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Rabbit Liver Lobes: An Anatomical Study of Experimental Surgical Approaches

Figen SEVIL KILIMCI

Adnan Menderes University, Faculty of Veterinary Medicine, Department of Anatomy, Aydın-TÜRKİYE.

Corresponding author: Figen Sevil-Kilimci; E-mail: fsevil@adu.edu.tr; ORCHID: 0000-0002-2291-0545
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Summary: A number of animal models have been developed for experimental liver surgery protocols such as lobectomy, ischemia and reperfusion studies, organ injuries, and drug trials. Though, some morphometric studies describe the liver lobes in rats and mice, such anatomical information is not sufficiently available in rabbits. The aim of this study was to evaluate the anatomical approaches for experimental liver resection in the rabbit, and to examine the proportional distribution of each lobe conforming to the whole organ, and to schematize the macroanatomical properties of each lobe.For this purpose, the liver lobes were dissected according to anatomical references. The volumes and weights of the whole organ and the individual lobes were measured. The percentages of the liver lobes were calculated according to the weight and volume of the total liver.The interlobar notch, especially between the medial and lateral parts of the left lobe was more prominent than that between the quadrate and the right lobe. The proportion of the left lateral and medial lobe was 27%, and 24% relative to the total liver weight, similarly, the right lobe, quadrate lobe and the caudate lobe was 19%, 7% and 23%, respectively. The volumetric ratios of liver lobes were also found close to the mass ratios.In conclusion, anatomical information from this study can be used as a reference in performing various experimental surgical studies on the rabbit liver.
Key words: Anatomy, liver, lobes, rabbit

Tavşan Karaciğer Lobları: Deneysel Cerrahi Yaklaşımlarına İlişkin Anatomik Bir Çalışma

Özet: Lobektomi, iskemi ve reperfüzyon çalışmaları, organ yaralanmaları, ilaç denemeleri gibi deneysel karaciğer cerrahisi protokolleri için farklı hayvan modelleri geliştirilmiştir. Rat ve farelerde karaciğer loblarını tanımlayan bazı morfometrik çalışmalar olmasına rağmen, bu anatomik bilgiler tavşanlarda yeterli değildir. Bu bilgiler ışığında, bu çalışmanın amacı bir deney hayvan olan tavşanlarda karaciğer rezeksiyonuna anatomik yaklaşımı ve her bir lobun tüm organa göre dağılım oranlarını değerlendirmek ve makroanatomik şemayı oluşturmaktır. Bu amaçla karaciğerlerde loblar anatomik referanslara göre diseke edilmiş. Tüm karaciğer ve daha sonra her bir lobun tek tek ağırlıkları ve hacimleri ölçülmüştür. Karaciğerin loblarının, total karaciğerin ağırlığına ve hacmine göre yüzde değerleri hesaplanmıştır. Çalışmada karaciğer lobları arasında bulunan incisura interlobaris, özellikle sol lobun medial ve lateral bölümleri arasında çok belirgin olduğu ve aynı zamanda bu lobların birbirinden tamamen ayrı iki lob olarak görüldüğü dikkati çekti. Ayrıca toplam karaciğer ağırlığına göre, sol lateral lobun oranı yaklaşık % 27, sol medial lob % 24, sağ lob % 19, kuadrat lob % 7 ve kaudat lob % 23 olarak bulundu. Hacim ölçümlerine göre lob oranları, kütle oranlarına yakın değerlere sahip olduğu bulundu. Sonuç olarak bu çalışmada; deneysel çalışmalarda kullanılmak üzere karaciğer rezeksiyonları başta olmak üzere çeşitli deneysel çalışmalarda operasyona referans olabilecek anatomik bilgi ile organın loblanmasının oransal verileri sunulmuştur.
Anahtar kelimeler: Anatomi, karaciğer, lob, tavşan

