left ventricular side it appears to become apparently parietal occupying the anterior wall of the left ventricle. This is due to the different geometrical configurations of the ventricles. Indeed, the right ventricular cavity is triangular and the septomarginal trabeculation occupies a septal position being posterior to the anterior septoparietal junction. In contrast, the left ventricular cavity is circular and no anterior septoparietal junction is identifiable. However, the outlet component of the septomarginal trabeculation although appearing parietal, once projected to the left, retains its septal identity. It would be anatomically unacceptable to consider a structure septal on one side and parietal on the opposite side. Furthermore, if hypothetically the left cranial limb of the septomarginal trabeculation is considered as a potential parietal structure once projected to the left ventricular side, then the dissection of such a structure performed in the present investigation would have inevitably perforated the anterior wall of the left ventricle. However, such a dissection produced a hole entering the subaortic left ventricular cavity as shown in Figure 8. In fact, the outlet component of the right ventricle shows a slightly convex configuration wrapping the aortic root and making the outlet surface of the left ventricle circularly concave and apparently reduced as compared to the right one. But this is only an optical appearance, indeed if we theoretically pull and stretch as much as possible the anterior wall of a dissected left ventricle until its circular concave shape becomes almost straight, then we would appreciate that the distance between the membranous septum and the anterior septoparietal boundary (only virtually on the left) would be the same on both sides of the ventricular septum. In summary, despite the different straight versus circular geometric configuration, the sagittal extension of the outlet septum is the same in both ventricles.

Summarizing, the triangular root of the crest (Figs. 1 and 2), if projected to the left ventricle, is related to the subaortic right coronary leaflet. More specifically, this root is related to the small portion of such a right coronary leaflet anterior to the membranous septum. Figures 5 and 7 show the corresponding triangular configuration of the crest root in both ventricles.

On the other hand, the left cranial limb of the septomarginal trabeculation is related to the subaortic area underlying the anterior portion of the left coronary leaflet (Figs. 6 and 8). This leaflet then makes a sort of bridge between this septal surface of the left ventricle and the parietal area attaching to the aortic leaflet of the mitral valve with the interposition of the left interleaflet triangle. Thus, strictly speaking, approximately the midpoint or nadir of the left coronary leaflet seems as if to mark a sort of virtual anterior septoparietal borderline of the left ventricular cavity.

From the present gross anatomy observations, it appears evident that the majority of extracavitary fibro-fatty tissue interposed between the parietal supraventricular crest and the aortic root behind, is mainly concentrated in the area posterior to the membranous septum. In light of our observations, we would be inclined to expect a lesser quantity of such extracavitary tissue anteriorly to the membranous septum, behind the root of the supraventricular crest and even less so behind the left cranial limb of the septomarginal trabeculation occupying the anterior outlet ventricular septal position. Indeed, we are currently planning a next histological investigation to confirm these present gross anatomy observations concerning presumable different quantities of extracavitary tissue in the different portions of the supraventricular crest. Furthermore, it must be reminded that the left cranial limb of the septomarginal trabeculation is developmentally out of the primordial mesenchymal conal cushions. So, it becomes even more difficult to conceptualize the source of such extracavitary tissue behind this specific structure considering that the source of this extracavitary tissue seems to be produced by some portions of non-muscularized fused conal or proximal outflow cushions according to the previously cited embryologic investigations (Anderson *et al*., 2019; Crucean *et al*., 2024).

To our knowledge, it is not entirely clear at present whether the mesenchymal conal cushions are invaded and replaced by flanking migrating myocardial cells, as originally proposed by Van Mierop *et al*. (1963) or whether these mesenchymal cells undergo direct myoblastic commitment and differentiation. A recent study by Van den Hoff & Wessels (2020) show, indeed, that myoblastic differentiation occurs contributing, with the flanking myocardial cells migration above the primary mesenchymal cushions, to the development of the embryonic conal septum. Nevertheless, it is not still clear whether an interplay between these two developmental mechanisms occurs or whether one of the two is predominant.

CONCLUSIONS

Summarizing, our previous study on 81 cases of fetal and neonatal normal human hearts found the anchorage of the subpulmonary infundibulum to the right ventricular septum through a direct parietal attachment of the root of the supraventricular crest to the ventricular septum itself in most cases. This confirms then the absence of infundibular septum in the normal heart. Very few cases, however, were found with an infundibular septal portion of the supraventricular crest (Fig. 1). So, it is shown that absence of infundibular septum in the normal heart is not an absolute rule.

