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Clinical anatomy of partial liver transplantation, a modified corrosion cast method

PhD thesis

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2 List of abbreviations

CHD	- common hepatic duct
CT	- computed tomography
EU	- European Union
FL	- falciform ligament
HCC	- hepatocellular carcinoma
HPB	- hepato-pancreato-biliary
HU	- Hounsfield unit
IHPBA	- International Hepato-Pancreato-Biliary Associaton
IVC	- inferior vena cava
KOH	- potassium hydroxide
LHA	- left hepatic artery
LHD	- left hepatic duct
LHV	- left hepatic vein
LDLT	- living donor liver transplantation
LLS	- left lateral segment (segments II and III)
LPV	- left portal vein
MHV	- middle hepatic vein
OLT	- orthotopic liver transplantation
RAHD	- right anterior hepatic duct
RAPV	- right anterior portal vein
RHA	- right hepatic artery
RHD	- right hepatic duct
RHV	- right hepatic vein
RPHD	- right posterior hepatic duct
RPPV	- right posterior portal vein
RPV	- right portal vein
SLT	- split liver transplantation
3D	- three dimension

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3 Introduction

3.1 History of liver transplantation

In the USA in 1968 Starzl performed the first successful orthotopic liver transplantation (OLT) using total hepatectomy. Calne and Williams (1968) announced similar achievements in the United Kingdom. Both teams greatly contributed to the development of liver transplantation and immunosuppressive therapy. The report of Fortner and co-workers (1970) on the first successful heterotopic (auxillary) liver homograft, was the forerunner of the oncoming development of heterotopic liver transplantation, split liver (SLT) and living donor related (LDLT) transplants. Liver transplantation has undergone continuous evolution although initially there was only one moderately effective immunosuppressive therapy within reach. The survival rates after the first year slowly approached 50% by 1979 [1, 2]. However, due to chronic rejection, infection and surgical infections there were only a small group of people among the long-term survivors. In 1979 Calne reported cyclosporine as immunosuppressive, which made a fast transformation [3]. A consensus conference held in 1983 announced liver transplantation to be an acceptable therapy from now on and ceased to be an experimental treatment. In 1987 Tacrolimus was declared to be another powerful immunosuppressive agent by Zeevi and colleagues [4]. Furthermore, de novo malignancy and other serious complications of immunosuppressive therapy for liver and other organ transplantations have been detailed [5, 6, 7]. In 1988, according to Iwatsuki, 54% of the patients survived the first five years [8]. There was a fast development and by 1992, more than 3000 OLT were carried out yearly in the United States (source: United Network for Organ Sharing, www.unos.org*).*

Treating liver cancer with total hepatectomy and liver transplantation was a disappointment at the beginning. Iwatsuki (1988) presented that three out of every four patients surviving the first two month had a recurrence of cancer [8]. Adjuvant chemotherapy made no demonstrable benefit. Ringe (1989) reported a 15.2% 5 year graft survival for such patients [9] and Calne and co-workers (1986) had come to similar conclusions 10]. The best results and apparent cure could be achieved when cancer was an incidental finding during the removal of the liver taken out for noncancerous disease

(e.g., alcoholic cirrhosis). Geevarghese (1998) reported an 85% 1-year survival and 78% 5-year survival for such cases [11]. Olthoff (1995) using fluorouracil, doxorubicin, and cisplatin declared a 45% 3-year survival, however, the size of the cancer was larger than 5cm only three cases [12]. Nowadays after liver transplantation no adjuvant chemotherapy is given. In 1996 Mazzaferro and co-workers established the so-called "Milan Criteria" for patients with hepatocellular carcinoma (HCC). A 75% survival at 4 years with a recurrence rate 17% after liver transplantation was unfolded in the case of patients with HCC 5 cm or less or with a maximum of three nodules each 3 cm or less without extrahepatic manifestations or vascular invasion. The case of the presence of vascular invasion or lymph node involvement went along with the increase at the risk of recurrence. Milan criteria was argued to be too restrictive considering liver transplantation, however a more lenient tumor criteria still would be beneficial. In 2002 Yao and the co-workers of the liver transplant group at the University of California at San Francisco (UCSF) has championed larger tumor sizes as criteria for liver transplantation and the result resembled to those ones which had been carried out while following the Milan criteria (UCSF criteria: single lesion ≤ 6.5 cm; multiple lesions ≤ 3 cm; largest tumor diameter if multiple ≤ 4.5 cm; total tumor diameter if multiple ≤ 8 cm).

The improvement of immunosuppression led to the boom of surgical methods. Reduced size orthotopic liver grafts in young patients were announced by Bismuth and Houssin (1984) [13]. In 1988 Pichlmayer used one donor liver for two recipients (SLT) [14]. Raia (1989) [15] and Strong (1990) [16] were the volunteers to produce LDLT with the usage of segments II and III. Yamaoka (1994) used the right liver lobe [17]. In Hungary it was Zoltán Máthé who carried out the first successful adult right-lobe LDLT on 19th November, 2007 [18].

Cultural restrictions and the shortage of donor organs greatly motivated the usage of split liver grafts and living related donors for both lobes. These techniques have been the main improvements in the field of liver surgery. The main ethical worry was the risk of mortality and morbidity for the recipients and also for the donors. Applying liver transplantation for tumors has begun significant with primary hepatocellular cancer. Although liver resection stays to be a treatment of choice, for HCC in the case of good liver function, or compromised liver function, and patients with hepatitis C and a little sized tumor in a unpropitious part of the liver (for resection) are presently thought to be

cured with the greatest effectiveness by liver transplantation. For patients with small HCC and patients with a wide range of benign diseases such as compromised liver function due to liver cirrhosis liver transplantation is widely used. Furthermore, it is accepted to treat the Budd-Chiari syndrome, the polycystic liver and kidney disease, sclerosing cholangitis, and other parenchymal and metabolic liver diseases. It is still being investigated if liver transplantation is the effective treatment for hilar cholangiocarcinoma. Time and again it is applied for patients with widespread neuroendocrine metastatic liver disease. Since people with metastatic disease from adenocarcinoma have shown insufficient outcomes, transplantation is not applied for in these cases [19].

So that the safety of the donors would improve in LDLT, Cherqui announced the first full laparoscopic left lateral segment (LLS) transplantation for adult-child LDLT in 2002 [20]. From that time on, numerous centres practice the laparoscopic technique which has a good standard by now, is linked to the decrease of the donors' blood loss and hospital stays and produces similar quality grafts to the open approach [21, 22]. On the other hand, presently there is no standardization for laparoscopic major right or left hepatectomies for adult-adult LDLT and several other methods for example the full laparoscopic approach [23, 24, 25, 26], the hand assisted approach [27, 28, 29] and the hybrid approach [23, 30, 31, 32, 33, 34, 35] have been presented. There was a publication about robot-assisted right lobe donor hepatectomy [36]. Although several publications point out the feasibility of these procedures, the real advantage of laparoscopy over laparotomy still needs to be fully investigated. For achieving it standardization is necessary and international registries from the Eastern countries are need to be created where LDLT is prosperous [22].

3.2 Segmental anatomy of the human liver

The major topics of modern hepatic anatomy instead of the surface marks are internal vascular and biliary textures. The inside set-up has been revealed by McIndoe and Counseller (1927) [37], Ton That Tung (1939, 1979) [38, 39], Hjörtsjö (1931) [40], Healey and Scroy (1953) [41], Goldsmith and Woodburne (1957) [42], Couinaud (1957) [43] and Bismuth's literary pieces (1982) [44]. Among these, it is Couinaud's work,

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which is the most useful and the most well-known for operations until 2000. The basis of Couinaid's terminology is based on the three main hepatic veins (within the scissurae) which divide the liver into four sectors, each with a portal pedicle, with alterations between the hepatic veins and portal pedicles. In 2000, the International Hepato-Pancreato-Biliary Associaton (IHPBA) modernised the classification of the structure of the liver and named it "The Brisbane terminology" [45]. This new terminology is mostly founded on hepatic artery and bile duct ramifications rather than the portal and hepatic venous system. In order to make the two terminologies clear and comparable, I would like to pay great attention to both of them in this chapter.

3.2.1 Couinaud's terminology

The inside structure of the liver is made of several parts which create sectors that are divided by scissurae containing the hepatic veins (*Figure 1*).

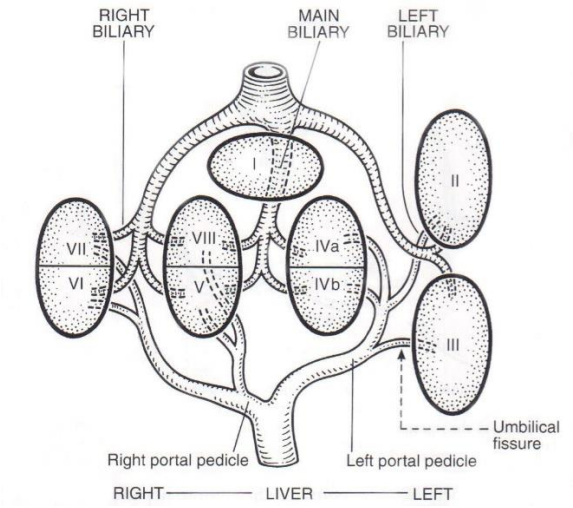

Figure 1: *"The portal vein, the hepatic artery, and the draining bile ducts are distributed within the liver in a beautifully symmetric pedicular pattern, which belies the asymmetric external appearance. Each segment (I-VIII) is supplied by a portal triad composed of a branch of the portal vein and hepatic artery and drained by a tributary of the right or left main hepatic ducts. The four sectors demarcated by the three main hepatic veins are called the portal sectors; these portions of parenchyma are supplied by independent portal pedicles. The hepatic veins run between the sectors in the portal scissurae; the scissurae containing portal pedicles are called the hepatic scissurae. The umbilical*

fissure corresponds to a hepatic scissura. The internal architecture of the liver consists of two livers, or hemilivers, the right and the left liver separated by the main portal scissura, also known as Cantlie's line. It is preferable to call them the right and the left liver rather than the right and left lobes because the latter nomenclature is erroneous, there being no visible mark that permits identification of a true hemiliver." (Source: Blumgart LH, Hann LE. Surgical and Radiologic Anatomy of the Liver, Biliary Tract, and Pancreas. In: Blumgart LH. (ed.), Surgery of the Liver, Biliary Tract, and Pancreas. Saunders, Philadelphia, 2007: 6.).

Basically, in the scissurae there are three main hepatic veins dividing the liver into four sectors, each has a portal pedicle, with alteration between the hepatic veins and portal pedicles. In the main portal scissura there is the middle hepatic vein (MHV) and goes to the left side of the cava from the centre of the gallbladder bed. The line of demarcation between the right and left parts of the liver is the main portal scissura, thus, these parts are self-contained in regards with of portal and arterial vascularization and of biliary drainage (*Figure 2*) [46].

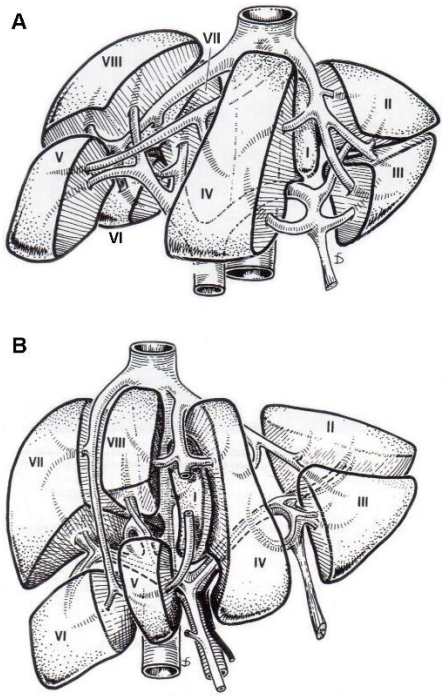

Figure 2: *"The functional division of the liver and of the liver segments according to Couinaud's nomenclature. A, as seen in the patient. B, In the ex vivo position." (Source: Blumgart LH, Hann LE. Surgical and Radiologic Anatomy of the Liver, Biliary Tract,*

and Pancreas. In: Blumgart LH. (ed.), Surgery of the Liver, Biliary Tract, and Pancreas. Saunders, Philadelphia, 2007: 6.).

The right and left parts of the liver are apportioned into two by the remaining portal scissurae. These four subdivisions are named as segments in Goldsmith and Woodburne's works [42] and called sectors in Couinaud's nomenclature [43] (*Figures 1-2*).

In his famous and worldwide extensively used peculiar book "Surgery of the Liver, Biliary Tract, and Pancreas" [46], Blumgart gives the most detailed anatomical description, based on Couinaud's terminology: "The right portal scissura separating the right liver into two sectors - anteromedial or anterior and posterolateral or posterior - is almost in the frontal plane with the body supine. The right hepatic vein (RHV) progresses inside the right scissura. The left portal scissura separates two distinct parts in the left liver. The left portal scissura is not within the umbilical fissure which is not a portal scissura and involves a portal pedicle. The place of the left portal scissura is posterior to the ligamentum teres inside the left next to the left hepatic vein. The anterior sector of the left liver is composed of a part of the right lobe (segment IV) that is to the left of the main portal scissura and of the anterior part of the left lobe (segment III). The left posterior sector is the only sector composed of one segment (segment II). At the hilus of the liver, the right portal triad pursues a short course of approximately 1 to 1.5 cm before entering the substance of the liver. In some cases the right anterior and posterior pedicles arise independently, and their origins may be separated by 2 cm. In some cases, it appears as if the left portal vein (LPV) arises from the right anterior portal vein (RAPV) (*Figure 3*). On the left side, however, the portal triad crosses over approximately 3 to 4 cm beneath the quadrate lobe embraced in a peritoneal sheath at the upper end of the gastrohepatic ligament and separated from the undersurface of the quadrate lobe by connective tissue (hilar plate). This prolongation of the left portal pedicle turns anteriorly and caudally within the umbilical fissure giving branches of supply to segments II and III and recurrent branches to segment IV. Beneath the quadrate lobe, the pedicle is composed of the left branch of the portal vein and the left hepatic duct (LHD), but it is joined at the base of the umbilical fissure by the left branch of the hepatic artery. The branching of the portal pedicle at the hilus, the distribution of the branches to the caudate lobe (segment I) on the

right and left side, and the distribution to the segments of the right (segments V-VIII) and left (segments II-IV) hemiliver follow a remarkably symmetric pattern and, as described by Scheele (1994) [47], allow separation of segment IV into segment IVa superiorly and segment IVb inferiorly. This arrangement of subsegments mimics the distributions to segments V and VIII on the right side. The umbilical vein provides drainage of, at least, parts of segment IVb after ligation of the middle hepatic vein and is important in the performance of segmental resection. The caudate lobe (segment I) is the dorsal portion of the liver lying posteriorly and embracing the retrohepatic inferior vena cava (IVC). The lobe lies between major vascular structures. On the left, the caudate lies between the IVC posteriorly and the left portal triad inferiorly and the IVC and the middle and left hepatic veins superiorly. This portion of the caudate is sometimes referred to as segment IX. The portion of the caudate on the right varies, but is usually quite small. The anterior surface within the parenchyma is covered by the posterior surface of segment IV, the limit being an oblique plane slanting from the LPV to the left hepatic vein (LHV). Thus, there is a caudate lobe (segment I) with a constantly present left portion and a right portion of variable size (*Figure 4*). The caudate lobe is supplied by blood vessels and drained by tributaries from the right and left portal triad. Small vessels from the portal vein and tributaries joining the biliary ducts also are found, usually two on the left side and one on the right. The right portion of the caudate lobe, including the caudate process, predominantly receives portal venous blood from the right portal vein (RPV) or the bifurcation of the main portal vein, whereas on the left side the portal supply arises from the left branch of the portal vein almost exclusively. Similarly, the arterial supply and biliary drainage of the right portion is most commonly associated with the right posterior sectoral vessels or pedicle and the left portion with the left main vessels. The hepatic venous drainage of the caudate is unique in that it is the only hepatic segment draining directly into the IVC. These veins sometimes can drain into the posterior aspect of the vena cava if there is a significant retrocaval caudate component. In the usual and common circumstance, the posterior edge of the caudate lobe on the left has a fibrous component, which fans out attaching lightly to the crural area of the diaphragm, but importantly extending posteriorly behind the vena cava to link with a similar component of fibrous tissue protruding from the posterior surface of segment VII and embracing the vena cava. In 50% of patients, this ligament is replaced, in whole or in part, by hepatic tissue, and

the caudate may completely encircle the IVC and contact segment VII on the right side. A significant retrocaval component may prevent a left-sided approach to the caudate veins. The caudal margin of the caudate lobe has a papillary process that occasionally may attach to the rest of the lobe via a narrow connection. It is bulky in 27% of cases and can be mistaken for an enlarged lymph node on computed tomography (CT) scan" [46].

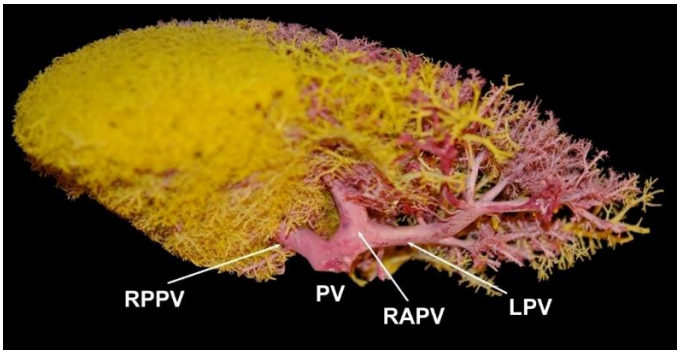

Figure 3*: An anatomical variation of the portal vein (PV) system. The left portal vein (LPV) arises from the right anterior portal vein (RAPV). (Source: author's own work. Co-workers: Ildikó Horti, Zsolt Pápai, Sándor Kovács, András Szuák).*

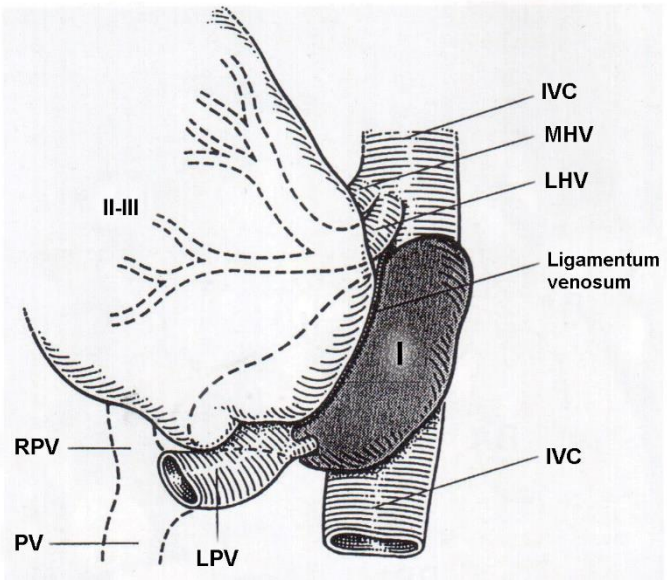

Figure 4: *"The caudate lobe (shaded)-segments II and III are rotated to the patient's right. Superiorly, the left portion of the caudate lobe is linked by a deep anterior portion, which is embedded in the parenchyma immediately under the middle hepatic vein (MHV), reaching inferiorly to the posterior margin of the hilus of the liver and fusing anterolaterally to the IVC on the right side to segment VI and VII of the right liver. The*

major blood supply arises from the left branch of the left portal vein (LPV) and the left hepatic artery close to the base of the umbilical fissure of the liver. The hepatic veins (MHV, LHV) are short in course and drain from the caudate directly into the anterior and left aspect of the vena cava. LHV, left hepatic vein; RPV, right portal vein; PV, main trunk of portal vein." (Source: Blumgart LH, Hann LE. Surgical and Radiologic Anatomy of the Liver, Biliary Tract, and Pancreas. In: Blumgart LH. (ed.), Surgery of the Liver, Biliary Tract, and Pancreas. Saunders, Philadelphia, 2007: 8.).

To summarize:

1. The main hepatic scissura divides the liver into two hemilivers in which the MHV can be found.

2. The left portal scissura containing the LHV partitions the liver into two sectors (*Figure 1*). In the posterior sector there is only one segment (segment II). The umbilical fissure partitions the anterior part into two segments, a medial segment (the quadrate lobe-segment IV) and the lateral segment (segment III).

3. The right portal scissura containing the RHV splits the right liver into two parts. Each sector is partitioned into two segments, an anterior sector (segment V inferiorly and segment VIII superiorly) and a posterior sector (segment VI inferiorly and segment VII superiorly) (*Figures 1-2*).

4. Segment I (the caudate lobe) is situated posteriorly to the IVC, it is adjacent with segments IV and VII [46] (*Figures 4-5*).

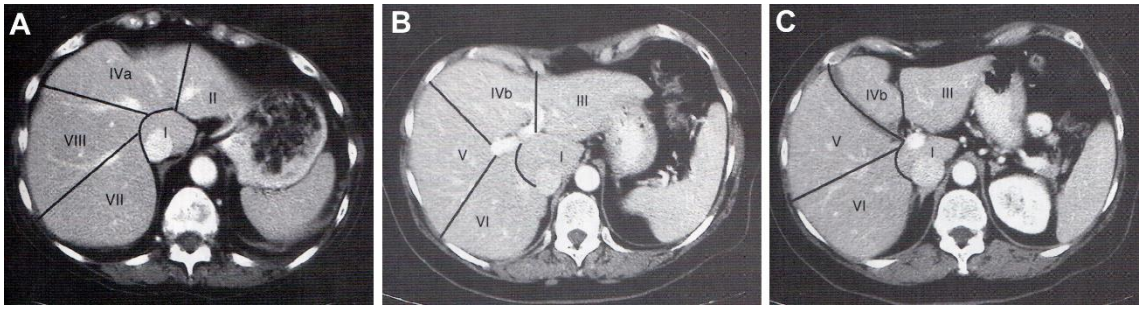

Figure 5: *"Hepatic segmental anatomy as shown by CT. A, At the level of the hepatic veins. B, At the portal vein bifurcation. C, Below the hepatic hilus. Roman numerals stand for liver segments." (Source: Blumgart LH, Hann LE. Surgical and Radiologic Anatomy of the Liver, Biliary Tract, and Pancreas. In: Blumgart LH. (ed.), Surgery of the Liver, Biliary Tract, and Pancreas. Saunders, Philadelphia, 2007: 9.).*

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3.2.2 "The Brisbane 2000 Terminology"

In December 1998, the Scientific Committee of the IHPBA had a meeting in Berne, Switzerland, to establish a Terminology Committee to address the confusion existing in the field of terminology of hepatic anatomy and liver resections. In the Committee there were eight hepato-pancreato-biliary (HPB) surgeons from all over the world. The Committee begun his work with seeking input from the IHPBA members, by publishing a survey questionnaire with 46 propositions in HPB. After almost 18 months' work the Terminology Committee initiated its suggestions in the Scientific Committee at the World Congress of the IHPBA in Brisbane, Australia in May, 2000. These recommendations contained a modern terminology labelled as "The Brisbane 2000 Terminology" of liver anatomy and resections. It was assumed with one accord by the Scientific Committee of the IHPBA and were presented to the members as the official terminology of the IHPBA on the last day of the meeting. A description of the new terminology follows [45, 48].