Introduction

In the liver, lobectomy is a surgical procedure that is required both in human and veterinary medicine for a variety of procedures such as tumor, trauma, and transplantation (Teh et al., 2007; Zhang et al., 2014; Tüzün et al., 2015). A good understanding of liver and lobes' volumes is not only important to estimate the vital functions of the body during lobectomy or transplants surgeries, but also during the functional remnant liver volume and the small size syndrome (Dahm et al., 2005; Tucker and Heaton, 2005). In addition, proportional measurements of lobes are also essential in hepatic ischemia and reperfusion studies (Graaf et al., 2011; Van Den Esschert et al., 2012; Huisman et al., 2014; Olthof et al., 2017). Due to above-mentioned facts, the knowledge of the liver anatomy is necessary in experimental surgical studies such as hepatectomy (Rahman and Hodgson, 2000; Madrahimov et al., 2006; Aller et al., 2009a-b; Alheani and Al-Kennany, 2013; Nevzorova et al., 2015), liver regeneration (Palmes and Spiegel, 2004; Bélanger and Butterworth, 2005), embolism (Graaf et al., 2011; Van Den Esschert et al., 2012; Huisman et al., 2014; Olthof et al., 2017), and liver tumors (Qi et al., 2007; Zou et al., 2012). These studies have been frequently carried out on rats and mice (Rahman and

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Hodgson, 2000; Palmes and Spiegel, 2004; Teh et al., 2007; Tuñón et al., 2009; Huisman et al., 2014; Torre et al., 2014; Zhang et al., 2014; Tedde et al., 2015) and only a few studies reported the proportions of liver lobes (Kubota et al., 1997; Martins et al., 2007). Given that the small size of these animals, as well as the variability of anatomical structures compared with humans, is considered to be a disadvantage for experimental surgical applications (Martins et al., 2007), rabbits may be preferred as anatomical model for these experimental surgical techniques, owing to the presence of gallbladder, larger volume than other rodents and closer functions to human liver (Olthof et al., 2017; Páramo et al., 2017).

In light of this information, the present study describes the macro-anatomical information and proportional distribution of organ lobes to support the research of experimental liver surgeries in rabbits.

Materials and Methods

This study was conducted with the permission of Animal Experiments Ethics Committee (HADYEK), 64583101/2018/125, Aydin Adnan Menderes University. Twenty New Zealand (Oryctolagus Cuniculus) female rabbit cadavers with a mean body weight of 2855.25 ± 680.05 grams were used. These animals had previously been used in the studies and no such application that could have affected the abdomen and the liver morphology. Macroscopically, organs with any suspected pathological formation were not used in the study.

The abdominal region was dissected in the cadavers used. After the resection of ligaments and vascular connections near the liver, organs were stored in the plastic boxes at 4^{o}C in 10% formalin solution. Before the lobes were separated, the organs were immersed in distilled water for one hour, thereafter, the volume of the whole organs was measured by "The Archimedes principle". Immedialtely after, the organs were dried with the towel paper and the total weight was measured. According to the studies (Stan, 2018 and Stamatova-Yovcheva et al., 2012) each lobe of the liver was carefully separated and weighed with precision scales (Precisa, XB-1200C), and volumes were measured by the Archimedes principle.

The ratios of the weight and volume of the liver lobes to the total weight and volume values of the liver were calculated. The weight ratios of the liver lobes to the live body weights of the animals and, also the Pearson's correlations for weights and volumes were calculated. The mean values ± SEM the proportional data were determined by the SPSS 19.00(IBM/SPSS, Armonk, New York, United States).

Results

At the midventral incision, the liver was seen situated caudally to the diaphragm at the cranial abdominal region. It was observed that it passed over the lesser curvatura of the stomach and found in close contact with the right kidney. The five lobes in the rabbit liver were presented as, the right lobe (RL), the left medial lobe (LML) and the left lateral lobe (LLL), the quadrate lobe (QL), the caudate lobe (CL), while the caudate lobe; the papillary process (PP) and the caudate process (CP) was again divided into two.

The interlobar notches were located between the liver lobes being more prominent, especially between the medial and lateral parts of the left lobe, and it was noted that these two subdivisions were seen as two completely separate lobes. Between the quadrate and the right lobe, the interlobar notch was less apparent. On the diaphragmatic surface of the liver, between the left medial lobe and the right lobe, a prominent structure of the falciform ligament was noted (along approximately 23-mm junction line) and extended to the portal region.

