

HEART TOPOGRAPHY AND PERICARDIC LIGAMENTS OF GUINEA PIGS

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Abstract:

Small rodents are the most used experimental models in research related to cardiovascular and respiratory system. The guinea pigs occupy a leading position. However, detailed anatomical descriptions of the thoracic cavity of this specie are relatively few in the literature. Compared to mice, rats or hamsters, widely used in research, electrocardiogram waves are similar to humans, making the guinea pigs to be the choice model for studies related to cardiac arrhythmias, and in particular, pharmacological studies. Using gross dissection of the thoracic cavity of ten guinea pigs, this study aims to achieve a detailed description of the heart topography and pericardial ligaments in guinea pigs. Occupying the majority of the narrow thoracic cavity, in the middle mediastinum, in guinea pigs, like all mammals, heart is double layer coated by the pericardium. It lies in the median plane, slightly oriented to the left at the level of 2nd-4th intercostals space and approximately at 1 cm cranial to the xiphoid appendix. External thin walls of the atria are separated from the ventricles by the grooves of coronary arteries and veins, showing multiple branches in all specimens studied. Ventrally and dorsally the ventricles are separated by two shallow interventricular sulci. Pericardial ligaments are well represented and are generated by reflection of the fibrous pericardium on the neighbouring structures, making heart attachment, mechanic protection of the heart and its great vessels.

The following ligaments were visualized in all subjects: sterno-pericardial ligaments (cranial and caudal), in four subjects being joined by a thin blade of adipose tissue; phreno-pericardial ligaments (central-strong, left-shorter, missing in two subjects and right-long); dorsally the vertebro-pericardial ligaments which connect the pericard to the spinal cord, more developed on the left side, forming sheaths for the aorta and for the large vessels. In conclusion, pericardial ligaments achieved a dynamic balance, constantly modified in relation to the phases of the cardiac cycle, their knowledge being necessary both practitioners and researchers which uses guinea pigs as experimental models in cardiovascular studies.

Key words: heart, pericardic ligaments, guinea pigs

INTRODUCTION

Although in recent years there is a conservative attitude of anatomists related to the resumption of anatomical studies or acceptance of new explicit theories or morphologically documented studies, the tendency to complete anatomical descriptions, especially of the animals used as experimental model, is unquestionable and must be accepted. In animals, cardiovascular system adaptation, are referred to morphological particularities due to taxonomic affiliation, environment and physical activity (Barone 1997, Cotofan et al., 2007). It is clearly stated that the heart of mammals share many similarities, beginning from embryonic developmental evolution, as long as the heart is the first organ to fully form and function during the vertebrate development

(Kent and Carr, 2001; Kirby 2002). Many of the researches findings claim the presence of the same underlying mechanisms in mammal's heart development, which are considered molecularly and developmentally similar (Harvey and Roshental 1998). However, in adult mammals the sizes, shape and positions of heart vary between species. Currently, in medical research, animal use as experimental model is fundamental in developing new therapies of cardiovascular disease, but the extrapolation of animal data requires that the animal model chosen for testing is similar in anatomy and physiology to that in humans (Paul and Paul 2001). Guinea pigs choice for cardiovascular studies must be primarily based on scientific hypothesis, the degree of species similarities to the human anatomy and the appropriate animal housing and care. This

involves a proper selection of the animal model and a detailed knowledge of its anatomy. The present study aims to provide a detailed description of topography, external conformation and pericardic ligaments of the heart in guinea pigs.

MATERIALS AND METHODS

Ten adult guinea pigs from ages between 1 and 3 years old, both sexes (4 male and 6 female) and varying weights (370-610g) were used. The subjects were part of an ongoing study related on digestive system and were provided by the “Iuliu Hațieganu” University of Medicine and Pharmacy, Cluj Napoca, Romania, bio base. Gross dissection was performed after euthanasia which was made by inhalation of an overdose of isoflurane (Baxter Health Care Corporation, USA). Thoracic cavity was opened by a double incision along the right and left side of the sternum to preserve the ligaments insertion. The ribs were carefully removed and the topography of thoracic organs and their ligaments were photographed using a Nikon D60 digital camera. Terms were used in agreement with NAV 2012. The Institutional Bioethics Committee of University of Agricultural Science and Veterinary Medicine approved the study.

