

The coronary circulation of the pig heart: comparison with the human heart

M. Rodrigues, A.C. Silva, A.P. Águas and N.R. Grande

Department of Anatomy, ICBAS (Abel Salazar Institute for Biomedical Science) and UMIB (Unit for Multidisciplinary for Biomedical Research), University of Porto, Portugal

SUMMARY

Over the last decades, the pig has been chosen as a feasible animal organ donor for the human species, namely regarding heart transplantation. This has led to the development of transgenic pigs with the goal of avoiding the rejection caused by xenotransplantation. It is therefore pertinent to characterize in detail the vascular anatomy of the pig heart and compare it with that of humans. In this study, 23 hearts from domestic pigs were subjected to two different anatomical techniques (resin vascular casting and injection/dissection with contrast suspension) in order to visualize their coronary circulation. After defining the arterial distribution and anastomoses of the branches of the coronary arteries of the pig, these features were compared with well-established descriptions of the coronary circulation in human hearts. The main contributions of this work are: (i) new features of the coronary vessels of the pig heart are documented; (ii) there is close resemblance in the architecture of the coronary arteries between the pig and humans; (iii) the frequency of anatomical variation in the arrangement of the coronary arteries is lower in the pig than in humans.

Key words: Angiology – Corrosion casts – Electron microscopy – Xenotransplantation

INTRODUCTION

Human Transplantation: Scarcity of donor organs

The current need of human organs for transplantation is not met by the availability of donors (Samstein and Platt, 2001). For instance, during the last decade, there was a 3-fold increase in the number of US patients waiting for organ transplantation (from around 22.000 to 72.000), while the number of transplant surgeries, using cadaveric or donor organs, underwent an increase of less than fifty percent (from 15.000 to 21.000). In the year 2000, while 60 patients received an organ each day, 17 patients on the waiting list died (Cooper et al., 2002).

Xenotransplantation: Non-limited availability of donor organs

Because of these limitations of allotransplantation in humans, xenotransplantation has long been envisioned as an alternative. If problems regarding graft rejection can be solved in the future, xenotransplantation will offer several advantages: i) non-limited availability of tissues and organs for transplants; ii) planning of all procedures, thus reducing some of the factors for graft rejection by the recipient; iii) control of donor organs to prevent transmission of infectious agents (Hammer, 2001; Samstein and Platt, 2001).

The first clinical experiments in xenotransplantation were performed as early as the seventeenth century, consisting mainly in blood transfusions from animals into humans. In the

nineteenth century, some tissue xenotransplants were attempted (reviewed in Cooper et al., 2002). Since 1960, vital organs such as the heart, liver and kidney have been thoroughly studied and tested in different experimental models aimed at xenotransplantation (Cooper, 1996). From 1964 to 2001, 10 attempts of heart transplantation from animals to humans were documented. Patients receiving organs from primates survived longer than those receiving non-primate organs (only a few hours) (Appel et al., 2001). The use of primates as organ donors is thus likely to be the most promising approach in xenotransplantation. However, the use of primate donors bears some disadvantages: the high cost of acquisition and maintenance of primates; most primates belong to endangered species; primate breeding is difficult and rare (one per year); increased risk of transmission of infectious diseases to humans, and, finally, genetic manipulation of primates is not yet possible (Igaz, 2001).

The Pig as an organ donor

As an alternative to primates, other animal species have been considered with the goal of obtaining organs for xenotransplantation. Among these, the pig seems to be the organ donor of choice for our species, because it is easy to breed, it has large litters, and is easily maintained in aseptic conditions. In addition, several studies have shown that the pig can be genetically modified, and also that the risk of porcine zoonoses affecting humans is much lower than in the case of primates. Another advantage is that the size of the organs of the pig corresponds to those of human adults. This is not the case in primates, since their organs are similar in size only to those of children (Igaz, 2001; Zhang et al., 2000). On the other hand, pigs belong to a species that is phylogenetically distant from humans, thus having greater immunologic and biochemical differences with humans (Platt et al., 2002; Hammer, 2001; Cooper et al., 2000).

Pig Anatomy: more Information is required

According to Hammer (1998), the anatomy of the pig as well as its physiology have not been sufficiently defined. Regarding cardiac anatomy, for example, there are only a few publications and, although it is a common saying that the pig's heart is similar to that of humans, there is a lack of comparative anatomy between the hearts in these two species.

Both Crick et al. (1998) and Hammer (1998) suggested that at a time when transgenic pigs are being produced there is a need to look back at the fundamental anatomical features of the pig. Crick et al (1998) examined the hearts of pigs and humans and reported several anatomical dif-

ferences, namely regarding the cardiac orientation, the morphology of the atria, the position of the openings of the caval veins, and the number of pulmonary veins. These authors also described differences in internal features, such as in the thickness of the left ventricular wall, in the disposition of the interventricular septum, in the prominence of the supraventricular crista, in the position and thickness of the trabecula septo-marginalis, and in the shape of the trabeculae carneae.

A look at the vascular anatomy of the pig heart

In this study, we have investigated the anatomy of the arterial blood supply of the pig heart. Using vascular injection techniques, which are adequate for detailed anatomical characterizations, we define here the detailed architectural arrangement of the coronary circulation of the domestic pig (*Sus scrofa domestica*). This animal species has several peculiar features in its coronary circulation, which this work documents and which will be discussed in a comparative manner with the heart of humans.

MATERIAL AND METHODS

Twenty-three hearts of adult pigs (*Sus scrofa domestica*) were collected at a local slaughterhouse. The thorax was opened by sternotomy immediately after the sacrifice of the animals and the heart was removed together with the pericardium and large vessels.

The coronary arteries of the heart samples were cannulated separately through their ostia. The cannulas were secured with ligatures and, after a thorough wash with warm saline solution (NaCl 0.9% at 37°C), the coronary arteries were perfused with different substances.

1. Vascular resin casting

The right and left coronary arteries of 20 hearts were injected with methyl methacrylate (Tensol nr 70) mixed with either a red (Ciba-Geigy, Rouge Irgalithe 108) or a green (Bayer, Green Moltopren 768) pigment. These pigmented resins were injected into the left and right coronary arteries, respectively. The injections were done simultaneously through both cannulas, and at the same pressure. During the whole procedure, the hearts were immersed in a warm saline bath (about 30°C).

After vascular injection, the cannulas were withdrawn and the aortic root was filled up with polymer to complete the cast. When resin polymerization was finished (approximately 10 hours later), the hearts were immersed in a 33% hydrochloric acid bath for 2 or 3 days for digestion of the cardiac tissue. The vascular casts were washed in water and dried.

These samples allowed the analysis of the distribution of each coronary artery, of vascular territories and of branches, including the deepest ones. It also enabled the identification of inter-arterial anastomoses.

2. Injection/dissection with contrast suspension

A contrast mixture (barium sulphate + jelly + saline solution) was injected in the coronary arteries of 3 of the hearts. The mixture injected in the right coronary artery also contained grey pigment ("Pelikan" Drawing Ink), to facilitate recognition of its branches.

During this procedure, the hearts were kept in a warm bath (about 30°C). Immediately after the injection, the samples were cooled down to 0-4°C, for polymerization of the contrast mixture. The hearts were then fixed by immersion in a 10% formaldehyde solution.

Two weeks later, the hearts were studied by X-ray, followed by dissection and were photographed. The dissection was performed after careful removal of the epicardium and adipose tissue.

Using this technique, it was possible to gain a radiographic view of the vascular casts of the coronary arteries and, at the same time, to study the superficial distribution of each of the coronary arteries. Because in these preparations the tissues were not corroded, the walls of the heart chambers and the large vessels at the base of the heart were visible, allowing the topography of the arterial branches to be defined and also serving as a comparative model to the corrosion vascular casts.

3. Scanning electron microscopy (SEM)

For this, 3 inter-arterial anastomoses were selected from the corrosion casts for observation under SEM. Using a magnifying glass (Zeiss), the small anastomoses were cut and applied on carbon surfaces over brass supports. For better stabilization, their ends were fixed using conductive carbon cement (Leit-C, Neubauer Chemik Alien). The anastomoses were further covered with a thin layer of gold (JEOL-Fine Coat Ion Sputter-JFC-1100). The SEM equipment used here was model JSM-6301F from JEOL.

SEM was used to study the three-dimensional arrangement of small arterial branches and also for the analysis of the endothelial surface of anastomotic branches.

RESULTS

The data obtained by observations of vascular casts and of angiograms of the coronary arteries of the pig can be organized into three parameters: 1) territorial distribution of each coronary artery; 2) description of the vascular course and number of branches, and 3) localization of the arterial anastomoses.

Vascular territories of the left (LCA) and right coronary arteries (RCA)

LCA

Comprehensive scrutiny of the samples suggested that each of the coronary arteries participated almost equally in the blood supply to the heart surface, to the large vessels at the base of the heart, and to the septa that divide the cardiac chambers. However, considering that the volume of the wall of the left ventricle is greater than that of the right ventricle, it may be concluded that the LCA supplied blood to a larger volume of myocardium than the RCA. The LCA supplied most of the left atrium and ventricle, a small portion of the right ventricle (adjacent to the interventricular paraconal groove), and the apex of the heart (Figure 1A, B and C). It also supplied the left half of the interventricular septum and its most central and dorsal portion. It also contributed to the supply to the atrial septum. The branches of the LCA spread to the caudal wall of the aorta and to the pulmonary veins, and also to the caudal vena cava and arterial conus. The blood supply to the trabecula septomarginalis was originated mainly from branches of the LCA, as occurred with the subauricular and subatrial papillary muscles.

RCA

This artery supplied the right atrium and ventricle, the peripheral right part of the interventricular septum and the left ventricular wall adjacent to the interventricular subsinuosal groove. The interatrial septum, the arterial conus, the cranial and right walls of the aorta and the walls of both vena cava were supplied by branches of the RCA (Figure 1A, C and D). The major papillary muscle, when identified, was supplied by branches arising from the RCA. In two samples, these branches also reached the trabecula septomarginalis. In a few cases, the RCA participated in the blood supply to the subatrial papillary muscle.

2. Origin, main courses and branches of the coronary arteries

2.1. Left coronary artery (LCA)

The LCA arose from the left sinus at the aortic bulbus, above the left semilunar valve. On average, it measured 4 mm in diameter and was usually wider than the RCA (Table 1).

The LCA ran under the left auricle, between the left atrium and the pulmonary trunk. Having reached the coronary groove, the LCA divided into two strong vessels: the interventricular paraconal branch (which followed the groove of the same name) and the left circumflex branch (running in the left part of the coronary groove) (Figure 2A). In most samples, the first branch was slightly wider than the latter. They had the same diameter in only 4 out

