CIÊNCIAS VETERINÁRIAS:

Pensamento científico e ético 2

ALÉCIO MATOS PEREIRA
GILCYVAN COSTA DE SOUSA
(ORGANIZADORES)

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CIÊNCIAS AGRÁRIAS

Ciências veterinárias: pensamento científico e ético 2

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CIÊNCIAS AGRÁRIAS

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APRESENTAÇÃO

Pautado no propósito de complementar e aprofundar cientificamente alguns dos principais assuntos no que concerne à ciência animal, a presente obra abrange relevantes temas de importância veterinária, especialmente casos clínicos, tratamentos preventivos, estudos patológicos... Ademais, todos os estudos foram desenvolvidos e alicerçados em metodologias científicas específicas, sendo que cada trabalho científico centralizou sua abordagem investigativa e descritiva nos principais pontos de seu assunto, de forma pontual e incisiva, no intuito de, profissionalmente, aperfeiçoar, aprimorar e capacitar ainda mais você, querido leitor (a).

A obra detalha com maestria assuntos complexos da clínica veterinária e trás, em sua redação, textos aprofundados e escritos pelos grandes pesquisadores da ciência animal, colocando esse e-book como leitura indicada para os alunos e profissionais que desejam uma fonte didática e atualizada sobre diversas temáticas dos estudos clínicos patológicos e zootécnicos da área animal.

Não obstante, o e-book que estás prestes a ler foi desenvolvido através de um árduo trabalho conjunto de pesquisadores de diferentes áreas do conhecimento, relacionadas aos animais, fato este que enaltece ainda mais a riqueza informativa do presente trabalho. Desde já desejamos uma ótima leitura!

Alécio Matos Pereira

Gilcyvan Costa de Sousa

THE HEART OF HUMANS AND DOMESTIC SWINE: A COMPARATIVE APPROACH - A LITERATURE REVIEW

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ABSTRACT: The swine model has been used since the mid-1980s, due to biological similarity with human species mainly when it comes to the cardiovascular system. The choice of a species for scientific experimentation is crucial, with no intention of offering greater practicality and veracity in the results. Thus, this model is considered to be the best about its morphophysiology. Both in humans and swine, there are two patterns of cardiac arterial distribution: in the first, a left coronary artery reaches the coronary sulcus by bifurcating into an anterior interventricular branch and in the left circumflex artery; the second pattern consists on a trifurcation in the coronary artery, giving rise to the anterior intermediate and interventricular branches. This information suggests that the heart may be an ideal model for acute myocardial infarction (AMI). Since cardiovascular diseases are responsible for the most significant number of deaths worldwide, AMI occurs when a coronary artery is obstructed, interrupting the use of oxygen in the cardiac tissue, being irreversible when not diagnosed early. In this context, the porcine model is used to evaluate and validate the techniques. In the future, it is expected to apply these techniques to humans. Information on comparative cardiac vascularity was addressed, supporting data for studies with acute myocardial infarction.

KEYWORDS: Cardiovascular diseases, Acute myocardial infarction, Swine Model.

INTRODUCTION

According to a recent estimate, it is believed that the number of human deaths from coronary artery disease reaches approximately 40 million in 2020, considering this to be the disease with the highest mortality worldwide (ISHITANI et al., 2006). In Brazil, although steadily decreasing over the past few years (from

120.4 / 100,000 inhabitants in 2000 to 92 / 100,000 inhabitants in 2013), ischemic heart disease has assumed the leading cause of death among all possible cardiovascular diseases (GUIMARÃES et al., 2015), which were responsible for 29.8% of deaths in the national territory in 2013 (SBC; SBH; SBN, 2016).

Heart failure has become one of the main specialties of applied scientific research (FIELD et al., 2010), however, the implementation of new pharmaceutical modalities and therapeutic techniques directly applied to human patients, in addition to interfering in ethical concepts, also finds significant genetic heterogeneity and different lifestyles characterized among patients. In this sense, the updating of animal models appear to be the most viable alternative to fill these gaps (LELOVAS, KOSTOMITSOPOULOS and XANTHOS, 2014).