The primary (first-order) partition divides the proper hepatic artery into the right (RHA) and left (LHA) hepatic arteries (*Figure 6*). The arterial inflow is provided by them to both hemilivers (*Figure 7*). The plane situated between the two distinct zones of vascular supply is named as a watershed the border of which at the first-order division is called the "midplane of the liver". It intersects the gallbladder fossa and the fossa for the IVC. The right liver is generally expected to have a bigger size than the left one (60:40), although it might change [45, 48].

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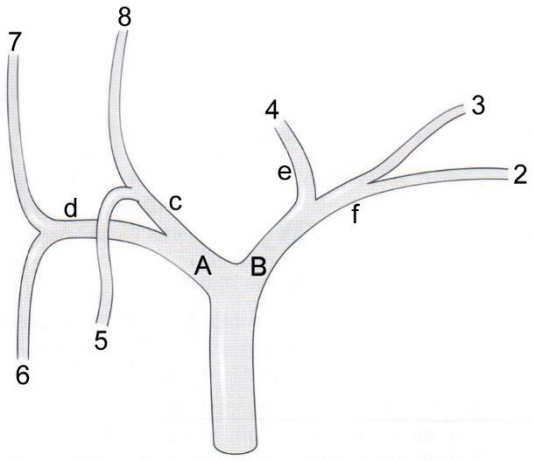

Figure 6: *"Ramification of the hepatic artery in the liver. The prevailing pattern is shown. The first-order division of the proper hepatic artery is into the right (A) and left (B) hepatic arteries, which supply right and left hemilivers respectively (Figure 7). The second-order division of the hepatic arteries, supplies the four sections (c, d, e, f) (Figure 8). The third order-division supply the segments (II-VIII) (Figure 9). The left medial section and segment four are the same. The caudate lobe is supplied by branches from A and B. Bile duct anatomy and nomenclature is similar to that of the hepatic artery. © Washington University in St Louis."* *(Source: Strasberg SM. Hepatic, biliary and pancreatic anatomy. In: Garden OJ, Parks RW. (eds.), Hepatobiliary and Pancreatic Surgery. A companion to specialist surgical practice. Fifth edition. Saunders, Edinburgh, 2014: 18.)*

The second-order divisions (*Figure 6 and 8*) of the hepatic artery makes the liver into four distinct parts, which are referred to sections. The right liver has two sections, the right anterior and the right posterior section. The blood supply comes into these sections from the right anterior and from the right posterior sectional hepatic arteries. The plane between these sections is the right intersectional plane. The right intersectional plane is difficult to be found due to the fact that it lacks all surface markings which would indicate its position. The left liver has two sections, also which are the following; (1) the left medial section, and (2) the left lateral section, both of which are supplied by the left medial sectional hepatic artery and the left lateral sectional hepatic artery. The left intersectional plane can be found between these sections. It has visible surface marks

which show its position – the umbilical fissure and the attachment line of the falciform ligament (FL) to the anterior surface of the liver [45, 48].

The third-order partitions of the hepatic artery distinguish segments II-VIII (*Figure 6 and 9*) in the right and left hemilivers. Each segment has its own supply via a segmental artery. The left lateral section contains segment II and III. It is impossible to subdivide the left medial section into segments due to the pattern or ramification of the vessels within it. Since it has an own arterial blood supply, the left medial section and segment IV are synonymous. On the other hand, segment IV can be arbitrarily divided into superior (segment IVa) and inferior (segment IVb) parts without an exact anatomical plane of separation since it is based on the internal ramification of the vessels. Two segments, segment V and segment VIII belongs to the right anterior section whereas segment VI and segment VII belongs to the right posterior section. The planes between segments are labelled as intersegmental planes. The ramifications of the bile ducts are identical with that has already been described for the arteries, as are the areas of the liver drained by the respective ducts [45, 48].

Segment I (caudate lobe) is a clearly distinct part of the liver, disparate from the right and left hemilivers (*Figure 10*). Appropriately called a lobe, bordered by visible fissures, containing three parts (1) the bulbous left part (Spiegelian lobe), gripping the left side of the IVC and is clearly visible through the lesser omentus; (2) the paracaval portion lying anterior to the IVC; finally (3) the caudate process, on the right. The caudate process is inseparable from the right hemiliver. Posterior to the hilum and the portal veins the caudate lobe can be found. The hepatic veins which lie anterior and superior to the paracaval portion, put a limit to the upper extension of the caudate lobe [41, 43] (*Figure 10*). Both the right and the left hepatic arteries (and portal veins) offer vascular supply for the caudate lobe. Its bile ducts drain into both right and left hepatic ducts [43]. There are several short caudate veins entering the IVC directly from the caudate lobe which drain it. The number and size of which are changeable. Sometimes a careful isolation and division is needed since the caudate veins might be quite short and wide. Generally the entering point of these veins into the IVC can be on either side of the midplane of the vessel, providing a possibility for the creation of a tunnel behind the liver on the surface of the IVC without touching the caudate veins. The “hanging manoeuvre” means lifting it up on a tape which is put through the tunnel mentioned before [45, 48].

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The basis of the terminology of hepatic resections is in complete accordance with the terminology of hepatic anatomy. When one side of the liver is resected it is called either a hepatectomy or hemihepatectomy (*Figure 7*). If it is a right or a left hepatectomy or hemihepatectomy it is decided by the side of the liver which is to be resected. When only a liver section is involved in the process it is called sectionectomy (*Figure 8*). When the liver is operated to the left side of the umbilical fissure it is a left lateral sectionectomy. Other sectionectomies are labelled accordingly, e.g. right anterior sectionectomy. Right trisectionectomy is a procedure when the right hemiliver plus segment IV are involved (*Figure 10*). Similarly, resection of the left hemiliver plus the right anterior section is named as a left trisectionectomy. Resection of one of the numbered segments is referred to as a segmentectomy (*Figure 9*). Resection of the caudate lobe is labelled as a caudate lobectomy or resection of segment I. It is always adequate to refer to a resection by the numbered segments. For instance, it would be appropriate to call a left lateral sectionectomy as resection of segment II and III [45, 48].

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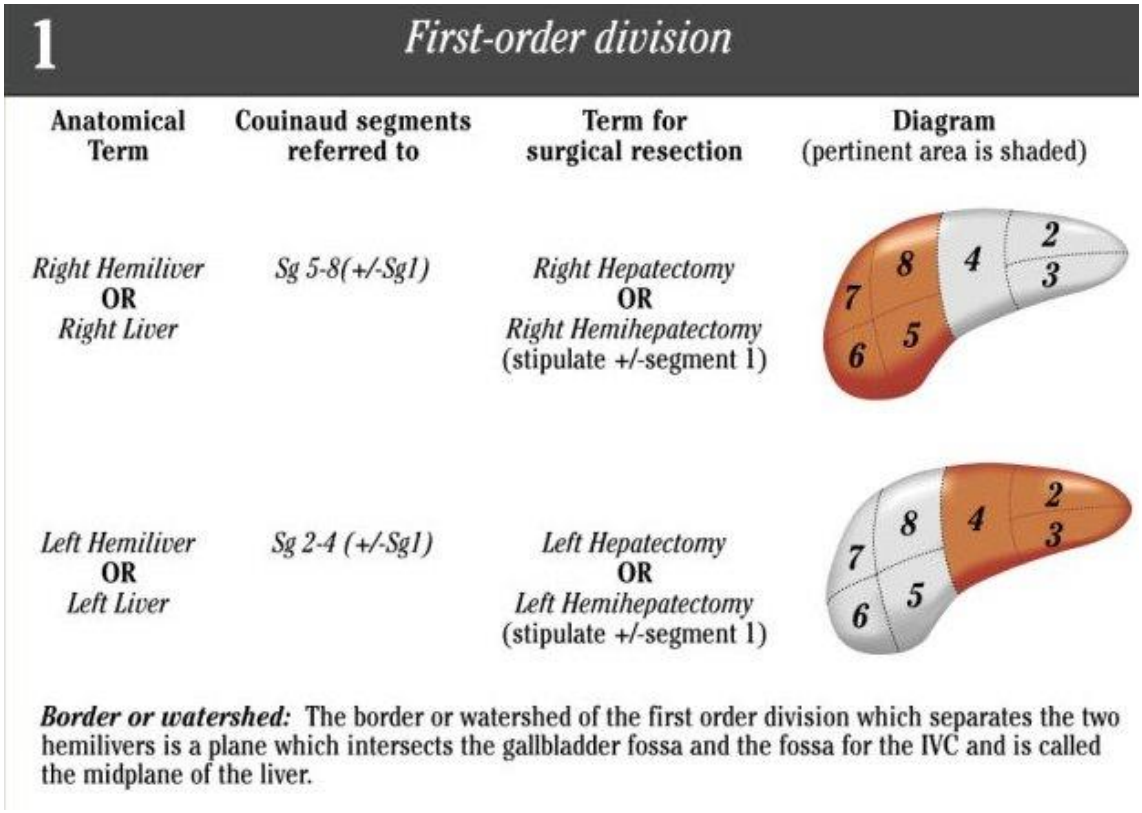

Figure 7: *First-order division (hemilivers, livers), nomenclature for anatomy and resections. (Source: Terminology Committee of the International Hepato-Pancreato-Biliary Association. (2000) The Brisbane 2000 Terminology of Liver Anatomy and Resections. HPB, 2: 333-339. https://www.ihpba.org/92_Liver-Resection-Guidelines.html).*

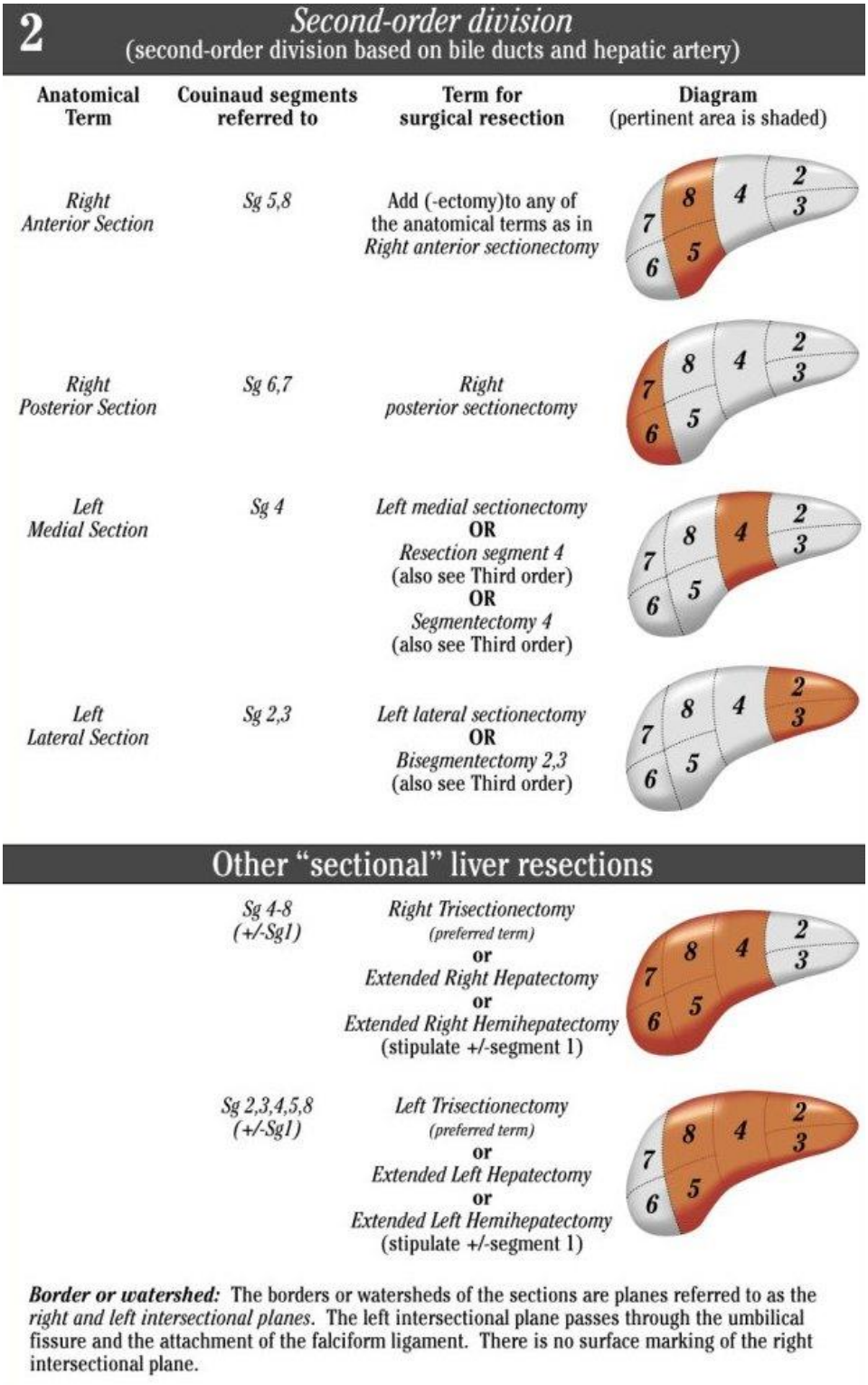

Figure 8: *Second-order division (sections), nomenclature for anatomy and resections. (Source: Terminology Committee of the International Hepato-Pancreato-Biliary Association. (2000) The Brisbane 2000 Terminology of Liver Anatomy and Resections. HPB, 2: 333-339. https://www.ihpba.org/92_Liver-Resection-Guidelines.html).*

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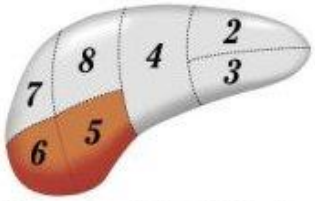
3 *Third-order division*

Anatomical Term	Couinaud segments referred to	Term for surgical resection	Diagram (pertinent area is shaded)
Segments 1-9	*Any one of Sg 1 to 9*	*Segmentectomy* (e.g. segmentectomy 6)	
2 contiguous segments	*Any two of Sg 1 to Sg 9 in continuity*	*Bisegmentectomy* (e.g. bisegmentectomy 5,6)	

For clarity Sg. 1 and 9 are not shown. It is also acceptable to refer to ANY resection by its third-order segments, eg. right hemihepatectomy can also be called resection sg 5-8.

Border or watersheds: The borders or watersheds of the segments are planes referred to as intersegmental planes.

Figure 9: *Third-order division (segments), nomenclature for anatomy and resections. (Source: Terminology Committee of the International Hepato-Pancreato-Biliary Association. (2000) The Brisbane 2000 Terminology of Liver Anatomy and Resections. HPB, 2: 333-339. https://www.ihpba.org/92_Liver-Resection-Guidelines.html).*

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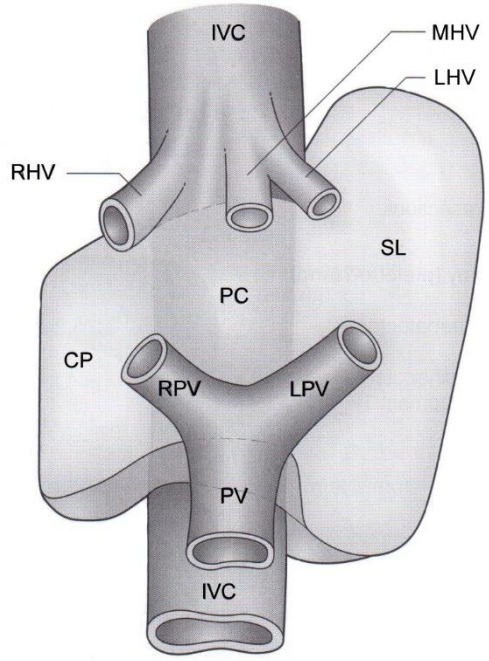

Figure 10: *"Schematic representation of the anatomy of the caudate lobe. The caudate lobe consists of three parts: the caudate process (CP), on the right, the paracaval portion anterior to the vena cava (PC) and the bulbous left part (Spiegelian lobe, SL). IVC, inferior vena cava; RHV; right hepatic vein, MHV; middle hepatic vein, LHV; left hepatic vein, PV; portal vin, RPV; right portal vein, LPV; left portal vein. © Washington University in St Louis." (Source: Strasberg SM. Hepatic, biliary and pancreatic anatomy. In: Garden OJ, Parks RW. (eds.), Hepatobiliary and Pancreatic Surgery. A companion to specialist surgical practice. Fifth edition. Saunders, Edinburgh, 2014: 20.).*

"The Brisbane Terminology" contains in the addendum of the original table an alternative and also adequate terminology for the second-order division. In the body of the table, the second-order partition is following Healey's and Couinaud's concept of apportionment of the artery and bile duct; in the addendum the second order rests on Couinaud's idea of portal vein divisions. It was necessary to include it in the addendum because it maintains the ability of naming particular rare resections on the left side according to Couinaud's concepts of the portal and hepatic veins, e.g. left paramedian sectorectomy [45] (*Figure 11*).

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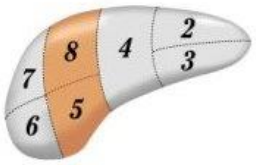
4 Addendum. *Alternative second-order division*
(second-order division based on portal vein)

Anatomical Term	Couinaud segments referred to	Term for surgical resection	Diagram (pertinent area is shaded)
Right Anterior Sector **OR** *Right paramedian Sector*	*Sg 5,8*	Add (-ectomy)to any of the anatomical terms as in *Right anterior sectorectomy* **OR** *Right paramedian sectorectomy*	
Right Posterior Sector **OR** *Right Lateral Sector*	*Sg 6,7*	*Right posterior sectorectomy* **OR** *Right lateral sectorectomy*	
Left Medial Sector **OR** *Left Paramedian Sector*	*Sg 3,4*	*Left medial sectorectomy* **OR** *Left paramedian sectorectomy* **OR** *Bisegmentectomy 3,4*	
Left Lateral Sector **OR** *Left Posterior Sector*	*Sg 2*	*Left lateral sectorectomy* **OR** *Left posterior sectorectomy* **OR** *Segmentectomy 2*	

Right anterior sector and Right anterior section are synonyms. Right posterior sector and Right posterior section are synonyms. Left medial sector and Left medial section are NOT synonyms and are NOT exchangeable terms. They do not describe the same anatomic areas. Left lateral sector and Left lateral section are also NOT synonyms *and are NOT exchangeable terms.*

Border or watersheds: The border or watersheds of second-order division based on PV are called right and left intesectoral planes. These have no surface markings.

Figure 11: *Alternative second-order division (sectors), nomenclature for anatomy and resections. (Source: Terminology Committee of the International Hepato-Pancreato-Biliary Association. (2000) The Brisbane 2000 Terminology of Liver Anatomy and Resections. HPB, 2: 333-339. https://www.ihpba.org/92_Liver-Resection-Guidelines.html).*

In the rest of this study "The Brisbane 2000 Terminology" will be used.

3.3 Technical aspects of split liver transplantation

One of the greatest advantage of Split liver transplantation (SLT) is, that it maximises the use of available cadaver donor organs, both at the case of adults and children, owing to the fact that the full liver can be utilised. Previously, in the reduced size liver transplantation it was impossible, thus it means a major profit compared to the earlier technique. In 1989, 2 patients were reported to be transplanted with 1 donor liver [14]. The basis of SLT and its varieties are cutting the liver into parts, each of which has a sufficiently functioning hepatic mass, a bile duct, a venous outflow and a vascular pedicle. [49]. SLT has two main types. With applying the regularly used splitting technique a left lateral graft (segments II and III) and a right extended graft (segments I and IV-VIII) are achieved and can be transplanted into a young child plus an adult. Whereas in the second type, the liver is cut along the Cantlie line, making two hemilivers - a left graft (segments I-IV) and a right graft (segments V-VIII) - which are sufficient for two grownup patients. The before mentioned splitting techniques however, show a great variety in the aspects of the challenges raised by anatomy, the required professional expertise and purpose [49].

Anatomical principles

As the result of dividing the hepatic parenchyma at the FL a segment II-III graft is obtained. In the case of pediatric recipients the size of the transplantable graft is about 250 cc in volume [50, 51], for adults it is one ‘right tri-segment’ graft, with the volume of 1100 cc, the rest of the Couinaud segment I, IV-VIII [49, 50]. Furthermore a ‘mono-segment graft’ (segment III) obtained from LLS graft is appropriate for new born babies and toddlers; for avoiding large-for size syndrome, we can apply a segment II mono-segment graft so that we can minimise the size of LLS grafts [49, 52, 53]. A fully developed cadaver liver may provide two grafts almost with the same size when cut along the MHV, suitable for giving them two adults with higher body mass. For people under the 60 kg weight, left-side 400-cc grafts are made from (segments I-IV) or without the caudate lobe (segments II-IV). Likewise, for patients who weigh 80 kg or more, right-

side grafts (segments I, V-VIII, or V-VIII) with the volume of 800-1000-cc are normally experienced to be adequate [49, 54, 55, 56, 57].

Donor selection

The efficiency and success of SLT has many factors out of which the most determining and critical one can be the adequate donor for the proper recipient. There is a criteria system for the donor selection. It involves age, serum sodium concentration, ABO match, liver function, similarity in size, no arrest period, vasopressor requirements, finally short donor hospitalization [49, 58, 59, 60]. Only hemodynamically stable cadaveric donors are suitable for SLT. Further requirements of the donors before left lateral splitting are that they have to be younger than 55, they should have not spent more than 5 days in intensive care, the fatty degeneration of their liver should be less than 30%, gamma-glutamyl transpeptidase is to be under 50 U/L, serum glutamic pyruvic transaminase less than 60 U/L, and serum Na less than 160 mmol/L [49, 61]. To get organs from adults with a full right - full left split, the donors have to be over 70kg. They are considered adequate for making grafts suitable for two adult recipients. Full left - full right split has greater requirements considering the quality of the organ and the donor should fulfil the oncoming requirements: younger than 40, should have not been in intensive care for more than 3 days, and fatty degeneration has to be less than 10% [62]. A liver biopsy has to be carried out the result of which, according to the macroscopic criteria, can be decisive considering the final decision if the quality of the graft is suitable for the splitting or not [49].

Recipient criteria

Before carrying out SLT on patients they need to be examined for some critical factors. The circumstances which are essential to be taken into account are the following; age, the history of illicit drug usage and examination for drugs, alcohol agreement, treatment agreement, evaluation of the possibility of relapse, and checking two types of hepatitis (B and C). All these circumstances are to be taken into consideration in every general liver transplantation, even with greater emphasis if SLT is carried out [49, 63]. It is worthy to remember that right split-liver graft recipients are more advanced in age than the recipients of left split-liver graft [64]. The graft variables of the recipient involves the

fraction, the mass, and the type of the reconstruction of the hepatic artery *ex vivo* before the operation begins, cold and warm ischemia time with the use of Roux limb biliary drainage, and finally multiple-duct biliary anastomoses. For SLT extended dissection has to be carried out either on the back table *ex vivo* or within the heart-beating donor. Increased blood loss is concerned when *in situ* SLT is made and the thoracic organ quality is to be taken into account as a result of volume replacement [49, 61]. A number of reports suggest that additional thoracic or abdominal organs with *in situ* SLT have no effect [49, 59, 65]. On average, *in situ* SLT for adults the extra time of the operation is 3 hours and one and half hours for children. Though, exceptions can happen and there has been a report of longer times [49, 66].