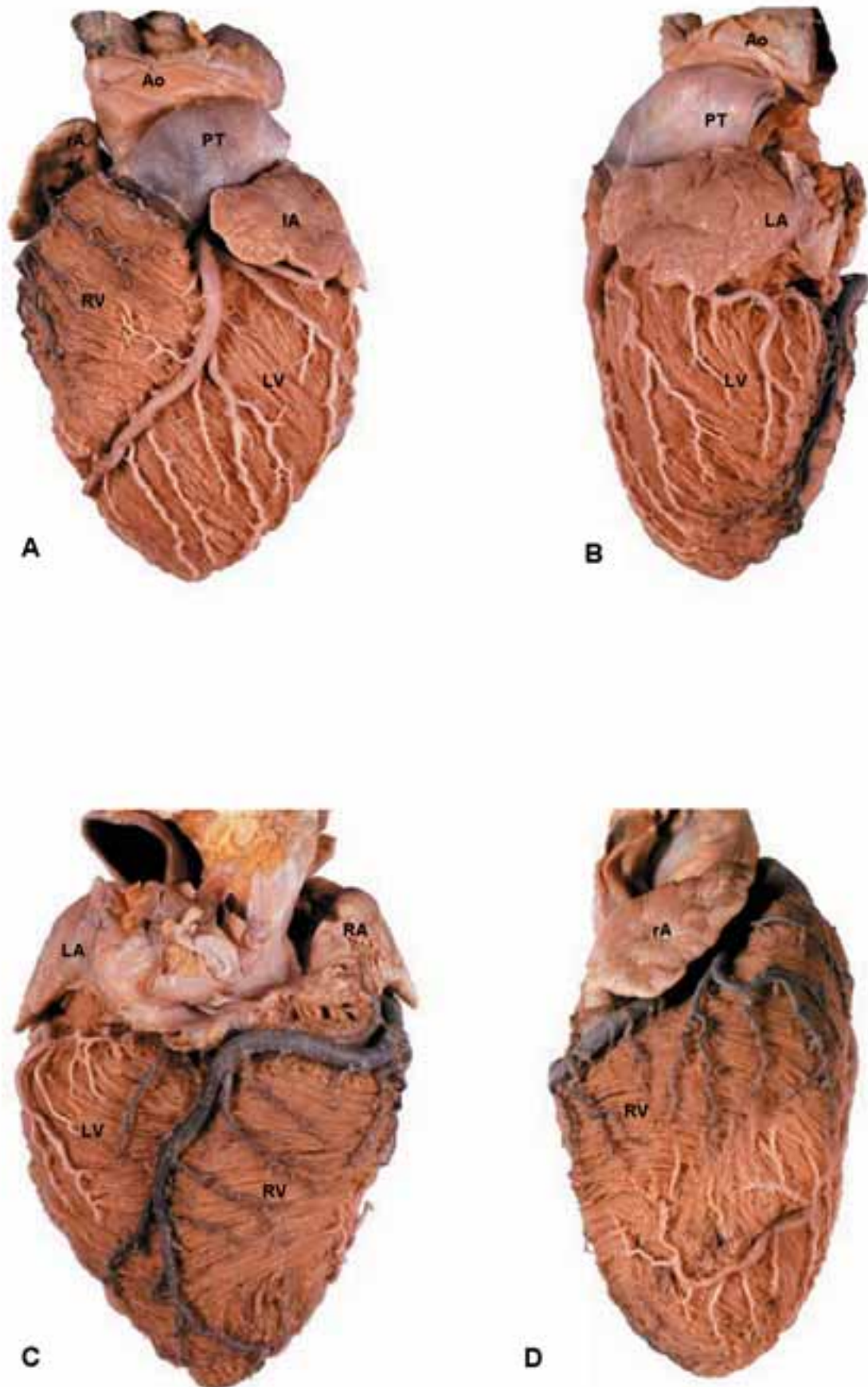


Fig. 1.- Pig heart injected with contrast suspension. The left coronary artery is in white and the right coronary artery is in grey. **A-** Auricular surface; **B-** Caudal border; **C-** Atrial surface; **D-** Cranial border. Ao- Aorta; PT- Pulmonary Trunk; rA- Right Auricle; lA- Left Auricle; RA- Right Atrium; LA-Left Atrium; RV- Right Ventricle; LV- Left Ventricle.

of 23 hearts. The ventricular and atrial branches ran first under the epicardium, and later penetrated the myocardium (Figure 2B). All these epicardial vessels gave off smaller myo-

our observations mainly on the epicardial branches (Diagram 1).

Table 1.- Differences in diameter observed between left and right coronary arteries.
LCA- Left Coronary Artery; RCA- Right Coronary Artery.

Diameters	Nr of hearts
LCA wider than RCA	12
LCA equal to RCA	9
RCA wider than LCA	2

cardial branches, usually at right angles, which branched extensively into a dense three-dimensional capillary network. We now focus

2.1.1. Interventricular paraconal branch

This is a wide vessel with a wavy course along the whole of the paraconal groove. In most of the samples (20 out of 23 hearts), it reached the apex and then changed its course obliquely to the other surface (atrial) of the heart. Along its course, it gave off 3 collateral branches – right ventricular, left ventricular and left septal, as seen in Table 2 (Figure 3).

The right ventricular branches were the thinnest and shortest of these branches; they spread over the right ventricular wall adjacent to the paraconal groove. The first right ventricular branch is called the left branch of the arterial conus, but it infrequently reached this structure and was only observed in 3 out of 23 hearts. The left ventricular branches were thick and long and

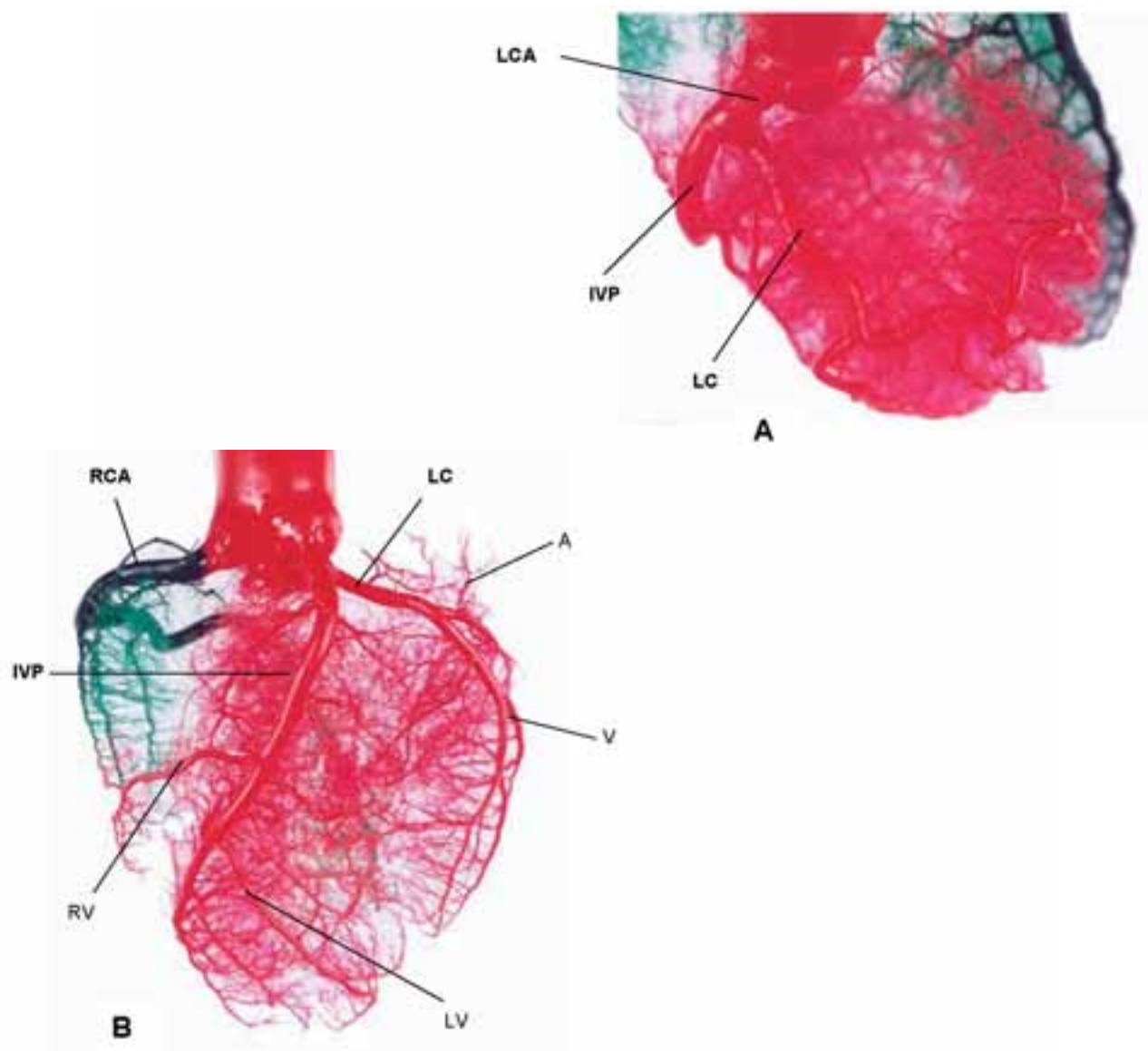


Fig. 2.- Corrosion casts of coronary arteries in the pig. **A-** Base of the heart; **B-** Auricular surface.
LCA- Left Coronary Artery; IVP- Interventricular Paraconal branch; LC- Left Circumflex branch; RCA- Right Coronary Artery; RV- Right Ventricular branch; LV- Left Ventricular branch; A- Atrial branch; V- Ventricular branch.

ran obliquely, parallel to the muscle fibers, towards the left ventricular border. A diagonal branch was seldom observed. The left septal branches were numerous, uniform and short. In their transversal or oblique course to the interventricular septum, they ramified extensively, making them broader than the right ventricular branches.

The first left septal branch was larger and much longer than all the others. It was called the interventricular septal branch, and it arose close to the end of the LCA. It followed on obliquely towards the apex of the heart, supplying the most dorsal and central part of the interventricular septum, while the other left septal branches supplied its left peripheral portion, close to the paraconal groove (Figure 4). In 3 out of 20 hearts, the interventricular septal branch was not identified, so that part of the interventricular septum was supplied instead by the atrioventricular branch (coming from the RCA). In one sample, two interventricular septal branches were identified.

Diagram 1.- Branches of the Left Coronary Artery.

IV- Interventricular; RV- Right Ventricular; LS- Left Septal; LV- Left Ventricular; LA- Left Atrium; LV- Left Ventricle; Prox.- Proximal; Interm.- Intermediate.

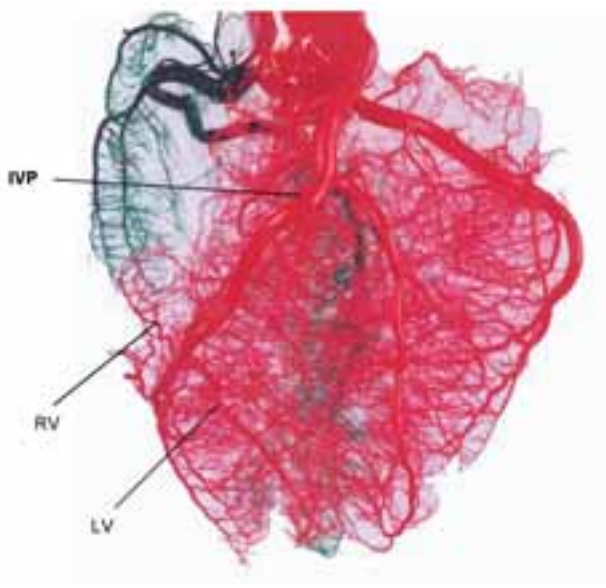
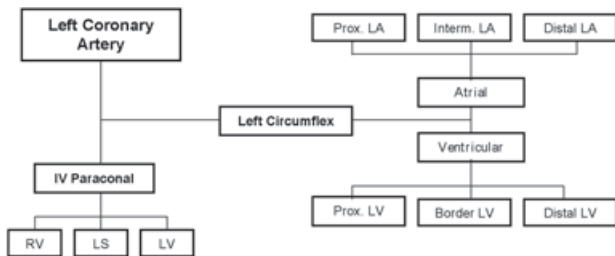


Fig. 3.- Auricular surface of corrosion cast of coronary arteries in the pig. IVP- Interventricular Paraconal branch; RV- Right Ventricular branch; LV- Left Ventricular branch.

Besides spreading to the interventricular septum, the interventricular branch gave off a trabecular branch that followed the trabecula septomarginalis (Figure 5). This branch was thin and was identified in 13 out of 20 hearts. In 2 hearts, there was a contribution from the branches of the RCA to the blood supply of the trabecula septomarginalis.

Table 2.- Variations in number of branches emerging from the Interventricular Paraconal Branch.

Branches of the Interventricular Paraconal Branch	Number (average)	Number (variations)
Right Ventricular	8	3 to 13
Left Ventricular	7	4 to 10
Left Septal	14	8 to 19

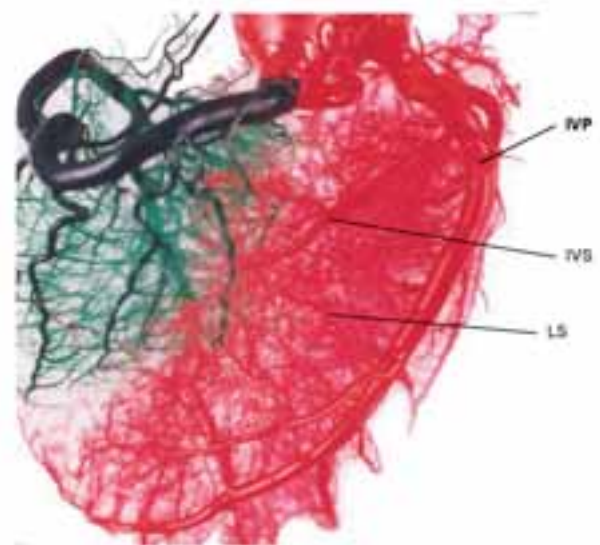


Fig. 4.- Cranial border of corrosion cast of coronary arteries in the pig. IVP- Interventricular Paraconal branch; IVS- Interventricular Septal branch; LS- Left Septal branch.

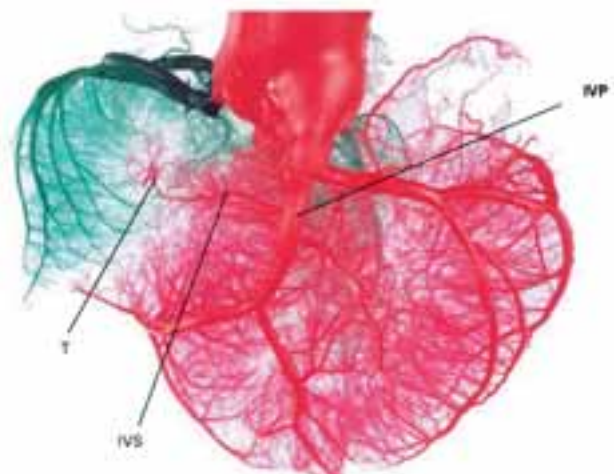


Fig. 5.- Corrosion cast of coronary arteries in the pig. IVP- Interventricular Paraconal branch; IVS- Interventricular Septal branch; T- Trabecular branch.