For Dixon and Spinale (2009), although the studies carried out with small animal models such as rodents, promote an understanding of the cellular and molecular bases of cardiovascular biology, the knowledge about the biological mechanisms and bases remains flawed in the extrapolation results for humans. They demonstrate that there are intrinsic differences in terms of heart rate, oxygen consumption, duration of action potential, and spontaneous reversal of experimentally induced ventricular fibrillation in the normal sinus rhythm (WINFREE, 1994; GREENE; BENSON, 2002; HAGHIGHI et al., 2003; GINIS et al., 2004). Therefore, the need to choose a species that accurately resembles human cardiovascular anatomy and physiology is paramount (LELOVAS, KOSTOMITSOPOULOS and XANTHOS, 2014). Such need elects the domestic swine species as a model of choice for such experiments (PLATT et al., 2002; VIDOTTI et al., 2008; PINTO et al., 2016).

From its use within laboratories, a significant advance in the production of knowledge has already been achieved, especially concerning the remodeling of the left ventricle and extension of the affected area after myocardial ischemia (PINTO et al., 2016). Therapies with stem cell transplantation were also related (MIN et al., 2012; LI et al., 2013) in addition to the use of angiogenic growth factors in infarcted patients (DIXON and SPINALE, 2009), which demonstrates their role vital in translational research (SWINDLE et al., 2012).

The objective was to carry out a literature review that compared the anatomy of the heart of humans and domestic swine, in order to expose a deeper understanding about the conformation and vascularization of this organ in both species, reporting on its behavior during acute myocardial infarction, in addition to describing the benefits of considering the swine species as an ideal model for medical progress.

GENERAL CONSIDERATIONS ABOUT CARDIAC ANATOMY

The period of embryogenesis marks the appearance of two distinct units that are formed concomitantly: the circulatory organs and the blood tissue. At this stage, clusters of mesenchymal cells from the outermost layer, organized on the wall of the yolk sac, compress and diffuse morphofunctionally like an endothelium, demarcating regions through which the hemocytoblasts will fill, floating in a fluid plasma (DYCE, 2019).

The heart of domestic animals, located in the center of the mediastinum of the thoracic cavity (more specifically in the middle of cardiac mediastinum), is the central muscular organ, intracavitary, which acts as two combined pumps (left and right) of suction and pressure, functionally determining the blood and lymphatic circuit due to the pressure difference caused by systole and diastole. Its morphology varies between species. However, there are many aspects in common. The layers (from internal to external) are composed of the endocardium, a smooth endothelial lining, myocardium, cardiac muscle, and epicardium, which is firmly attached to the cardiac muscle through the serous pericardium (GETTY, 1975; DYCE, 2019).

Geometrically, the heart appears as an irregular cone, and its anchoring is done through the vessels of the base; the atrial and auricular surfaces, margins, and the apex remain permanently free in the pericardial sac. Such a structure is strictly a closed serous sacculation that, when fixed in the heart, becomes strictly invaginated, reducing its flame to a mere capillary slit. The organ arrangement is asymmetrical, where the major axis (from the center of the base to the apex) is located at the ventral-caudal (GETTY, 1975; KÖNIG, 2016; DYCE, 2019).

The cardiac base (hilum) runs in the dorsal-cranial region, and its highest portion is located at the connection of the dorsal and median thirds of the dorsoventral diameter of the thoracic cavity; in this region, the right and left atria are organized, where the cranial and caudal vena cava and pulmonary veins flow, respectively. In the right antimere, the cardiac margin is extremely convex, and curves in a ventrocaudal direction. In the left antimere, the margin is shorter and practically vertical. The atrial (right, diaphragmatic - atrial face) and auricular (left, sternocostal - auricular) surfaces are convex and pleated by grooves that indicate the separation of the organ into four cavities: the two atria more cranially and distinct from each other by the interatrial septum, and the two ventricles more caudally, also distinguished from each other by the interventricular septum, oriented obliquely. The region of the septum located dorsally to the valves is called the atrioventricular. The apex is disposed at the central region, limiting dorsally the stern (GETTY, 1975).