Left lateral splitting

In the case of small children who had end-stage liver problems there was an eager demand for the development of new techniques in the 1980s since the waiting list was unacceptably high, and the mortality rate almost reached the 40%. The evolution of left lateral splitting began when the first successful segmental graft was transplanted into a child from an adult through living donation and with the size reduction of the cadaver liver. Similarly, the transplantation of a whole adult organ to a child resulted in a significant reduction of the need for the living donations. It is essential to point out that the left lateral splitting does not compromises the adult graft pool and the remaining extended right graft is suitable for even large-sized adults, too without involving a small-for-size condition [67]. Due to its relatively great weight variability the LLS potentially can be given to recipients whose weight is less than 40 kg. Since the beginning of SLT, *ex situ* and *in situ* transplantation methods have been developed [68], which were comparably successful, if carried out in accordance with the logistical proportions. However, the final result is greatly influenced by the selection of donor and recipients and the optimal technique, also. To identify the LHA, the hepatoduodenal ligament is cut from the left side. It is determined by the individual anatomy, if the right graft main arterial trunk may remain in continuity with the segment IV artery it may need to be anastomosed with the stump of gastroduodenal or LHA so as to minimize any risks of necrotizing of segment IV [49, 61]. Due to this, LPV is dissected down to the main bifurcation. Arising at segment I and IV portal branches, the main LPV, has to be

transected. Just right of the FL, the parenchyma is dissected. A flat surface is created out of the parenchyma when cutting it sharply into a single even plane in the *ex situ* technique, to create an efficient hemostasis. With the application of the already existing liver resection procedures combined with suture ligation of vessels and vessel clipping in *the in situ* technique the parenchyma is suitably transected. For the optimal hemostasis, the donor's coagulation system is made use of in this technique. A LHV which surrounds the vessel loop, between the LHV and MHV can give a guidance to the surgeon while doing *in situ* splitting [49, 69]. With avoiding the isolation and dissection of the main LHD, the bile ducts and parabiliary vascular plexus of segments I and IV can be saved. The hilar plate, which includes the segment II and III hepatic duct(s), is to be divided sharply at the longitudinal part of the left portal vein (Rex Recessus). We have to divide the left side of the IVC right next to the LHV. The IVC to the right graft is kept in continuity with the MHV and RHV. The left lateral splitting is shown in *Figure 12*. All has to be done to prevent the possibility of right graft bile leakage risks. In case of necessity an intraoperative cholangiography might be included to save the segment I and IV draining bile ducts. Due to split-liver and LLS LDLT the waiting list fatalities in case of children has deeply fallen. Considering safety and surgery, the complete graft seems to be the safest; although, in young patients, successful outcomes were reported with SLT [49, 60, 70, 71, 72, 73]. LLS LDLT can lead to equal results with left lateral splitting of a cadaveric donor liver and transplantation of the created grafts [60, 74]. Therefore, in places where cadaveric livers are within easier reach SLT is suggested to be used to reduce the risks for the living donors. In the existing literature there is no mentioning of the availability of inferior graft or patient survival or higher surgical complication rates for right extended graft transplantation. As a result of this, considering security, when a right extended graft is transplanted it can be equal with the process when a whole organ is given. [49, 71, 75, 76].

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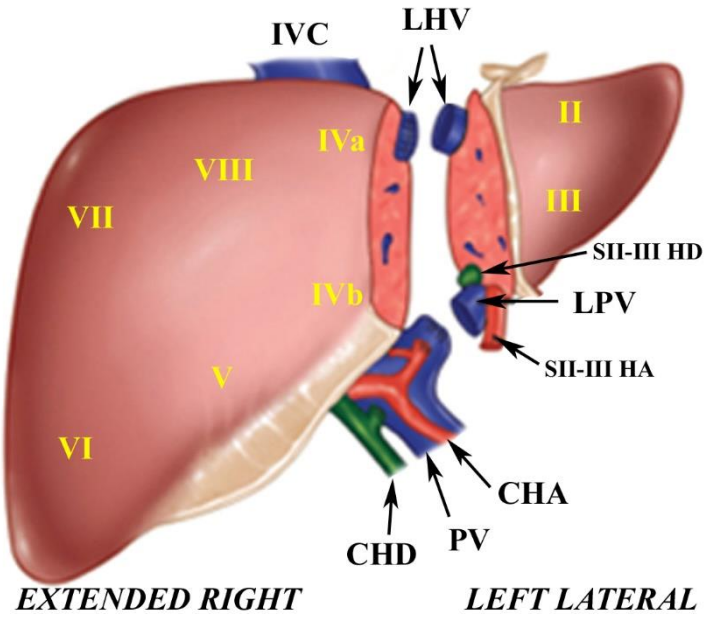

Figure 12: *Left lateral splitting: left lateral (segments II and III) and extended right (segments IV-VIII) liver grafts. IVC, inferior vena cava; LHV, left hepatic vein; SII-III HD, segment II and III hepatic duct; LPV, left portal vein; SII-III HA, segment II and III hepatic artery; CHA, common hepatic artery; PV, portal vein; CHD, common hepatic duct; Roman numerals stand for liver segments. (Original source: http://accessmedicine.mhmedical.com/data/books/980/bru_ch11_f17.png).*

Full left - full right splitting

As a result of routine use of left lateral splitting and using alive donors the lack of available organs in the cases of young patients has notably dropped. On the other hand, for adults and older children the want of organs was still pressing. In 1989, Bismuth and his colleagues [77] presented an operation in which one cadaveric liver was given to two adults for the first time. Since then, full left - full right splitting of liver became an essential factor for adult liver graft pool expansion since it doubles the grafts to be given to adult recipients (*Figure 13*), therefore decreasing the want for alive donors and the dangers involved in that method. The previous technique provides one graft (segments V-VIII) for an adult recipient with average size and one graft (segments I-IV) for a larger pediatric or for an adult with a smaller body weight. Full left - full right splitting, however, is such a complex liver transplantation form that it requires special knowledge of the

anatomic variations, furthermore high level of skills and expertise without which the success of the procedure cannot be granted. The complexities are the following; liver splitting for two adults should be done in places where skills and knowledge are based on the performance of many liver transplantations yearly. Where there is an ongoing hepatobiliary surgical program deeply experienced in left lateral splitting. The aspects of SLT for two grownup recipients has two critical issues: managing to ensure the safe biliary drainage for every implanted segments and sharing of blood vessels, especially the IVC and hepatic veins. The main alterations in left lateral splitting are that, the transection plane is larger, bile drainage of the implanted parts, higher possibility of the disturbance of the vascularization, and where to set the resection line, since there is no indicating anatomic structure (such as the FL). In these circumstances, the *in situ* splitting has a further advantage, which is the ability of identifying the ideal dissection plane. It can be identified by blocking the inflow of one of the hemilivers. Prior to perfusion, adequate venous outflow and arterial/portal inflow (especially at segments V and VIII) is to be guaranteed after the parenchymal transection. Finally, the donor's own coagulation system is to be applied in this method to achieve a biliostasis and hemostasis. Intraoperative cholangiography is used to identify the anatomical hepatic duct variations, which can completely prohibit liver splitting or can point out a left lateral splitting [49, 61]. The place of common hepatic duct (CHD) either to the right or left of the hemiliver is determined by individual anatomy. The CHD regularly belongs to the right graft since frequent anatomical variations have been noted with the right lobe where the RHD is shorter than in the left. To assure sufficient perfusion the hepatic ducts are to be shortened to every possible extent. Arteriography is advised in some literature [64], but hilar dissection can be applied for the safe identification of the arterial anatomy for the most part. The arterial trunk sharing, especially segment IV artery origin is specified by individual donor anatomy. In general, the left graft is considered with the main arterial trunks. When using traditional methods, the IVC remains with the right graft and the MHV stays with the left graft. The viability of the liver segment I is in question when the division of the caudate lobe veins is needed. In this case a resection can be necessary [49]. The split vena cava method [78] has been introduced to provide both hemiliver grafts with optimal venous drainage. This method includes IVC division, and the sustenance of venous drainage of dorsal parts and segment I of right lobe through retrohepatic veins.

On the other hand, the venous congestion of segment V and VIII is impossible to be averted by this technique when the left graft contains the MHV. Thus, there is a requirement of these veins on the cut surface to undergo further venous reconstruction. The literature published about full left - full right splitting is much less than on splitting for an adult and a child. This procedure, however, has not been widely accepted since it resulted in poor success at the beginning and the fatalities were high, especially after left hemiliver grafting [49, 64, 79, 80, 81]. The main barriers of the expansion of this technique are that of logic and technic, furthermore, there is normally a risk for the development of a small-for-size problem when a full left - full right splitting for two adults is carried out. The essential factors of having positive outcomes with full left - full right SLT compared to whole-size organ transplantation are: proper technical abilities ideal size match of graft recipients, and suitable graft quality. Graft quality has to be evaluated by an experienced surgeon with SLT knowledge, and when possible, a liver biopsy should help. If we compare it to left lateral splitting, donor selection has much higher requirements. Not only the individual recipient's needs but also an absolutely transplantable functioning liver mass has to be assessed during the selection of the recipient. The transplanted graft should reach the minimum of 1.0% of the recipient's body mass weight [49, 59]. There can be a possibility of increasing the functional liver mass if general worsening condition of the recipient may occur. This limit can only be exceeded in individually evaluated elective cases where there is no portal hypertension. Therefore no compromises can be made when selecting the donor and the recipient since they are essential for the most successful outcomes [49].

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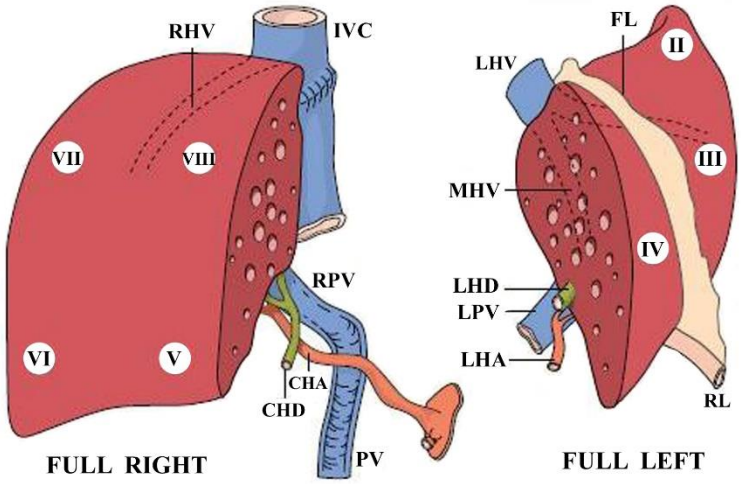

Figure 13: *Schematic illustration of full left - full right liver grafts. IVC, inferior vena cava; RHV, right hepatic vein; LHV, left hepatic vein; MHV, middle hepatic vein; LHD, left hepatic duct; LPV, left portal vein; LHA, left hepatic artery; RPV, right portal vein; CHA, common hepatic artery; CHD, common hepatic duct; PV, portal vein; FL, falciform ligament; RL, round ligament; Roman numerals stand for liver segments. (Original source: https://optn.transplant.hrsa.gov/media/2016/fig2_split_liver.jpg?width=359px& height=233px).*

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4 Objectives

The detailed surgical anatomy is one of the basics of major liver surgery including liver resection and transplantation. Since the lack of cadaveric organs, all over the world the number of liver transplantation was limited, Pichlmayr (1988) and Raia (1989) carried out the first successful SLT and LDLT [14, 15] two decades after the first human liver transplantation. Subsequently, Broelsch initiated the idea of LLS LDLT for transplantation in young patients [82].

Partial liver graft transplantation is a process in which the surgeon creates a liver graft from a living-donor [82, 83, 84], that reduces a larger cadaveric graft [13, 85], or divides an adult cadaveric liver during SLT [68, 86, 87, 88]. The use of partial liver graft transplantation techniques led to a rise in the number of pediatric donor organs and lessened the pretransplant complications and mortality [82, 88, 89] but the SLT predisposes to specific complications [84, 91, 92, 93, 94]. Biliary complications can be the following (1) biliary stricture and (2) anastomotic leakage which are still considered to be stressing problems to address during partial liver graft transplantation and are often originate from an ischemia of the biliary tract or the lack of complete anatomic expertise of the bile duct system [95, 96, 97, 98]. The reported incidence of the biliary complications' rate is announced to be 5% - 38% which made some authors to consider biliary anastomoses as the "Achilles heel" of segmental liver transplantation [99]. Owing to the previously mentioned worries anatomical and clinical researchers are eager to make a deeper clarification of anatomic variations and surgical techniques to eliminate the risk of these complications [100, 101, 103, 104, 105, 106]. Owing to these reasons it is absolutely necessary that liver surgeons should be full-trained in the anatomy of the bile duct system and have the ability to realise the existence and the implications of the anatomical variations [107]. Since the data published on the biliary anatomy and statistics display significant differences, altered incidences in different countries and/or limitations of different methods cannot be excluded. Therefore we aimed to investigate the incidence of bile duct variations in the Hungarian population. With the increasing prevalence of partial liver transplantation and liver resections a detailed preoperative assessment of biliary anatomy is mandatory. More and more sophisticated high resolution diagnostic imaging methods provide accurate preoperative evaluation of hepatobiliary anatomy.

Moreover, new data are of special importance since the development of a new system of common transplantable organ pool in Europe is in progress. It is known that the European Union (EU) started already the implementation of EU directives including safety and quality standards in transplantation. The investigation and findings of the anatomical variations can improve the level of education and can help the standardization of surgical techniques.

Since the incidence of biliary variations is far more numerous in the right lobe, the right lobe LDLT is widely accepted for adult patients, the complications are concomitants of reconstruction of complex biliary routes after right lobe harvesting [108]. The detailed knowledge of hilar anatomy is also essential in case of full-left full-right, split or in case of left lobe living donor liver transplantation when the resection line goes through the LHD at the hilum. An unforeseen biliary variant may extend graft ischemia time and increase the risk of postoperative complications. Therefore the first aim of this study was to complete the data on the surgical anatomy of the hilar biliary tree by investigating the types and incidence of hilar biliary variants in the Hungarian population.

The most commonly used LDLT technique is LLS transplantation for children. Recently, the survival rates have significantly improved, however, biliary complications are still the major source of morbidity after pediatric LDLT [109, 110, 111, 112]. The incidence of biliary complications after LLS transplantation is higher when multiple bile ducts are present [99], hence it is important to choose a line of hepatotomy that results in the fewest possible surface ducts that need to be anastomosed in the recipient. Therefore the second aim of this study was to investigate the optimal division line of hepatotomy for an LLS donation, based on the anatomical variations of left hepatic duct system.

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5 Methods

5.1 Working out of the corrosion cast technique

Although several researcher have used corrosion cast techniques to study the anatomy of different vessels in humans or in animals we aimed to work out our own vessel lumen filling and modified corrosion technique for the best possible results. If a researcher decides to use corrosion technique to get the required data one will face a great number of questions, e.g.:

- Should conventional corrosion technique or vessel lumen filling technique without corrosion be used?
- Which resin is the best for the planned research work (investigation of the hepatic ducts system)?
- Is the use of CT scan wanted? – Is any extra contrast material needed?
- Does it need to be coloured?
- Special additives?
- Special circumstances during preparation?

We summarise here our answers for the above mentioned questions.

Conventional corrosion cast or vessel lumen filling without corrosion technique?

The main difference between the two techniques is that while the conventional corrosion technique results "just" in the resin cast without any organic tissue around the vessels or on the preparation, the vessel lumen filling technique does not use corrosive material to remove the organic tissue so by the end of the procedure the preparation does have the organic tissue with its vessels filled up with resin. To decide which technique is better to get the aimed data mainly depends on the followings:

If the resin cast analysis is simply enough and we do not plan to do any further preparations which require the original organic tissue, we need to choose the conventional corrosion technique (e.g. the study of the „hilar variations of the hepatic duct system" in this work) (*Figure 14*). However, if we need to keep the organic tissue e.g. we need it in order to be able to perform surgical procedure on the preparation (e.g. LLS hepatectomy)

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or to be able to determine the exact place of an intra organic anatomical structure in the view of surface markings on a CT scan (e.g. the study of “optimal line of hepatotomy for left lateral living donor liver transplantation” in this current work), in these cases the lumen filling technique without removing the organic tissue is the choice (*Figure 15*).

Both techniques are suitable for CT scans but if there are soft tissues around the resin cast, more investigation will be needed to find the optimal CT density because of the higher background density of the organic tissue.

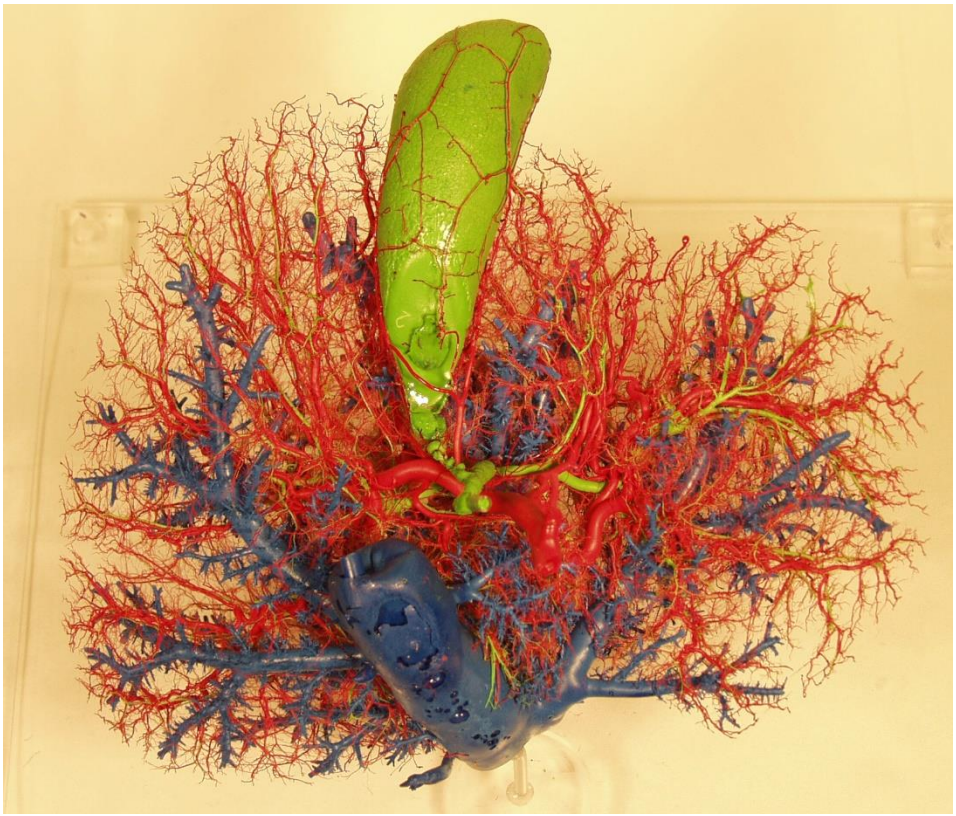

Figure 14: *Corrosion cast preparation of human liver. Liver parenchyma is removed with potassium hydroxide. IVC and hepatic veins - blue, bile ducts and gallbladder – green, hepatic artery - red, (Source: author’s own work).*

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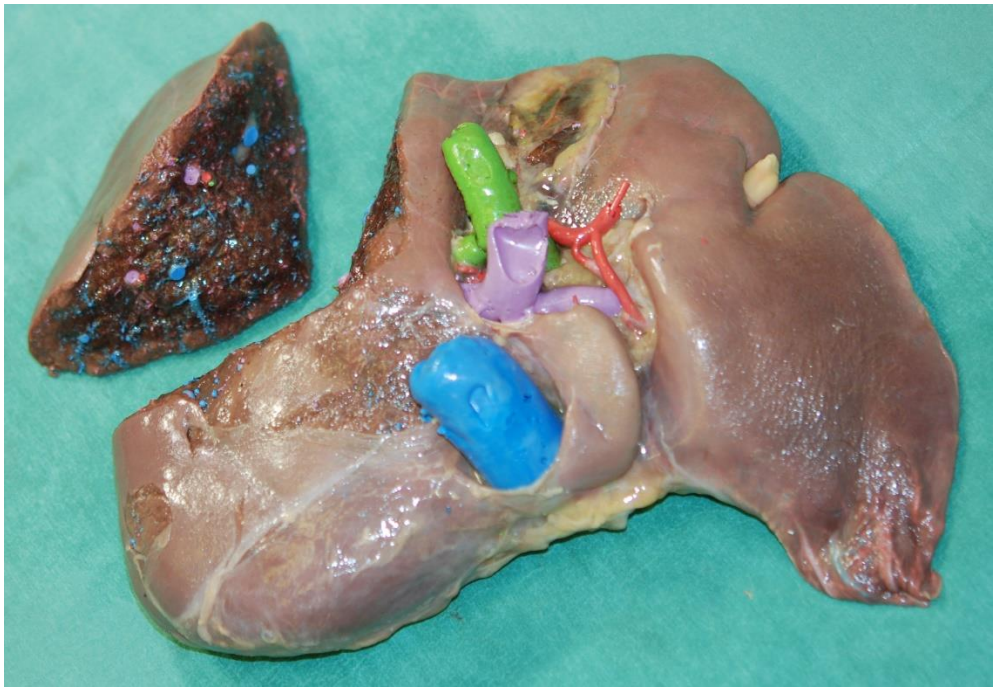

Figure 15: *Vessel lumen filling technique. Liver parenchyma is fixed around the resin cast. IVC and hepatic veins - blue, portal vein – purple, bile duct – green, hepatic artery – red. (Source: author's own work. Co-workers: Zsuzsanna Kürti, Zsolt Pápai, András Szuák).*

Find the best resin

Synthetic resins are materials which possess the qualities of the natural plant resins: they are viscous liquids which are able to harden permanently. From a chemical point of view they show a great alteration from the different resinous compounds secreted by plants.

In the time of chemical inventions numerous different types of synthetic resins are available to perform corrosion cast studies. These resins have been mainly in use for industrial flooring, tool-making, car and boat making and repairing purposes since the 1960's (source: https://en.wikipedia.org/wiki/Synthetic_resin). There are at least five main types of resins to be considered for corrosion casts:

1. Polyester
2. Vinyl ester
3. Epoxy ester
4. Polyurethane
5. Acrylic resin

From the corrosion cast study point of view the main physicochemical parameters must be considered are:

1. **viscosity** of the liquid resin mixture
2. **flexibility** of the hardened resin
3. **durability** of the hardened resin
4. **acid resistance** of the hardened resin
5. **CT density** of the hardened resin

The viscosity is one of the most important features of the resin. If it is too high, the resin is not able to be injected deeply enough into the small vessels or ducts. On the other hand, if the viscosity is too low researchers have to be very careful not to overfill the structures make the preparations inaccessibly dens (e.g. in case of injecting too low viscosity resin injection into the hepatic veins the resin can go as deep as the liver sinusoids without staying just in the level of the hepatic veins). In 2014, in collaboration with the 1st Department of Surgery, Semmelweis University, Károly Németh from our Clinical Anatomy Research Laboratory, took part in the study of the „Collateral circulation of the rat lower limb and its significance in ischemia - reperfusion studies". For this unique work, the research team needed to use an extreme low viscosity resin with extreme durability and perfect acid resistance. After the trials of different resins, an acrylic resin, Methyl Methacrylate (UZIN KR 416, http://www.uzin.com/products/product-search/details/uzin-kr-416-219/) was chosen that was worked out by Bence Dorogi. This resin was found very useful for the study of the smallest vessels and their anastomoses but was not ideal for wider diameter structures since it always filled up even the smallest vessels making the casts unnecessarily dense for the planned investigations of the ramification of bile duct system (*Figure 16*).