RESULTS

Heart topography

In guinea pigs the heart occupies a relatively

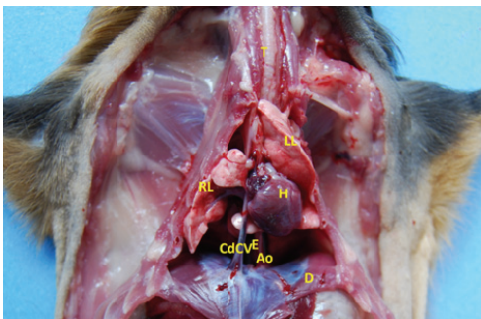


Fig. 1 Heart topography in guinea pigs. H-heart; T-trachea; LL-left lobe of lungs ; RL-right lobe of lungs;-CdCV-caudal cava vein; E-esophagus; Ao-aorta; D-diaphragm

large space in the thoracic cavity, extending from the sternum to the vertebral column and leaves only a narrow space for the lungs on each side. Its base, dorsocranially oriented, lies in the midline, at the level of 2nd-4th intercostals space, the apex caudoventrally directed was situated at 1cm distance from xiphoid appendix (Fig. 1). The overall orientation was slightly to the left in caudal direction and a more ventrally tilted long axis of the heart (Fig. 2).

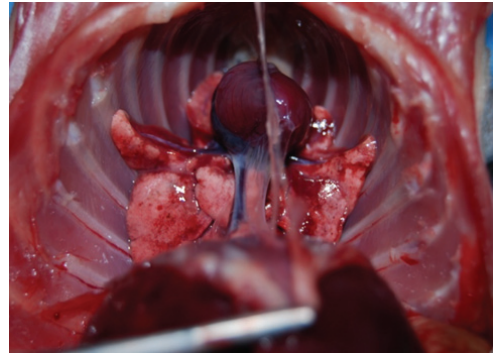


Fig. 2 Note the slightly left orientation in caudal direction and a tilted long axis of the heart

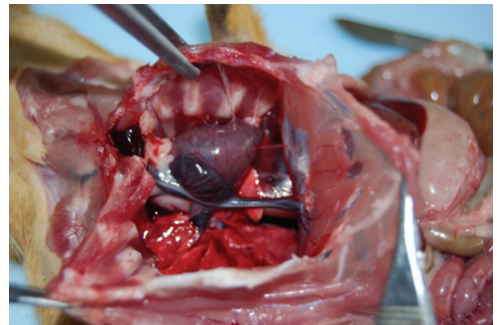


Fig. 3 Right lateral view of the thoracic cavity in guinea pigs. Extended course of the caudal vena cava after passing the diaphragm

The tilted of the heart was limited due to the extensive attachments of the pericardium to the sternum and diaphragm. The auricles were visible on both, right and left sides with the pulmonary trunk located between them and to the left oriented. The caudal vena cava has an extended course on the right side of median plane (Fig. 3).

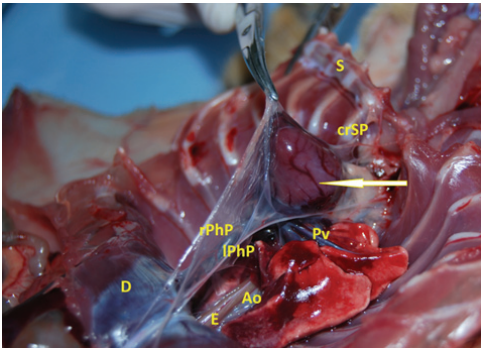


Fig. 4 Well represented arterial vascular supply and venous drainage of the heart-arrow. (S-sternum; crSP-cranial sternal pericardial lig.; rPhP-right phrenico-pericardial lig.; lPhP-left phrenico-pericardial lig.; Ao-aorta; E-esophagus; D-diaphragm; Pv-pulmonary veins)

The aortic arch projects caudally, first on the right then to the left being accompanied by the pulmonary trunk.

In all subjects, the coronary arteries were well observed on the external aspect of the heart running into the shallow coronary groove, with an extensive collateralization of the arteries. Also, an extensive network of intercommunicating veins provides the venous drainage of the heart (Fig 4).

Pericardic ligaments

The heart was enclosed by the fibrous pericardium (*Pericardium fibrosum*), which in cranial direction was fixed at the base of the heart, extends upward on the great arteries and veins, enclosing these vessels; ventrally the fibrous pericardium was attached to the sternum and to the diaphragm by several and obvious ligaments.