2.1.2. Left circumflex branch

This artery was quite long, although slightly shorter than the interventricular paraconal branch. Initially covered by the left auricle, the left circumflex branch followed the coronary groove caudally and crossed the left ventricular border to reach the atrial surface of the heart. Along its course, it gave off several branches and ended close to the origin of the interventricular subnuosal groove. The collateral branches of the left circumflex branch can be classified as atrial and ventricular (Table 3). According to their origin and distribution, the left atrial branches are named proximal (located on the auricular surface), intermediate (close to the left border) and distal (on the atrial surface) (Figure 6).

The proximal branches to the left atrium (Figure 6A) were single or multiple. They were the widest and longest of the atrial branches. When they were multiple, the first branch was always the largest. The proximal branches supplied mainly the left auricle, the dorsal surface of the left atrium, and usually the pulmonary veins too. In 4 out of 23 hearts, the proximal branch bifurcated: one branch reaching the left atrium and the other running between the aorta and the base of the left atrium to finish at the most caudal part of the right atrium, at the interatrial septum and at the vena cava. There was usually one single intermediate atrial branch (Figure 6A). When this branch was absent, it was replaced by other atrial branches. The intermediate atrial branch supplied the caudal-most area of the left

Table 3.- Frequency of the number of branches emerging from the Left Circumflex Branch.
 ++ More common; + Less common; - Not observed.

Branches of the Left Circumflex Branch	Number of branches					
	0	1	2	3	4	5
Proximal Atrial	-	++	++	+	-	-
Intermediate Atrial	+	++	+	+	-	-
Distal Atrial	+	++	+	+	-	-
Proximal Ventricular	-	+	+	-	-	-
Branch to the Left Ventricular Border	+	++	-	-	-	-
Distal Ventricular	-	-	++	++	+	+

atrium and then sometimes continued to the auricle. In 8 out of 23 hearts, it also contributed to the blood supply of the pulmonary veins. The distal atrial branches (Figure 6B) were the thinnest and shortest of the atrial branches. They were usually multiple. These vessels spread to the base of the atrium, but could also run dorsally to the pulmonary veins (observed in 6 hearts) or to the caudal vena cava and interatrial septum (in 8 samples).

The left ventricular branches, classified as proximal, of the left ventricular border and distal were wider and more numerous than the corresponding atrial branches (Figure 7). The proximal branches to the left ventricle (Figure 7A) were large and long. They ran obliquely towards the caudal border and apex of the heart, supplying the dorsal-most part of the auricular surface of the left ventricle. They were longer when run-

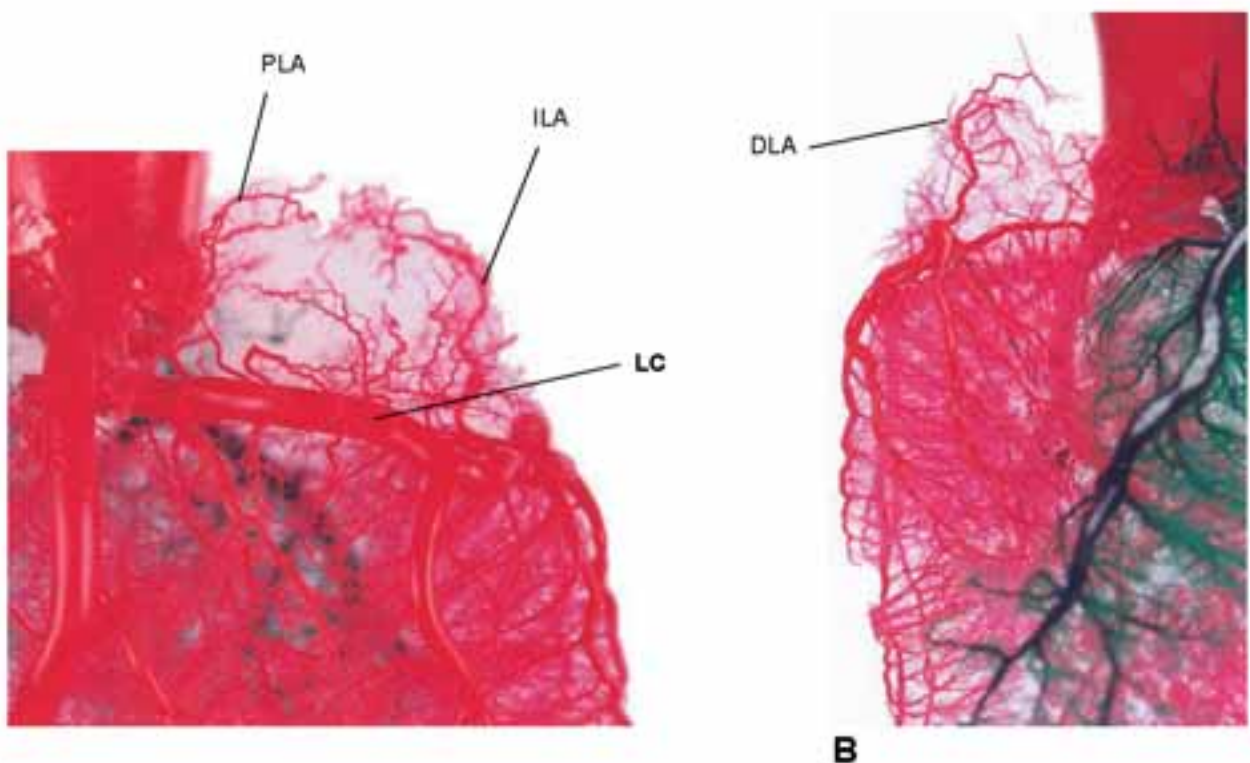


Fig. 6.- Corrosion casts of coronary arteries in the pig. **A**- Auricular surface; **B**- Atrial surface.
 LC- Left Circumflex branch; PLA- Proximal branch to Left Atrium; ILA- Intermediate branch to Left Atrium; DLA- Distal branch to Left Atrium.

ning parallel to the muscle fibers and to the left ventricular branches from the interventricular paraconal branch. In 4 out of 23 hearts, the proximal branch to the left ventricle was very large, as the circumflex branch continued as a proximal branch to the left ventricle and gave off another branch which followed the caudal part of the coronary groove. The branch to the left ventricular border (Figure 7A) followed the caudal border of the heart towards the apex, but never reached it. It was large and, in 3 samples, it was actually the continuation of the left circumflex branch itself. When this branch was absent, the left ventricular border was supplied by the proximal branch to the left ventricle. The distal branches to the left ventricle (Figure 7B) were usually shorter and thinner and supplied the left ventricular wall between the left ventricular border and the interventricular subsinuosal groove, i.e., the atrial surface of the left ventricle. In 5 out of 23 hearts, one of these branches was wider as it continued and ended the left circumflex branch.

2.2. Right coronary artery (RCA)

The right coronary ostium was located at the right sinus of the aortic bulb, above the right semilunar valve. In one of the hearts, two right coronary ostia were identified.

The RCA ran between the right atrium and the base of the pulmonary trunk and then followed the right part of the coronary groove until it reached the interventricular subsinuosal groove. The length of the RCA was similar to that of the left circumflex branch. When one of these bran-

ches was shorter, the other ran a longer distance on the coronary sulcus.

Once the interventricular subsinuosal groove had been reached, the RCA gave off a short atrioventricular branch to the septa and then continued as an interventricular subsinuosal branch descending along this groove (Figure 8A). Like the left circumflex branch, the RCA gave off two types of branches: to the right atrium and to the right ventricle wall, as seen in Table 4 (Figure 8B, Diagram 2).

The right atrial branches were ascendant and very thin (Figure 9). The first one, called the proximal branch to the right atrium, was usually wider (Figure 9A and B). It was either single or double. When absent, it was compensated by other branches. This branch supplied the right auricle and in most cases ran dorsally between this auricle and the walls of the aorta to spread over the cranial vena cava (in 13 samples), the pulmonary veins (in 6 samples) and the caudal vena cava (in 4 samples). In 5 hearts, it also supplied the interatrial septum. The intermediate atrial branch (Figure 9A and B) was also single or double. It spread mainly over the cranial-most wall of the right atrium and then sometimes reached its auricle. In some cases (4 hearts), it ran along the cranial wall of the aorta to give off branches to the cranial vena cava. The distal atrial branches (Figure 9A and B) were very thin. They spread over the base of the right atrium and, in 8 samples, they also supplied the cranial vena cava.

The right ventricular branches were larger than the atrial ones, but not as much as the left

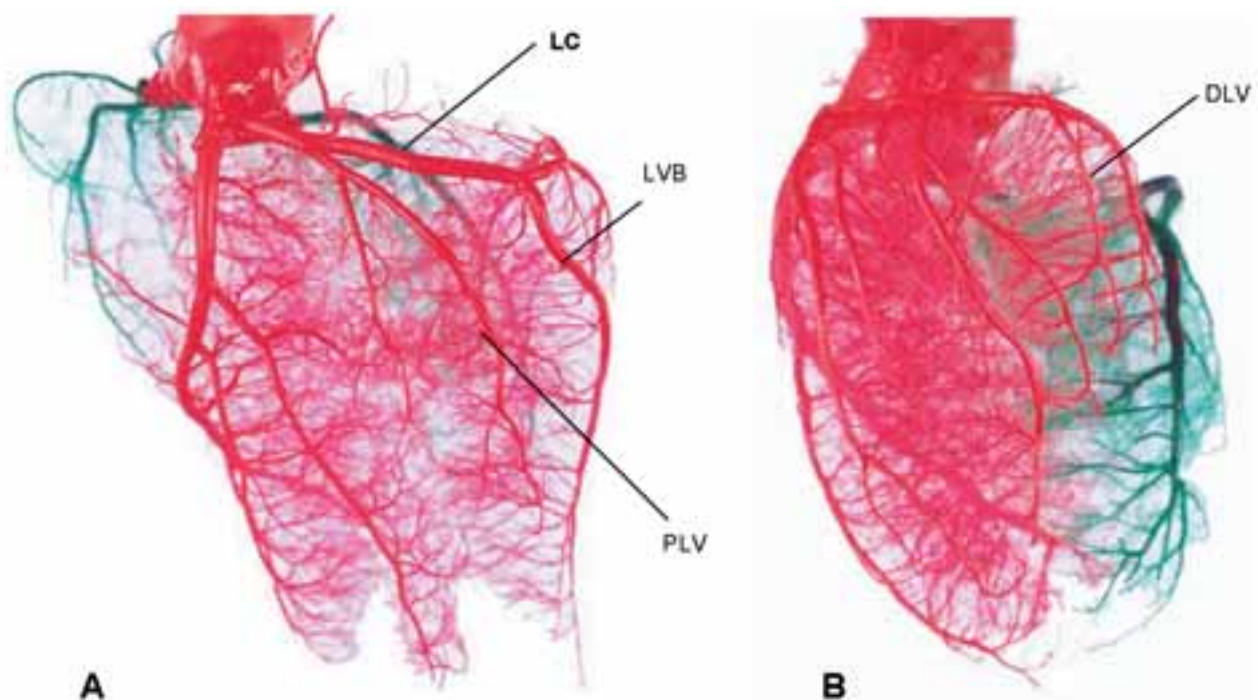


Fig. 7.- Corrosion casts of coronary arteries in the pig. **A-** Auricular surface; **B-** Caudal Border.

LC- Left Circumflex branch; PLV- Proximal branch to Left Ventricle; LVB- branch to Left Ventricular Border; DLV- Distal branch to Left Ventricle.