Between the atria and the ventricles, there is the coronary sulcus, which represents the limit between the two cranial chambers and the two caudal chambers. Through a circumference, it girds almost entirely the heart, where it ends, in an uninterrupted way, in the ascendancy of the pulmonary trunk, originating the paraconal and circumflex interventricular grooves. These grooves contain the arterial and venous vessels that irrigate and perfuse the organ. The lateral plane of the left antimere reveals the paraconal interventricular groove, which externally borders and delimits the two ventricular chambers, the right being cranial-ventrally, and the left caudodorsally; it comes from the coronary sulcus, caudally to the origin of the pulmonary trunk, descending in parallel to the caudal border. Conversely, the lateral plane of the right antimere points to the subsinuous interventricular groove; it occurs at the level of the ventral coronary groove in the closing of the caudal vena cava towards the cardiac apex (GETTY, 1975).

CARDIAC VASCULARITY COMPARED

As previously presented, cardiovascular diseases are characterized as the leading cause of death worldwide, with coronary diseases being the most frequently observed condition (CLAES et al., 2008). In each specific case, the anatomical knowledge of the coronary circulation is essential for establishing the region of the affected tissue, the expected prognosis and the most appropriate therapy (STANDRING, 2010), whether during the performance of imaging procedures, hemodynamic interventions or surgical procedures (CAVALCANTI et al., 1995).

According to Borelli (2014), cardiac vascularization can be segmented into a left coronary system and a right coronary system, which tends to meet at their ends, defining a longitudinal circle (in non-human animals; transversal in humans). It bypasses the base of the heart through the coronary sulcus, defining a transversal circle (in non-human animals; sagittal in humans) that converges to the apex of the heart through the paraconal and subsinuous interventricular grooves (anterior and posterior in humans). In this way, all arteries directed to the organ depart, the first yielding atrial ascending and ventricular descending branches; and the second, giving only ventricular branches to the various myocardial segments (BORELLI, 2014).

The two coronary arteries, one left and one right, originate directly from the base of the aorta (GETTY, 1986; BATISTA; PORTO; MOLINA, 2011) from, respectively, the left and right coronary ostia (NETTER, 2008; STANDRING, 2010; MOORE; DALLEY; AGUR, 2011; GÓMEZ; BALLESTEROS, 2013; GÓMEZ; BALLESTEROS, 2014; KÖNIG; LIEBICH, 2016). The blood directed here, approximately 10% of the total volume in left ventricular systole (SHUMMER et al., 1981), comes from aortic reflux that does not return to the organ after the closure of the aortic valve and, therefore, is directed to cardiac nutrition tissue (HURST et al., 1981).

After extending through the defined space between the pulmonary trunk artery and the left auricle, the left coronary artery reaches the coronary sulcus for, in humans (SPALTEHOLZ; SPANNER, 2006; STANDRING, 2010; MOORE; DALLEY; AGUR, 2011), forking in the anterior interventricular branch and the left circumflex artery in 54.7% (BAPTISTA et al., 1991), 59.58% (BATISTA; PORTO; MOLINA, 2011) 61.3% (FALCI JÚNIOR; CABRAL; PRATES, 1993) or 92% (ABUCHAIM et al., 2009) of the cases. Respectively, these structures are positioned in the anterior interventricular groove towards the apex and posterior region of the heart; and in the coronary groove to the diaphragmatic face of this same organ (MOORE; DALLEY; AGUR, 2011), irrigating most of the left ventricle and, even if slightly, the right ventricle (WILLIAMS et al., 1995).