Using NAV we systematized the pericardic ligaments in ventral, cranial, dorsal and caudal ligaments.

In all subjects, ventrally, the pericardium was attached to the sternum through the cranial and caudal sterno-pericardic ligaments (*Lig. sternopericardiacum*), which was continuous in seven subjects, showing a small amount of adipose tissue within. The *cranial sterno-pericardic ligament* emerges from the ventral cranial region of heart to be inserted on the dorsal side of the manubrium and on the two

small cylindrical vestigial clavicles on the each side. This ligament was a direct continuation of the vertebro-pericardic ligament (right and left), delimiting a space which houses a small amount of adipose tissue, a reminiscent of the thymus in adult animals. The *caudal sterno-pericardic ligament* was detached from the ventral margin of the heart, above the interventricular sulcus to be inserted of the xifoid appendix of the sternum (Fig. 5). This ligament too, was fulfilled with adipose tissue.

Cranially, the parietal pericardium (*Lamina parietalis*) surrounds the aorta and the pulmonary trunk, the inferior and superior vena cava together with the pulmonary veins, being the reflection on visceral layer (*Lamina visceralis-epicardium*) of serous pericardium (*Pericardium serosus*) creating the *pericardial cavity (Cavum pericardii)*. The fusion of the parietal serous pericardium with the fibrous pericardium creates one layer with two surfaces. The fibrous pericardium has little elasticity and by its fusion with the base of the great vessels creates a closed space in which the heart is disposed.

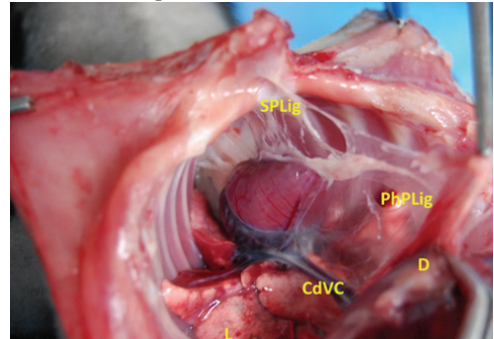


Fig. 5 Overall patern of fibrous pericardium. SPLig-sternal pericardial lig.; PhPLig. Phreno-pericardial lig.; CdVC-caudal cava vein; D-diaphragm; L-lungs

In all subjects, dorsal cranial pericardial ligament was short being represented by the *aorto-pericardic ligament* which anchors the pericardium from the aortic arch in cranial direction. This ligament was almost imperceptible due to the relative large place occupied by the heart in thoracic cavity and the close proximity of the heart to the thoracic

inlet. Also, in the middle mediastinum the fibrous pericardium cover the descending aorta making the connection of the pericardium to the vertebral column.

Between the dorsal pericardium and the lungs hilum, covering the vascular and the bronchial elements, the tiny but well visualized *pericardo-pedicular ligaments* were noted. Besides the mentioned ligaments which stabilize relations between the mediastinal organs, in all subjects were identified the connection ligaments between the esophagus and trachea, esophagus and bronchi, and between the esophagus and fibrous pericardium.

The caudal pericardic ligaments were represented by the obvious *phreno-pericardic ligaments*, (*Lig. phrenopericardiacum* which connect the caudal margin of the heart with the diaphragm (Fig. 6).

Three ligaments were observed in eight subjects, while in two subjects the left phreno pericardial ligament was missing. The *right phreno-pericardial ligament* was detached from the cranial right ventricle to be inserted on the tendineous center (*centrum tendineum*) of the diaphragm. The *left phreno pericardial ligament* emerges from the apex having an oblique direction for its insertion half divided: one part on the tendinous diaphragm and one part on the costal muscular diaphragm close to the 8th intercostals space. The *central phrenico-*

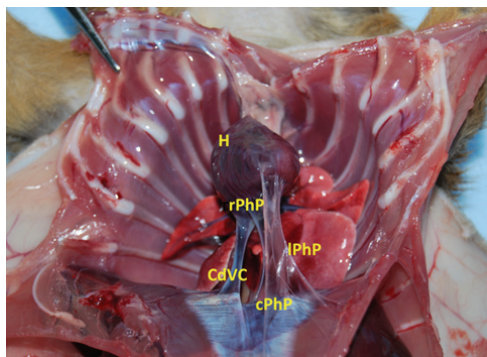


Fig. 6 Phreno-pericardial ligaments and their insertion. rPhp-rightphreno-pericardial lig. ; lPhp-leftphreno-pericardial lig. ; CdVC-caudal cava vein; cPhP-central or ventral phreno-pericardial ligament.