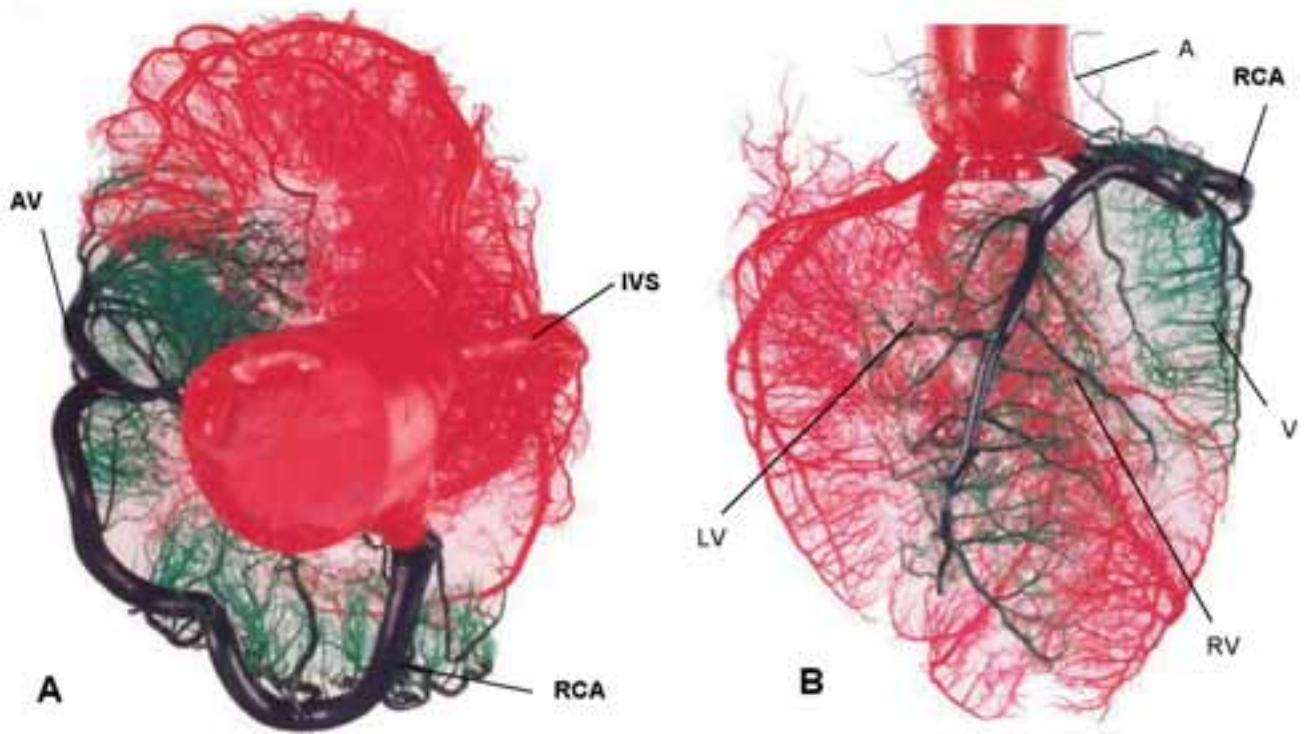
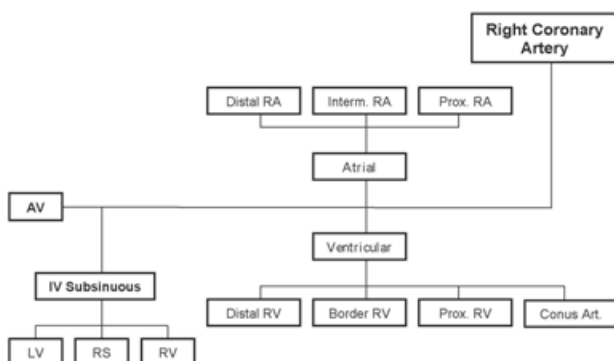


Fig. 8.- Corrosion casts of coronary arteries in the pig. **A-** Base of the heart; **B-** Atrial surface. RCA- Right Coronary Artery; AV- Atrioventricular branch; IVS- Interventricular Subsinoous branch; A- Atrial branch; V- Ventricular branch; RV- Right Ventricular branch; LV- Left Ventricular branch.

Table 4.- Frequency of the number of branches arising from the Right Coronary Artery.
++ More common; + Less common; - Not observed.

Branches of Right Coronary Artery	Number of branches			
	0	1	2	3
Proximal Atrial	+	++	++	+
Intermediate Atrial	+	++	++	+
Distal Atrial	+	++	-	-
Right Branch to the Conus Arteriosus	-	++	+	-
Proximal Ventricular	-	++	++	+
Branch to the Right Ventricular Border	-	++	+	-
Distal Ventricular	-	-	++	++

Diagram 2.- Branches of the Right Coronary Artery.
AV- Atrioventricular; IV- Interventricular; LV- Left Ventricular; RS- Right Septal; RV- Right Ventricular; RA- Right Atrium; RV- Right Ventricle; Prox.-Proximal; R- Right; Art.- Arterial.



ventricular branches (Figure 10). The right branch to the conus arteriosus (Figure 10A and B), unlike the left one, was easily identified, spreading to the right side of this structure. The proximal branch to the right ventricle (Figure 10A and B), slightly wider than the branch to the conus arteriosus, supplied the auricular surface of the right ventricle. In 7 hearts, these two branches arose together from the right coronary artery. The branch to the right ventricular border (Figure 10A) was quite large and sometimes double. It extended towards the apex of the heart without reaching it. The distal branches to the right ventricle (Figure 10C), usually multiple, short and thin, supplied a small area between the right ventricular border and the interventricular subsinoosal groove, i.e., the dorsal-most part of the right ventricle wall on the atrial surface.

As stated above, the RCA gave off an atrioventricular branch before continuing as an interventricular subsinoous branch on this groove.

2.2.1. Atrioventricular branch

The atrioventricular branch was very thin, but usually easy to recognize (except in 2 hearts where it was indistinct from the other right septal branches). The atrioventricular branch turned medially towards the septa and/or continued caudally for a short course on the coronary groove. It divided into 2 or 3 thinner branches to participate in the blood supply to both the interventricular and interatrial septa and also to a small part of the dorsal wall of the left ventricle

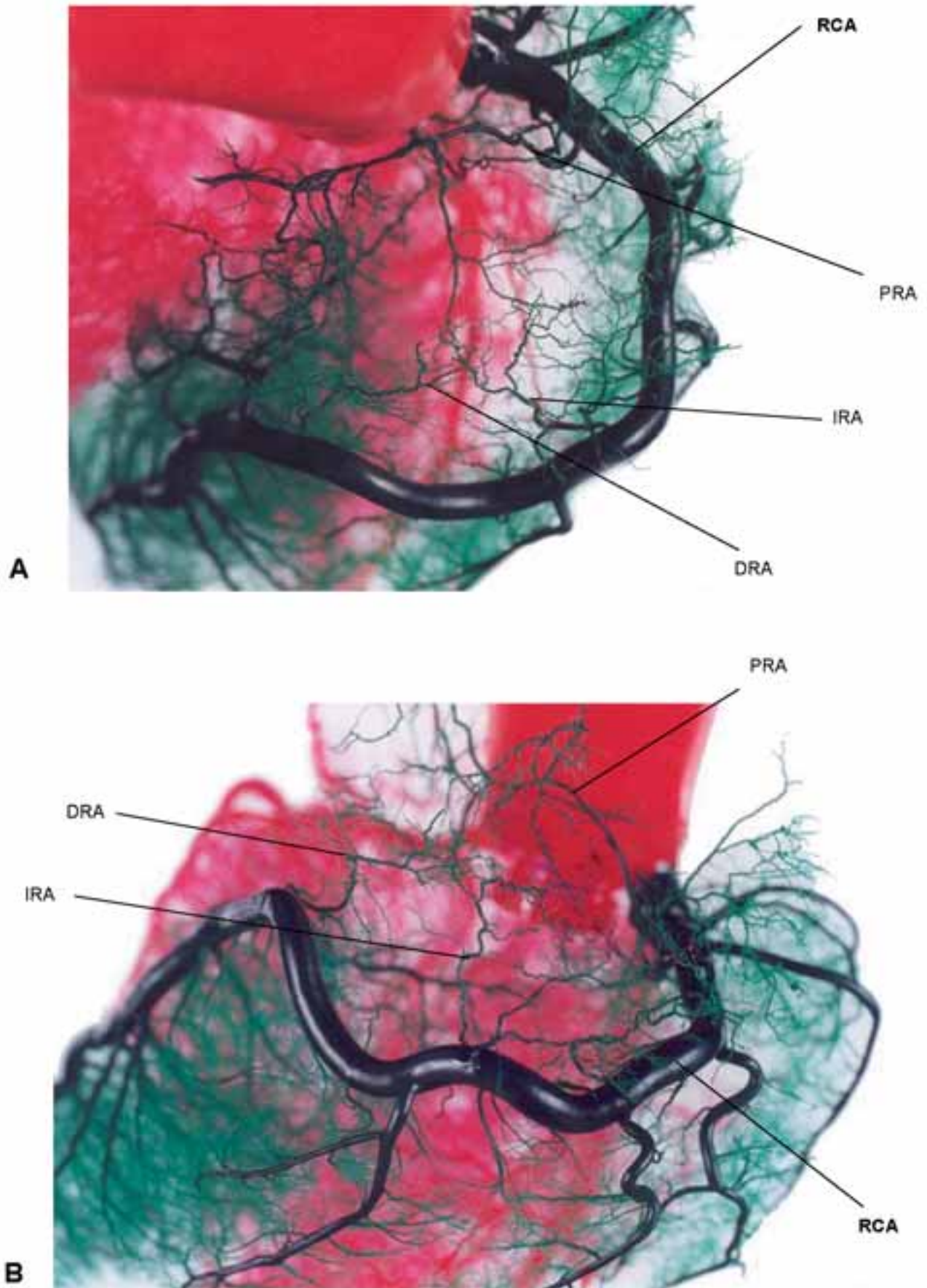


Fig. 9.- Corrosion casts of coronary arteries in the pig. **A-** Base of the heart; **B-** Cranial Border.
RCA- Right Coronary Artery; PRA- Proximal branch to Right Atrium; IRA- Intermediate branch to Right Atrium; DRA- Distal branch to Right Atrium.

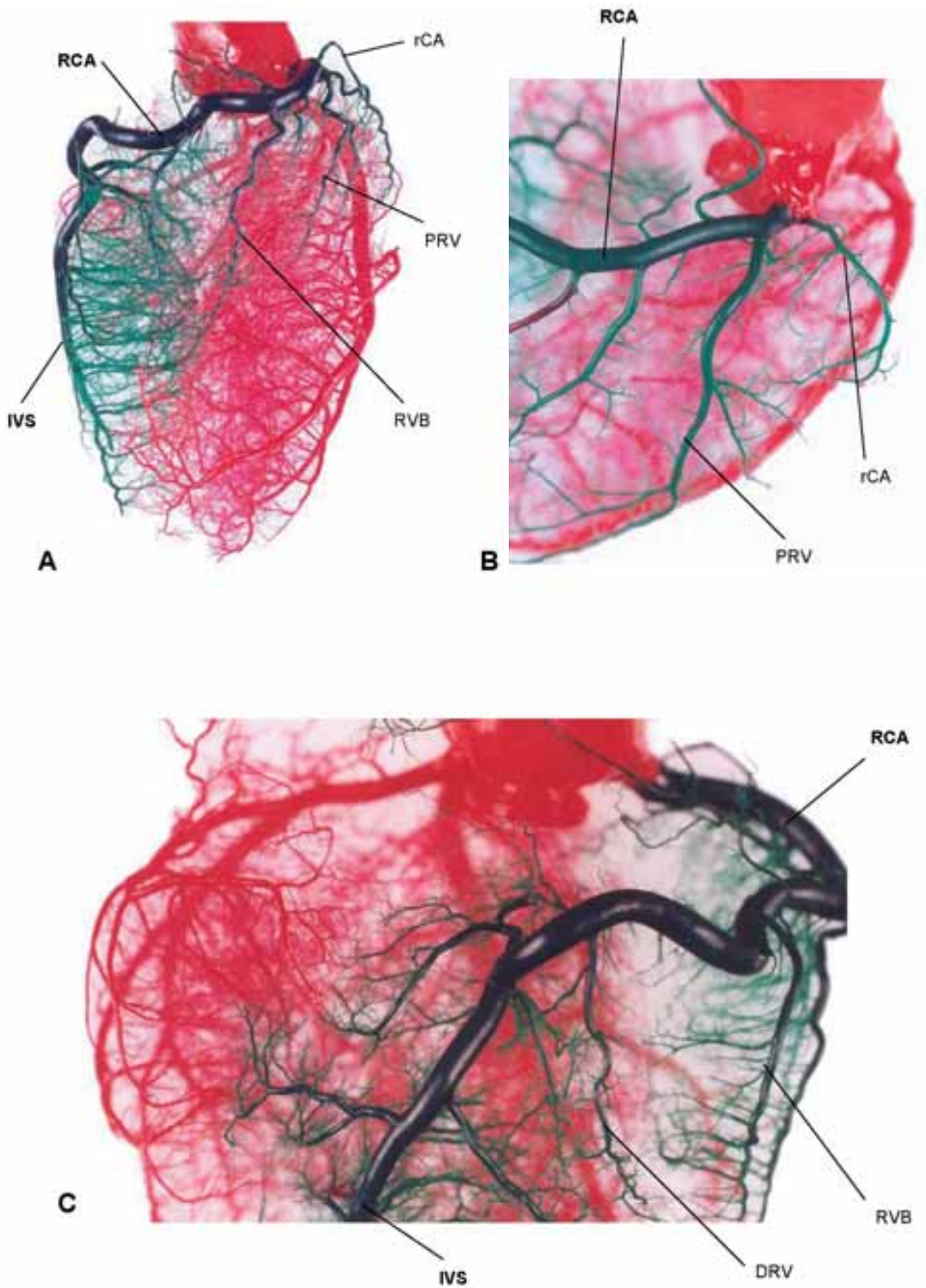


Fig. 10.- Corrosion casts of coronary arteries in pig. **A-** Cranial Border; **B-** Base of the heart; **C-** Atrial Surface.
 RCA- Right Coronary Artery; IVS- Interventricular Subsinoous branch; rCA- Right branch to Conus Arteriosus; PRV- Proximal branch to Right Ventricle; RVB- branch to Right Ventricular Border; DRV- Distal branch to Right Ventricle.

close to the coronary groove (Figure 11). At least in 2 hearts, it also gave off a branch to the caudal vena cava.