The second pattern of distribution of the left coronary artery consists of its trifurcation, giving rise to the intermediate and anterior interventricular branches, and the left circumflex artery, already being reported in the proportions of 8% (ABUCHAIM et al., 2009), 36, 18% (BATISTA; PORTO; MOLINA, 2011), 38.7% (FALCI JÚNIOR; CABRAL; PRATES, 1993) and 45.3% of the humans studied (BAPTISTA et al., 1991). This variation seems to play a role of supplementary irrigation in cases of vascular obliteration (PAULA, 1972).

In domestic swine, these two conformations of arterial distribution are also present (JORDÃO et al., 1999; GÓMEZ; BALLESTEROS, 2014; MOURA JÚNIOR et al., 2008) for the bifurcation in the left circumflex artery [traversing the coronary groove] and branch paraconal interventricular artery of the left coronary artery [crossing the groove of the same name]; and 20% (JORDÃO et al., 1999), 20% (MOURA JÚNIOR et al., 2008) and 21% (GÓMEZ; BALLESTEROS, 2014) for trifurcation in the left circumflex artery and diagonal and paraconal interventricular branches.

Noteworthy is the lack of definition as to the name used for the third branch from the left coronary artery trifurcation, time treated as an intermediate in humans (BAPTISTA et al., 1991; FALCI JÚNIOR; CABRAL; PRATES, 1993; ABUCHAIM et al., 2009; BATISTA; PORTO; MOLINA, 2011), time treated as diagonal in swine (JORDÃO et al., 1999; MOURA JÚNIOR et al., 2008; GÓMEZ; BALLESTEROS, 2014). More recently, Borges et al. (2019) used the denomination of oblique branch in a study involving Boars, in an unprecedented way, it is the only one that relies entirely on the indicative terms of position and direction for the nomination of the referred structure.

As for the right coronary artery, in humans, it follows from its origin at an anterior direction to the right, emitting branches to the area between the right auricle and pulmonary trunk artery. Then, it travels through the coronary sulcus and emits the right marginal branches (MOORE; DALLEY; AGUR, 2011) and to the arterial cone, ending, in about 72% (ABUCHAIM et al., 2009) or 75% of the cases, in the condition of the posterior interventricular branch (WILLIAMS et al., 1995), resting in the groove of the same name (MOORE; DALLEY; AGUR, 2011).

In domestic swine, the right coronary artery also ran through the coronary sulcus and was always responsible for emitting its marginal branch (MOURA JÚNIOR et al., 2008). Also in 100% of the cases (MOURA JÚNIOR et al., 2008; SAHNI et al., 2008; GÓMEZ; BALLESTEROS, 2013), or 96.7% (VIEIRA et al., 2008), this artery gave rise to the branch subsinuous interventricular, which also travels along the groove of the same name and irrigates the right and left ventricles, however from its right face (MOURA JÚNIOR et al., 2008; GÓMEZ; BALLESTEROS, 2013).

COMPARED CORONARY DOMINANCE

Schlesinger's study (1940) created the concept of coronary dominance, determining whether it will be right or left, depending on which coronary artery will supply the branch that reaches and exceeds Crux cordis. For the human species, Zoll (1951) described in his coronary study that these dominances are described in the same proportions for the cone branch of cases with the direct origin of the aorta. It was also noted that the pigs had the same similarity since there is no development of coronary anastomoses in most cases.

In humans, Didio and Wakefield (1975) described that right dominance was observed in 73.5%, balanced in 7.1%, and left in 19.4%. FALCI JÚNIOR and PRATES (1994) attributed that in the case of an anterior interventricular artery extrapolating the cardiac apex, emitting the posterior septal branches, even with the posterior interventricular branch coming from the right coronary, the dominance should be classified as left. In 1995, Kyriakidis and collaborators explained that the anatomical differences between men and women are of paramount importance concerning the control and evolution of coronary diseases in the measured patients.