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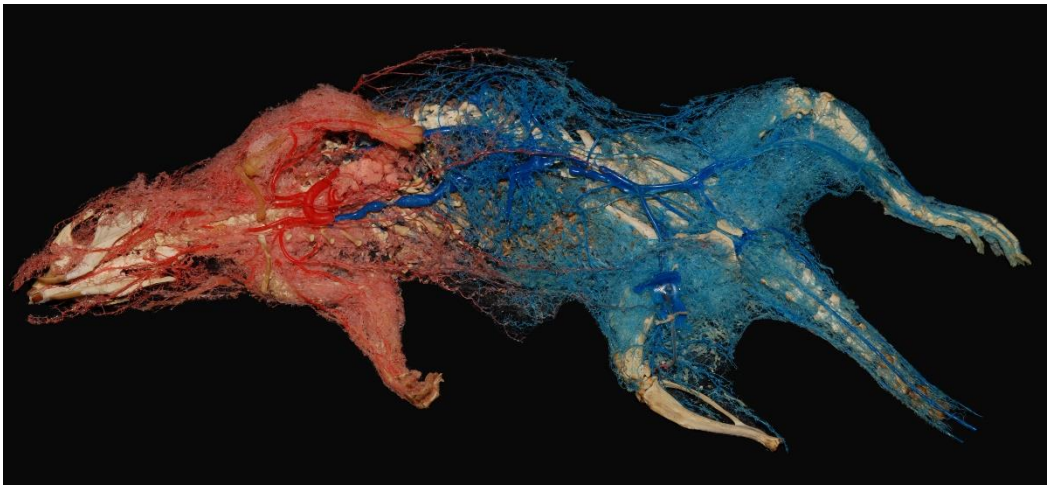

Figure 16: *Corrosion cast of a male Wistar rat's arterial system for the study of the „Collateral circulation of the rat lower limb and its significance in ischemia - reperfusion studies" by Rosero et al. In this study an extreme low viscosity Methyl Methacrylate resin mixture was used by Németh Károly's guide, as advised by Bence Dorogi. The arterial system of the rat's head, upper limbs and upper trunk is red, while the lower limbs, lower trunk and tail are blue. Anastomoses can be identified between the two systems. (Source: Rosero O, Nemeth K, Turoczi Z, Fulop A, Garbaisz D, Gyorffy A, Szuak A, Dorogi B, Kiss M, Nemeskeri A, Harsanyi L, Szijarto A. (2014) Collateral circulation of the rat lower limb and its significance in ischemia - reperfusion studies. Surg Today, 44: 2345-2353.).*

As regards flexibility, generally speaking it can be said that for a conventional corrosion cast technique high flexibility is a disadvantage because the cast will not have a stable frame and will lose its original shape without a supporting organic tissue around the flexible resin. However, if the aim is to perform/simulate surgical procedures on the preparations, a hard framed cast can be easily broken in the soft organic tissue during the simulation or the hard resin cast cannot be cut with a conventional surgical scalpel. That is why a flexible resin generally is more preferred for a vessel lumen filling technique (*Figure 15 and 17*).

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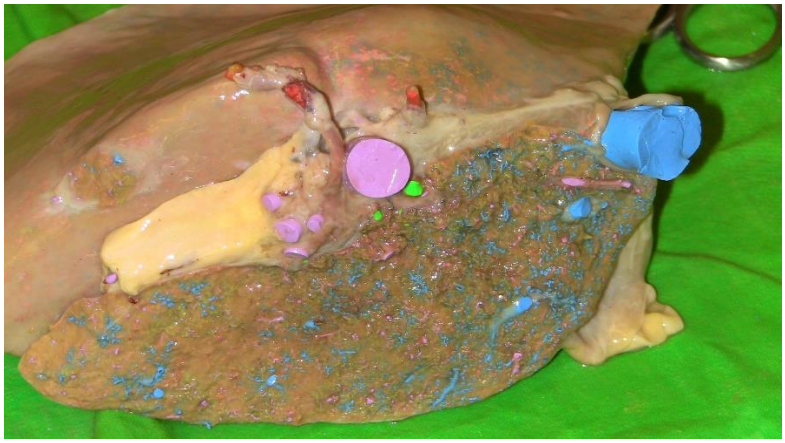

Figure 17: *Left lateral segment graft of human liver vessel lumen filling technique preparation. High flexibility resins were used at this preparation (liquid urethane rubber-Vytaflex by Smooth-on was used for the artery and bile ducts; Köraform, a two-component silicone mould-making compound by Alpina Technische Produkte GmbH was used for the portal and hepatic veins) which kept the liver soft and easy to cut, while creating a graft from the whole size liver on hands on course. Preparation from the „First Donor Surgery Masterclass" Hungary, Budapest 2014.01.30-31. IVC and hepatic veins - blue, portal vein - purple, hepatic duct - green, hepatic artery - red (Source: author's own work. Co-workers: András Szuák, Zsuzsanna Kürti, Zsolt Pápai, Sándor Kovács).*

If there is a need for further preparation of a hard resin filled liver, super durable resin is essential (*Figure 18*).

Figure 18: *Human liver vessel lumen filling technique preparation after further preparation of the hepatic duct system. This technique requires „super durable" resin (Source: Zsolt Pápai).*

For a vessel lumen filling technique there is no need for acid resistance since the parenchyma will not be removed by acid from the cast, but this is a really important feature of the resin in case of conventional corrosion cast technique. We have tried many different resins from this aspect and the Novolac-based Epoxy Vinyl Ester Resin (Derekane 470-300 by Ashland) was proved to be the most acid resistant.

For CT scan examination we need to know the density of the resin itself to make sure we can set up the optimal density of the resin mixtures that go into the different vessels or bile ducts. The average density of the different resins is about 200 Hounsfield unit (HU) (e.g. Derekane 470-300), but occasionally some resins has a higher value (e.g. Köraform, a two-component silicone mould-making compound by Alpina Technische Produkte GmbH has a CT density of 400HU). Naturally, higher density resins require less contrast materials in the resin mixture.

Contrast material

If a certain research work calls for the CT scan of the cast, the proper CT density of the resin mixture needs to be set up in advance in order to be able to make difference between the resin in the different vessels and the surrounding organic tissues on the CT scan.

Hounsfield unit is a standard form of quantity widespread in CT scanning to express CT. Hounsfield units, labelled after their creator Sir Godfrey Hounsfield, originate from the measured attenuation coefficients, which undergoes a linear transformation. This transformation is founded on the peremptory definitions of water (0 HU) and air (-1000 HU) [113]. In our series of formaldehyde fixed human liver preparations the average CT density of the liver parenchyma was 100 HU. If the aim is to fill up more than one vessels on a certain preparation (and we want to visualise all of them separately on the CT scan), we need to keep at least 300-400 HU difference between the different structures since the density of the resin drops in the vessels from proximal to distal. On the other hand, the highest density of any of the structures must not be more than 1900-2000 HU because it would cause severe secondary products. The preparation shown on *Figure 19*, we set up the density of the resin mixtures as follow: hepatic vein - 600 HU, portal vein - 1000 HU, hepatic duct – 1400 HU, hepatic artery – 1800 HU. Since the density of formaldehyde fixed liver parenchyma is about 100 HU we could keep the

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required 400 HU difference with these densities. As a result of this, the different vessels could be visualised (and colour coded) separately or all together (with or without the parenchyma) on the CT pictures (*Figure 19*).

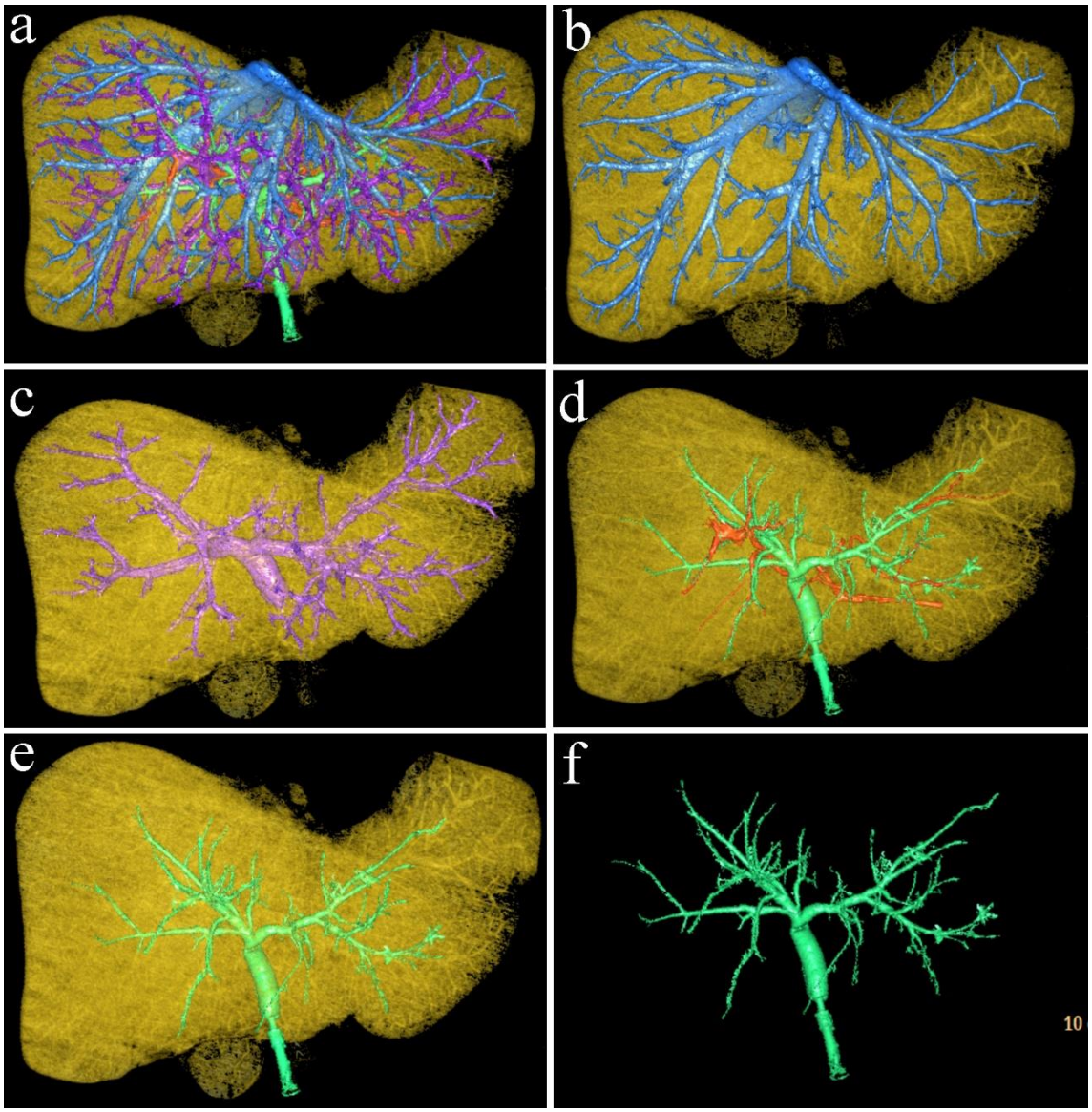

Figure 19: *CT scans of a human liver preparation with specially adjusted CT density for the different vessels and bile ducts. The different structures can be visualised (and colour coded) separately or all together (with or without the parenchyma) because of the appropriately different CT density. IVC and hepatic veins - blue, portal vein - purple, hepatic duct - green, hepatic artery - red (Source: author's own work. Co-workers: Zsuzsanna Kürti, Ibolyka Dudás, Zsolt Pápai, András Szuák).*

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Various contrast materials could be considered to set up the required CT density if those meet the following requirements:

- compose a homogenous resin mixture
- reproducible with the same density
- available on the market (on acceptable price)

In our studies we practically used Lipiodol, Gastrographin or Barium powder. While the first two are liquid, barium is a powder. We made dilution series with the different contrast materials to check their homogeneity, reproducibility and their enhancement of CT density. It was found, that 1% m/m Lipiodol adds 150 HU extra density to the resin while 0.25% m/m barium powder gives the same enhancement (*Figure20*).

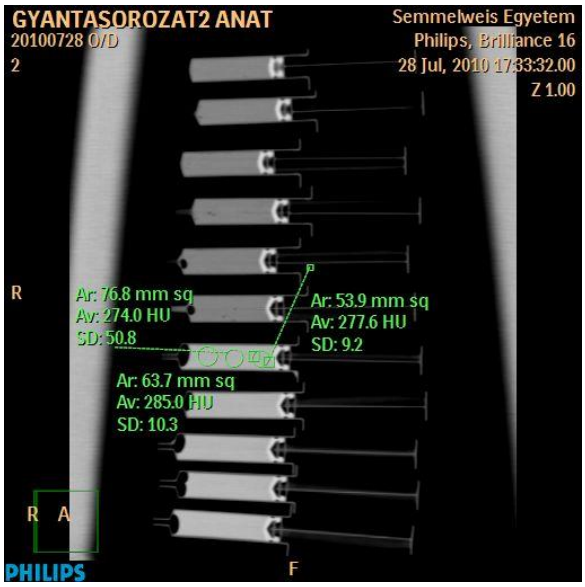

Figure 20: *Dilution series with the different contrast materials to check the homogeneity, reproducibility and enhancement of CT density (Source: author's own work. CT scan was done by Dr. Ibolyka Dudás)*

Additives

1. Most resin requires a Catalyst for the polymerization.
2. Many resin (e.g. Derekane 470-300 by Ashland) requires accelerator to speed the polymerization time up.
3. In most studies there is a need for pigments to set the required colours of the resin mixtures. After we tried various colourants, Pigments FP 6018 yellow-

green, FP 3000 red, FP 5010 blue and FP 4215 purple by Surface Specialties Austria GmbH were chosen for our studies since these were homogenous enough and also reproducible with the same shades.

4. In some of our studies we needed to fill up a relatively bigger vessel e.g. portal vein and a smaller one e.g. bile duct in the liver. Usually it is enough to see just the bigger or segmental branches of the portal vein so we can check where and how the bile ducts run around it. In this case if the viscosity of the resin mixture is too low it can easily go too deeply into the portal vein, making the resin cast far too dense so actually the bile ducts cannot be assessed properly. As a solution for this problem we have found an additive called Q-Cel hollow spheres by Potters Industries (www.pottersbeads.com) which can be added to the resin mixture up to 100% v/v to elevate its viscosity to the aimed level.

Special circumstances

1. Fresh organ/tissue. This is a basic and natural requirement for any kind of corrosion or vessel lumen filling technique to use a fresh organ for the study. Vessels can easily break and leakage can happen if the preparation is not fresh enough.
2. Flush the organ through before resin injection. It can remove any remained blood, open the vessels and in case if it is a liver it gives back its original “round” shape.
3. Put the organ into water, so the resin can equally go into the vessels independently of whether it is just under the top surface or just above the “bottom”.
4. Set the water temperature to a certain degree. In our series we usually used 30°C water temperature to make sure that the polymerization time does not change. Even if we use the same resin compounds and additives exactly in the same ratio, the polymerization time can be changed drastically according to the temperature of the resin mixture. Higher temperature speed the polymerization time up (allow less time for injection), meanwhile lower temperature elongate it.

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5.2 New corrosion cast technique to study the hilar variations of the hepatic duct system

Having spent some years on investigating the corrosion techniques [114, 115, 116, 117, 118, 119] we worked out a suitable method for this current study. A total of 106 fresh human adult livers without signs of liver disease or trauma were recovered at autopsy. Written permission had been obtained beforehand from the Ethical Commission of the Semmelweis University (Number: 185-1/2004).

Livers were carefully removed en block with preservation of the extrahepatic biliary and vascular pedicle. The cystic duct was ligated 1-2 cm far from its drainage into the CHD. The portal vein and the CHD underwent a cannulation process using a polyethylene tube and the liver was subtly perfused with tap water through the portal vein to flush the organ. Liver was taken into a 14 l plastic box then 7 l tap water (temperature 30°C) was poured into it. While the liver was floating in the plastic box the common hepatic duct was injected with special Vinyl Ester resin mixture (1.4 ml resin / 100gr liver tissue), worked out by our research team with the following components:

1. Resin: Novolac-based Epoxy Vinyl Ester Resin (Derekane 470-300 by Ashland);
2. Pigment (5%): FP6018 green (by Cytec Surface Specialties Austria GmbH);
3. Accelerator (1%): Cobalt 2-ethylhexanoate, N,N-Dimethyl aniline (Accelerator NL-23 by AkzoNobel);
4. Catalyst (2%): Methyl Ethyl Ketone Peroxid (Butanox M-50 by AkzoNobel).

After infusion, the resin was polymerized for approximately 20 minutes at 30°C. Hepatic parenchyma was corroded by whole-organ immersion in potassium hydroxide (KOH) solution. After 3-4 days, the remnant of hepatic tissue was removed with water jets from the surface of the biliary cast. The air-dried casts were macroscopically analyzed.

Computer tomography scans were made by Philips Brilliance 16 multidetector CT (tube voltage: 90 kV, tube current: 30 mAs, thickness: 0.8 mm, increment: 0.4 mm) after which 3D volume rendering postprocessing technique was applied by Philips workstation (Extended Brilliance Workspace, version number: V3.5.0.2254).

The confluence of left and right hepatic ducts and those of segmental ducts participating in the formation of common hepatic duct in the absence of left or right hepatic ducts were analyzed and categorized according to the modified Couinaud's classification [43, 120] both in the liver casts and their CT scans.

5.3 Vessel lumen filling without corrosion technique to study the optimal line of hepatotomy for left lateral living donor liver transplantation

A vessel lumen filling technique we worked out and made 30 human liver preparations with it for this study is very similar to the corrosion cast method described previously in details with some important differences. Fresh livers were used with written permission from the Ethical Commission of Semmelweis University. The livers were prepared carefully on the same way we described it in chapter 5.1 till the resin injection (livers were removed en block, CHD was cannulated while cystic duct was ligated, livers were flushed through the portal vein). Components of the resin mixture:

1. Resin: Vinyl Ester Resin (Viapal VUP 4652 by Cytec Surface Specialties Austria GmbH);

2. Pigment (5%): FP6018 green (by Cytec Surface Specialties Austria GmbH);

3. Accelerator (1%): Cobalt 2-ethylhexanoate, N,N-Dimethyl aniline (Accelerator NL-23 by AkzoNobel);

4. Catalyst (1.5%): Methyl Ethyl Ketone Peroxid (Butanox M-50 by AkzoNobel).

As an average 1.4 ml resin mixture / 100gr of liver tissue was injected into the CHD. After polymerization the liver parenchyma was not corroded but was fixed with 8% of formaldehyde solution. CT scans were performed with Philips Brilliance 16 multidetector CT (tube voltage: 90 kV, tube current: 30 mAs, thickness: 0.8 mm, increment: 0.4 mm). The branching pattern of the left hepatic duct and the distance between the falciform ligament (FL) and the confluence of segment II and III ducts was analyzed using 3D VR (volume rendering) CT reconstruction. The number of bile ducts on the surface of virtual hepatotomy was estimated for three different virtual division lines.

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6 Results

6.1 Hilar variations of the hepatic duct system

We prepared 106 high quality human liver casts with our newly developed corrosion technique. The casts were durable enough for complete analysis, and provided suitable density for the CT scans.

Though several researchers have conducted investigations into the detailed anatomy of the liver [40, 41, 42, 121], Couinaud created a segmental division more than half century ago which is still remained universally accepted [43]. The classification presented in this thesis uses Couinaud's segmental anatomy based on the absence or presence of the left (LHD) and right (RHD) hepatic duct (1957) [43] and modified by Smadja and Blumgart [120]:

I. Presence of the LHD and RHD. Normal anatomy.

II. Absence of the RHD. This group of livers was subdivided into six further classes of variations (a,b,c,d,e,h).

III. Absence of the LHD and presence of the RHD. None of the Couinaud's preparations displayed this variation out of 100.

IV. Absence of the LHD and RHD. Group IV was also subdivided into two further classes of variations (g,f).

Smadja and Blumgart revised this classification into six main types (A, B, C, D, E, F) [120]. Applying the most commonly used classification of Smadja and Blumgart, in our series barely more than half of the casts displayed the "normal" biliary branching pattern (*Table 1*).

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Table 1. *Classification of biliary variants according to Couinaud and Smadja and Blumgart.*

Couinaud 1957		Smadja and Blumgart 1994
I. Presence of LHD and RHD	normal anatomy	A
II. Absence of RHD and Presence of LHD	a	B
	b	C1
	c	C2
	d	D1
	e	D2
	h	F
III. Absence of LHD and Presence of RHD	_	_
IV. Absence of LHD and Absence of RHD	g	E1
	f	E2

RHD, right hepatic duct; LHD, left hepatic duct

6.1.1 Group I: Presence of left and right hepatic ducts, normal biliary anatomy: Type "A" (54.74%)

The right and left lobes are drained by the RHD and LHD, respectively; this configuration is commonly considered as normal biliary anatomy (*Figure 21*). The right anterior hepatic duct (RAHD) draining segments V and VIII, join the right posterior hepatic duct (RPHD) draining the segments VI and VII. Their confluence gives rise to the right hepatic duct. The left hepatic duct (LHD) drains segments II, III and IV *(Figure 21*). In full left - full right split, the cutting plane is on the right side of the joining segmental duct IV, through the LHD. The preparation which is presented on *Figure 21* is also optimal for left lateral split since the segmental ducts II and III form a common trunk. The optimal place for split is the common trunk before the duct from segment IV joins into it. The caudate lobe (segment I) has its own biliary drainage. In our series, the frequency of the “typical” biliary configuration is found to be only 54.74%.