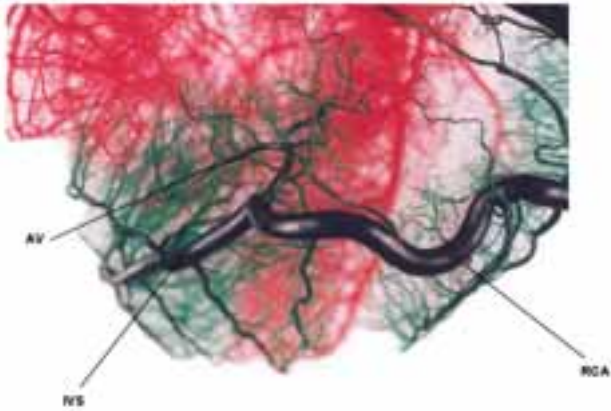


Fig. 11.- Corrosion cast of coronary arteries in the pig - base of the heart.
RCA- Right Coronary Artery; IVS- Interventricular Subsinoous branch; AV- Atrioventricular branch.

2.2.2. Interventricular subsinoous branch

This branch was wide and was the continuation of the RCA, describing a wavy course along the interventricular subsinoosal groove and ending close to the apex of the heart. This branch was always shorter than the interventricular paraconal branch. In fact, the shorter the interventricular subsinoous branch, the longer the other one.

Like the interventricular paraconal branch, the interventricular subsinoous branch gave off 3 types of divisions: the right ventricular, left ventricular and right septal branches, as seen in Table 5 (Figure 12). The right ventricular branches (Figure 12A) were usually the largest and ran obliquely to the right ventricular border, supplying this wall of the right ventricle. The left ventricular branches (Figure 12A) were shorter and thinner. They coursed towards the left ventricular border. In most cases, they had a distal origin at the interventricular subsinoous branch. Proximally, the dorsal wall of the left

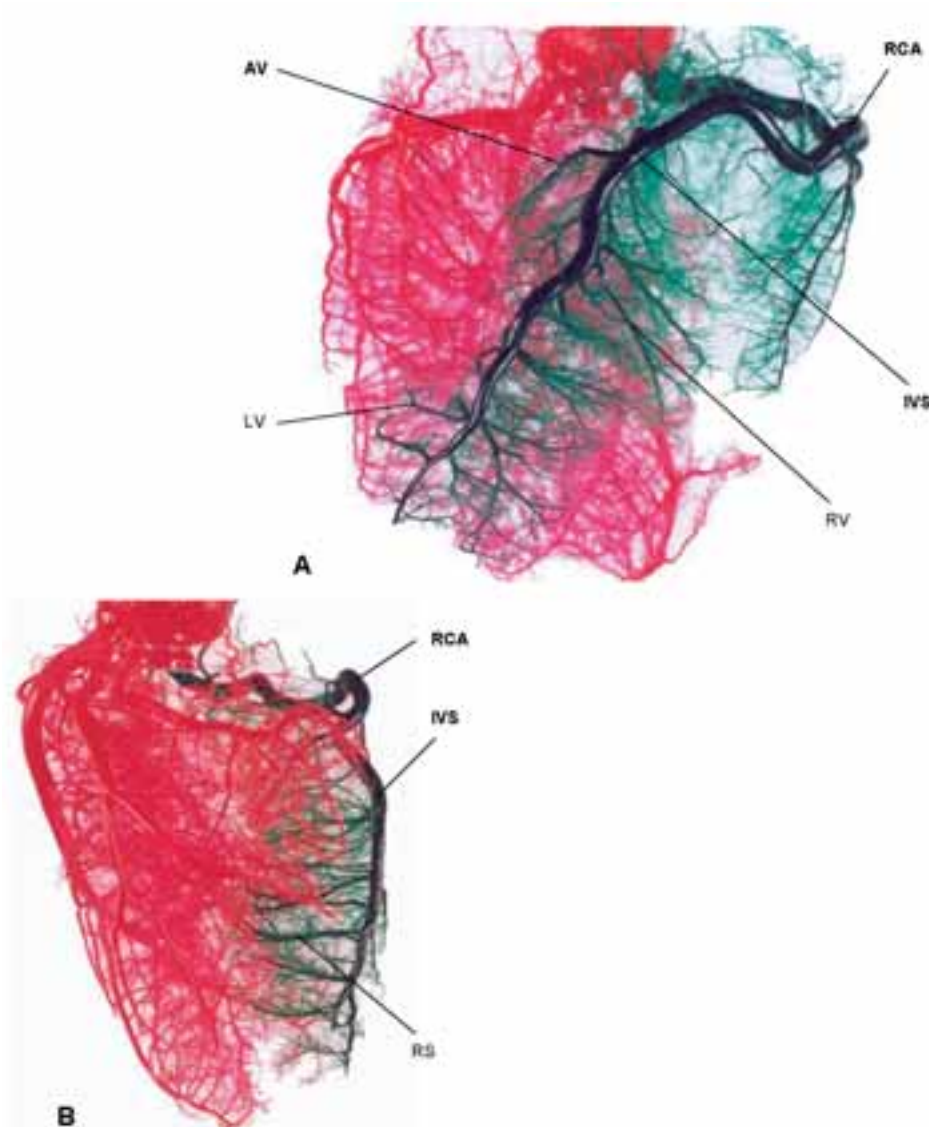


Fig. 12.- Corrosion casts of coronary arteries in pig. **A**- Atrial Surface; **B**- Caudal Border.
RCA- Right Coronary Artery; AV- Atrioventricular branch; IVS- Interventricular Subsinoous branch; LV- Left Ventricular branch; RV- Right Ventricular branch; RS- Right Septal branch.

ventricle was supplied either by the distal ventricular branches (in 10 hearts) or by divisions from the atrioventricular branch (in 4 hearts). The right septal branches (Figure 12B) were more uniform and numerous. They plunged into the interventricular septum to supply its right peripheral part. They were as short and ramified as their counterparts, the left septal branches.

Table 5.- Variations in the number of branches emerging from the Interventricular Subsinuous Branch.

Branches of the Interventricular Subsinuous Branch	Number (average)	Number (variations)
Right Ventricular	6	0 a 9
Left Ventricular	3	0 a 8
Right Septal	11	7 a 14

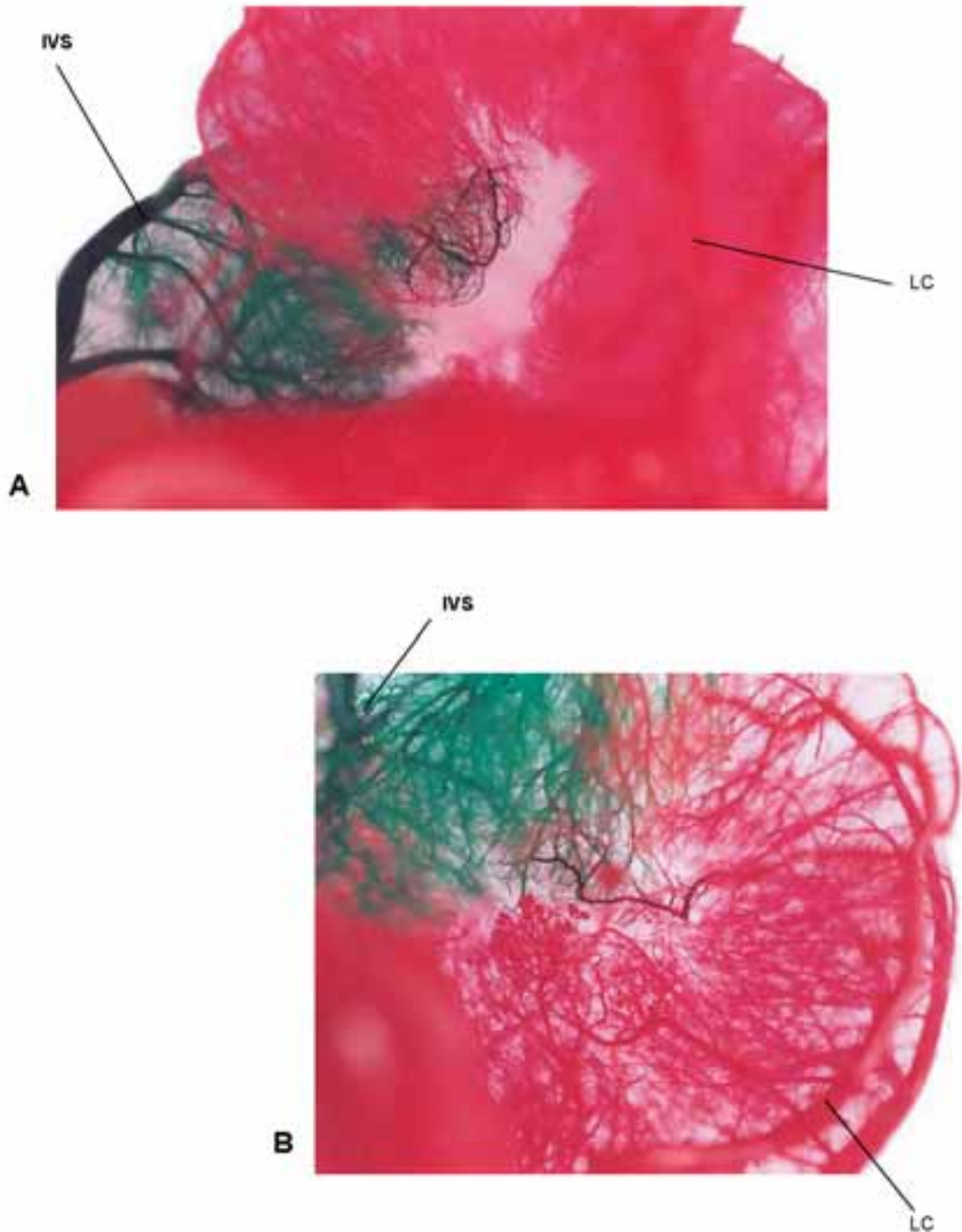


Fig. 13.- Corrosion casts of coronary arteries in pig. **A-** Anastomosis between one Distal branch to Left Ventricle and one Right Septal branch at the subatrial papillary muscle; **B-** Anastomosis between the branch to Left Ventricular Border and one Right Septal branch at the subatrial papillary muscle

3. Inter-arterial anastomoses

3.1. Corrosion casts

The anastomoses between the branches of the RCA and LCA were thin but macroscopically visible (Figure 13). They did not occur between the main branches from the coronary arteries, but between thinner branches. Each heart presented on average 2 anastomoses. In 2 samples, we identified 4 anastomoses in each. Only in one heart were these inter-arterial connections not recognized.

Most of these anastomoses occurred between the branches that supplied the papillary muscles. Thirty per cent of all anastomoses were observed between branches to the subatrial papillary muscle at the left ventricle (left ventricular branches connecting to right septal branches) (Figure 13A and B). At the major papillary muscle, in the right ventricle, the anastomoses occurred between the trabecular branch and the right ventricular branches (20% of the total of anastomoses identified) (Figure 13C and D).