These observations lead us also to emphasize that the outlet septum, in the normal heart, includes an anterior component (anterior ventricular septum), which is interposed between the pulmonary valve root and the left ventricle, and which is always present. On the other hand, the posterior component of the outlet septum, that is the infundibular septum interposed between the subarterial outflow tracts, is absent in most cases.

Additional and most recent dissections performed on pig hearts allowed us also to correlate these right ventricular outlet septal regions with the left ventricular counterparts which were found to correspond, respectively, with the subaortic right and left coronary leaflets.

We also found the presence of extensive extracavitary fibro-adipose tissue interposed between the supraventricular crest and the aortic root which confirmed the free-standing structure and position of the subpulmonary infundibulum supporting most of the pulmonary valve root.

However, a small portion of the pulmonary root, coinciding with the left pulmonary valve leaflet, was not supported by the free-standing subulmonary infundibulum but rather by the anterior outlet ventricular septum which then represents the point of anchorage of the pulmonary valve root to the ventricular septum itself.

All this of course creates a lot of difficult correlative aspects between normal heart and congenital cardiac anomalies involving the cardiac outflow tract and more particularly the infundibular ventricular septal defects. Thus, most probably a huge prospective of future correlative morphologic, embryologic and molecular genetic work must be expected out of this context.

Addendum. We notify that the first 3 Figures were originally produced (1988) in black and white, so we preferred to produce the following 5 recent Figures in black and white as well to maintain a color uniformity of the illustrative material.

Author Contributions. **Angelo Restivo** conceived the study, made all the anatomic observations, and wrote the manuscript. **Giovanni Botta** performed the dissections on pig hearts and took active part in this study. **Massimiliano Tursi** provided the pig hearts, took active part in this study and was of help in the production of photographic material. He also organized the submission of the whole material to the Editor taking the editorial correspondence commitment. **Carolina Putotto** took an active part in this study. **Enrico Chiappa** took active part in this study and encouraged this investigation since the very beginning. **Andrei A. Iakimov** provided much contribution to this investigation and provided final suggestions, being much dedicated to cardiac anatomy in his University and it is much appreciated that he has accepted our invitation to join us in this study.

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RESTIVO, A.; BOTTA, G.; TURSI, M.; PUTOTTO, C.; CHIAPPA, E. & IAKIMOV, A. A. El infundíbulo subpulmonar en el corazón normal. Estudio morfológico y consideraciones embriológicas. *Int. J. Morphol., 44(2)*:698-706.

RESUMEN: Una investigación morfológica previa realizada por uno de nosotros sobre la trabeculación septomarginal de 81 corazones humanos fetales y neonatales normales mostró que el compartimento de salida del ventrículo derecho incluía la raíz de la cresta supraventricular y la rama craneal izquierda de la trabeculación septomarginal, esta última ocupando una posición septal ventricular anterior. Este estudio también mostró que la raíz de la cresta supraventricular se unía parietalmente al tabique ventricular, estando presente una superficie septal de esta raíz (tabique infundibular) solo en muy pocos casos. Además, basándose únicamente en observaciones anatómicas, se encontró que la raíz de la cresta supraventricular y la rama craneal izquierda de la trabeculación septomarginal correspondían, en el lado ventricular izquierdo, a las regiones de las válvulas coronarias derecha e izquierda subaórticas, respectivamente. Estas observaciones fueron confirmadas recientemente mediante disecciones realizadas en corazones de cerdo normales. Este estudio también destaca la estructura y posición independientes del infundíbulo subpulmonar, que es esencialmente la cresta supraventricular, en condiciones normales, debido a la interposición de tejido fibroadiposo extracavitario entre la raíz aórtica y el propio infundíbulo subpulmonar. En este sentido, se subraya que la raíz de la valva pulmonar está sostenida principalmente independiente por el infundíbulo subpulmonar; sin embargo, una pequeña porción, correspondiente a la válvula izquierda de la valva pulmonar, se encuentra fuera de los límites del infundíbulo subpulmonar y en relación con el septo ventricular anterior subyacente, representando así el punto de anclaje de la raíz pulmonar al propio septo ventricular.

PALABRAS CLAVE: infundibulum subpulmonar; Cresta supraventricular; Trabécula septomarginal; Septum; Raiz aórtica.

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