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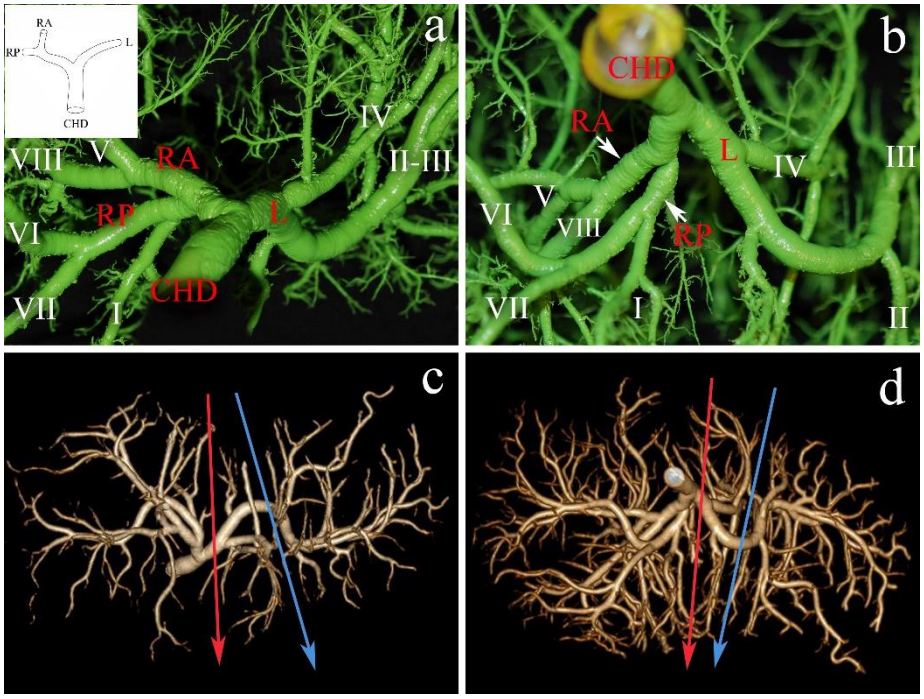

Figure 21: *Normal biliary confluence: Type "A". a) Biliary cast; antero-inferior view. The insert shows the schematic illustration of Type "A" configuration. b) postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the plane of the left lateral split while the red arrow shows the plane of the full left - full right split. CHD, common hepatic duct; RA, right anterior hepatic duct; RP, right posterior hepatic duct; L, left hepatic duct. Roman numerals stand for the segmental ducts.(Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

6.1.2 Group II: Absence of the right hepatic duct - presence of the left hepatic duct (41.49%)

Variation Type "B"

A triple confluence forming the common hepatic duct is the main feature of variation Type "B". The RAHD and RPHD join to the LHD without forming a considerable length of the RHD (*Figure 33*). In full left - full right split, the optimal transection line runs through the LHD just before the LHD joins CHD. This particular preparation which is on *Figure 22* is not optimal for left lateral split since the duct of

segment III forms a common trunk with the duct of segment IV instead of segment II. Graft after left lateral split has two bile ducts to be reconstructed - ducts of segment II and III. (*Figure 22*). Variation Type "B" has 8.49% prevalence.

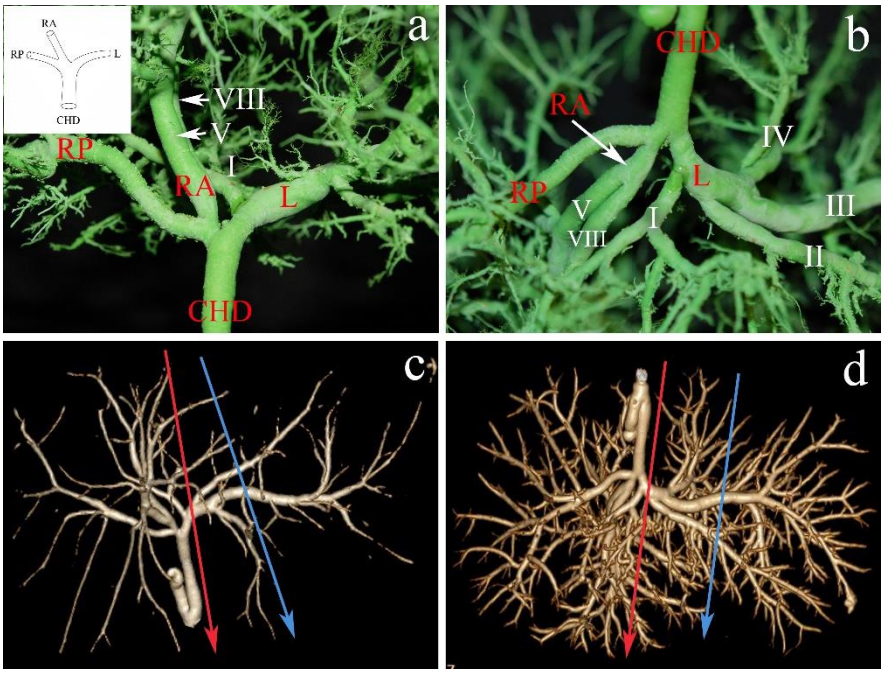

Figure 22: *Type "B" configuration: trifurcation of the common hepatic duct (CHD) into right anterior (RA), right posterior (RP) and left (L) hepatic ducts. a) Biliary cast; antero-superior view. The insert shows the schematic illustration of Type „B" configuration. b) postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the plane of the left lateral split while the red arrow shows the plane of the full left - full right split. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Variation Type "C1"

In type "C1" the RAHD drains directly into the CHD as its continuation, and the RPHD crosses the RAHD on reaching the confluence (*Figure 33*). It is easy to perform full left - full right split in this variation just before the LHD drains into the CHD. The preparation which is presented on *Figure 23* is also optimal for left lateral split since there is a common trunk of the segmental ducts II and III. The optimal place is this common

trunk before the segmental duct IV joins into it (*Figure 23*). The incidence of variation "C1" was 5.66%.

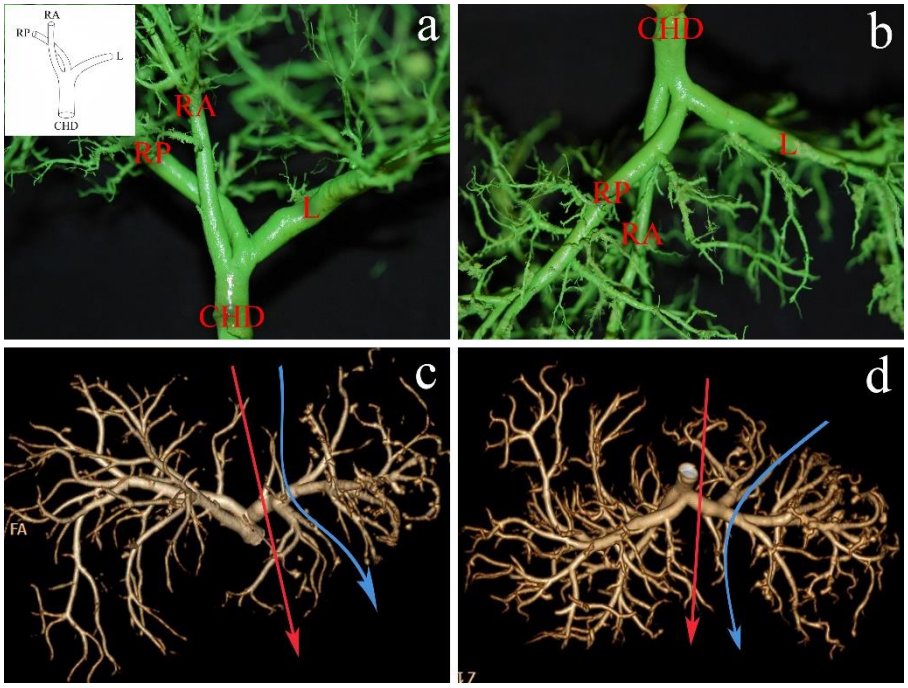

Figure 23: *Type "C1": Continuation of the right anterior hepatic duct (RA) into the common hepatic duct (CHD), while the right posterior hepatic duct (RP) crosses the right anterior duct. a) Biliary cast; anterior view. The insert shows the schematic illustration of Type "C1" configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; infero-posterior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. L, left hepatic duct. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Variation Type "C2"

An ectopic drainage of RPHD into the CHD characterizes this variant (*Figure 33*). In full left - full right split, the resection is just before the LHD merges into the RAHP. Since no common duct of segment II and III is present on this particular cast which can be seen on *Figure 24*, (two ducts drain into the duct of segment III) after left lateral split two ducts remain on the surface of resection to be reconstructed. Type "C2" variant was found in 1.87% in this study.

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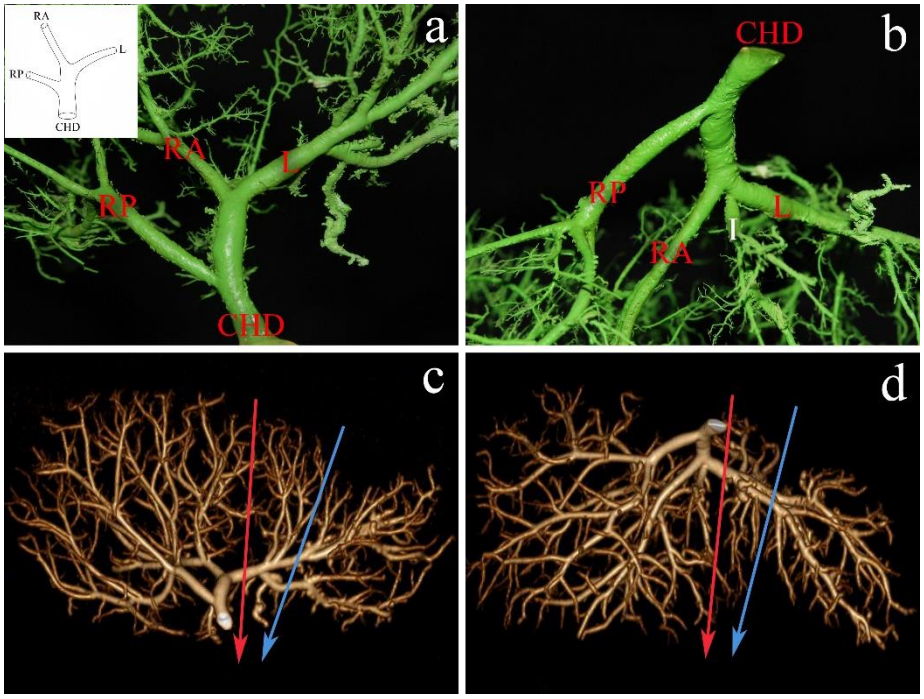

Figure 24: *Type "C2" configuration: The right posterior hepatic duct (RP) drains into the common hepatic duct (CHD). a) Biliary cast; anterior view. The insert shows the schematic illustration of Type „C1" configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-inferior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. RA, right anterior hepatic duct; L, left hepatic duct. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Subvariant of Type "C2"

The cystic duct drains into the bile duct ("common hepatic duct") between the merging site of RPHD distally and the union of RAHP with the LHD proximally (*Figure 33*). This subvariation is also ideal for full left - full right split. The preparation which is presented on *Figure 25* the site for the left lateral split is optimal through the LHD before the RAHD joins it. This anomalous subvariant of Type "C2" was observed in 0.94%.

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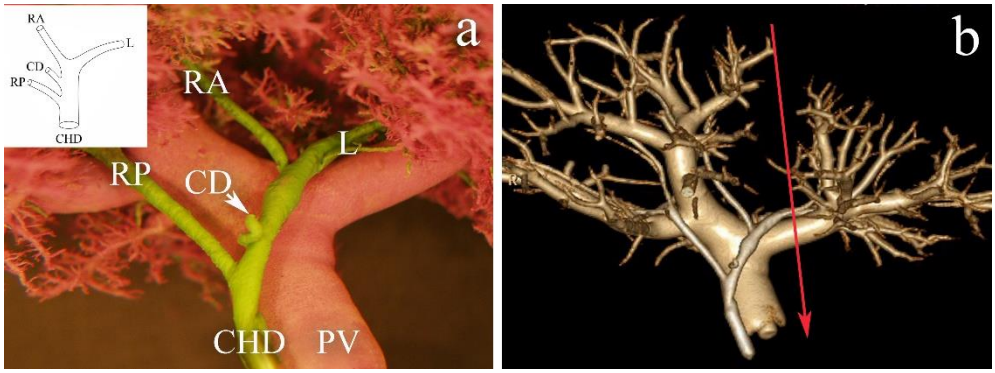

Figure 25: *Configuration of Type "C2" subvariant. The right posterior hepatic duct (RP) drains into the common hepatic duct (CHD) distally to the confluence of cystic duct (CD). a) Biliary cast; anterior view of the hilum. The insert shows the schematic illustration of Type "C2" subvariant configuration. Beside the biliary tree, the portal vein (PV) was also injected with purple coloured resin. b) 3D volume rendering reconstruction; anterior view. On the CT image the red arrow shows the site of the full left - full right split. RA, right anterior hepatic duct; L, left hepatic duct. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Variation Type "D1"

In type "D1" variation the RPHD drains into the LHD. In full left - full right split, the adequate site of transection is through the LHD before the RPHD drains into it (*Figure 33*). Since several ducts drain segment II and III on this particular cast (*Figure 26*), the left lateral split may result in more than two ducts on the surface of resection to be reconstructed. Out of the total of 106 casts 24 cases displaying "D1" variation. The distance between the origin of the right posterior and the right anterior ducts was less than 9 mm in 95.83%, in one case (4.17%) it was 24.15 mm. Type "D1"accounted for 22.64%.

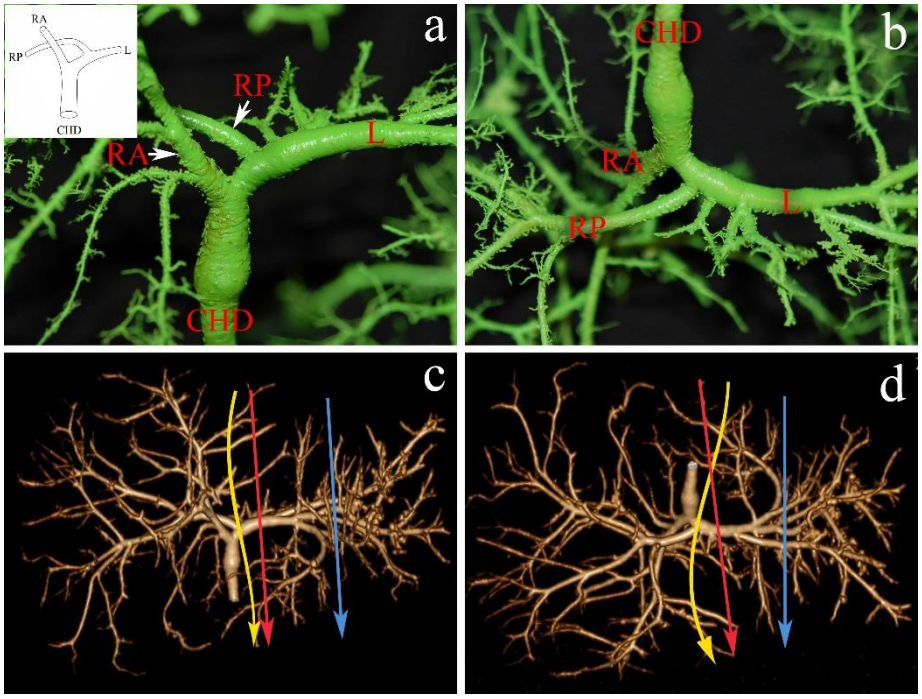

Figure 26: *Type "D1" configuration: The right posterior duct (RP) drains into the left hepatic duct (L). a) Biliary cast; antero-superior view. The insert shows the schematic illustration of Type „D1" configuration. b) Infero-posterior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior visceral view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the plane of the full left - full right split. The yellow arrow shows the site of the erroneously designed full left - full right split. CHD, common hepatic duct; RA, right anterior hepatic duct. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Variation Type "D2"

The RAHD collecting the bile from segments V and VIII drains into the LHD (*Figure 33*). It is easy to perform full left - full right split in this variation just before LHD drains into the CHD. This preparation on *Figure 27* is also optimal for left lateral split since there is a common trunk of the ducts of segment II and III. The optimal place is this common trunk before the duct from segment IV joins into it. The incidence of variant "D2" was low: 0.94%.

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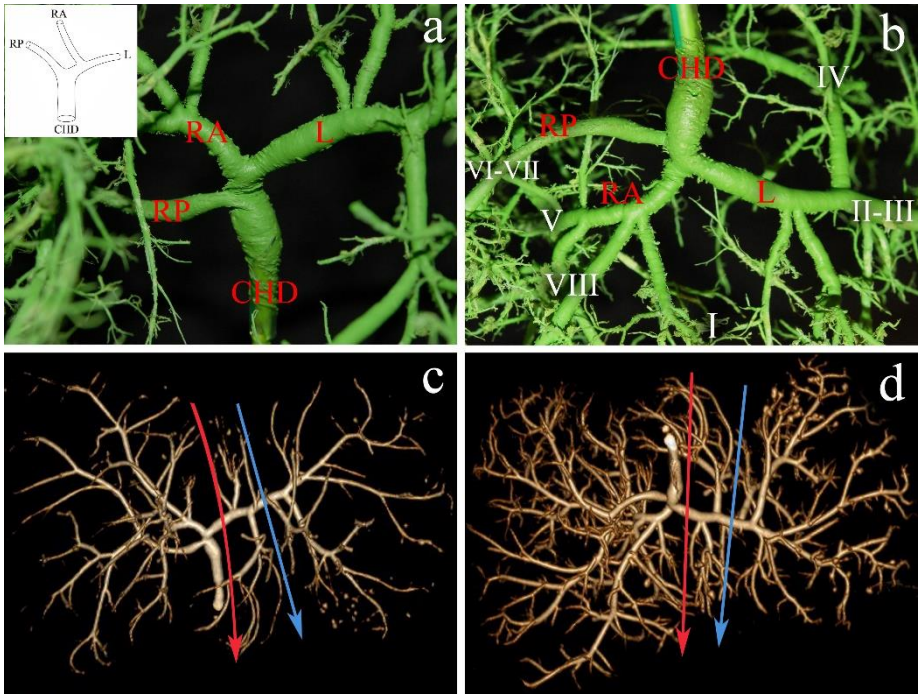

Figure 27: *Type "D2" configuration: The right anterior hepatic duct (RA) drains into the left hepatic duct (L). a) Biliary cast; antero-superior view. The insert shows the schematic illustration of Type „D2" configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. CHD, common hepatic duct; RP, right posterior hepatic duct; Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Variation Type "F"

The RPHD drains into the common trunk of the RAHD and LHD. There is a confluence of the RPHD and cystic ducts (*Figure 28 and 33*). According to the course and diameter of merging RPHD and cystic ducts the possibility arises to distinguish two subtypes. In one subtype the RPHD displays larger diameter than the cystic duct and it clearly continues into the CHD as in our preparation. The other subtype (Couinaud described this anomaly) the RPHD drains into the cystic duct (similar diameters) which continues distinctly into CHD. This variation is optimal for full left - full right split, LHD can be transected before the RHD joins into it. This particular preparation on *Figure 28*

is also optimal for left lateral split since there is a common trunk of the ducts of segment II and III. Type "F" occurs also rarely; one preparation displayed it (0.94%).

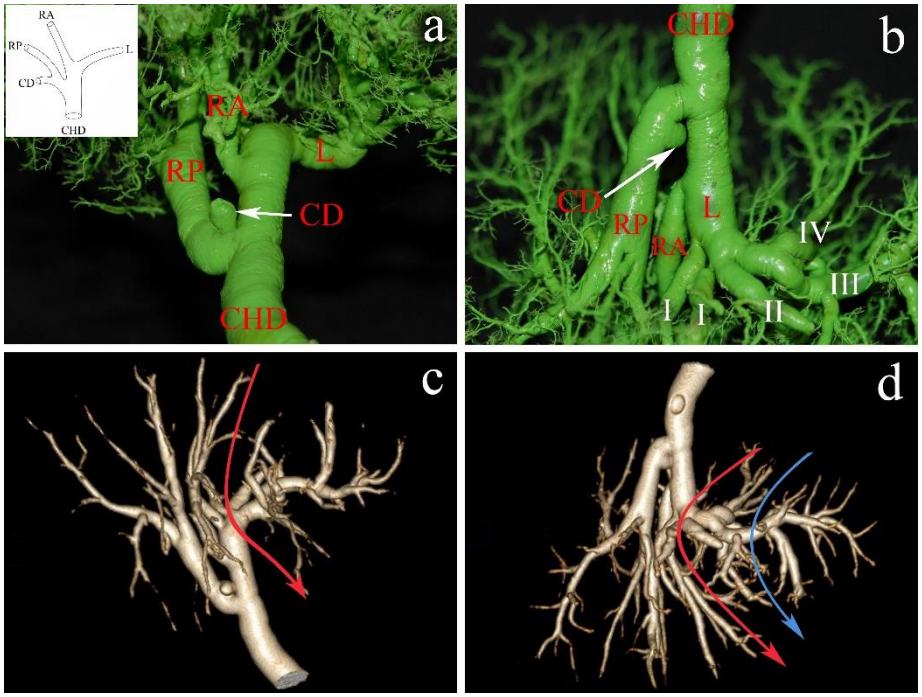

Figure 28: *Type "F" configuration: The cystic duct (CD) joins to the right posterior duct (RP) that forms a confluence with the common trunk of the left (L) and right anterior (RA) hepatic ducts. a) Biliary cast; anterior view. The insert shows the schematic illustration of Type "F" configuration. b) Infero-posterior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. CHD, common hepatic duct; Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Newly described variation Type "G"

Revealing a biliary configuration that has not yet been recorded until present, we have further extended the Couinaud's classification modified by Smadja and Blumgart by a new category of variation: "Type G". Since this anomalous biliary tree has no RHD, but bears a usual LHD it would fit into the group II: absence of the RHD, presence of the

LHD. However, on the right side, only the RAHD can be identified, while the duct from segment VI drains separately into the main confluence. Moreover, the duct from the segment VII has a common entry with the RAHD into the terminal part of the LHD (*Figure 29 and 33*). Performing full left - full right split, the LHD can be transected before the duct from segment VII drains into it. This preparation on *Figure 29* is also optimal for left lateral split since there is a common bile trunk from segment II and III. The optimal place of it is this common trunk before the duct from segment IV joins into it. One biliary cast displayed this variant (0.94%).

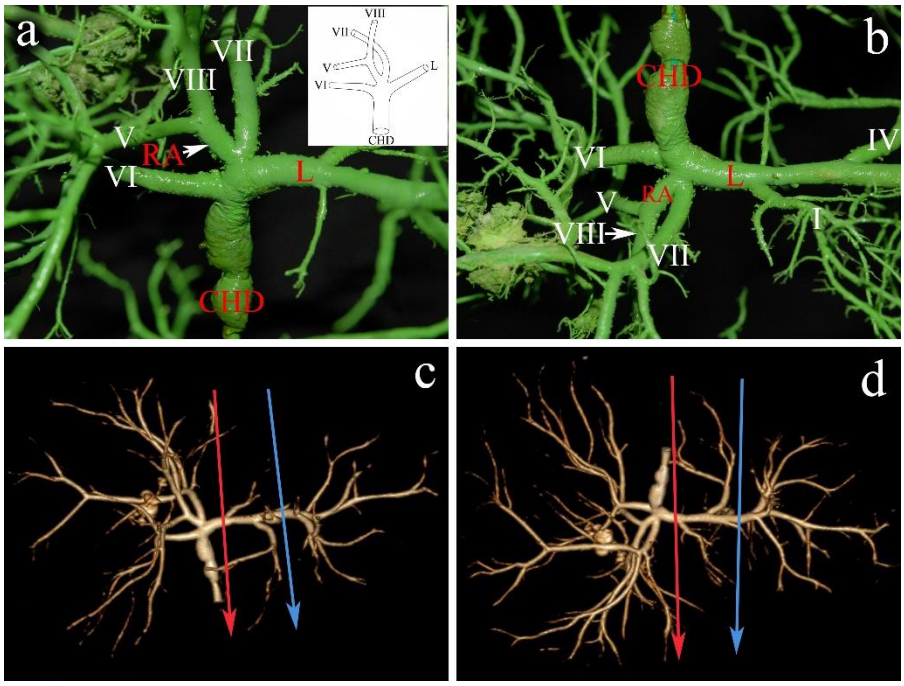

Figure 29: *Type "G" configuration: Presence of left hepatic duct and absence of right posterior hepatic duct and right hepatic duct. Note the common ostium of the right anterior hepatic duct (RA) and the duct of segment VII into the left hepatic duct (L). The duct of segment VI joins the common hepatic duct (CHD). a) Biliary cast; antero-superior view. The insert shows the schematic illustration of Type „G" configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

6.1.3 Group III: Absence of the left hepatic duct - presence of the right hepatic duct (0 %)

Of the 106 biliary casts none had such biliary configuration.