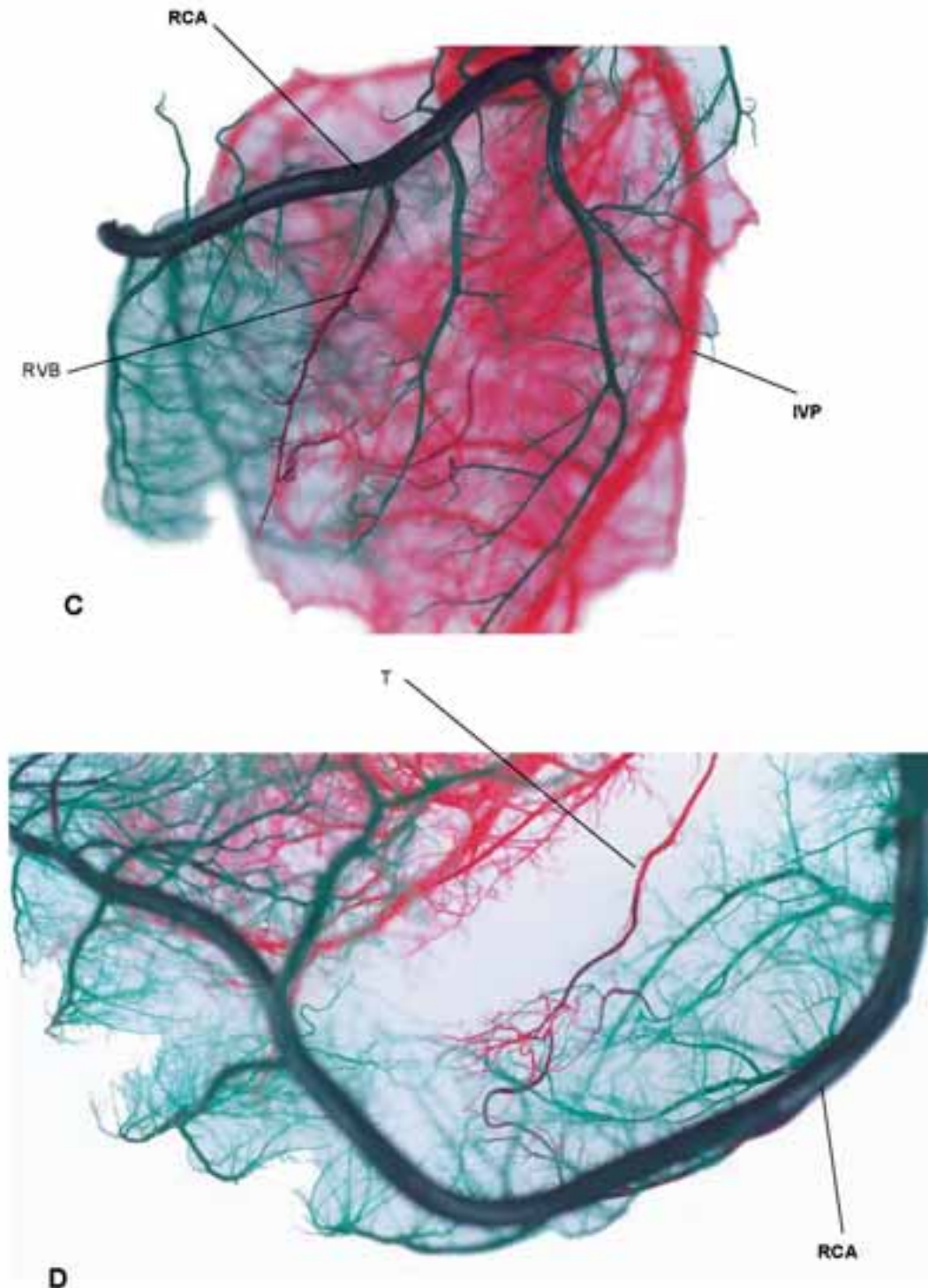


Fig. 13.- C and D- Anastomosis between the Trabecular branch and the branch to the Right Ventricular Border at the major papillary muscle

Another 20% were connections between the atrioventricular branch and other branches: namely, the interventricular septal branch, the trabecular branch and the distal branches to the left ventricle (Figure 13E). Other less common anastomoses were observed between opposite atrial branches and between opposite septal branches.

3.1.1. Blood supply to papillary muscles

Because most of the anastomoses occurred on the papillary muscles, it seemed important to describe their blood supply. The branches that most commonly supplied each papillary muscle were identified and percentages were calculated.

At the left ventricle, the subauricular papillary muscle was supplied by left ventricular branches from the interventricular paraconal branch (65%) or by proximal branches to the left ventricle (35%). The subatrial papillary muscle was supplied by right septal branches (45%), by the end of the left circumflex branch (25%), by distal branches to the left ventricle (20%), by the branch to the left ventricular border (4%), by the interventricular septal branch (3%) or even by the atrioventricular branch (3%).

At the right ventricle, when the major papillary muscle was identified it was supplied by

the branch to the right ventricular border (55%), by proximal (20%) or by distal (20%) branches to the right ventricle, or also by the end of the right coronary artery (5%).

3.2. Scanning electron microscopy

The 3 anastomotic samples obtained from corrosion casts were analysed. We observed that the diameter of the branches was always greater than 100 μm (between 300 and 600 μm), indicating that all of them were small arteries.

There was no evidence of any constrictions or sphincters on the surface of the anastomotic area. The diameter of these branches did not show any changes, throughout the course from the branch from the RCA, along the anastomotic area, to the branch from the LCA (Figure 14).

At higher magnification, 3 different areas were observed: one in the branch from the RCA; another in the transitional area, and another in the branch from the LCA. In all of them, the surface showed longitudinal folds and sulci (Figure 14: Z1, Z2 and Z3). These irregularities are evidence of the contraction of the wall of the arteries due to low viscosity of the methyl methacrylate. The impressions of the endothelial nuclei were always elongated, oriented parallel to the longer axis of the vessel. This feature is typical of arterial vessels.

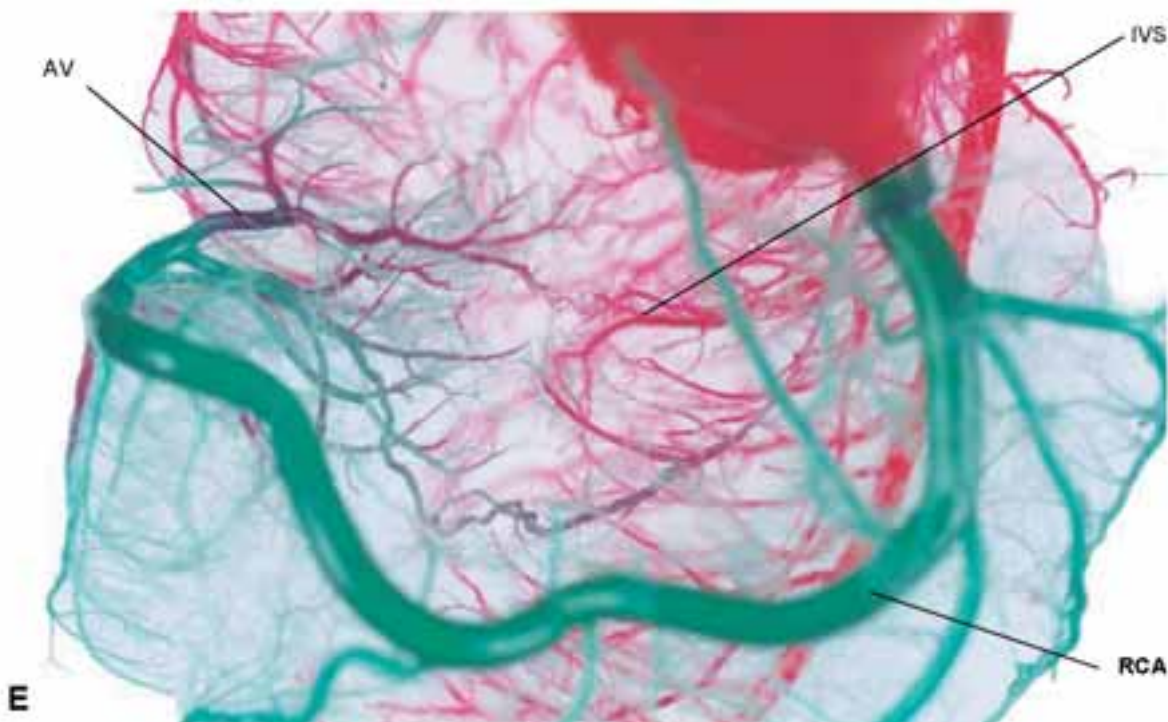


Fig. 13.- E- Anastomosis between the Interventricular Septal branch and the Atrioventricular branch.
 IVS- Interventricular Subsinoous branch; LC- Left Circumflex branch; RCA- Right Coronary Artery; IVP- Interventricular Paraconal branch; RVB- branch to Right Ventricular Border; T- Trabecular branch; AV- Atrioventricular branch; IVS- Interventricular Septal branch.

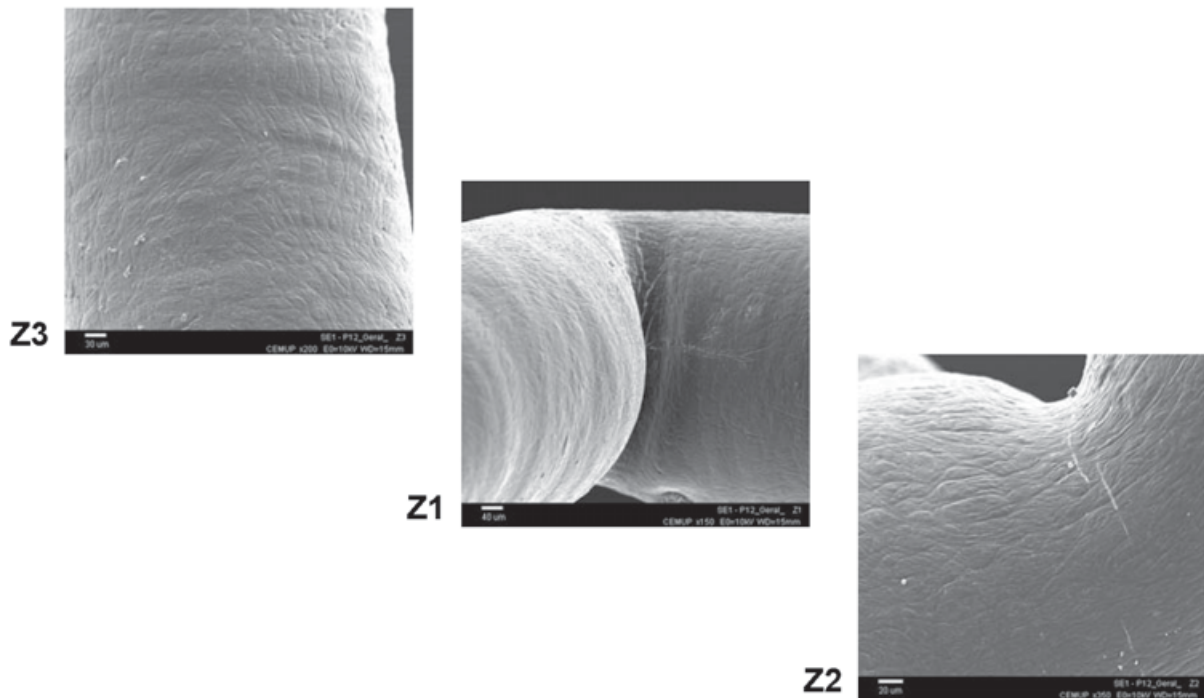
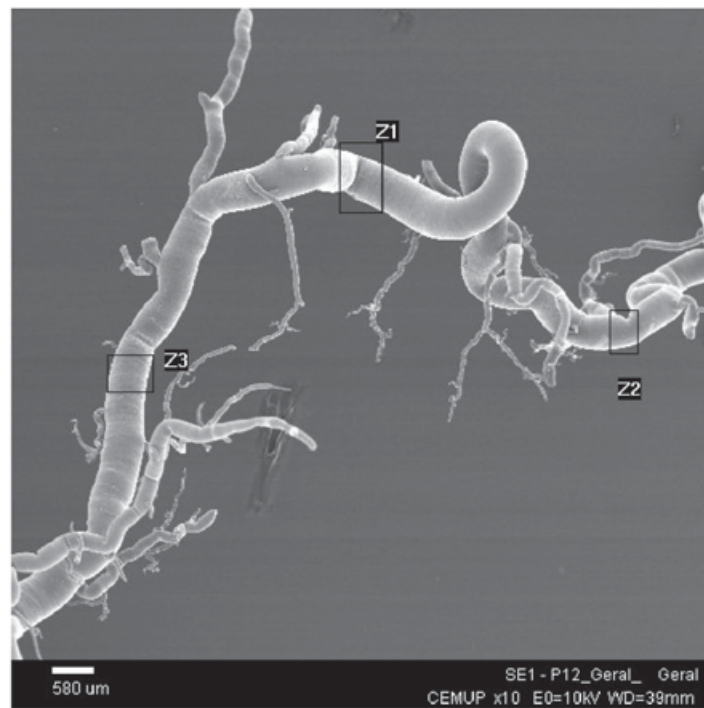


Fig. 14. - Electron micrographs of anastomosis in a corrosion cast of coronary arteries in the pig. **Z1**- transitional anastomotic area; **Z2**- branch from Right Coronary Artery; **Z3**- branch from Left Coronary Artery.

DISCUSSION

The present data on the microanatomy of the coronary arterial supply of the pig heart are discussed at two levels: i) comparison with previous reports on the arterial supply of the pig heart; ii) major differences in heart arteries between pigs and humans.

Anatomical terms are different in Human and Veterinary Medicine. The major differences regarding the heart arteries are that the interven-tricular paraconal branch in veterinary anatomy is always named interven-tricular anterior branch (or anterior descending) in human anatomy and the interven-tricular subsinu-ous branch is also named interven-tricular posterior branch (or pos-

terior descending). The collateral branches have different designations too, depending on the author, either as human or veterinary anatomists. Therefore, it does not seem very important to mention each of these terms. We chose the ones proposed by the *Nomenclatura Anatomica Veterinaria* (Simoens and De Vos, 1999) and some veterinary anatomy books: Schummer et al. (1981), Getty (1986), Ghoshal (1986), Barone (1996), Dyce et al. (1997) and Evans (1993).