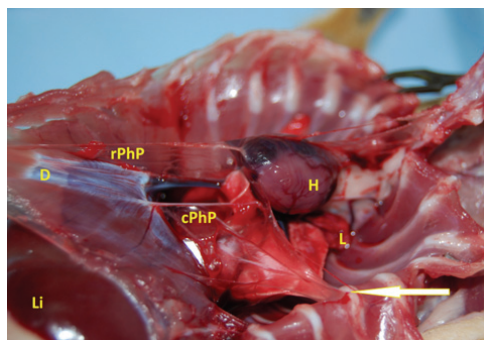


Fig. 7 The left insertion on the 7th rib of pericardium- white arrow

pericardial ligament connected the central part of the tendinous diaphragm with the apex.

This ligament was attached to the right pericardial ligament in five subjects. In two subjects in which the left phrenopericardial ligament was missing, it was well defined a *left lateral pericardial ligament* which emerges from the apex to be inserted on the 7th rib and intercostals space (Fig 7).

Division of the mediastinum A clear division of mediastinum was possible due to the accurate topography of the composing structures in all examined subjects. The cranial mediastinum (*Mediastinum craniale*) was the space between the dorsal side of the sternal manubrium, cranial mediastinal pleura on each side, upper pericardium and the first thoracic vertebrae. It contains several important structures like aortic arch, the final course of superior vena cava, the trachea, the esophagus, thoracic duct, vagus and phrenic nerves. Also, in the cranial mediastinum a small amount of adipose tissue, a reminiscent of involuted thymus, lying close to the thoracic inlet was found in all subjects. The middle mediastinum



Fig.8 Size, shape and external conformation of guinea pig heart. B-base of the heart; RA-right atrium under the right auricle; RV-right ventricle; A-apex; LV-left ventricle; PTr-pulmonary trunk

(*Mediastinum medium*) was further divided into three spaces: ventral, middle and dorsal. Ventrally, the ventral mediastinum (*Mediastinum ventrale*) was bounded by the sternum and the pericardium dorsally. In this space the sterno-pericardial ligaments, internal thoracic vessels, small lymph nodes were found. The central (middle) space of middle mediastinum was occupied by the great vessels (superior and inferior vena cava, aorta, pulmonary trunk and pulmonary vessels), pericardium and heart. The caudal vena enters into the right atrium after an extended course after passing the diaphragm and caudal mediastinum: the same long trajectory was present of cranial vena cava after the confluence of the right and left brachiocephalic veins. In all subjects the pulmonary veins were well individualized emerging from the well delineated pulmonary lobes. The pulmonary trunk ascends from right ventricle, dorsal and to the left oriented, passing in front of the aorta (Fig. 8). The aorta leaves the left ventricle primary on right oriented, curves dorsally to the left becoming the aortic arch. After the aorta exit the pericardium it arches over the right pulmonary trunk, passing to the left of the trachea and esophagus and entering into the dorsal mediastinum as descending aorta. Dorsal mediastinum (*Mediastinum dorsale*) was the space between the dorsal pericardium and the posterior thoracic walls containing descending

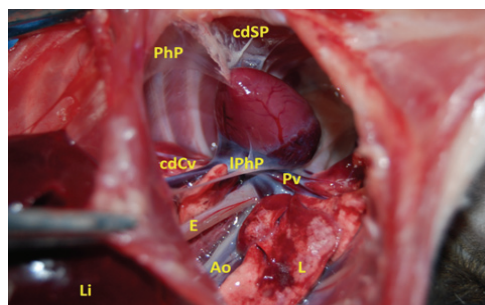


Fig. 9 Caudal view of the thoracic cavity in guinea pigs and its principal structures. cdSP-caudalsterno-pericardiclig.; PhP-phreno-pericardiclig.; cdCv-caudal vena vein,; Ao-aorta; L-left caudal lung lobe; Pv-pulmonary veins; IPhP-left phreno-pericardiclig.

aorta, thoracic duct, thoracic sympathetic trunk and the thoracic splanchnic nerves. Esophagus passes along the right side of the descending aorta in dorsal mediastinum.