6.1.4 Group IV: Absence of the left hepatic duct - absence of the right hepatic duct: Type "E"

(3.75 %)

A proportion of 3.75% in our series formed this group of biliary variations. In such biliary trees neither the RHD nor the LHD develop but the confluence of the right sectional and/or segmental ducts and ducts from the left hepatic lobe forms the CHD. According to the duct joining, two types can be distinguished: Type “E1” and “E2”.

Variation Type "E1"

In this configuration the ducts from segments II and III after receiving the segmental duct I and IV, respectively, separately drain into the RPHD; while the RAHD joins these merged ducts. None of our casts showed this variation; however, we found two preparations that fit into this group, except, the ducts from segments II and III do not join separately to form the CHD with the right sectional ducts. We extended the Couinaud’s classification modified by Smadja and Blumgart by two subvariations.

Type "E1a" subvariant

In Type “E1a” configuration the ducts from segment II and III form a common trunk with the RPHD which receives then the duct from segment IV. Most distally (towards the duodenum) the RAHD joins into this common trunk resulting in the formation of the CHD (*Figure 30 and 33*). This variation is not ideal for full left - full right split since there would be two separate bile ducts (one from segment IV and one from segments II and III) on the surface of resection, instead of one LHD. This particular preparation on *Figure 30* is optimal for left lateral split since there is a common bile trunk from segment II and III. The occurrence of subvariation "E1a" was 1.87% (n=2).

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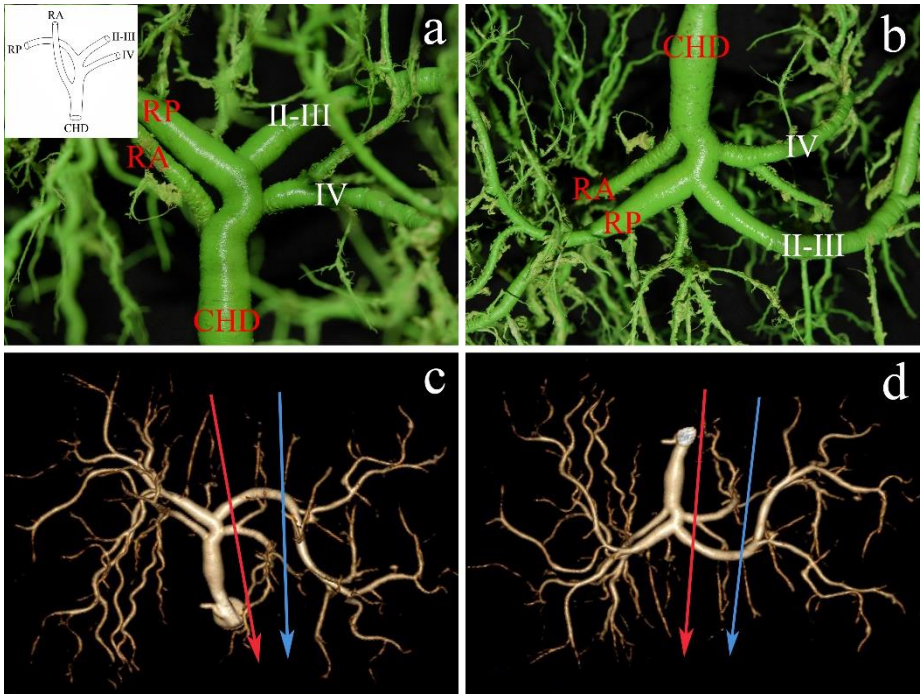

Figure 30: *Type "E1a" configuration: Ducts draining segment II and III form a common duct that joins the right posterior hepatic duct (RP), forming a common trunk. Then from the left it receives the duct of segment IV and from the right lobe the right anterior hepatic duct (RA) forming the common hepatic duct (CHD). a) Biliary cast; antero-superior view. The insert shows the schematic illustration of Type „E1a" configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Type "E1b" subvariant

Type "E1b" biliary anomaly exhibits one particular dissimilarity compared to variation "E1a", namely the entry of the duct of segment IV is distal (in duodenal direction) to that of the RAHD (*Figure 31 and 33*). This variation is not ideal for full left - full right split since there would be two separate bile ducts (one from segment IV and one from segments II and III) on the surface of resection, instead of one LHD. This

particular preparation on *Figure 31* is optimal for left lateral split since there is a common bile trunk from segment II and III. Type “E1b” accounted for 0.94% (n=1).

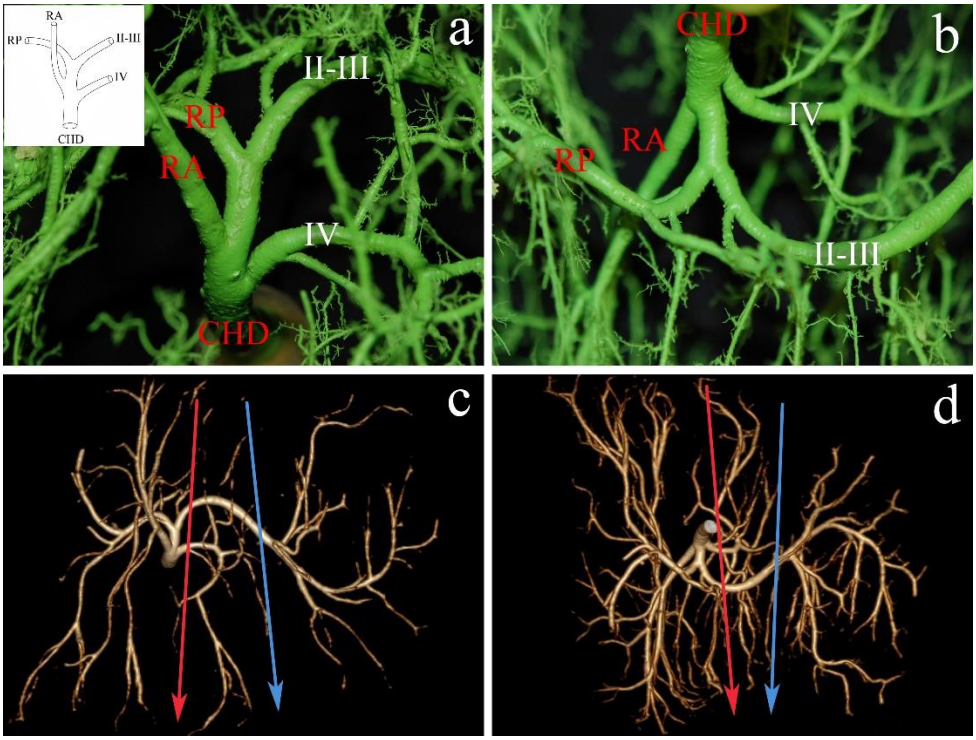

Figure 31: *Type "E1b" configuration: The duct draining segment II and III forms a common trunk with the right posterior hepatic duct (RP) that receives the right anterior hepatic duct (RA) and then most distally the duct from segment IV joins into this common trunk forming the common hepatic duct (CHD). a) Biliary cast; antero-superior view. The insert shows the schematic illustration of Type “E1b” configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; infero-posterior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the line of the full left - full right split. Roman numerals stand for the segmental ducts. (Source: author’s own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

Variation Type "E2"

Biliary tree in this group has also double hepatic duct on the left side (IV - III and II - I) like in group “E1” and the right sectional ducts join the CHD separately at the same level. Of 106 casts none of them bears this variation; however, we observed a

configuration that fits into this group, except, the double hepatic ducts on the left side are formed by the segmental duct IV and by a duct from segments III, II, and I, respectively. Moreover, right sectional ducts (RAHD and RPHD) are also absent. We inserted this variant into the Couinaud's classification modified by Smadja and Blumgart as subvariant of type "E2".

Subvariant of type "E2"

Instead of the right anterior and posterior hepatic ducts a highly complex drainage pattern is present in this variant. One branch from segment VIII forms a common trunk with the segmental duct VII, while the other branch from segment VIII forms a common trunk with the segmental duct V. Furthermore, these two common trunks and the duct from segment VI form a trifurcation. On the left side, there is a common stem of segmental ducts II and III that receives duct from segment I, while the duct from segment IV joins independently and most distally (towards the duodenum) into the common hepatic duct (*Figure 32 and 33*). This variation is not ideal for full left - full right split since there would be two separate bile ducts (one from segment IV and one from segment II and III) on the surface of resection, instead of one left hepatic duct. This particular preparation on *Figure 32* is optimal for left lateral split since there is a common bile trunk from segment II and III. The occurrence of subvariant of type "E2" was found in 0.94% (n=1).

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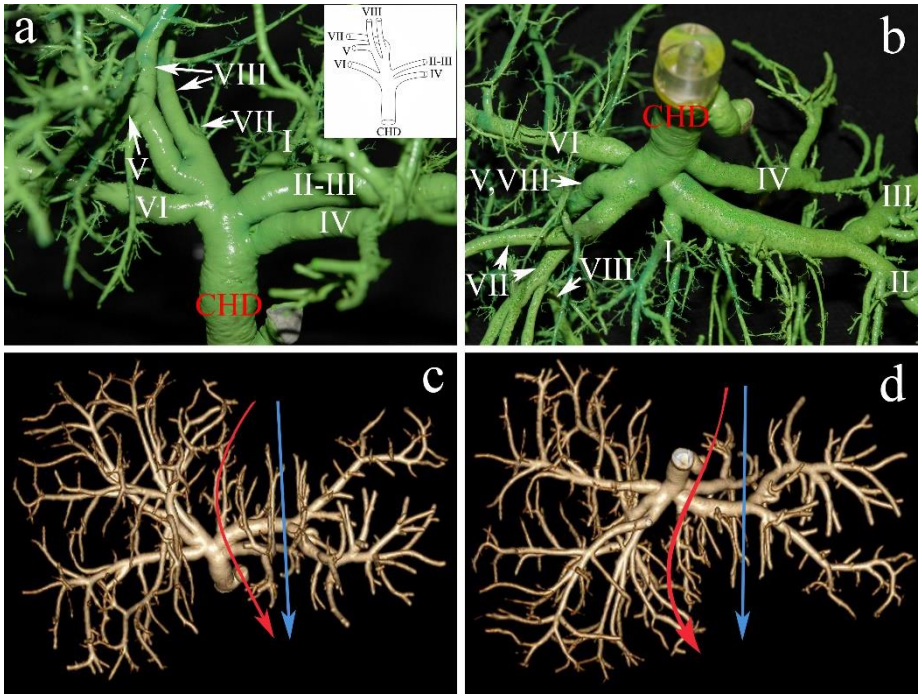

Figure 32: *Subvariant of type "E2" configuration: There are neither RAHD (RA) nor RPHD (RP) and LHD. a) Biliary cast; antero-superior view. The insert shows the schematic illustration of subvariant of type "E2" configuration. b) Postero-inferior view of the cast. c) 3D volume rendering reconstruction; antero-superior view. d) 3D volume rendering reconstruction; postero-inferior view. On the CT images the blue arrow indicates the site of the left lateral split while the red arrow shows the site of the full left - full right split. CHD, common hepatic duct; Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Zsolt Pápai, Sándor Kovács. CT pictures made by Ibolyka Dudás).*

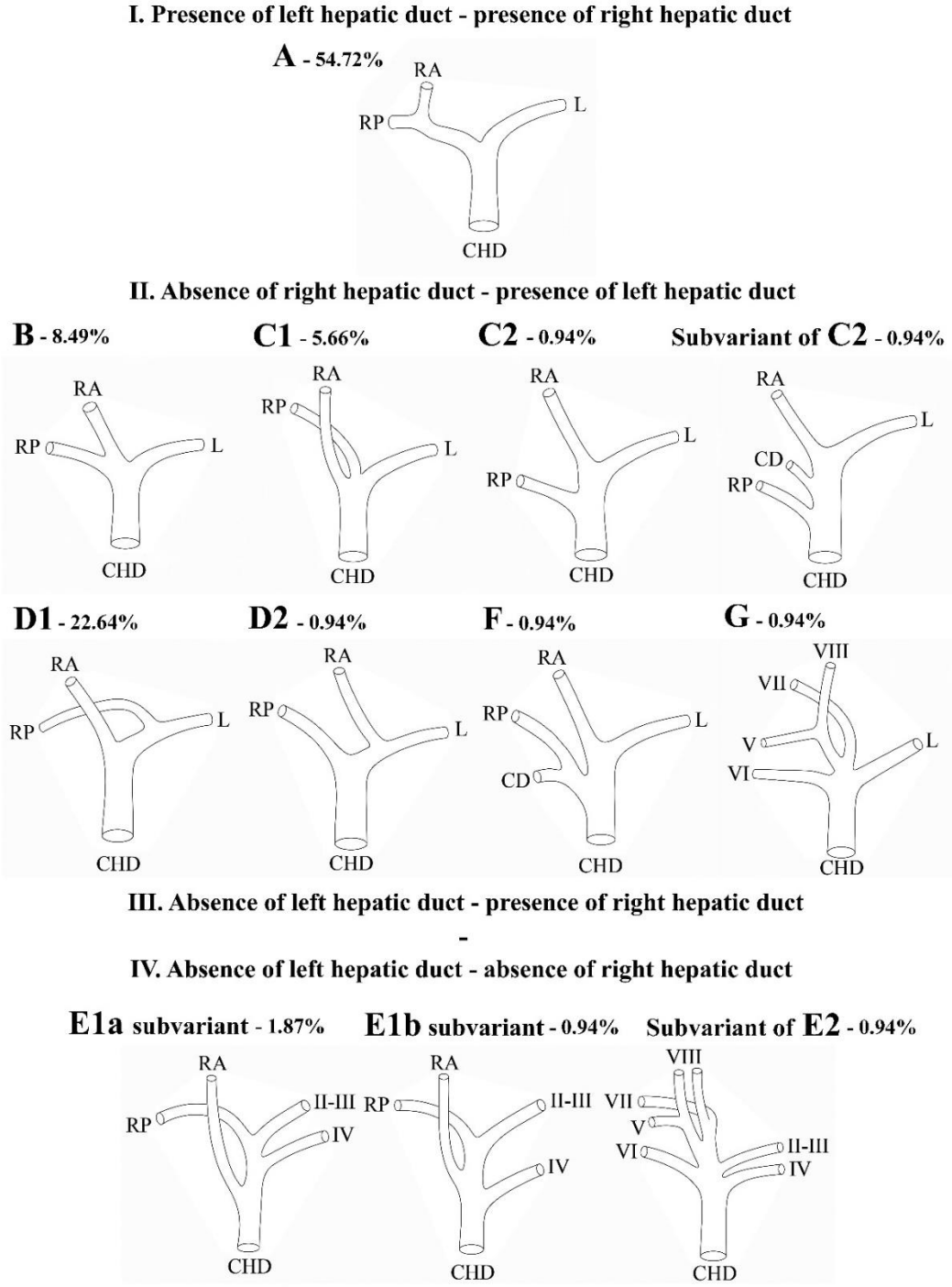

Figure 33: *Branching patterns of hepatic ducts in 106 human biliary casts classified according to Couinaud's classification modified by Smadja and Blumgart and by the present author. Newly inserted variants: C2 subvariant, E1a subvariant, E1b subvariant, E2 subvariant. "G" a recently observed new variant. CHD, common hepatic duct; RA, right anterior hepatic duct; RP, right posterior hepatic duct; L, left hepatic duct; Roman numerals stand for the segmental ducts.*

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6.2 Variations of the left hepatic duct, optimal line of hepatotomy for left lateral living donor liver transplantation

With our newly developed vessel lumen filling technique with preserved liver parenchyma we made 30 high quality human liver preparations to study the anatomical variations of the LHD and the optimal line of hepatotomy for the simulation of the left lateral LDLT [118].

6.2.1 Branching patterns of left hepatic duct

According to the confluences of bile ducts segment II, III and IV, three different main types with subtypes were found (*Figures 34 - 37*).

In variation Type I. the bile ducts from segments II and III form a common trunk. The duct from segment IV joins into this common trunk in the subtype named: Type I.a (*Figure 34*). In another subtype, segment IV duct merges into the common hepatic duct/one of the hilar ducts; we have designated it as Type I.b (*Figure 34*).

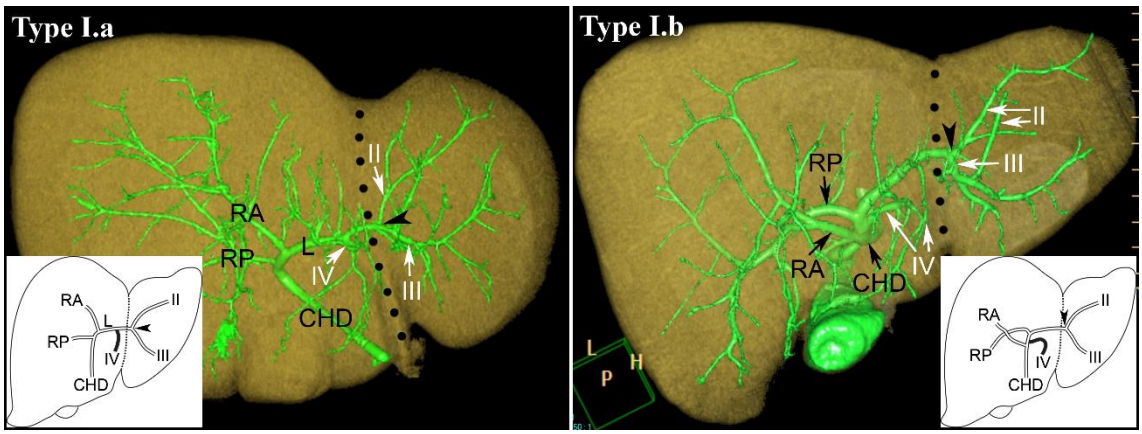

Figure 34: *Type I.a and Type I.b. FL is indicated by the black dotted line, while a black arrowhead shows the junction of segment II and III ducts. RA, right anterior hepatic duct; RP, right posterior hepatic duct; L, left hepatic duct; CHD, common hepatic duct; Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Tien Nguyen. CT pictures made by Ibolyka Dudás).*

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A surgically notable subvariant fitting into this group was observed in livers where the left hepatic duct was formed by multiple ducts from segments II and III. Moreover, the confluence was localized closer to the hilum, than to the FL (*Figure 35*).

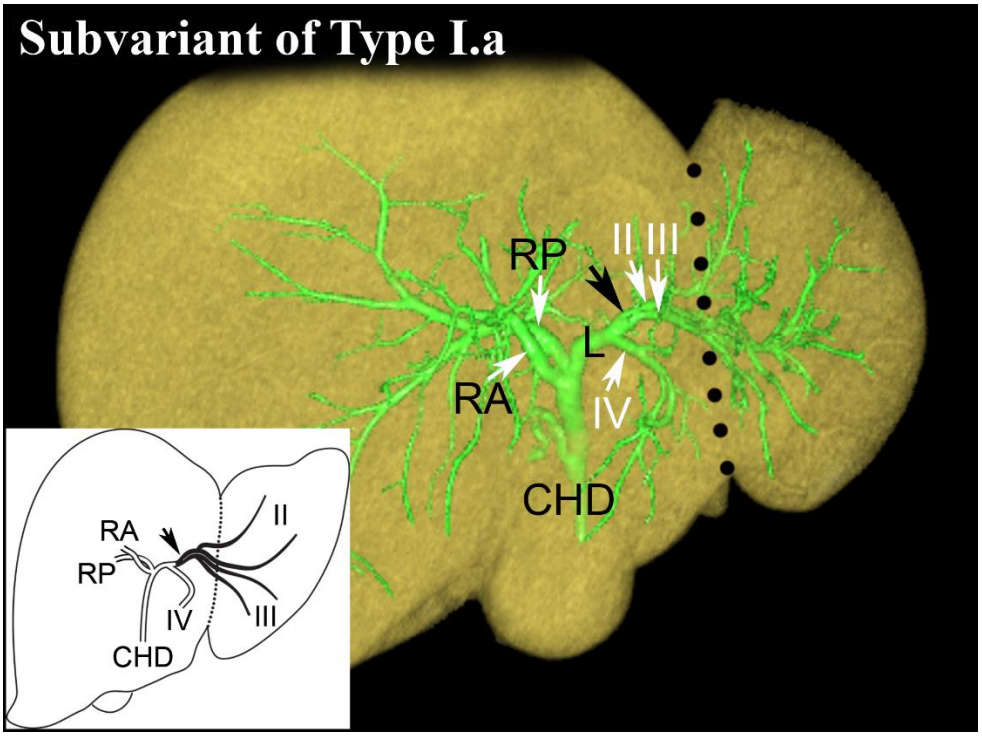

Figure 35: *Subvariant of Type I.a. There are more ducts from segment II and segment III as well, which form the LHD close to the hilum, far away from the FL (black dotted line). Black arrow shows the junction of segment II and III ducts. RA, right anterior duct; RP, right posterior duct, L, left hepatic duct, CHD, common hepatic duct. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Tien Nguyen. CT pictures made by Ibolyka Dudás).*

In variation Type II. the duct of segment IV drains into segment II or segment III or both ducts proximally from the confluence of segment II and III ducts. When segment IV duct drains into segment III duct, we named it as Type II.a. Theoretically segment IV duct could drain into segment II duct, it should be named as Type II.b in this classification, however there was no liver found in our series like this. When segment IV duct drained into both segment II and segment III ducts, we labelled it as Type II.c (*Figure 36*).

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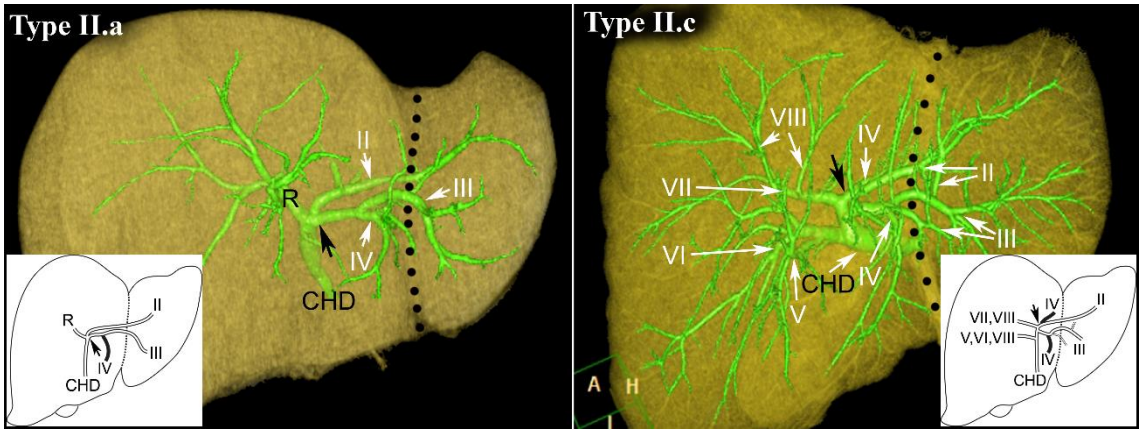

Figure 36. *Type II.a and Type II.c. FL is indicated by the black dotted line, while a black arrow shows the junction of segment II and III ducts. R, right hepatic duct, CHD, common hepatic duct. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Tien Nguyen. CT pictures made by Ibolyka Dudás).*

Variation Type III. denotes a trifurcating confluence of segment II, III and IV ducts forming the LHD (*Figure 37*).