1. Neither the LCA nor RCA is dominant in the superficial arterial supply of the pig heart in contrast with the right dominance in the human heart.

The meaning of dominance regarding the vascular territory of a coronary artery must first be defined. In fact, some authors consider that a coronary artery is dominant when its superficial distribution is broader, while other authors use dominance to refer to the ventricular mass supplied by the artery.

Concerning superficial arterial distribution, three different concepts may be considered. According to Gabella (1999), Crick et al. (1998), Weaver et al. (1986), Christidès and Cabrol (1976), and Kamimura et al. (1996), right or left dominance of the coronary system is given to the artery that originates the interventricular posterior (subsinoous) branch. Alternatively, Hadžiselimović et al. (1980) consider that the dominant artery is the one going beyond the crossing between the interventricular subsinoosal groove and the coronary groove, the so-called "cardiac cross". Grande et al. (1994) and Dodge et al. (1993) integrated these definitions on proposing that there is right dominance when the right coronary artery gives off the interventricular posterior (subsinoous) branch and supplies the posterior (atrial) surface of the left ventricular wall (in this case, the left circumflex branch is of a "short" type, and does not reach the cardiac cross). There is left dominance when the interventricular posterior (subsinoous) branch is given off by the LCA, and these authors consider that there is no dominance when the interventricular posterior (subsinoous) branch arises from the RCA and the left circumflex branch is "long".

In the present study no interventricular subsinoous branch was seen to spring from the LCA or from any other branch following a parallel course to the interventricular subsinoous branch arising from the RCA. In light of this, and because each coronary artery ran a similar distance along the coronary groove and each one gave off an interventricular branch, regarding the superficial arterial supply, it may be assumed that there is no dominance of the coronary arteries in the pig. This observation is in agreement with previous observations by several authors, e.g. Barone (1996), Getty (1986), Ghoshal (1986)

and Schummer et al. (1981). In contrast, Weaver et al. (1986) and Crick et al. (1998) stated that around 80% of domestic pigs presented right dominance in the distribution of the coronary arteries in the heart. A possible explanation for this interpretation may be found in their assumption that there was no dominance only when both coronary arteries gave off branches running along the interventricular subsinoosal groove.

In human hearts, the studies by Hadžiselimović et al. (1980), Grande et al. (1994), Dodge et al. (1993), Christidès and Cabrol (1976), Barone (1996) and Lumb and Singletary (1962) reported high percentages (63% a 93%) of hearts with right dominance. These authors observed that the RCA often gave off the interventricular posterior (subsinoous) branch and spread over the posterior (atrial) surface of the left ventricle. They also noticed that the left ventricular branch was usually short, ending close to the left ventricular border. Interestingly, in different editions of Gray's classical textbook of Human Gross Anatomy (35th and 38th) there are different statements concerning the organization of human coronary arteries. In fact, Williams and Warwick (35th edition) say that in the human heart the interventricular posterior (subsinoous) branch arises most frequently from the RCA and spreads to the right and posterior (atrial) walls of both ventricles. Later, Gabella (38th edition) states that in most cases (70%), there is left dominance of the coronary arterial supply in human hearts. In the remaining 30%, the same author reports that the interventricular posterior (subsinoous) branch proceeded from both coronary arteries or could be absent.

2. Regarding the volume of myocardium supplied by the coronary arteries, the LCA is dominant in both species

The LCA was usually wider and proportionally larger than the RCA and this difference reflected the greater left ventricular mass in comparison to the right one in the pig heart. We observed that in 12 animals the LCA was wider than the right one; only in 2 hearts was the opposite observed. The remaining 9 hearts presented a LCA and a RCA of the same calibre. Considering that a higher calibre of one coronary artery supplies a greater myocardial volume (according to Vieweg et al., 1976), then the LCA is the dominant coronary artery in the pig heart. There is also left dominance in the human heart, but it is less significant because the difference between the right and left ventricular masses is not so marked in this species (Gabella, 1999; Crick et al., 1998; Ghoshal, 1986).

Studies by Elizaga et al. (1985), White and Bloor (1981) and Kassab and Fung (1994) confirm the left dominance (in terms of ventricular mass supplied) in the pig heart. All these authors considered the existence of three independent

coronary arteries (the RCA, the interventricular paraconal branch and the left circumflex branch). In the study by White and Bloor (1981), only 38% of the heart tissue was supplied by the RCA. Kassab and Fung (1994) studied the arrangement of the coronary capillaries in pigs. These authors calculated a total number of 1187 capillaries arising from the RCA; 1273 capillaries from the interventricular paraconal branch, and 516 from the left circumflex branch. These numbers document left coronary dominance, since addition of the two last figures show that the LCA contributes with 1789 capillaries, while the RCA only gives off 1187.

3. The existence of a single coronary ostium is very rare. The presence of supranumerary ostia is also not usual in pigs, but occurs with some frequency in humans, especially at the right aortic sinus

Barone (1996) and Ghoshal (1986) reported that in some animal species, although seldom, both coronary arteries may spring from a common trunk. This vascular architecture was not observed in any of our samples.

In the human heart, Grande et al. (1982) observed some variation in the localisation of coronary ostia: in a total of 710 hearts, they found that both coronary arteries proceeded from the same aortic sinus in 2% of cases. Gabella (1999) and Santos et al. (1991) also described rare situations in human patients in which the coronary arteries sprung from the same sinus.

The presence of supranumerary coronary ostia is more usual than the existence of a single ostium for both coronary arteries, both in humans and in domestic animal species (Christidès and Cabrol, 1976; Gabella, 1999).

We identified two right coronary ostia in one sample, from which proceeded the right branch to the conus arteriosus and the RCA itself. We never recognized more than one left coronary ostia. Barone (1996), however, described "two branches of the LCA arising side by side or very closely on the aorta". That author considers this situation very rare in domestic animal species, and never reports the possibility of supranumerary ostia at the right aortic sinus.

In human hearts, most authors agree that supranumerary ostia are more commonly found at the right than at the left aortic sinus (Gabella, 1999; Edwards et al., 1981). Three different patterns were described by Edwards et al. (1981): one in which the right branch to the conus arteriosus proceeded from the aorta; a second one in which this branch and the RCA arose from the same ostium; and a third one in which only the RCA arose from the right aortic sinus. Regarding the left sinus, there may be two ostia for each of the main branches: the interventricular anterior (paraconal) branch, and the left circumflex branch (Gabella, 1999). In their studies of 710 human

hearts, Grande et al. (1982) found two ostia in 87% of cases, but they identified supranumerary ostia (3 or 4) in 12% of cases, the majority of them at the right sinus. The same authors observed one exceptional case in which 5 ostia were present.

4. Three major differences in LCA branching between the pig and human heart

Our observations in the distribution of the collateral branches of the LCA in the pig revealed 3 major differences in comparison with their organization in humans:

a. - Absence of the left branch to the conus arteriosus in the pig. This branch was described by Barone (1996) and Schummer et al. (1981), but in our study it was only recognized in 3 of the hearts. This left branch to the conus arteriosus is not mentioned in the Nomenclatura Anatomica Veterinaria (Simoens and De Vos, 1999). In humans, however, the prevalence of this branch is quite high (Christidès and Cabrol, 1976). Grande et al. (1994) identified two left branches to the conus arteriosus in all of 70 hearts.

b. - Lack of a distinct diagonal branch in the pig hearts, as reported by Barone (1996). We observed that this branch could be double or triple, or mingled with the rest of the ventricular branches due to their similar caliber. The Nomenclatura Anatomica Veterinaria (Simoens and De Vos, 1999) does not report any diagonal branches. Schummer et al. (1981) consider that there are two larger ventricular branches and call them proximal and distal collateral branches.

Diagonal branches of the LCA are usually considered in the human heart. The Nomenclatura Anatómica Humana (Feneis and Dauber, 2000) calls them lateral branches. Dodge et al. (1993) and Christidès and Cabrol (1976) consider that these branches include the two or three first left ventricular branches from the interventricular anterior (paraconal) branch and they are the widest and longest. On the other hand, Grande et al. (1994) described a diagonal branch as the one arising from the LCA when it ends as a trifurcation. Grande et al. (1994) and Gabella (1999) identified this branch in 33-50% of cases.

c. - The length of the left circumflex branch. This branch had a very constant length: always the "long" type in the pig heart. It gave off distal atrial and ventricular branches and usually ended at the cardiac cross. This branch never followed the interventricular subsinuuous groove.

In contrast, in humans this branch is not constant in terms of length. It may end close to the ventricular border (in most cases) or reach and follow the interventricular posterior (subsinuuous) branch (Gabella, 1999; Barone, 1996; Grande et al., 1994; Dodge et al., 1993; Hadžiselimović et al., 1980; Christidès and Cabrol, 1976, Lumb and Singletary, 1962). Christidès and Cabrol (1976) identified distal branches to the left atrium in only 50% of cases, explained by the shortness of

the left circumflex branch. For the same reason, the *Nomenclatura Anatómica Humana* (Feneis and Dauber, 2000) also reports that the distal branches to the left ventricle are not constant.

It seems relevant to point out the importance of the interventricular septal branch arising from the LCA. The *Nomenclatura Anatomica Veterinaria* (Simoens and De Vos, 1999) and Barone (1996) do not mention any interventricular septal branch in the pig heart. Christensen and Campeti (1959), quoted by Ghoshal, 1986 and Schummer et al. (1981) are the only authors who distinguished it from the other left septal branches. They report that it spreads to the central part of the interventricular septum.

We found that the interventricular septal branch is responsible for more than one third of the blood supply of the septum, especially its most dorsal and central part. The other left septal branches supplied the left periphery and apical part of the septum. The remaining part of the interventricular septum was supplied by divisions from the interventricular subsinuuous branch and atrioventricular branch. The LCA thus had a higher contribution (60 to 80%) to the blood supply of the septum compared to that of the RCA (Barone, 1996; Weaver et al., 1986).

This branch is present in human hearts and has a similar distribution. It is mentioned by several authors (Dodge et al., 1993; Christidés and Cabrol, 1976; Williams and Warwick, 1973; Lumb and Singletary, 1962).

5. Three major differences in RCA branching between the pig and human heart.

Regarding the RCA and in agreement with the *Nomenclatura Anatomica Veterinaria* (Simoens and De Vos, 1999), Barone (1996) and Getty (1986), we did not consider a right circumflex branch. We describe the course of the RCA as beginning in the aortic sinus, following the right part of the coronary groove until it bifurcates in an atrioventricular branch and an interventricular subsinuuous branch. However, Schummer et al. (1981) describe a right coronary artery arising from the right aortic sinus, its right circumflex branch that first follows the right part of the coronary groove and then as an interventricular subsinuuous branch through this groove until the apex of the heart.

We identified two differences between the branches of the RCA in pigs and humans:

a. - The collateral branches of the RCA are less developed than those from the LCA in the pig. This situation also occurs in humans (Barone, 1996), although the difference between the right and left ventricular mass is not as significant as in the pig.

b. - The extent of the atrioventricular branch. In the pig, it spreads only to a restricted area close to the cardiac cross while in humans it usually continues along the coronary groove, almost rea-

ching the left ventricular border. Barone (1996) reports that the atrioventricular branch is almost rudimentary in pigs in comparison with humans.

With the exception of Schummer et al. (1981), most authors do not mention that in pig hearts the atrioventricular branch, besides spreading to both interatrial and interventricular septa, also branches over the adjacent left ventricular wall. Our observations also revealed that in at least two hearts the atrioventricular branch gave off a branch to the caudal vena cava.

Another particular feature not mentioned in previous studies is the fact that the proximal branch to the right ventricle could arise from a common branch with the right branch to the conus arteriosus. We identified this common trunk in 30% of the pig hearts studied.

6. As in humans, the inter-coronary anastomoses in the pig are common. They usually occur sub-endocardially

In the pig heart, anastomoses were multiple and small, usually involving small arterioles. In more than 70% of the samples, these anastomoses occurred sub-endocardially, especially between branches that supplied the papillary muscles and the interventricular septum. The other 30% were more superficial anastomoses: between opposite atrial branches, or between the atrioventricular branch and distal branches to the left ventricle.

In contrast with our observations, Stowe *et al.* (1978), Schaper *et al.* (1990), Sakai *et al.* (1985) and Elízaga *et al.* (1985) claim that inter-coronary anastomoses in the pig are virtually inexistent because they are capillary connections. This conclusion was probably based on observations done epicardially, where there are only a few and very small anastomoses in the pig. Dyce *et al.* (1997), Barone (1996), Schummer *et al.* (1981) and Fedor *et al.* (1978) support our results. Barone (1996) reports that in most species the distribution of branches from coronary arteries is of a terminal type, i.e., their final divisions present very thin, almost microscopic anastomoses. In the pig, however, this author defends the notion that they are macroscopic and numerous. Schummer *et al.* (1981) and Fedor *et al.* (1978) add that they are more common between small branches of sub-endocardial arteries.