The papillary process of the caudate lobe was relatively round and located at the front aspect of the lesser curvature of the stomach, while the caudate process was cylindrical, and extended from the back of the curvature ventriculus minor to the right kidney.

The renal impression of the liver was markedly deep. It was also noted that there was a thin-long liver tissue (paracaval portion of the caudal lobe-CLparacaval) between the papillary process and caudate process at the level of the lesser curvature of the stomach. Some vessels such as the caudal vena cava, hepatic artery and portal vein were also visible in this region. The esophagus also passed closer to papillary process. It was seen that the gallbladder was embedded in the visceral surface of the right lobe and did not reach the ventral edge of the lobe.

The mean ± SEM the percentage of weight and volume of liver lobes were presented in Table 1 and Figure 1-B. The weight (TL_{Weight}%) and volume (TL_{Wolume}%) ratios of lobes relative to the total liver were similar (Table 1). It was noted that the largest lobe was left lateral lobe and the smallest lobe was the papillary process. While the sum of the left lobes measurements was approximately half of the total liver (~ 50%), the papillary process was found to constitute 5% of the total liver. It was also noted that one-fourth of the total liver was formed by the right lobe and the quadrate lobe. On the other hand, the left lobe and the right lobe together constituted ~ 70% of the liver. In addition, the volume of the paracaval portion was 3%. The correlations for weights and volumes were also presented in Table 2 and Table 3. The left lateral lobe weight showed positive high correlation with the total liver weight (r=0.933) and the body weight (r=0.593). At the same time, the left lateral lobe volume showed positive high correlation with the total liver volume (r=0.892).

Table 1. Weight and volume percentage of liver lobes to total liver and body weight (N=20)

Lobes	BW% Mean±SEM	TL_{Weight}% Mean± SEM	TL_{volume}% Mean± SEM
LLL	0.67±0.04	27±0.083	29±1.02
LML	0.60±0.04	24±0.082	23±1.05
RL	0.48±0.03	19±0.62	17±0.67
QL	0.19±0.01	7±0.50	8±0.75
PC	0.40±0.04	16±0.83	15±1.04
$CL_{paracaval}$	0.08±0.01	3±0.23	3±0.27
PP	0.09±0.01	4±0.28	5±1.15
TLL	2.51±0.12	100	100

TLL: Total Liver lobes. **BW%:** Body weight percentage, **TL_{Weight}%:** Total liver weight percentage, **TL_{volume}%:** Total liver volume percentage **LLL:** Left lateral lobe of liver, **LML:** Left medial lobe of liver, **RL:** Right lobe **QL:** quadrate lobe, **PP:** papillary process. **PC:** caudate process, **$CL_{paracaval}$:** paracaval portion of caudal lobe.

Table 2. The Correlation table showing weight of body, total liver and individual liver lobes

	TLL	LLL	LML	PP	PC	CLparacaval	QL	RL
BW	0.575**	0.593**	0.470*	0.260	0.163	0.569**	0.303	0.583**
TLL		0.933**	0.852**	0.596**	0.665**	0.640**	0.495*	0.858**
LLL			0.748**	0.531*	0.571*	0.675**	0.413	0.781**
LML				0.428	0.341	0.486*	0.428	0.758**
PP					0.455	0.454*	0.240	0.470*
PC						0.207	0.190	0.529*
CLparacaval							0.540*	0.454*
QL								0.382
RL								1

*: P< 0.05; **: P< 0.01.

BW: Body weight, **TLL:** Total Liver lobes, **LLL:** Left lateral lobe of liver, **LML:** Left medial lobe of liver, **RL:** Right lobe **QL:** quadrate lobe, **PP:** papillary process. **PC:** caudate process, **$CL_{paracaval}$:** paracaval portion of caudal lobe.