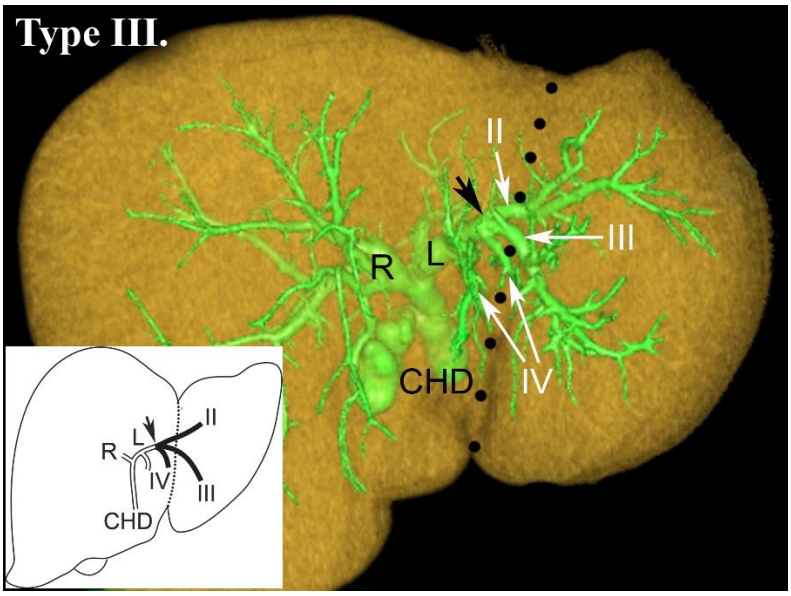

Figure 37: *Type III. FL is indicated by the black dotted line, while a black arrow shows the junction of segment II and III ducts. R, right hepatic duct; L, left hepatic duct; CHD, common hepatic duct. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Tien Nguyen. CT pictures made by Ibolyka Dudás).*

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Variation Type I. compared to Types II. and III. was found to be the dominant one (76.67%) in our series, furthermore, its subtype "a" (Type I.a) constituted the highest relative frequency in the investigated livers (66.67%). Type I.a may be considered as the "normal" anatomical variation (*Table 2*).

Table 2: *Types and prevalences of left hepatic duct variations in 30 cadaveric liver preparations*

Type	Subtype	Frequency			
		No.		%	
I.	a	20	23	66.67	76.67
	b	3		10	
II.	a	5	6	16.67	20
	b	0		3.33	
	c	1		0	
III.		1		3.33	

6.2.2 Topographical relationship of the falciform ligament and the confluence of segment II and III ducts

In Type I. variation, the localization of the confluence related to the FL showed three topographical patterns:

Pattern Left - segment II and III ducts join at the left side of the FL.

Pattern Right - segment II and III ducts join at the right side of the FL.

Pattern Middle - segment II and III ducts join at the level of the FL (*Figure 38*).

The relative incidence of Pattern Middle and Left were equally 20-20%, while the percentage of Pattern Right was the highest: 36.67% (*Table 3*).

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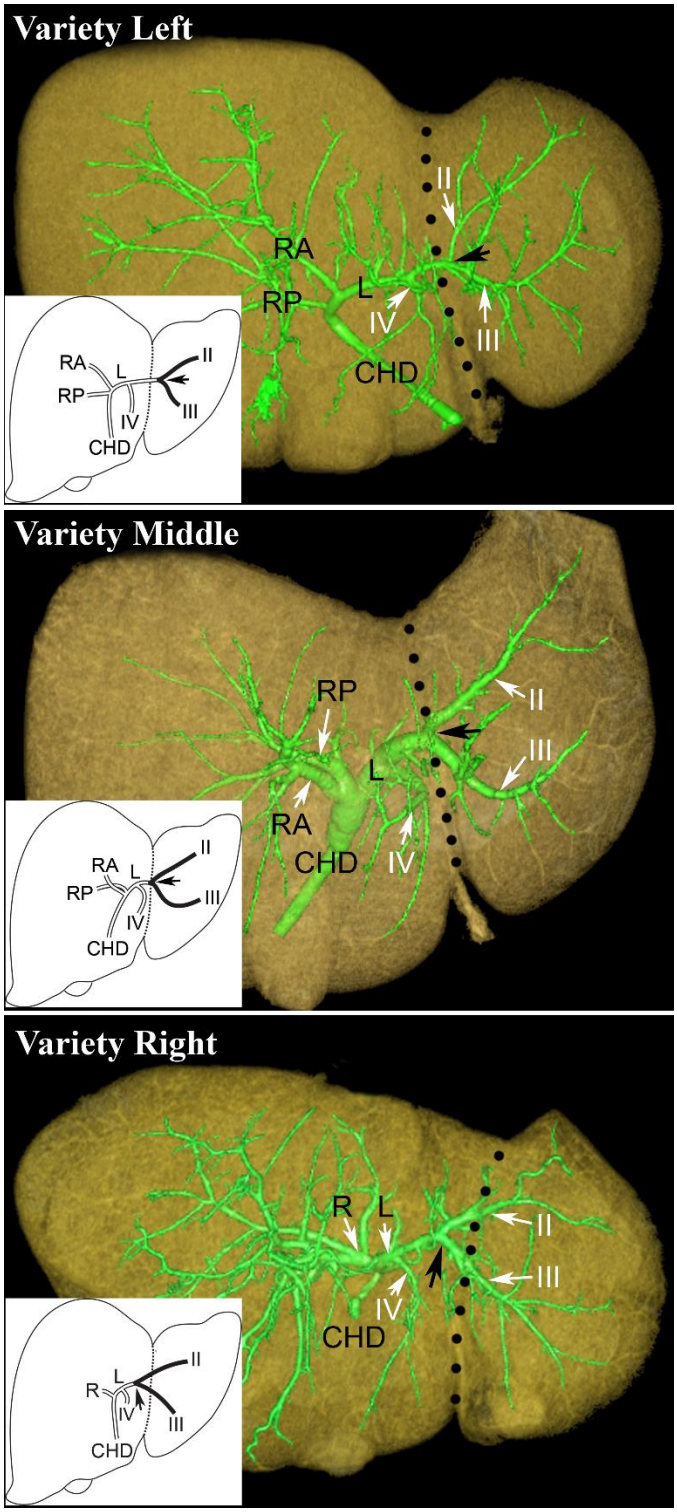

Figure 38: *Correlation of the confluence of segment II and III ducts (black arrow) to the site of the FL (dotted line). R, right hepatic duct; RA, right anterior hepatic duct; RP, right posterior hepatic duct; L, left hepatic duct; CHD, common hepatic duct. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Tien Nguyen. CT pictures made by Ibolyka Dudás).*

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Table 3: *Topographical pattern of segment II and III ducts' confluence in Type I variation*

Type	Subtype	Pattern	Frequency / 30 livers			
			No.		%	
I.	a	Left	5	6	16.67	20
	b	Left	1		3.33	
	a	Middle	6	6	20	20
	b	Middle	0		0	
	a	Right	9	11	30	36.67
	b	Right	2		6.67	

6.2.3 Evaluation of the number of bile ducts in three different division lines

The surgical relevance of the LHD variations described above was evaluated by counting the number of bile ducts on the surface of virtual hepatotomy in three different division lines. When the virtual division line was on the FL, there was a single duct for anastomosis in just 30% of cases and there were 2, 3 or 4 ducts in 53.3%, 10.0%, and 3.3%, respectively. The optimal line of division was achieved when virtual hepatotomy was performed one cm to the right of the FL resulting in one hepatic duct only to be anastomosed in about two thirds (70%) of the investigated livers (*Table 4*).

Table 4: *Number of bile ducts on the surface of virtual hepatotomy in case of three different division lines*

Number of bile ducts on the surface of virtual hepatotomy	Division line: 1 cm to the right of FL	Division line: 0.5 cm to the right of FL	Division line: on FL
1	21/30 (70%)	15/30 (50%)	9/30 (30%)
2	8/30 (26.6%)	11/30 (36.7%)	16/30 (53.3%)
3	1/30 (3.3%)	3/30 (10%)	3/30 (10%)
4	0/30 (0%)	1/30 (3.3%)	1/30 (3.3%)

FL, falciform ligament

However, dividing the liver 1 cm to the right of the FL, impairs segment IV duct in 46.7% of cases (*Figure 39*).

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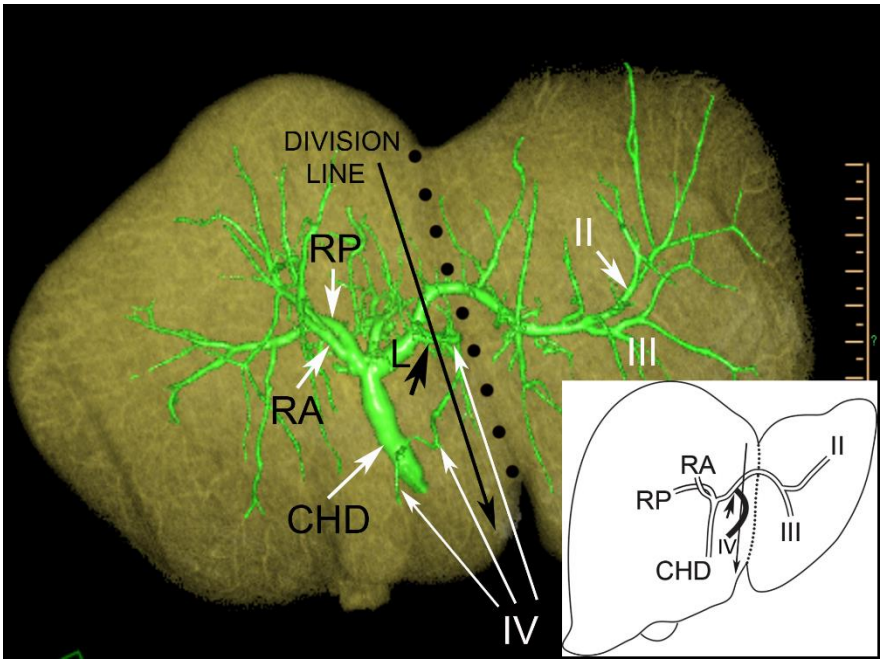

Figure 39: *Dividing the liver 1 cm to the right of the FL may impair the bile drainage of segment IV in the remaining liver. Resection line is shown by the long black arrow, and FL is indicated by the black dotted line, while ducts draining segment IV are indicated by long white arrows. Short black arrow shows the joining of segment IV duct into the LHD. RA, right anterior hepatic duct; RP, right posterior hepatic duct; L, left hepatic duct; CHD, common hepatic duct. Roman numerals stand for the segmental ducts. (Source: author's own work. Co-workers: András Szuák, Tien Nguyen. CT pictures made by Ibolyka Dudás).*

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7 Discussion

Both of our newly developed corrosion cast- and vessel lumen filling without corrosion techniques were perfectly suitable to perform our planned studies and get the aimed data. The resin mixture could fill up even the small subsegmental ducts, after the polymerization the liver preparations were hard enough to keep their shape, provided excellent density for CT scans and also kept their colours even in case of corrosion with cc KOH.

7.1 Hilar variations of the hepatic duct system

Of the vascular and biliary anatomic variants, the most challenging are the variations of biliary branching pattern since their frequency is the highest according to recent and old classic publications [43, 100, 122]. Thus the majority of postoperative complications in SLT and segment resections proves to be related to biliary duct system including biliary leakage, long-term segmental atrophy and strictures [123, 124]. The hilar variations of the hepatic duct system has a great importance in case of full left-full right split, when the LHD needs to be cut at this level just before it drains into the CHD. The knowledge of these variations is also essential in case of right lobe LDLT, when the RHD needs to be dissected in the liver hilum. Our results in a series of 106 livers showed 45.28% (58/106) perihilar biliary variants (*Tables 5 and 6*). This result indicates that the biliary modality classified as "normal" occurs only little more than half of the specimens. Present data confirm the supposition that in categorizations, instead of "normal biliary anatomy" the use of "most frequent variation" would be reasonable. Some investigators [43, 125] also published data on the high frequency of biliary variations (43 % and 45 %, respectively) (*Tables 6 and 7*). However, a striking difference in incidences of perihilar biliary variations comes into view comparing our data to those deducted from investigations in far-east countries (Japan, Korea) displaying lower percentages of perihilar variants (30.7%, 31.58%, 35%, 37%, 28%) [100, 126, 127, 128, 129]. One should avoid the misconclusion; however, our present records together with the above mentioned literary data strongly suggest the presence of existing population differences.

Analysing the literary data some of them describe biliary duct variations in specimens derived only from left or right hepatectomies [127, 129]. Their findings clearly indicate a significantly lower incidence of bile duct variations in the left liver lobe than in the right one. Sorting our data by sides confirmed that the right liver lobe exhibits far higher frequency of bile duct variation (41.9% versus 3.75%) than the left one (*Tables 7 and 8*). Since the right liver harvesting is prevalent, it follows that a higher risk of postoperative biliary complications is likely. Sorting out our casts depriving the RHD, near upon half of them (48/106 = 45.28 %) displayed this variant being in close accordance with Couinaud's [130] figuring (50/107 = 46.73 %). Ohkubo et al. [129] reported 29 right livers of the 110 cases (26 %) without a RHD on the other hand the LHD was absent only in one left liver lobe out of 55 cases (2 %) (*Table 8*).

Among the biliary duct variations recorded in our study the incidence of "D1" configuration exceeds all "D1" figures reported by other authors (22.4% versus 5%, 13%, 8%, 15.8%, 11%, 12%, 11.6%), although, except Yoshida et al. [126] and Couinaud [43], several investigators described this variation as the most numerous [100, 125, 127, 128, 129]. The clinical importance of this variant is obvious since the surgeon has to be careful not to hurt the aberrant RPHD -which drains into the LHD- during surgical interventions e.g. left hepatectomy. If the RPHD damaged, not only the left lobe will be removed but segments VI and VII will also be isolated, leaving the patient with only two viable segments, V and VIII. It is advisable to perform preresection cholangiography before the left hepatectomy. In this study the distance between the ostia of the RPHD and the RAHD was less than 9 mm in 95.83%. In the case of full left - full right split or in case of left lobe LDLT, when the LHD needs to be dissected from the CHD for the left liver graft, this last 9 mm of the LHD should be preserved for the right liver lobe in case if there is a hilar variation type "D1". This finding probably has less importance in those countries where the occurrence of this variation is lower (e.g. 5% in France [43, 130]) but it can have great importance in those countries where type "D1" occurs much more frequently, e.g. 22.64% in this current Hungarian study. Edward Russel et. al found that 36% of 47 patients who had sclerosing cholangitis showed this type of variation [125].

Since a considerable number of variations in the hepatic ducts persist in the hilar region, it is necessary to have a profound knowledge of the actual variations in the hepatic ducts in the hilar area around the hilar confluence to perform safe right or left liver lobe

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transplantation. Our data stress on the high incidence of perihilar biliary variations in the livers taken from Hungarian deceased.

Table 5. *Authors who have published data on the biliary variations. Country of investigation, number of investigated cases, and the method of investigation*

	Year of the study	Number of cases	Method	Country
Present study	2017	106	Corrosion casts	Hungary
Couinaud	1957 & 1989	100	Corrosion casts	France
Russell et al.	1990	838	Cholangiography	USA - Miami
Yoshida J. et al.	1996	1094	Cholangiography	Japan
Nakamura et al.	2002	120	Intraoperative cholangiography	Japan
Choi et al.	2003	300	Intraoperative cholangiography	Korea
Ohkubo et al.	2004	165	Postmortem cholangiography & serial section reconstr.	Japan
Kishi et al.	2010	361	Intraoperative cholangiography	Japan

Table 6. *Classification and frequencies of biliary variations in the present study and those of variations reported by other authors*

Classification of biliary configurations			Frequency of biliary tract variations (%)							
Couinaud 1957	Smadja and Blumgart 1994	Present study 2017	Present study 2017	Couinaud 1957 & 1989	Russel et al. 1990	Yoshida J. et al. 1996	Nakamura et al. 2002	Choi et al. 2003	Ohkubo et al. 2004	Kishi et al. 2010
I. Presence LHD Presence RHD	A	A	54.72 (n=58)	57	55	68.42	65	63	72	69.3
II. Absence RHD Presence LHD	B	B	8.49 (n=9)	12	-	17.7	8.3	6	-	-
	C1	C1	5.66 (n=6)	16	8	-	9.2	10	5	6.9
	C2	C2	0.94 (n=1)	4	5	6.0	-	-	5	6.9
		C2 subv.	0.94 (n=1)	-	-	0.09	-	-	-	-
	D1	D1	22.64 (n=24)	5	13	8.0	15.8	11	12	11.6
	D2	D2	0.94 (n=1)	1	-	-	-	-	-	-
	F	F	0.94 (n=1)	1	-	-	-	-	-	-
	-	**G**	0.94 (n=1)	-	-	-	-	-	-	-
III. Absence LHD Presence RHD	-	-	0.00	0	-	0.18*	-	1	-	-
IV. Absence LHD Absence RHD	E1	E1	0.00	2	-	0.09*	-	-	-	-
		E1a subv.	1.87 (n=2)	-	-	-	-	-	-	-
		E1b subv.	0.94 (n=1)	-	-	-	-	-	-	-
	E2	E2	0.00	1	-	0.18*	-	-	-	-
		E2 subv.	0.94 (n=1)	-	-	-	-	-	-	-

*RHD, right hepatic duct; L, left hepatic duct; -: no data; *: calculated on the basis of percentages and numbers of cases presented by the authors*

Table 7. *Confluence pattern of left and right perihilar bile ducts*

		Present study 2017	Couinaud 1957 & 1989	Russel et al. 1990	Yoshida J. et al. 1996	Nakamura et al. 2002	Choi et al. 2003	Ohkubo et al. 2004	Kishi et al. 2010
No variation (%)	I. Presence LHD Presence RHD	54.72	57	55	68.1*	65	63	81.8*	69.3
Variations of LHD (%)	III. Absence LHD Presence RHD, IV. Absence LHD Absence RHD	3.75	3	-	0.5	-	1	0.6*	0.6*
Variations of RHD (%)	II. Absence RHD Presence LHD	41.49	39	26.1*	31.4*	35*	35.8*	18.1*	29.1*

*RHD, right hepatic duct; LHD, left hepatic duct; -: no data; *: calculated on the basis of percentages and numbers of cases presented by the authors*

Table 8. *Distribution of biliary variations according to the presence or absence of the right and left hepatic duct*

	Present study 2017	Couinaud 1989	Russel et al. 1990	Yoshida J. et al. 1996	Nakamura et al. 2002	Choi et al. 2003	Ohkubo et al. 2004	Kishi et al. 2010
Presence LHD Presence RHD (%)	54.72	57	55	67.7	65	63	-	69.3
Absence of LHD (%)	3.77	3	-	0.5	-	1	2	0.8
Absence of RHD (%)	45.28	46.73	-	~34.1	35	29	26.3	~20.2

RHD, right hepatic duct; LHD, left hepatic duct; -: no data

7.2 Variations of the left hepatic duct - Optimal line of hepatotomy for left lateral living donor liver transplantation

Between Nov. 1989 and Febr. 1991 Broelsch performed 20 LDLT for children less than 2 years of age. He introduced the left lateral segmentectomy for LDLT instead of the full left hepatectomy [82]. Prior studies reported that the use of pediatric LDLT substantially decreased the pediatric death on the waiting list, however, the post transplantation morbidity increased mainly because of the biliary complications including bile leak and biliary strictures, frequently due to technical difficulties of multiple duct anastomoses [99, 109, 110, 111, 112]. Xu et al. [131] performed a total of 118 LDLT and assessed the biliary complications in the light of the graft's duct orifice. It was found, that cases with graft duct orifice ≤5mm showed a significant higher incidence of total biliary complications (21.1% vs. 6.6%, P=0.028) and biliary stricture (10.5% vs. 1.6%, P=0.041) compared with cases with larger duct orifice >5mm. Naturally, multiple ducts involve smaller diameters individually. Darius et al. [132] assessed the biliary complications in the light of different graft types. He performed 429 pediatric liver transplantations between 1993 and 2010 with the use of four graft types: whole, reduced size, split, and living donor grafts. It was found that most of the biliary complications were anastomotic complications not influenced by the type of graft, which looks contrary to the above mentioned authors' results [99, 109, 110, 111, 112]. In our opinion the type of the graft (whole, reduced size, split, or living donor) does not necessarily determine the number of bile ducts needs to be anastomosed during liver transplantation. It also depends on the

surgical technique and the exact plane of hepatotomy, however, naturally the whole size graft has the higher chance to have just one bile duct for the anastomoses. Hence, Darius has not classified any particular graft types into subtypes according to the number of bile ducts orifice. While it can be said that biliary complications are not influenced by the type of the graft (whole, reduced size, split, or living donor) [132], it does not mean that the LLS graft with one bile duct (left lateral graft subtype I.) has the same complication rate as subtype II, III or IV with two three or four bile ducts opening. Despite the fact that multiple duct anastomoses involve higher number of biliary complications, few authors focused on the advantageous resection surface of lateral segment grafts in respect of the duct numbers to be reconstructed [98, 133, 107]. Since biliary complications are high in pediatric LDLT, the prevention and thereby reduction of patient morbidity is henceforward crucial.

The current study strongly supports the view that if the division line is precisely on the falciform ligament, the implantable graft will have a single bile duct for the anastomoses in only 30% of cases and a surgeon should prepare multiple ductal anastomoses during implantation. Contrary to our expectations, the division surface of standard hepatotomy just at the FL displayed surprisingly high percentage of two (53.3%), three (10%) and moreover four (3,3%) biliary ducts which must be anastomosed individually. These experimental results are consistent with the findings of some other studies [82, 112, 134, 135]. In Broelsch's very first series of LLS LDLT separate ducts were found in 7 of 17 cases (41%) in which the transection was carried out at the round ligament [82]. Salvalaggio et al. [112] retrospectively analyzed the database of 50 LLS graft transplantations for exploring the impact of multiple ducts on patient and graft survival. Forty per cent of their patients needed 2 biliary anastomoses, 8% required 3 anastomoses, and 2% (1 graft) required 4 anastomoses. The authors conclude that the risk of biliary complications is associated with the number of bile ducts on the graft surface. Russell evaluated the left hepatic duct anatomy of 838 patients who had biliary interventional procedures and found that 55% of the patients had a single LHD that was formed by the intrahepatic union of ducts draining segments II and III lateral to the FL [125].Thus the surface marking of the FL, which usually determines the plane of division may not necessarily correspond to the LLS duct.

