Comparative Study of the Liver Anatomy in the Rat, Rabbit, Guinea Pig and Chinchilla

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Bulletin UASVM Veterinary Medicine 75(1)/2018

Print ISSN 1843-5270; Electronic ISSN 1843-5378

doi:10.15835/buasvmcn-vm:002717

Abstract

In liver surgical and histological research, small rodents are the most used experimental models. Although the small animals liver is typically lobulated and its macroscopic appearance do not resemble that of the compact human liver, a high degree of lobulation equivalence, allow the use of small rodents in biomedical research. The macroscopic anatomy of the liver of the rat, rabbit, guinea pig and chinchilla was studied from a comparative standpoint. The topography, lobulation and the connection elements of the liver were examined by detailed in situ observation and explanted liver of forty specimens.

The rat liver (*Hepar*) consists of four distinct lobes of different size: the left lateral lobe - LLL (*Lobus hepatis sinister lateralis*), the median lobe - ML, the right lobe - RL (*Lobus hepatis dexter*) and the caudate lobe CL (*Lobus caudatus*). The largest lobe was the median lobe. The rabbit liver consists of five lobes: left lateral lobe - LLL, left medial lobe - LML (*Lobus hepatis sinister medialis*), right lobe - RL, quadrate lobe - QL (*Lobus quadratus*) and caudate lobe - CL. The most developed lobe was the left lateral lobe. The caudate lobe had a very narrow attachment on the hilar region. The guinea pig liver show six lobes: left lateral lobe - LLL, left medial lobe - LML, right lateral lobe - RLL (*Lobus hepatis dexter lateralis*), right medial lobe - RML (*Lobus hepatis dexter medialis*), quadrate lobe - QL and caudate lobe - CL. The largest lobe of this specie was the left lateral lobe. In chinchilla liver showed four lobes like in the rat. In the rats the most developed hepatic ligament was the falciform ligament (*Lig. Falciforme hepatis*) which spans from xyphoid process of the sternum and diaphragm to the liver, beginning at the interlobular fissure. The coronary ligament (*Lig. Coronarium hepatis*) was well developed in all rats. Interlobular ligaments connect the left lateral lobe with the upper caudate lobe. In rabbits, guinea pigs and chinchillas the connection elements were represented by the falciform ligament, coronary ligament, right (*Lig. triangulare dextrum*) and left triangular ligaments (*Lig. Triangulare sinistrum*), hepatorenal ligament (*Lig. hepatorenale*) and hepatoduodenal ligament (*Lig. hepatoduodenale*) with varying degrees of development.

Based on detailed study of the macroscopic anatomy of rat, rabbit, guinea pig and chinchilla a proper experimental model in liver research, could be assessed. In this regard, the vascular anatomy of the liver in the mentioned species is of a great importance and it is subject of another report.

Keywords: anatomy, experimental models, hepatic ligaments, liver lobes

Introduction

In recent years, mice and rats are the most used animals both in morphological and functional studies of the liver. Starting from the models used in experimental liver transplantation, anatomical and physiological studies, metabolic and immunological research, the area of interest has expanded in the field of regenerative and

pathological studies. In this context, experimental lobar resections of the liver have been practiced on both healthy liver and liver tumors. Particularly of the rodents is that they have the same anatomical organization of the liver, in the sense that each liver lobe has its own pedicle containing a portal triad, namely the corresponding branch of the portal vein, its own biliary pathway and the