Observing some patients in which the right coronary artery had a higher distribution, Nerantzis and collaborators (1996) recommended the term of true right dominance for hearts that presented a posterior interventricular and a marginal branch in the left ventricle. In these cases, infarction of the right coronary artery would cause ischemia of the posterolateral wall and mitral insufficiency. This shape had been observed in 38% of the hearts studied. Such results added to those found by Adams and Treasure (1985), who reported the right dominance in 90% of the cases, citing that the posterior interventricular branch has its origin before the Crux cordis in 32% of the cases, later following the path in the posterior interventricular groove. Both authors attributed that this form should be recognized in order to have a better result in surgical treatment.

Regarding the cardiac tissue perfusion assessment method, Vasko, Gutelius and Sabiston (1961) described a higher incidence of left dominance. When evaluated by arteriography, 48% had the right dominance, while left and balanced were the same. Mandarin (1990) also describes that the cardiac mass irrigated by the left coronary was higher. Weaver and collaborators (1986) studied pig hearts and considered the circulation and distribution of the branches to be superimposable to humans, considering the pig as the best experimental model for studies consistent with coronary circulation, with left dominance.

Didio and Rodrigues (1983) recommended anatomic-surgical segments, according to the distribution of the main branches, presenting three segments of the right portion of the heart, namely: cone, right marginal and posterior interventricular; and four segments of the left portion: anterior, lateral, left marginal and posterior ventricular interventricular. This cardiac segmentation is crucial to delimit the resection area of the left ventricles in partial ventriculectomy surgeries aiming at the treatment of dilated cardiomyopathy, where the connection of the marginal branch and its satellite veins would cause an area of ischemia, indicating the resection site (DIDIO et al., 1998).

When considering domestic swine, Sahni et al. (2008), Moura Júnior et al. (2008), and Gómez and Ballesteros (2015) reported that the right dominance was observed in all studied specimens. In addition to this, with a percentage of 96.7%, Vieira et al. (2008) also mention a balanced dominance in 3.3% of specimens, and Weaver et al. (1986) reported 17% and 5% of cases with balanced and left dominance, respectively, in 75 hearts. Subtype dominance has also been reported in swines Duroc, Landrace, and Mongrel, the balanced form being the most frequent [42.2%], however, with values very close to the right type [40%] (PINTO et al., 2016). These distributions can be seen in Figure 1, which shows the arterial vascularization patterns found in swine hearts.