In their study of coronary capillary arrangement in pigs, Kassab and Fung (1994) identified several types of connections. The most interesting one was the H type, which allows the fluids in two parallel vessels to communicate. They reported that these anastomoses are very important and serve different functions: they make the distribution pressure in the capillary network more uniform; they may affect the transport of oxygen if there are countercurrent flows prevailing; and they may serve as a mechanical support for capillaries during ventricular contraction.

Christidès and Cabrol (1976) and Reig-Vilallonga et al. (1988) suggest that these anastomoses become functional only when the system is unstable, i.e., when one coronary system is deficient, these connections allow the blood to flow from the other coronary artery.

Hadžiselimović and Secerov (1979) studied all types of anastomoses (inter-arterial, intra-arterial, arterio-venous and veno-venous) in 100 human hearts. They identified inter-arterial anastomoses in 33% of cases, but they did not mention their position. Gabella (1999) reports the existence of anastomoses at all levels: sub-epicardial, myocardial and sub-endocardial. Although some of the techniques used were not the most appropriate, several other studies in human hearts mention anastomoses at the cardiac cross, at the apex, and at the conus arteriosus (Williams and Warwick, 1973; Christidès and Cabrol, 1976; Hadžiselimović et al., 1980). Christidès and Cabrol (1976) and Reig-Vilallonga et al. (1988) also identified anastomoses between right and left septal branches. Reig-Vilallonga et al. (1988) examined 100 human hearts and recognized inter-coronary anastomoses in 96 of them, of which 76% were located at the supraventricular crest. This study reinforces the similarity between the hearts of pigs and humans, provided that most of the connections happen between sub-endocardial branches, as we observed in our study of the pig heart.

The fact that the anastomoses identified by us were located mostly at the papillary muscles is somewhat intriguing. This prompted us to perform a more detailed analysis of the blood supply to these structures. With the exception of two articles (Teixeira Filho et al., 2001 and Lorenz and Guski, 1990), this issue does not seem to be addressed. The first authors studied the blood supply to the papillary muscles in oxen and the second authors examined the existing vessels at the trabecula septomarginalis in pigs, goats and oxen.

From comparison of the vascular anatomy of the pig and human heart, it may be concluded that the similarities are greater than the differences in the anatomical arrangement of the coronary arteries. The most important *similarities* are:

- The myocardial volume supplied by the LCA is higher and therefore dominant as compared to the RCA;
- The coronary arteries arise from the aortic bulb in a similar way in both species;
- The LCA is very short and divides into an interventricular paraconal (anterior) branch and a left circumflex branch. These latter give off collateral branches, mainly to the left atrium and ventricle;
- The interventricular paraconal (anterior) branch gives off proximally a wider left septal branch, the interventricular septal branch, which

spreads to the most dorsal and central part of the septum;

- The RCA supplies mainly the right atrium and ventricle, always continuing as an interventricular branch in the pig and, in most cases, also in humans;
- The atrioventricular branch supplies a small area of the interventricular septum, dorsally and to the right;
- The anastomoses between the branches from the coronary arteries are common and occur between small arteries, usually sub-endocardially.

From the *differences* between the coronary circulation in the pig and in humans, we point out the following:

- In the pig, each of the coronary arteries runs a course of a similar length and gives off an interventricular branch. In humans, however, the length and origin of the interventricular posterior (subsinoventricular) branch are highly variable;
- There is right coronary dominance in most human hearts, but there is no dominance in the hearts of pigs as regards to the surface distribution of the coronary arteries;
- In the pig, the right atrial and ventricular branches are less developed than their counterparts, the left atrial and ventricular branches. In humans, this difference is not so clear;
- It is not possible to recognize diagonal branches or left branches to the conus arteriosus in the pig.

We may therefore conclude that, from a strictly anatomical point of view, it is not possible to find important reasons for objecting to the compatibility between the hearts of these two species. On the other hand, the type of coronary dominance present in a specific human heart and the calibres of its coronary arteries should be analysed when considering the need for xenotransplantation of a pig heart to a human patient.

ACKNOWLEDGEMENTS

The authors are grateful to Dr M. Costa, Mr E. Monteiro and Mr C. Frias for the expert technical assistance; Mr D. Monteiro for the artwork, and Dr A. Roldão for photographic work. This research was funded by the FCT.

REFERENCES

- BARONE R (1996). Angiologie. In: *Anatomie comparée des mammifères domestiques*. Vigot Frères, Paris, 5: 5-443.
- CHRISTIDÈS C and CABROL C (1976). *Anatomie des artères coronaires du cœur*. Lafarge, Paris, pp 9-119.
- COOPER DK, KEOGH AM, BRINK J, CORRIS PA, KLEPETKO W, PIERSON RN, SCHMOECKEL M, SHIRAKURA R and WARNER SL (2000). Report of the Xenotransplantation Advisory Committee of the International Society for Heart and Lung Transplantation: the present status of xenotrans-

- plantation and its potential role in the treatment of end-stage cardiac and pulmonary diseases. *J Heart Lung Transplant*, 19: 1125-1165.
- COOPER DKC (1996). Xenotransplantation – State of the Art. *Front Biosci*, 1: d248-265.
- COOPER DKC, GOLLACKNER B and SACHS DH (2002). Will the pig solve the transplantation backlog? *Annu Rev Med*, 53: 133-147.
- CRICK SJ, SHEPPARD MN, HO SY, GEBSTEIN L and ANDERSON RH (1998). Anatomy of the pig heart: comparisons with normal human cardiac structure. *J Anat*, 193: 105-119.
- DODGE JT JR, BROWN BG, BOLSON EL and DODGE EHT (1993). Diâmetro do lúmen de artérias coronárias humanas normais. *Circulação*, 13: 111-130.
- DYCE KM, SACK WO and WENSING CJG (1997). O Sistema Cardiovascular. In: *Tratado de Anatomia Veterinária*, 2nd edition. Guanabara Koogan S.A., Rio de Janeiro, pp 171-179.
- EDWARDS BS, EDWARDS WD and EDWARDS JE (1981). Aortic origin of conus coronary artery. Evidence of postnatal coronary development. *Br Heart J*, 45: 555-558.
- ELÍZAGA J, GARCÍA DORADO D, GALIÑANES M, SOLARES J and FERNÁNDEZ AVILÉS F (1985). Estudio cuantitativo de las diferencias en los territorios de distribución de las arterias coronarias epicárdicas en el perro y en el cerdo. *Rev Esp Cardiol*, 38: 348-350.
- EVANS HE (1993). The Heart and Arteries. In: *Miller's Anatomy of the Dog*, 3rd edition. W.B. Saunders Company, Philadelphia, pp 586-601.
- FEDOR JM, MCINTOSH DM, REMBERT JC and GREENFIELD JC JR (1978). Coronary and transmural myocardial blood flow responses in awake domestic pigs. *Am J Physiol*, 235: H435-444.
- FENEIS H and DAUBER W (2000). Corazón e Arterias. In: *Nomenclatura anatómica ilustrada*, 4th edition. Masson S.A., Barcelona, pp 184-193.
- GABELLA G (1999). Cardiovascular System. In: *Gray's Anatomy*, 38th edition. Churchill Livingstone, London, pp 1505-1510.
- GETTY R (1986). Generalidades sobre o coração e os vasos sanguíneos. In: *Sisson/Grossman Anatomia dos animais domésticos*, 5th edition. Guanabara Koogan, Rio de Janeiro, 1: 153-162.
- GHOSHAL NG (1986). Coração e artérias do suíno. In: *Sisson/Grossman Anatomia dos animais domésticos*, 5th edition. Guanabara Koogan, Rio de Janeiro, 2: 1224-1227.
- GRANDE N, CASTELO BRANCO N and RIBEIRO A (1982). Coronary arterial circulation in the Bantu. *Ohio Acad Sci*, 82: 146-151.
- GRANDE NR, TAVEIRA D, SILVA AC, PEREIRA AS and ÁGUAS AP (1994). Anatomical basis for the separation of four cardiac zones in the walls of human heart ventricles. *Surg Radiol Anat*, 16: 355-361.
- HADŽISELIMOVIĆ H and SECEROV D (1979). Superficial anastomoses of blood vessels in the human heart. *Acta Anat (Basel)*, 104 (3): 268-278.
- HADŽISELIMOVIĆ H, DILBEROVIĆ F and OVČINA F (1980). Blood vessels of the human heart: coronarography and dissection. *Acta Anat*, 106: 443-449.
- HAMMER C (1998). Physiologic obstacles after xenotransplantation. *Ann N Y Acad Sci*, 862: 19-27.
- HAMMER C (2001). Xenotransplantation: perspectives and limits. *Blood Purif*, 19: 322-328.
- IGAZ P (2001). Recent strategies to overcome the hyperacute rejection in pig to human xenotransplantation. *Yale J Biol Med*, 74: 329-340.
- KAMIMURA R, SUZUKI S, NOZAKI S, SAKAMOTO H, MARUNO H and KAWAIDA H (1996). Branching patterns in coronary artery and ischemic areas induced by coronary arterial occlusion in the CLAWN miniature pig. *Exp Anim*, 45: 149-153.
- KASSAB GS and FUNG YC (1994). Topology and dimensions of pig coronary capillary network. *Am J Physiol*, 267: H319-325.
- LORENZ G and GUSKI H (1990). Histotopographic and morphometric studies of the intramural coronary arteries in the trabecula septomarginalis of swine and pigmy goats. *Zentralbl Allg Pathol*, 136: 87-95.
- LUMB G and SINGLETARY HP (1962). Blood supply to the atrioventricular node and bundle of His: a comparative study in pig, dog, and man. *Am J Pathol*, 41: 65-71.
- PLATT J, DISESA V, GAIL D and MASSICOT-FISHER J (2002). Recommendations of the National Heart, Lung, and Blood Institute Heart and Lung Xenotransplantation Working Group. *Circulation*, 106: 1043-1047.
- REIG-VILALLONGA J, LONCAN-VIDAL MP and DOMENECH-MATEU JM (1988). Coronary arterial anastomoses. Study of their distribution in adult hearts specially emphasizing the crista supraventricularis. *Anat Anz*, 166: 285-295.
- SAKAI K, WATANABE K and MILLARD RW (1985). Defining the mechanical border zone: a study in the pig heart. *Am J Physiol*, 249: H88-94.
- SAMSTEIN B and PLATT JL (2001). Physiologic and immunologic hurdles to xenotransplantation. *J Am Soc Nephrol*, 12: 182-193.
- SCHAPER W, SHARMA HS, QUINKLER W, MARKERT T, WUNSCH M and SCHAPER J (1990). Molecular biologic concepts of coronary anastomoses. *J Am Coll Cardiol*, 15: 513-518.
- SCHUMMER A, WILKENS H, VOLLMERHAUS B and HABERMEHL KH (1981). Heart. In: Nickel R, Schummer A, Seiferle E (eds). *The Anatomy of the Domestic Animals*. Springer-Verlag, New York, 3: 15-70.
- SIMOENS PJ and DE VOS NR (1999). Angiologia. In: *Nomenclatura Anatómica Veterinária Ilustrada*. Manole Ltda, São Paulo, pp 234-243.
- STOWE DF, MATHEY DG, MOORES WY, GLANTZ SA, TOWNSEND RM, KABRA P, CHATTERJEE K, PARMLEY WW and TYBERG JV (1978). Segment stroke work and metabolism depend on coronary blood flow in the pig. *Am J Physiol*, 234: H597-607.
- TEIXEIRA FILHO A, ROLL C, SOARES CL and CARAMBULA SF (2001). The blood supply of the papillary muscles of the left ventricle in the Hereford cattle. *Ital J Anat Embryol*, 106: 293-298.
- VIEWEG WV, ALPERT JS and HAGAN AD (1976). Caliber and distribution of normal coronary arterial anatomy. *Cathet Cardiovasc Diagn*, 2: 269-280.
- WEAVER ME, PANTELY GA, BRISTOW JD and LADLEY HD (1986). A quantitative study of the anatomy and distribution of coronary arteries in swine in comparison with other animals and man. *Cardiovasc Res*, 20: 907-917.
- WHITE FC and BLOOR CM (1981). Coronary collateral circulation in the pig: correlation of collateral flow with coronary bed size. *Basic Res Cardiol*, 76: 189-196.
- WILLIAMS PL and WARWICK R (1973). Angiology. In: *Gray's Anatomy*, 35th edition. Jarrold and Sons Ltd, Norwich, pp 616-619.
- ZHANG Z, BÉDARD E, LUO Y, WANG H, DENG S, KELVIN D and ZHONG R (2000). Animal models in xenotransplantation. *Exp Opin Invest Drugs*, 9: 1-17.