arterial branch (Popesco *et al.*, 1997; Stamatova *et al.*, 2012; Quesenberry et Carpenter, 2012). Due to this fact, lobar resections, more or less extensive (Madrahimov *et al.*, 2006) are possible. All these interventions requires a good understanding of the liver's macroscopic anatomy and its vasculature. Due to the facts that rats are the most commonly used in biomedical research because they are easy to maintain and their procurement is cheap, anatomical liver studies have been made most often on this rodent. The rat and chinchillas liver is described as having four main lobes: the right lobe (*Lobus hepatis dexter*), the medial lobe, the left lobe (*Lobus hepatis sinister*) and the caudate lobe (*Lobus caudatus*) (Martins and Neuhaus 2007; Stan 2013; Novak *et al.*, 2015), while the guinea pig liver is divided into six lobes, the right and left lobes being subdivided in lateral and medial part (Breazile and Brown, 1976), topography determined by position on the falciform ligament (*Lig. Falciforme hepatis*) and median plane. Thus, the right lateral lobe (*Lobus hepatis dexter lateralis*) - RLL, the right medial lobe (*Lobus hepatis dexter medialis*) - RML, the left medial lobe (*Lobus hepatis sinister medialis*) - LML, the left lateral lobe (*Lobus hepatis sinister lateralis*) - LLL, besides the caudate lobe (*Lobus caudatus*) - CL and the quadrate lobe (*Lobus quadratus*) - QL, are described. An intermediate situation is encountered in the rabbit, in which the liver has five lobes, the right lobe being undivided (Barone, 1997; Stamatova *et al.*, 2012). Another distinguishing characteristic of rats compared to the other three species is the absence of gallbladder (Kongure *etv al.*, 1999; Martins and Neuhaus, 2007). Taking into account the fact that the rodents share the same ancestor with the lagomorphs on the one hand and on the other hand the rabbits are used as much as experimental models as the rodents, this anatomical study performs the comparative description of the lobes of the liver at rat, rabbit, guinea pig and chinchilla.

Materials and methods

Forty animals (ten of each species) were examined. Ten adult male Wistar rats (mean body weight 460 ± 40 g) provided from the UMF (University of Medicine and Pharmacy Cluj-Napoca) bio base, were used. Also, ten domestic rabbits (mean body weight 980 ± 250 g), ten guinea pigs (mean body weight 420 ± 50 g), and ten

chinchillas (mean body weight 350 ± 60 g) were brought from breeding farms in the day of the examination. All animals received care according to the criteria outlined in the "Guide for care and Use of Laboratory Animals". The study was performed with approval of the Bioethics Committee of the University of Agricultural Sciences and Veterinary Medicine, Cluj Napoca. Euthanasia was performed by administration of an overdose of isoflurane (AErrane, Baxter, USA) in all animals. A midline incision of abdominal cavity was performed and the liver, its topography, and connecting elements were recorded. The hepatic ligaments were incised and the liver was extracted from abdominal cavity to be examined separately. Terms were used in accordance with NAV 2012.

Results and discussions

- Topography, borders surfaces and relations with adjacent structures

In the rats, the firm, smooth, dark red liver (*Hepar*) was placed on the cranial abdominal region, half of its volume being situated in the intrathoracic part of abdominal cavity (Figure 1A). It has a compact appearance and a central position, the caudal edges reaching approximately the same level on both sides of the abdominal cavity. On the right side, the caudal edge was made by the right inferior lobe and on the left side by the left lateral lobe. The diaphragmatic or parietal surface (*Facies diaphragmatica*) was smooth and convex, being mostly made by the medial lobes and by the left lateral lobe, and completely covered by the peritoneum. *In situ*, on this surface were visible three lobes: the median lobe, the left lateral lobe (*Lobus hepatis sinister lateralis*), and the right lobe (*Lobus hepatis dexter*). Between the caudate lobe (*Lobus caudatus*), caudal vena cava and the two layers of coronary ligament (*Lig. Coronarium hepatis*), a part of the liver was uncovered by the peritoneum, (*Area nuda*) being in direct contact with the diaphragm. The visceral surface (*Facies visceralis*) was deeply concave being in relation with the stomach, descending duodenum, pancreas, transverse colon and right flexure, spleen, right kidney and right suprarenal gland. With the exception of the right kidney, that made the renal imprint (*Impressio renalis*), the mentioned structures did not leave visible imprints on the liver lobes. On the visceral surface,

Figure 1. *In situ* visceral surface of the rat-A and chinchilla-B, liver.