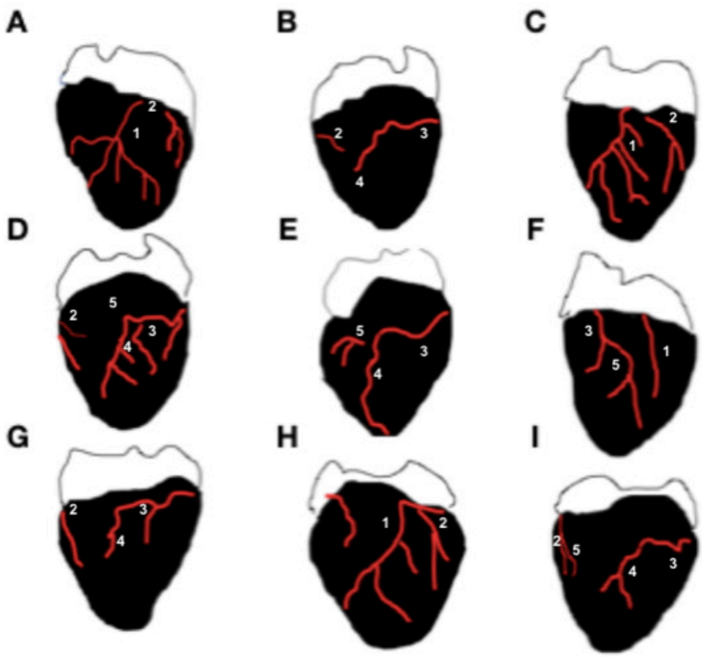

Figure 1: Swine cardiac vascularization patterns. In A- auricular face and B- Atrial face of the Mongrel swine heart, with balanced circulation. In A1, paraconal interventricular branch, A2 and B2 left circumflex branch, B3, right circumflex branch. In B4, subsinuous interventricular branch. In the same race, circulation of the right type, C- auricular face, D and E atrial face, was also found. It is noted that the direct circumflex branch in D5 in the form of C invading the left coronary sulcus through the collateral sulcus. In D4, subsinuous interventricular branch and left circumflex branch. In E3, left coronary sulcus invading the left coronary sulcus through the collateral sulcus (E5) and subsinuous interventricular branch, The right circulation was observed in Landrace pigs (F). In F1, paraconal interventricular branch running through the dorsal half of the left interventricular groove (F3). In F2 there is the left circumflex branch, and you will stick the right circumflex branch in F5, bypassing the pulmonary cone to run through the ventral half of the left interventricular groove. Left-type circulation in crossbred pigs is also observed in G (atrial face), H (auricular face) and I (atrial face). In G3, the right circumflex branch, G4 the subsinuous interventricular branch that runs through the dorsal and middle thirds of the right interventricular groove and the paradoxical interventricular branch (G1), reaching the ventral third of the right interventricular groove and the left circumflex branch (G2). In I, the subsinuous interventricular branch I4 is seen running through the dorsal and middle thirds of the right interventricular groove and the left circumflex branch (I2) and the collateral branches of the left circumflex branch I5 running towards the left ventricular wall and the dorsal third of the left ventricle. right interventricular groove. Adapted from PINTO el al., 2016.

Acute myocardial infarction

Three main arteries establish the blood supply to the heart in humans: anterior descending (AD), right coronary (DC), and circumflex (CX) (GORDELS et al. 2008, apud FERREIRA et al., 2016). AMI occurs when coronary blood flow is decreased, as previously mentioned. To better understand AMI and its diagnosis, Mansur et al. (2006) explained how the electrocardiogram (ECG) is performed, measuring the electrical impulses of the heart, allowing the identification of possible heart diseases. The correct analysis of this exam is fundamental to identify the place of AMI, as reported by (PESARO, SERRANO JUNIOR and NICOLAU, 2004).

For topographic analysis of ECG ischemic manifestations, using the Guidelines of the Brazilian Society of Cardiology (2016):

a) Anteroseptal wall - leads V1, V2, and V3.

b) Anterior wall - leads V1, V2, V3, and V4.

c) Localized anterior wall - leads V3, V4, or V3-V5.

d) Anterolateral wall - leads V4 to V5, V6, D1, and aVL.

e) Extensive anterior wall - V1 to V6, D1, and aVL.

f) Low lateral wall - leads V5 and V6.

g) High sidewall - D1 and aVL.

h) Lower wall - D2, D3, and aVF.

These topographic variations are best seen in Figure 2.