Table 3. The Correlation table showing volume of whole liver and individual liver lobes

	LLLv	LMLv	PPv	PCv	CLparacaval V	QLv	RLv
TLLv	0.892**	0.712**	0.161	0.695**	0.525*	0.518*	0.766**
LLLv		0.465*	0.231	0.584**	0.410	0.469*	0.612**
LMLv			0.009	0.292	0.309	0.502*	0.613**
PPv				-0.012	0.071	0.017	0.167
PCv					0.313	0.115	0.569*
CLparacaval V						0.038	0.462*
QLv							0.195
RLv							1

*:P< 0.05 ; **: P< 0.01

TLLv: Total Liver lobes volume. **LLLv:** Left lateral lobe of liver volume, **LMLv:** Left medial lobe of liver volume, **RLv:** Right lobe volume **QLv:** quadrate lobe volume, **PPv:** papillary process volume. **PCv:** caudate process volume, **$CL_{paracaval}$ V:** paracaval portion of caudal lobe volume.

Discussion and Conclusion

In experimental lobectomy, it is important to distinguish each liver lobe term anatomically (Martins et al., 2007), but it is noteworthy that in various studies, there is confusion in using the terms for liver lobes. While various studies reported four liver lobes (Van Lienden et al., 2011; Van Den Esschert et al., 2012; Huisman et al., 2014; Olthof et al., 2017; Páramo et al., 2017) in rabbit and some studies report five lobes (Stamatova-Yovcheva et al., 2012; Stamatova-Yovcheva et al., 2018; Stan, 2018). Moreover, some investigators describe the liver lobes in the rabbit as cranial and caudal lobes. The caudal lobe is defined only as the caudate process, while all the other lobes are defined as the cranial lobes (Van Den Esschert et al., 2012; Huisman et al., 2014; Olthof et al., 2017; Páramo et al., 2017). Some researchers define the

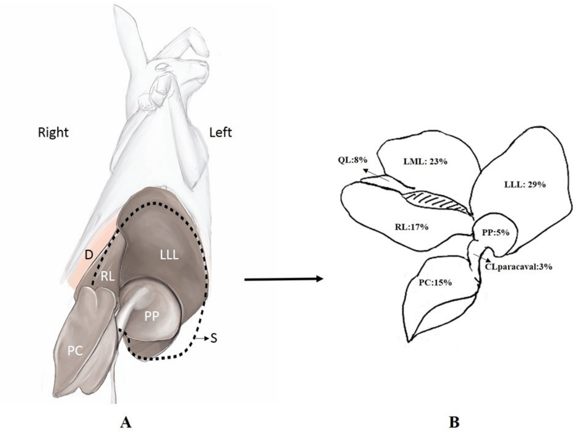

Figure 1: **A:**Liver position on rabbit, **B:** The distribution of liver lobes. Left lateral lobe (LLL), left medial lobe (LML),quadrate lobe (QL), right lobe (RL), caudate process (PC), papillary process (PP), parcaval portion ($CL_{paracaval}$), diaphragm (D), stomach boundaries (S)

lobes according to the course of the portal vein (Páramo et al., 2017). The gross anatomical divisions of the liver comprise the right, left, caudate and quadrate lobes (König and Liebich, 2007; Ellis, 2011). In the guidance of the reports of Stan (2018) and Stamatova-Yovcheva et al. (2012), the rabbit liver was divided into 5 lobes in this study according to anatomical terminology as left lateral, left medial, right, quadrate and caudate lobes. Apart from these standard lobes, the presence of paracaval region in the rabbit liver should also be considered. In addition to the similarities and differences in the definitions of the lobes, it is recommended that the researchers who work on experimental lobectomy in rabbits, also pay attention to the presence of the paracaval region.

The classical terminology of the gross anatomical lobes does not correspond to the functional division into eight hepatic segments, each with their own blood supply and the biliary drainage of human liver (Ellis, 2011). In liver surgery, the terms of segmentation of human liver is defined by the Terminology Committee of the International Hepato-Pancreato-Biliary Association (Strasberg et al., 2000; Abdala et al., 2004; Ellis, 2011; Strasberg, 2016). Although these terms do not not completely correspond to this segmentation, and there few studies comparing rat liver with human liver segments (Kogure et al., 1999; Martins et al., 2007). There are also studies describing macro-anatomically, the biliary drainage and vascularization of the liver in rabbits (Tam et al., 2014; Stamatova-Yovcheva et al., 2018). However, considering the experimental surgical studies of the liver in rabbits, further studies are needed to define the functional liver segments as in humans.