LLL-left lateral lobe; LML-left medial lobe; RML-right medial lobe; DRL-dorsal right lobe and VRL-ventral right lobe; FL-falciform ligament; Interlobar ligament-arrow; S-stomach; RK-right kidney; P-pancreas; RL-right lobe; CP- caudate process; PP-papillary process;

covered almost completely by the peritoneum, four lobes were recognized.

In the rabbits, the red-brown liver was positioned almost in intrathoracic part of abdominal cavity. The diaphragmatic surface (*Facies diaphragmatica*) was convex applied on the diaphragm and the visceral surface (*Facies visceralis*) was concave, moulded on the convexity of the stomach (Figure 2C). On the diaphragmatic surface three lobes were visualized, namely two left lobes and one right lobe. Visceral surface show five lobes, separated by deep fissures. The dorsal margin (*Margo dorsalis*) was almost transversally positioned in the manner in which the left lobes of the liver reach the same level as the right lobe. The right margin (*Margo dexter*) is deeply hidden under the hypochondrium and only the caudate process reaches the level of the last rib. The ventral margin (*Margo ventralis*) extends in the epigastric region, stretching between the two costal arcs, up to the level of the seventh rib to the right, and the ninth rib to the left.

In the guinea pigs, two thirds of the red-brown, smooth liver was located in the intrathoracic part of abdominal cavity. It was multilobulated having deep fissures (Figure 2D). Concav diaphragmatic and convex visceral surfaces were noted. On the diaphragmatic surface four lobes were visualized while on the visceral surface six lobes were identified. The visceral surface was in relation with stomach, duodenum, right colic flexure, pancreas and right kidney. The ventral margin of the gallbladder exceeds the ventral border of the liver. On the visceral surface the gallbladder

was attached to its fossa (*Fossa vesicae felleae*), between the right medial lobe and quadrate lobe.

In chinchillas, as in guinea pigs, two-thirds of the liver mass was situated in intrathoracic part of abdominal cavity (Figure 1B). Diaphragmatic concave surface showed three lobes, while the convex visceral surface showed four main lobes. The visceral surface was in contact with stomach, duodenum, duodenal lobe of the pancreas, jejunum, and right kidney. It has a light brown colour and a smooth appearance.

• Liver lobes and hepatic ligaments

In the rats, the liver presented four lobes: left lateral lobe - LLL, middle or median lobe - ML, right lobe - RL and caudate lobe - CL, of varying sizes. Except for of LLL the rest of the lobes presented subdivisions (Figure 3A).

The left lateral lobe - LLL, occupied the left part of the epigastric region and the left hypochondriac region. It has no subdivisions. The free part of this lobe was placed ventral to the stomach, covering two third of the stomach, cranial to the caudate lobe and slightly dorsal to the middle lobe. Its medial part was covered by the left middle lobe but the dorsal part of the lobe lies in close relation with the diaphragm. It has an oval shape and has no fissures. The left lateral lobe presented a narrow pedicle bound with the intrahepatic cava vein and a small base attached to the left median lobe.

The middle lobe of the rat liver - ML, was the largest lobe of the liver. It was located just under the diaphragm, and makes a large part

Figure 2. *In situ* liver of the rabbit-C and guinea pig-D.

LLL-left lateral lobe; LML-left medial lobe; RL-right lobe; RML-right medial lobe; RLL-right lateral lobe; CP-caudate process; PP-papillary process; QL-quadrato lobe; GB-gallbladder; RK-right kidney. S-stomach; P-pancreas; D-duodenum;

of the parietal surface. A deep fissure (the main fissure or umbilical fissure, divides the lobe in two portions: a small left middle lobe - LML and a large right middle lobe - RML. The ratio between the two middle lobe divisions was 1:3. The left middle lobe was bound with left lateral lobe. A large base of the middle lobe surrounded almost entire circumference of the cava vein.