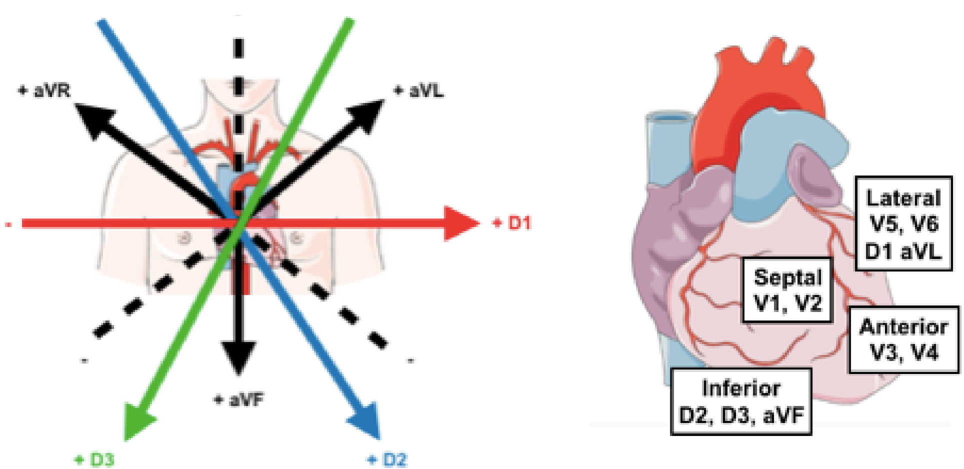

Figure 2: Peripheral derivations and topographic diagnosis (adapted from FIGUINHA, 2014; MOREIRA, 2020).

On ECG, lower infarction is characterized if the ST-segment elevation in D3 is more significant than in D2, and there is an unevenness in D1 and aVL greater than 1 mm, showing some lesion in the right coronary.

When there is an association with V4R elevation, it is possible to say that the right ventricle is involved in AMI. The CX artery is involved when there is an elevation in D1, aVL, V5, V6, and infra in V1, V2, and V3. Anterior infarction with elevation in V1, V2, and V3, if the elevation is greater than 2.5 mm in V1. If there is an associated depression in D2 and D3, the highest probability is in a proximal lesion of the AD (PESARO, SERRANO JUNIOR, and NICOLAU, 2004).

Although this test is inexpensive and easy to access, it can be performed late, with no effective pharmacological and surgical intervention, since the heart has a small capacity to repair and regenerate (CUI, YANG, and LI, 2016). Although survival rates in people affected by AMI are increasing due to improved health care, real recovery depends on restoring blood flow and cardiac function.

THE SWINE HEART AS A MODEL IN TRANSLATIONAL MEDICINE AND FUTURE PERSPECTIVES

The use of the swine model in translational medicine has been dated since the 1980s. These animals have been widely applied in biomedical research, as a general standard for preclinical studies. The morphophysiological characteristic mus be shared between humans and swines to generate a consistent cardiovascular modelo; there is then a significant difference in pigs, which is the presence of the azygos vein that drains the intercostal vessels in the coronary sinus of the heart, thus characterizing the return of mixed blood flow of systemic and myocardial blood. If necessary, this vessel can be connected to the total coronary blood flow (SWINDLER and SMITH, 2008).

As previously discussed, the hearts of humans and pigs are characterized by right coronary dominance, given that 90% of the human population does not have significant collateral circulation in coronary vascularization. However, the left coronary artery can supply most of the myocardium (SWINDLER and SMITH, 2008). These data are essential for the study of AMI since obstruction of a coronary vessel can result in this condition, making it an area of intensive research in swine to verify surgical and therapeutic approaches (LELOVAS, KOSTOMITSOPOULOS and XANTHOS, 2014).

In addition to this morphofunctional advantage of the heart, we must highlight other benefits related to the use of these animals, such as size, availability, useful life, being able to perform various surgical experiments, and to collect a good number of samples. Since they are omnivores, they are more similar when human physiology, the life span of pigs can reach 20 years, among other advantages cited by MAURENS et al., 2012.

All of this information provides for a new scenario in studies about heart transplants.

In Brazil, the first heart transplant was performed by Dr. Euryclides de Jesus Zerbini on May 26, 1968, at the Hospital das Clínicas in São Paulo, noted for being the first transplant performed in Latin America and the fifth in the world (STOLF and BRAILE, 2012). Advances in animal studies provided the use of grafts in heterologous transplants (between different species) began in 1974, with the use of artisanal valves of porcine and bovine pericardium preserved in glutaraldehyde, based on studies by HARKEN et al., 1951.