The caudal mediastinum (*Mediastinum caudale*) was a relative large space between the caudal sagittal plan which passes under the apex, and diaphragm. It contains the caudal thoracic segments of caudal vena cava, descending aorta, esophagus guarded by the vagus branch (Fig. 9).

DISCUSSION

The heart is located in ventral part of middle mediastinum in large mammals, tend to have a less pronounced left side orientation and a more ventral tilted long axis (Getty 1995; Barone 1997; Crick et al., 2001) if we compare to humans (Goss 1949; Barone 1997). Also, the heart of most animals tends to be elongated having a pointed apex. This feature is absent in dogs which have an ovoid heart with a blunt apex (Evans, 1993), ruminants, which have a pointed apex and a conical shape heart, compare with the blunted apex in sheep (Ghoshal, 1975, Kent 2001) and pigs in which the blunt apex is medially oriented (Cotofan et al., 2007). The conical, elongated heart and pointed apex in rabbit (Schiffmann, 2002) is similar to the guinea pigs heart, but in guinea pigs the heart tend to be more large related on thoracic cavity size, occupying a

disproportionally large part of the thorax and leaves only a narrow space for the lungs on each side. This is in agreement with the report of other studies about the differences that exist in the ratio of heart weight to body weight, which show that adult sheep and adult pigs have a smaller ratio of heart weight to body weight compare to adult dogs, whom ratio was as much as twice the heart weight to body weight than in mentioned animals (Ghoshal et al., 1975; Evans, 1993). The earliest literature data show that the body weight is inversely related to the heart rate and directly related to blood volume and heart weight (Holt 1970; Getty 1975).

In all mammals the apex is formed only by left ventricle, but differences exist in heart orientation. In quadruped standing animals, the heart long axis is oblique, ventro-caudally oriented and slightly to the left. Due to the quadruped posture of animals, the apex of the heart is more ventrally tilted toward to the sternum, than in humans, but in guinea pigs this tilting is limited because of extensive attachment of the pericardium both to the sternum and to the diaphragm. Most quadruped mammals tend to have a less pronounced left side orientation and a more tilted long axis of the heart compare to humans, in which the heart is situated with the right atrium on the right, the right ventricle anterior, the left ventricle to the left and posterior, and the left atrium entirely posterior. The apex is projected inferiorly and to the left.

All mammalian hearts lies in the middle mediastinum being enclosed into the pericardium which creates the pericardial cavity around the heart (Barone 1997; Kent and Carr 2001; Cotofan et al., 2007). The mechanical function of the pericardium including the heart fixation in the thorax, prevention of the heart dilatation by maintenance of the heart shape, preventing of excessive movement of the heart with changes in body position and a physical barrier to infection and malignancy are of great importance but not the major one. Also, the pericardium has a secretory function accomplished by visceral layer of serous

pericardium, which secrete the pericardium liquid which allows the inner visceral pericardium to glide against the outer parietal pericardium. However, it was proved that the pericardium is not essential for survival, as long as the congenital absence or pericardiectomized human and animals, have no severe adversereaction to removal, or congenital absence (Hammond et al., 1992; Abel et al., 1995). Moreover, in certain condition, the presence of the pericardium, physically constrains the heart function by a depressive hemodynamic influence that limits cardiac output by affecting and reducing diastolic ventricular function (Saunders 2012, Ware 2012; Majoy 2013), feature frequent present in humans too. Equally true is that clinically pericardial disease is one of the most infrequent type of cardiac disease, but morphologically is common, both in humans (Roberts 2005) and animals (Dempsey and Ewing 2011; DeFrancesco 2013). This could be explaining by the differences related to pericardium thickness. Generally, pericardium wall thickness increases with increasing heart and cavities size between the various species. If ovine have $0.32\pm 0.1\text{mm}$ wall pericardial thickness, porcine $0.20\pm 0.1\text{mm}$, dogs $0.19\pm 0.1\text{mm}$, humans have between 1-3.5mm wall pericardial thicknesses. Our description of guinea pig pericardium is in concordance with the features found in most of the mammals. Also, in animals the differences of the amount of pericardial fluid are related to the heart dimensions and animal weight. Holt (1970) reported various volume of pericardial liquid in dogs, ranging from 0.5-2.5ml or more in large breed dogs up to 15ml. In small animals, like guinea pigs, chinchilla, rat there are no reports of pericardial liquid volume, further studies are necessary.