The right lobe - RL, was divided by a deep horizontal fissure into two small overlapped portions: the dorsal - DRL, or superior, right lobe and the ventral - VRL, or inferior, right lobe. The two right lobes were located on the right side of the cava vein. On the parietal surface the right lobes were almost completely covered by the right middle lobe. The dorsal right lobe has a large base. The ventral right lobe shows an obvious renal imprint.

The caudate lobe was located ventral to the left lateral lobe, on the left part of the cava vein. A small paracaval portion of the caudate lobe surrounded the cava vein making the connection between the caudate lobe and the ventral right lobe. The proper caudate lobe (or Spiegel lobe) was split into two portions, one as ventral caudate lobe - VCL or anterior, and a dorsal portion as dorsal caudate lobe - DCL or posterior caudate lobe. The VCL has a narrow pedicle, and it lies on the ventral surface of the stomach, being covered by the ventral layer of the lesser omentum. The DCL lies on the dorsal surface of the stomach being in close relation with the gastric lobe of the pancreas and with the spleen. Also, the DCL was covered by the dorsal layer of the lesser omentum.

The falciform ligament was complete in all subjects, making the attachments of the liver with the diaphragm and ventral abdominal wall. In its free margin, the round ligament (*Lig. teres*) was present. The coronary ligament has two layers: the upper layer and the lower layer. The upper layer extended from the upper margin of the bare area to the diaphragm. The coronary ligament was continued on the right side by the small right triangular ligament. This ligament connected the right margin of the DRL to the diaphragm. The left triangular ligament connected the dorsal part of the parietal surface of the left lateral lobe to the diaphragm. Between the LLL and the DCL an obvious interlobular ligament was present.

In all examined rats the caudal cava vein has an extended intrahepatic path.

The gallbladder was absent, usually each lobe being drained by its own bile duct. The common bile duct was formed by the union of the main hepatic ducts.

In the rabbits, the liver presented five lobes: the left lateral lobe - LLL, the left medial lobe - LML, the right lobe - RL, the caudate lobe - CL and the quadrato lobe - QL (Figure 4C). In rabbit the right lobe was single, while the left lobe was subdivided in left lateral and left medial lobes. Almost the half of left lateral lobe was covered by left medial lobe, the first one being entire visualized on the visceral surface. On the lateral edges, the left lateral lobe showed small incisures, less numerous and smaller on the other lobes. The right lobe had an oval shape, twice long as wide and covered the half of the left medial lobe on the diaphragmatic surface. The caudate lobe was well

Figure 3. The rat – A and the chinchilla – B liver lobes.

LLL – left lateral lobe; LML – left middle lobe; RML – right middle lobe; DRL- dorsal right lobe; VRL – ventral right lobe; ICV – inferior cava vein ligated; PC – paracaval portion; VCL – ventral caudate lobe; DCL - dorsal caudate lobe. In chinchilla, the notch of the middle lobe - ML and the divisions of the right lobe - RL are not shown in this picture. CP – caudate process;

developed having a narrow attachment on the hilar region. The caudate lobe was divided into two parts: the caudate process (*Processus caudatus*) and the papillary process (*Processus papillaris*). The caudate process exceeds the right liver lobe and shows an obvious renal imprint. The papillary process was rounded in rabbit. The quadrate lobe was small, less visualized, being attached to the gallbladder fossa.

Regarding the hepatic ligaments in rabbit, the absence of the round ligament (*Lig. teres*) was noted. The falciform ligament starting from hillus, was large but very thin on its insertion on diaphragm and was found in all rabbits. In eight rabbits the right triangular ligament was small, being attached to the right lobe of liver near the caudate process. We noticed the presence of a well developed left triangular ligament extended from the left lateral lobe to the diaphragm in all rabbits. The hepatorenal ligament connected the right lobe of liver to the right abdominal wall having a long parietal insertion.

The gall bladder lies in a deep depression of the caudal surface of right lobe, had cylindrical shape, its ventral border did not exceed the ventral edge of the liver.