For more than 40 years, the pig has been studied as an organ donor for humans (GALVÃO and ALBUQUERQUE, 2020), initially the use of xenografts and, in the future, the partial or total replacement of tissues and organs. Taking into account that the number of organs available for transplants is still not able to meet the stipulated need, a new area of multidisciplinary research emerges, called tissue engineering, aimed at regenerative medicine and, thinking about the bioengineering of cardiac tissue, aims to generate clinically functional products, restoring the damaged heart's functionality (DELGADO, 2019).

FINAL CONSIDERATIONS

Given the above, the swine model remains a promising option in matters related to the understanding and improvement of therapeutic and surgical approaches, in addition to advances in tissue engineering. All the information about the swine model contributes to the understanding that this is still a current model, being extremely important for a better understanding of AMI and its therapeutic implications. Studies related to comparative cardiac vascularization were necessary for our approach so that the mechanisms involved in AMI were better elucidated, helping both in its diagnosis and in the treatment to be addressed.

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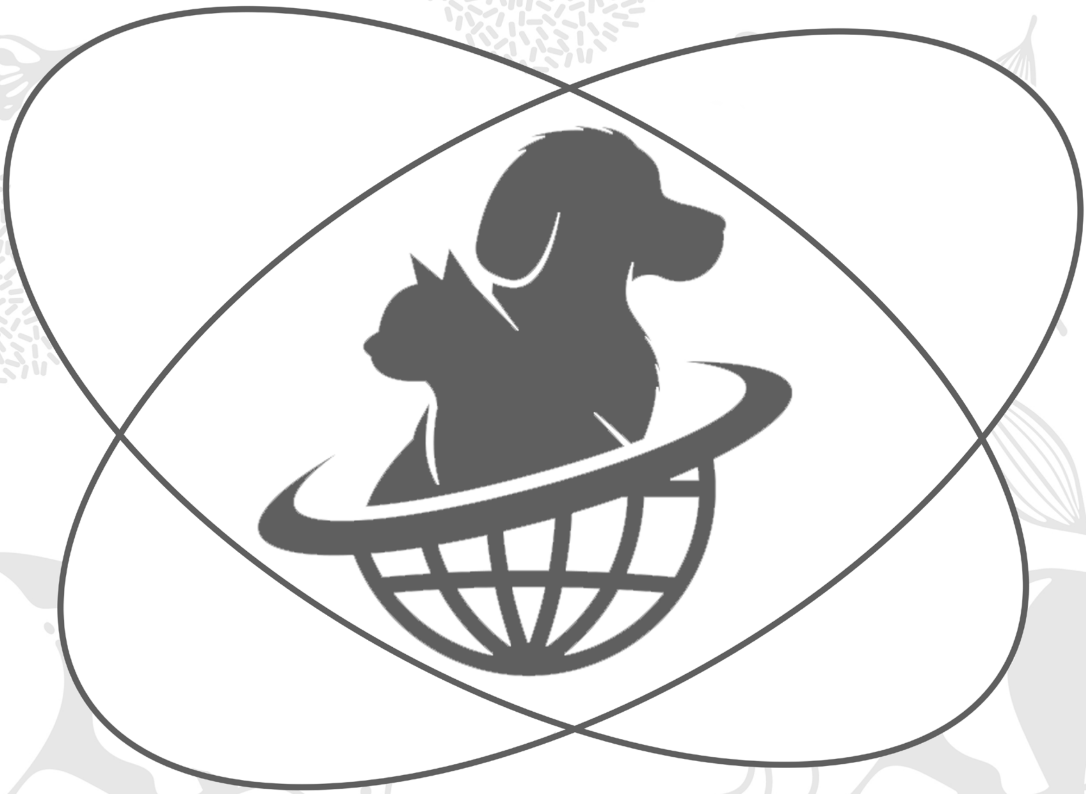
ÍNDICE REMISSIVO

CIÊNCIAS VETERINÁRIAS:

Pensamento científico e ético 2



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