Various studies reporting surgical procedures like liver resection, lobectomy, embolism, and tumor always take into account the proportional distribution of liver sections. It is also important to follow the amount of tissue loss in the liver, and determine postoperative liver volume with minimal functional remnant liver volume. In several studies, human liver is divided into lobes or segments and their proportional data are presented (Leelaudomlipi et al., 2002; Abdalla et al., 2004; Mise et al., 2014). The proportional distribution of each liver lobe relative to total liver weight is presented in detail in rats and mice which are commonly used animal models for such studies (Madrahimov et al., 2006; Martins et al., 2007; Aller et al., 2009b). Rabbits are also used as common laboratory animals for experimental hepatic surgical operations. There is scarce information about proportions of lobes (Dupre et al., 2012; Huisman, 2014; Liao et al., 2017), however, the ratios of each liver lobes to the total liver have not been reported in rabbit. Liao et al. (2017) indicated that it is 50% of the left lobe and 20% of the caudate lobe according to the total liver mass in rabbit. Dupre et al. (2012) stated that according to preliminary study data, it is 27.9% of the total liver volume of the left lateral lobe, while Huisman (2014) reported it as 25%. In this study, the detailed proportional values of each liver lobe's weight and volume were presented with respect to anatomical structures. According to total liver weight, the proportion of the left lateral lobe was approximately 27%, the left medial lobe 24%, the right lobe 19%, the quadrate lobe 7% and the caudate lobe was 23%. The volumetric ratios of lobes were close to the mass ratios.

The experimental hepatectomy models that are based on the removal of defined liver lobe combinations use approximately 30%, 50%, 70% and 90% resected liver volume (Madrahimov et al., 2006). The macro-anatomical and morphometric findings in this study showed that the lobes for rabbit liver surgery can be easily accessed (considering the depth of interlober notch) in the following order, the left lateral lobe (approximately 27-29%)> the caudate process (15-16%)> the papillar process (4-5%) for resection.

Research in experimental surgery suggests that the left lateral lobe should be removed for easy partial hepatectomy in rabbits (Dupre et al., 2012). In addition, if a partial hepatectomy, including the other lobes, is planned, the presence of a shallow incisura between the quadrate lobe and both the right lobe and the left medial lobe along with gallbladder in the region, can make it diffcult to remove/ressect. Furthermore, in order to prevent the development of small size syndrome the determination of postoperative liver volume is important in liver transplantation cases. In a healthy young person, 20-25% minimal functional remnant liver volume is sufficient, while, 30 -60% remnant liver volume is needed in elderly or liver patient (Tucker and Heaton, 2005; Tüzün et al., 2015). As mentioned above, according to the morphological data the caudate and papillary process are easily removed together with the left lateral lobe, therefore, the minimal functional remnant liver may remain in respect to the numerical data in the rabbit liver.

In some studies, the ratio of liver or lobes to live weight was also used (Urayama et al., 1999; Aller et al., 2009b). Therefore, these ratios were calculated for rabbits in the study. It is about 2% of total liver to body weight in human. The mice used as experimental animals are 3-5% BW (2-3 g) and the rat is 2-3% BW (4-5 g) (Rogers and Dintzis, 2018). In this study, mean liver weight was calculated as 2.51% BW in rabbits.

The ratio of caudate process to the total liver volume was defined as 15% in this study, while the volume of this segment is also stated as 22-26% in the experimental liver embolism studies in rabbit. The volume of the lobe was calculated using compure tomography in these studies (Van Lienden et al., 2011; Van Den Esschert et al., 2012; Páramo et al., 2017). Graaf et al. (2011) reported that the values measured by computed tomography are significantly larger than the direct volume measurements of liver lobes. Accordingly, investigators should consider the method of liver measurement in their studies.

The method of storage is limitation during which the water which may enter the blood vessels or bile ducts of liver or their contents change after discontinuation. However, as mentioned above, it is also worth noting that the computed tomographic volumetry calculates different results from direct anatomical measurements.

In conclusion; anatomical information may be a reference in performing various experimental surgical studies in rabbit liver. This study suggests that, the caudate and papalillary processes together with the left lateral lobe are the easiest part of the liver for lobectomy, and approximately 50% functional remnant liver can continue to perform normal functions.

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