In the guinea pigs, the liver showed six lobes: the right lateral lobe - RLL, the right medial, lobe - RML, quadrate lobe - QL, left medial lobe - LML, left lateral lobe - LLL and caudate lobe - CL (Figure 4D). The most developed lobe was the left lateral lobe. This lobe showed no incisures as in rabbits, only a small incision on the lateral edge of the left lateral lobe was noted. The quadrate lobe was well

defined in the left side of gall bladder. The rounded shape of gall bladder exceeded the ventral border of the liver. The gall bladder was attached to a fossa on the quadrate lobe and showed an obvious swelling on the beginning of the cystic duct. The caudate process was well demarcated showing the right kidney imprint. The papillary process has triangular shape and was subdivided by a deep cleft in two small segments. Regarding the liver connection elements, in guinea pigs, the presence of a large falciform ligament which connects the diaphragmatic margin of quadrate lobe to xiphoid process of the sternum, extending backward to the ventral abdominal wall, was visualized. The position of this ligament indicates the line division of the liver into right and left territories. The dorsal extremity of falciform ligament was continued by a conspicuous coronary ligament, like a short circular fold, connecting the dorsal border of the liver with the middle aponevrotic region of the diaphragm. Also, a small bare area was present. The left triangular ligament, a lateral continuation of the coronary ligament on the left side, was present in all subjects, connecting the left lateral lobe of the liver with the diaphragm. Regarding the right triangular ligament, this structure was present in seven subjects. The hepatoduodenal ligament was made by the lesser omentum passing from the lesser curvature of the stomach and from the duodenal ampulla to the visceral surface of the liver. In its thickened margin on the right side three important structures were identified, namely the common bile duct, hepatic artery and portal vein. Also, a free edge of this

Figure 4. Visceral surface of the rabbit-C and guinea pig-D liver.

LLL-left lateral lobe; LML-left medial lobe; RL-right lobe; RML-right medial lobe; RLL-right lateral lobe; CP-caudate process; PP-papillary process; QL-quadrate lobe; GB-gallbladder; RK-right kidney.

ligament with cranial insertion on the cystic duct, has descended along to the common bile duct to make the caudal insertion on the duodenal lobe of the pancreas. Gastrohepatic ligament was well individualized connecting the lesser curvature near to the right side of the esophagus with the papillary process of caudate lobe. The hepatorenal ligament has a particular insertion. Cranial insertion of hepatorenal ligament was visualized on the ventral border of the caudate process, then glide down medial to the ventral surface of the right kidney and on the ascending duodenum.

In the chinchillas, the liver showed four distinct lobes: the left lateral lobe – LLL, the middle lobe – ML, the right lobe – RL and the caudate lobe – CL. The LLL was unique without divisions (Figure 3B). It has an oval shape, its visceral surface covering the stomach fundus and the ventral surface of this organ. The ML was the largest lobe being subdivided into two portions: a largest left middle lobe (LML) and a smaller right middle lobe (RML). The RL was divided into two pyramidal parts: a lateral part and a medial part. The caudate lobe or Spiegel lobe was well developed. The larger caudate process located at the right side of the cava vein has a wide renal imprint and the small papillary process was located on the small curvature of the stomach. On its base the caudate lobe was attached to the left lobe.

The falciform ligament connected the middle lobes with the diaphragm extending to the level of the umbilicus. The coronary ligament was very small and the left and right triangular ligaments were almost untraceable. The wide hepatoduodenal ligament contained a system of

parallel bile ducts which opens at several points in the proximal duodenum.

The oval shape gallbladder has been visualised on the visceral surface, sitting on its fossa on the delineation between the right middle lobe and the right lobe of the liver, its ventral border being covered by the right lobe.

In scientific literature there are numerous descriptions of the gross anatomy of the mammalian liver, but most of them lack of in situ presentation and pictures. This paper performed a thorough description of the macroscopic anatomy of the liver of the most common small animals used in liver research in order to provide comparative macroscopic anatomical details of the liver of the rats, rabbits, guinea pigs and chinchillas. Also with a great importance in liver comparative studies, especially in surgical approach, is the liver vasculature, but this aspect is subject of another ongoing research.