In animals, the tiny pericardium is fixed to the great vessels at the base of the heart and is attached to the sternum and diaphragm, although the degree of attachment varies between the species. More specific, the attachment to the tendineus center of the diaphragm is firm and broad in dogs, the phreno-pericardial ligament being the only

constant pericardial ligament reported in dogs. Nevertheless, in dogs, there are reports of the presence of a tiny ligament which detached from the dorsal caudal pericardium to be inserted on the 6th costal cartilage (Kent and Carr 2001). Our results are in agreement with this reports, we describe in two subjects the presence of this pericardio costal ligaments in absence of the left phreno-pericardial ligaments. In ruminants the caudal pericardium is attached to the sternum by a strong sterno-pericardial ligament, only the apex being in contact with the sternum, compare to the extensive attachment to the sternum, in absence of the phreno-pericardial ligaments in horse (Barone 1997; Cotofan et al., 2007).

The presence of a rich coronary collateral circulation in guinea pigs revealed in this study is in accordance with that described in dogs (Ghoshal 1975; Koke and Bittar 1978). In the earliest studies related to heart ischemia and in pharmacological therapies for reducing the ischemic size, the dogs were the preferred animal model, but, due to anatomical particularities of coronary irrigation these studies lead to false claim about the efficacy of medication as long as administration in humans did not produce the same results as those observed in dogs. Nowadays, it is well known that the dog have a much more extensive collateral circulation compare to sheep and pigs (Abel et al., 1995). Morphologically, the pig's heart is more similar to the human heart, due to limited collateral coronary circulation, making the swine heart, ideal for acute ischemia studies (Crik et al., 1998). In recent years, small animals are commonly used in cardiovascular disease; the rats have a sparse collateral circulation being a suitable model to heart ischemia (Chorro et al 2009). Due to the extensive collateral circulation in guinea pigs, normal perfusion of heart is maintained after a coronary artery occlusion and infarction does not develop. Another morphological feature of the guinea pigs heart is the smallest diameter of the mentioned vessels which are hard to be verified if the spontaneous or induced reperfusion appears. Nevertheless, the use of guinea pigs as experimental model remains

quite important for arrhythmia studies on humans due to the similar electrocardiographic waves (Guo et al., 2009). It was demonstrated that the polarity of T waves is the same of that of QRS complex from human subjects (Watanabe et al., 1985, Roberts et al., 2003, Zaragoza et al., 2011).

Regarding the mediastinum, based on the obvious anatomical components, we realized a detailed division and description of mediastinum spaces. In human the mediastinum is divided by a transversal plane that connects the sternal angle, passes over the pericardium to the intervertebral disc of 4th and 5th thoracic vertebra, into superior and inferior mediastinum, the later being subdivided in anterior, middle and posterior (Goss 1949, Gray's Anatomy, 2008). In animals anatomical descriptions recognizes three spaces: cranial, middle and caudal, with a double division of middle mediastinum in ventral and dorsal (Barone 1997, Cotofan et al., 2007) From a morphologic point of view, and due to extensive feature of pericardic ligaments in guinea pigs, our division of middle mediastinum in ventral, middle (central) and dorsal is justified. The same simple landmarks as in humans could be made: the ventral mediastinum is dorsal to the sternum and ventral to the pericardium, the middle mediastinum contains the pericardium and its components and the dorsal mediastinum is behind the pericardium and ventral to the vertebral column.

All these considerations mentioned above are the base of using both large and small animals as experimental models for the cardiovascular studies. The advantages of large animal models are primarily based to their similarities in heart physiology to humans and ease of instrumentation, but equally true is that maintenance costs are higher which make small animal models more attractive.

CONCLUSIONS

Apart from the differences in size the guinea pig heart is anatomically similar with the most of the mammal's heart.

Guinea pigs have a different type of heart vascularisation meaning the presence of a well developed collateralisation of heart supplying vessels offering a natural degree of protection of ischemic disease.

The tiny but obvious sterno-pericardial and phreno-pericardial ligaments give the guinea pigs heart, a strong insertion and protection into thoracic cavity.

The middle mediastinum in guinea pigs can be divided in three obvious spaces: ventral, middle (or central) and dorsal, each of them containing important and obvious anatomical structures.

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