The most studied model in liver research is undoubtedly the rat. Its liver macroscopic anatomy was rated as being closest to the human liver anatomy. Kongure *et al.*, (1999) have compared the rat and humans livers, showing that the divisions of the rat liver correspond to the human liver segmentation made by Couinaud (1994). However, differences exist, and were pointed out by the Martins and Neuhaus (2007). Among them and in concordance with this research are those related to the macroscopic anatomy. The rats liver is multilobulated, divisions of the lobes are distinct, and the left and right territories has approximately the same volume, the gallbladder is absent, while human liver is compact, the lobes

have no clear external divisions, the gallbladder is present and the left territory is smaller than the right territory (Martins and Neuhaus, 2007). Moreover, the fact that each lobe has its own pedicle containing a portal triad, makes the rats the most suitable animal models in liver surgical research.

Between rats, rabbits, guinea pigs and chinchillas there are numerous similarities and differences. The similarities are related to the division in two main territories, the right and the left territory with approximately the same sizes in mentioned species. This aspect is less mentioned in anatomical studies cited (Nowak *et al.*, 2015; Stamatova *et al.*, 2012; Pérez *et al.*, 2005; Pérez and Lima, 2007). Using as delineation landmark the falciform ligament, in this report, the lobes were delimited as right lobes and left lobes.

However, in rat in chinchilla, the middle lobe was shared of both territories, but in rats the right middle lobe was largest compare to the smallest right middle lobe in chinchillas.

The liver surfaces are the same in most of mammals: parietal and visceral surfaces. In rats, the diaphragmatic surface was continued with a surface in direct contact with the diaphragm, aspect mentioned by the Martin and Neuhaus too. The degree of convexity of the diaphragmatic surface was less pronounced in rabbit, due to the presence of a voluminous cecum in this specie.

The rat liver is multilobulated as in other mammals (Barone, 1997) and lobes nomination is made after portal vein ramifications (Couinaud, 1994; Kongure *et al.*, 1999; Martins and Neuhaus, 2007). Our macroscopic assessment is similar with the mentioned authors. However, the rat liver divisions are differently interpreted by various authors due to a great individual variability (Madrahimov *et al.*, 2006; Popesco *et al.*, 1990). In this report, the caudate lobe and the right lobe subdivisions have been named according to the veterinary medicine nomenclature, after their dorsal or ventral position corresponding to the superior or inferior denomination of other authors (Kogure *et al.*, 1999; Madrahimov *et al.*, 2006; Martin and Neuhaus, 2007).

Commonly in rodents there are described four liver lobes: left, right, caudate, and middle lobe (Quesenberry, 2012).). In rabbits subdivision of the left lateral lobe into left lateral and left medial parts and the presence of quadrate lobe pointed

out the presence of five lobes (Barone, 1997; Stamatova *et al.*, 2012). In the guinea pigs the presence of deep notches between the lobes lead to the identification of six distinct lobes, which is similar to those reported by Cooper and Schiller (1975), Breazile and Brown (1976). In chinchilla, the presence of four lobes was reported by the Novak *et al.* (2015) too, but they don't mention a clear division of the caudate lobe.

Regarding the hepatic elements, the present report described in all mentioned specie the presence of the five hepatic ligaments, with variable degree of development (Stan, 2013, 2014). The most constant was the falciform ligament, which was complete in rats, guinea pigs and chinchilla, being reduced at hepato-diaphragmatic part in rabbits (Barone, 1997). A noteworthy aspect is the presence of an interlobular ligament in rats, between dorsal caudate lobe and left lateral lobe, pattern which was described by the Madrahimov (2006) too.

Conclusion

The present study shows that an accurate knowledge of the morphology of the liver in experimental models underpins the achievement of safely experimental surgery, organ transplantation and training in liver research.

Acknowledgments. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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