Based on our CT analysis of the left duct branching pattern and its topographical relationship to surface markings, we could also define the optimal plane of division for LLS transplantation. Only a single bile duct for anastomosis was present when we performed the virtual hepatotomy one cm to the right of the attachment of FL on the diaphragmatic surface and equally one cm to the right of umbilical fissure on the visceral surface, in 70% of the investigated livers. These results agree with those of other studies published by Reichert and co-workers [98, 133]. Although our basic findings are comparable, there are some differences. These authors state that in 90% of their cases, transection of the liver through segment IV, in a plane one cm to the right of the umbilical fissure yields a single LLS duct, and the need for dual anastomoses was found in 10% of their cases. The authors have not mentioned 3 or 4 bile ducts on their graft surfaces. In comparison, in our series the percentage of multiple ducts in this plane of resection was about three times more. A possible explanation for their higher number of the cases (90% versus 70%) exhibiting the ideal resection surface one cm to the right from the umbilical fissure might be that Reichert and co-workers [98, 133] estimated the site of this plane on corrosion casts in one part of their study and that method is rather speculative compared to our procedure. Despite the fact that we have a large collection of liver casts, this series cannot be used for precise measurements in this order of magnitude (1-10 mm). For this reason and because of the clinical use of preoperative cholangiographic imaging modalities in donor patients we chose livers for this investigation, injected with CT-density coded resin mixture, therefore we could achieve precise measurements on 3D VR CT reconstructions.

However, dividing the liver well to the right of the FL, can cause accidental damage of segment IV ducts in the remaining liver in 46.7% of our cases.

In relation to LDLT the incidence of biliary complications are likely to increase if segment IV duct in the donor liver remnant is tied off. If segment IV in the donor is small or if the duct is minor, the consequences should be minimal and the chances of postoperative liver dysfunction are negligible. However, long-term complications may potentially arise related to a larger excluded segment IV, in the form of biliary stasis and low-grade biliary infections. A much more serious donor complication can result from the non-identification of segment IV drainage into the left ductal system, where the duct is left unligated on the donor resection margin. This can lead to an ongoing bile leak

which may be difficult to manage by conservative means alone, leading to a higher risk of donor morbidity and even mortality. Many authors state that intraoperative cholangiography is the most appropriate way (even better than preoperative MRCP) to decide where the bile duct should be transected minimizing the risk of postoperative bile leakage [131, 136, 137]. A completion cholangiogram or a 'blue-dye test' after a donor hepatectomy can identify such unligated ducts, thereby potentially minimising postoperative bile leaks in the donor [138, 139].

In case of SLT or LDLT some surgeons discard the compromised segment IV after split/hepatectomy to prevent complications such as segment IV necrosis or abscess [140, 141]. Seda-Neto et al. [141] performed partial segment IV resection in 107 cases out of 204 (52.5%) left lateral segmentectomy for pediatric LDLT, because of parenchymal discoloration. Sepulveda did not routinely remove segment IV during SLT using extended right graft, but segment IV related complications developed out in 8 cases out of 36 (22%) which significantly decreased graft survival [142].

In accordance with Reichert and co-workers [98, 133] the variation that we found to be the commonest and most promising for LLS graft recovery, was Type I.a (66.67%). In this group the bile ducts from segments II and III form a common trunk that was joined by a single or more segment IV duct/s. It is notable that in Reichert's series this percentage (85%) was substantially higher (Table 4).

Some variations (I.b and II.c) that we have described were not mentioned in the above cited papers [98, 133]. These differences may be due to population variances or the low number of specimens in our and their studies.

As discussed before, the ideal situation for an LLS LDLT would be to end up with needing as few recipient anastomoses as possible, ideally one. The standard technique of a LDLT usually involves dividing the liver just at the FL [61]. It would seem, then, that with this technique, the only chance of needing a single recipient anastomosis would be if the donor liver had a Type I. variation. However, even with that type, the exact plane of hepatotomy would eventually determine whether one ends up with more than one anastomoses, since in 36.67% of Type I. livers, the mode of confluence shows Right pattern.

Workup for a LDLT now routinely includes multidetector CT reconstructions and MR cholangiography. Hence one should be able to foresee the biliary anomalies and in

case of any doubts, intraoperative cholangiography can verify the concrete anatomical situation [131, 136, 137]. In addition, it should also be possible to plan a plane of division beforehand based on the surface marking of the FL. Since liver dysfunction due to small-for-size syndrome is rarely an issue in the adult donor after an LLS donation, it may be better to routinely perform a hepatotomy one cm to the right of the FL, particularly if vascular variations are not an issue [107]. It could be equally employed if there is some uncertainty about the confluence pattern of the left ducts. This would also potentially create a slightly larger graft avoiding small-for-size syndrome in a larger recipient. Due care would, however, need to be employed in dealing with segment IV duct in the donor, ensuring minimization of postoperative bile leaks. If there are related vascular or other contraindications or if it is absolutely essential to preserve segment IV in the donor, then the hepatotomy should be performed at the FL, accepting the relatively higher chance of needing multi-ductal anastomoses in the recipient.

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8 Conclusions

The use of partial liver transplantation made more donor organs within easier reach led to the reduction of the pre-transplant complications and mortality on the waiting list, and also can provide available grafts in case of emergency situations. On the other hand, the SLT should face specific complications. Biliary complications for example biliary stricture and anastomotic leakage are still considered to be reportedly stressful problems to address in partial liver graft transplantation. The source of them can originate from an ischemia of the biliary tract or the fact that we do not possess adequate anatomic knowledge about the bile duct system. The hepatic biliary anatomy is highly variable and some variants require reconsideration of the surgical techniques.

Both of our newly developed corrosion cast- and vessel lumen filling without corrosion techniques were perfectly suitable to perform our planned studies and get the aimed data. The resin mixture could fill up even the small subsegmental ducts, after the polymerization the liver preparations were hard enough to keep their shape, provided excellent density for CT scans and also kept their colours.

Hilar variations of the hepatic duct system, according to the absence or presence of the LHD and RHD four different groups could be identified: Our results in a series of 106 livers showed 45.28% (58/106) perihilar biliary variants. These data confirm the supposition that in categorizations, instead of “normal biliary anatomy” the use of “most frequent variation” would be reasonable.

Among the biliary duct variations recorded in our study, the incidence of “D1” configuration exceeds all “D1” figures reported by others (22.4% versus 5%, 13%, 8%, 15.8%, 11%, 12%, 11.6%). In full left–full right split or in case of left lobe LDLT, the LHD needs to be dissected from the CHD for the left liver graft. The last 9 mm of the LHD should be preserved for the right liver lobe in cases of hilar variation type ”D1”, since according to this current study the distance between the ostia of the RAHD (joining the CHD) and the RPHD (joining the LHD) is less than 9 mm in 95.83% in variation type ”D1”. In view of the fact that a considerable number of variations in the hepatic ducts persist in the hilar region, it is necessary to have a profound knowledge of the actual to perform safe right or left liver lobe transplantation. Our data stress on the high incidence of perihilar biliary variations in the livers taken from Hungarian deceased.

The current study strongly supports the view that if the division line of LLS hepatectomy is precisely on the FL, the implantable graft will have a single bile duct for the anastomosis in only 30% of cases and in 70 % the surgeon should prepare multiple ductal anastomoses during implantation. Contrary to our expectations, the division surface of standard hepatotomy just at the FL displayed high percentage of two (53.3%), three (10%) and even more four (3.3%) biliary ducts which must be anastomosed individually. Only a single bile duct for anastomosis was present when we performed the virtual hepatotomy one cm to the right of the attachment of FL on the diaphragmatic surface and equally one cm to the right of umbilical fissure on the visceral surface, in 70% of the investigated livers. However, dividing the liver well to the right of the falciform ligament, can cause accidental damage of segment IV ducts in the remaining liver in 46.7% of our cases. Our conclusion is, that ideally the division line of LLS hepatectomy for LDLT is one cm to the right of the FL. However, if there are related vascular or other contraindications or if it is absolutely essential to preserve segment IV in the donor, then the hepatotomy should be performed at the FL, accepting the relatively higher chance of needing multi-ductal anastomoses in the recipient.

Statistical analysis of the observed anomalous branching patterns in the hepatic duct system and comparison of that to the literary data together with the recognition of new biliary variants may help to make easier the preoperative preparations for transplantations. We believe that our hereby presented data and new techniques can contribute to the more perfect knowledge of the biliary duct system of the human liver and therefore may lead to the reduction of post-transplantation complications in the partial liver transplantation and in the LDLT.

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9 Summary

Aims The severe lack of cadaveric liver grafts evoked a major development both in the surgery of partial liver transplantation and in the clinical anatomy research of hilar and intrahepatic variations. Of the vascular and biliary anatomic variants, the most challenging are the variations of hepatic duct branching pattern since their frequency is the highest causing the elevated incidence of post-transplantation biliary complications. Therefore the aim of our study was to investigate the surgical relevance of the hilar- and left hepatic duct's anatomical variations, which are the most relevant in case of partial liver transplantation, in the Hungarian population. For macroscopic analysis of branching patterns and for the simulation of preoperative planning and the split surgery we developed new methods.

Methods Fresh human livers (106) were injected with a new colour and CT density coded Vinyl Ester resin mixture and the liver parenchyma was corroded by cc. KOH solution. Casts were macroscopically analyzed, photo documented and CT scanned. In another series the elastic resin injected livers (30) were CT scaned and immersed in formaldehyde fixative. Bile duct system was analyzed using 3D CT reconstruction. Number of bile ducts in three differently placed virtual left lateral hepatotomy planes was surveyed.

Results Application of our newly developed techniques proved to be profitable in revealing the surgically important biliary variants. Normal perihilar biliary anatomy was observed only ~ 55% of cases and variant anatomy in near half of the examined livers. A clinically important variant showing the drainage of the RPHD into the LHD (type"D1") occurred in markedly higher percentage in our series compared to available data on this issue. Such dissimilarity in the incidences may indicate population differences and it is a hint for the Hungarian transplant surgeons to expect this variant in one-fourth of patients. In our series a new unpublished biliary configuration and four subvariants were observed which are optimal for left lateral split. Our virtual hepatotomy studies revealed that when the virtual split was performed 1 cm to the right from the FL only one bile duct for anastomosis was present in 70 % of our cases and split at the line of FL resulted two (53%), three (10%) or four (3.3%) bile duct cut profiles.

Conclusion With the use of partial liver transplantation techniques more donor organs became available, reducing the complications before the transplantation and the fatalities

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on the waiting list, and also can provide available grafts in case of emergency situations. On the other hand, the SLT should face specific complications which are normally associated with the bile. These biliary complications can be a biliary stricture, anastomotic leakage which a still considered to be stressful problems to handle in partial liver graft transplantation. The cause of these can be an ischemia of the biliary tract or the lack of suitable knowledge considering the surgical anatomy of the bile duct system. The hepatic biliary anatomy is highly variable and some variants require reconsideration of the surgical techniques. We are greatly committed to contribute to a deeper understanding of the biliary duct system of the human liver with our data introduced in this thesis so that the number of the post-transplantation complications can be subdued in the partial liver transplantation and in the LDLT.

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10 Összefoglalás

Célkitűzés A cadaverekből eltávolítható máj graftok számának elégtelen volta a májmegosztás sebészi technikájának megjelenését és rohamos fejlődését indukálta és ezzel párhuzamosan a hiláris és intrahepatikus variációk kerültek a klinikai anatómiai kutatások fókuszába. A vasculáris és epeúti variációk közül sebészi szempontból a legnagyobb kihívást a ductus hepaticus oszlási variációi jelentik mindmáig. Ennek magyarázata az epeúti variációk legmagasabb előfordulási aránya és ebből következik a parciális máj-transzplantációk után fellépő epeúti komplikációk kedvezőtlen magas száma.

Mivel a parciális máj transzplantáció szempontjából a hiláris área epeútjainak, valamint kiemelten a bal ductus hepaticus anatómiai variációinak kiemelt a sebészi fontossága, ezért ennek ismeretében tűztük ki kutatásunk céljául e régiók epeúti anomáliáinak további feltárását a magyar populációban, valamint ezek májsebészeti jelentőségének vizsgálatát. Az epeúti oszlási variációk vizsgálatára valamint a parciális máj transzplantáció tervezésének és végrehajtásának szimulálására új módszerek kidolgozását terveztük.

Módszerek 106 friss, fixálatlan humán májat töltöttünk fel egy általunk kidolgozott új, szín- és CT denzitás kódolt Vinyl Ester gyanta keverékkel, majd a májparenchymát cc. KOH oldattal eltávolítottuk. Az öntvényeket makroszkóposan elemeztük, fotódokumentáció és CT vizsgálat készült. Egy másik sorozatban egy rugalmasabb gyantakeveréket használva 30 máj epeútjait töltöttük fel, majd CT vizsgálatot követően formaldehid oldatban fixáltuk. Az epeútrendszert 3D CT rekonstrukciós képeken elemeztük. Három különböző rezekciós síkú virtuális bal laterális hepatotómia során elemeztük az epeutak átmetszetének számát.

Eredmények Az általunk kifejlesztett technikák eredményesnek bizonyultak a máj sebészet szempontjából fontos epeúti variációk feltárásában. A perihiláris régióban, a normál epeúti anatómiaként ismert biliáris struktúrát az eseteink alig több, mint felében (55%) figyeltünk meg, így a vizsgált májak közel fele (45%) hiláris epeúti variációt mutatott. Az a variáció, melyben a RPHD az LHD-hoz csatlakozott (D1-es variáció), egy sebészi szempontból kiemelten jelentős variációként ismert. Ez az anomália, a mi vizsgálati sorozatunkban sokkal magasabb arányban fordult elő, mint a témával foglalkozó kutatók közleményeiben szerepel. A D1-es variáció jelentősen eltérő

előfordulási aránya felhívja a magyarországi máj transzplantációs sebészek figyelmét arra a tényre, miszerint betegeik egynegyedében számítaniuk kell erre az anatómiai szituációra. Sorozatunkban azonosítottunk egy még nem publikált új variációt, amit a használt klasszifikációs rendszerbe nem lehetett beilleszteni, így annak javasoljuk a kibővítését egy új kategóriával (G típusú variáció). Továbbá négy új alvariációt figyeltünk meg, amelyek a bal laterális split elvégzéséhez ideális anatómiai változatok, ezekkel is bővítettük az epeúti variációk osztályozását. Máj preparátumaink CT rekonstrukcióin végrehajtott virtuális hepatotomia során kapott adataink szerint, ha a virtuális split síkja a ligamentum falciformétól 1 cm-re jobbra vezetett, akkor csak egy epeút átmetszet figyelhető meg az eseteink 70 %-ában. Ha split síkját a ligamentum falciforme hepatis vonalában vezettük, akkor kettő (53 %), három (10 %) vagy négy (3.3) epeút átmetszetet találtunk.

Konklúzió A részleges máj transzplantációk elterjedése megnövelte a beültethető graftok számát, és a gyorsabb transzplantációra kerülés csökkentette a sebészi beavatkozás előtt kialakuló komplikációk számát és súlyosságát, a várólistán lévő betegek halálozási arányát, és lehetőséget nyújtott akut vészhelyzetben történő transzplantációra is. Ugyanakkor a transzplantációs sebészeknek szembesülni kellett parciális májbeültetés jellegzetes komplikációival. Legnagyobb számban az epeúti szövődmények, mint az anasztomizált epeút szűkülete, az anasztomózis elégtelensége miatti epecsorgás jelentettek súlyos poszt operatív problémát. Az irodalmi adatok szerint a szövődmények hátterében a rekonstruált epeutak ischemiája és a biliáris rendszer sebészi anatómiájának elégtelen ismerete állhatnak. Munkánk is egyértelműen igazolja, hogy a máj epeút rendszere rendkívül variábilis és a szövődmények csökkentése érdekében bizonyos variációk esetében a sebészi technikák felülvizsgálata szükséges. A jelen munkánkban bemutatott kutatási eredményeink remélhetőleg hozzájárulhatnak a humán máj epeúti anatómiájának teljesebb megismeréséhez. E tudás elterjedtebb alkalmazása pedig a cadaver máj megosztásból vagy élő donorból származó parciális máj átültetés utáni epeúti szövődmények számát jelentősen csökkentheti.

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11 Bibliography

1. Calne RY, Williams R. (1979) Liver transplantation. Curr Probl Surg, 16:1-44.

2. Starzl TE, Koep LJ, Halgrimson CG, Hood J, Schroter GP, Porter KA, Weil R 3rd. (1979) Fifteen years of clinical liver transplantation. Gastroenterology, 77: 375-88.

3. Calne RY, Rolles K, White DJ, Thiru S, Evans DB, McMaster P, Dunn DC, Craddock GN, Henderson RG, Aziz S, Lewis P. (1979) Cyclosporin A initially as the only immunosuppressant in 34 recipients of cadaveric organs: 32 kidneys, 2 pancreas and 2 livers. Lancet, 2: 1033-1036.

4. Zeevi A, Duquesnoy R, Eiras G, Rabinowich H, Todo S, Makowka L, Starzl TE. (1987) Immunosuppresive effect of FK-506 on in vitro lymphocyte alloactivation: synergism with cyclosporin A. Transplant Proc 19: 40-44.

5. Penn I, Starzl TE. (1972) Malignant tumors arising de novo in immunosuppressed organ transplant recipients. Transplantation, 14: 407-417.

6. Penn I. (1988) Secondary neoplasm as a consequence of transplantation and cancer therapy. Cancer Detect Prev, 12: 39-57.

7. Penn I, Brunson ME. (1988) Cancers after cyclosporine therapy. Transplant Proc 20: 885-892.

8. Iwatsuki S, Starzl TE, Todo S, Gordon RD, Esquivel CO, Tzakis AG, Makowka L, Marsh JW, Koneru B, Stieber A, Klintmalm G, Husberg B. (1988) Experience in 1000 liver transplants under cyclosporine-steroid therapy: a survival report. Transplant Proc 20: 498-504.

9. Ringe B, Wittekind C, Bechstein WO, Bunzendahl H, Pichlmayr R. (1989) The role of liver transplantation in hepatobiliary malignancy: a retrospective analysis of 95 patients with particular regard to tumor stage and recurrence. Ann Surg, 209: 88-98.

10. Calne RY, Williams R, Rolles K. (1986) Liver transplantation in the adult. World J Surg, 10: 422-431.

11. Geevarghese SK, Bradley AE, Wright JK, Chapman WC, Feurer I, Payne JL, Hunter EB, Pinson CW. (1998) Outcomes analysis in 100 liver transplantation patients. Am J Surg, 175: 348-353.

12. Olthoff KM, Rosove MH, Shackleton CR, Imagawa DK, Farmer DG, Northcross P, Pakrasi AL, Martin P, Goldstein LI, Shaked A. (1995) Adjuvant chemotherapy improves survival after liver transplantation for hepatocellular carcinoma. Ann Surg, 221: 734-741.

13. Bismuth H, Houssin D. (1984) Reduced-sized orthotopic liver graft in hepatic transplantation in children. Surgery, 95: 367-370.

14. Pichlmayr R, Ringe B, Gubernatis G, Hauss J, Bunzendahl H. (1988) Transplantation of a donor liver to 2 recipients (splitting transplantation)--a new method in the further development of segmental liver transplantation. Langenbecks Arch Chir, 373: 127-130.

15. Raia S, Nery JR, Mies S. (1989) Liver transplantation from live donors. Lancet, 2: 497.

16. Strong RW, Lynch SV, Ong TH, Matsunami H, Koido Y, Balderson GA. (1990) Successful liver transplantation from a living donor to her son. N England J Med, 322: 1505-1507.

17. Yamaoka Y, Washida M, Honda K, Tanaka K, Mori K, Shimahara Y, Okamoto S, Ueda M, Hayashi M, Tanaka A. (1994) Liver transplantation using a right lobe graft from a living related donor. Transplantation, 57: 1127-1130.

18. Máthé Z, Kóbori L, Görög D, Fehérvári I, Nemes B, Gerlei Zs, Doros A, Németh A, Mándli T, Fazakas J, Járay J. (2010) The first successful adult right-lobe living donor liver transplantation in Hungary. Orv Hetil, 151: 3-7.

19. Varela M, Fuster J, Bruix J. Liver Transplantation for Tumors. In: Blumgart LH. (ed.), Surgery of the Liver, Biliary Tract, and Pancreas. Saunders, Philadelphia, 2007.

20. Cherqui D, Soubrane O, Husson E, Barshasz E, Vignaux O, Ghimouz M, Branchereau S, Chardot C, Gauthier F, Fahniez PL, Houssin D. (2002) Laparoscopic living donor hepatectomy for liver transplantation in children. Lancet 2002, 359: 392-396.

21. Soubrane O, Cherqui D, Scatton O, Stenard F, Bernard D, Branchereau S, Martelli H, Gauthier F. (2006) Laparoscopic left lateral sectionectomy in living donors: safety and reproducibility of the technique in a single center. Ann Surg, 244: 815-820.

22. Cauchy F, Schwarz L, Scatton O, Soubrane O. (2014) Laparoscopic liver resection for living donation: Where do we stand? World J Gastroenterol, 20: 15590-15598.

23. Soubrane O, Perdigao Cotta F, Scatton O. (2013) Pure laparoscopic right hepatectomy in a living donor. Am J Transplant, 13: 2467-2471.

24. Rotellar F, Pardo F, Benito A, Martí-Cruchaga P, Zozaya G, Lopez L, Hidalgo F, Sangro B, Herrero I. (2013) Totally laparoscopic right-lobe hepatectomy for adult living donor liver transplantation: useful strategies to enhance safety. Am J Transplant, 13: 3269-3273.

25. Samstein B, Cherqui D, Rotellar F, Griesemer A, Halazun KJ, Kato T, Guarrera J, Emond JC. (2013) Totally laparoscopic full left hepatectomy for living donor liver transplantation in adolescents and adults. Am J Transplant, 13: 2462-2466.

26. Troisi RI, Wojcicki M, Tomassini F, Houtmeyers P, Vanlander A, Berrevoet F, Smeets P, Van Vlierberghe H, Rogiers X. (2013) Pure laparoscopic full-left living donor hepatectomy for calculated small-for-size LDLT in adults: proof of concept. Am J Transplant,13: 2472-2478.

27. Suh KS, Yi NJ, Kim T, Kim J, Shin WY, Lee HW, Han HS, Lee KU. (2009) Laparoscopy-assisted donor right hepatectomy using a hand port system preserving the middle hepatic vein branches. World J Surg, 33: 526-533.

28. Choi HJ, You YK, Na GH, Hong TH, Shetty GS, Kim DG. (2012) Single-port laparoscopy-assisted donor right hepatectomy in living donor liver transplantation: sensible approach or unnecessary hindrance? Transplant Proc, 44: 347-352.

29. Hwang S, Ahn CS, Kim KH, Moon DB, Ha TY, Song GW, Jung DH, Park GC, Namgoong JM, Yoon SY, Jung SW, Lee SG. (2012) Standardization of modified right lobe grafts to minimize vascular outflow complications for adult living donor liver transplantation. Transplant Proc, 44: 457-459.

30. Koffron AJ, Kung R, Baker T, Fryer J, Clark L, Abecassis M. (2006) Laparoscopic-assisted right lobe donor hepatectomy. Am J Transplant, 6: 2522-2525.

31. Kurosaki I, Yamamoto S, Kitami C, Yokoyama N, Nakatsuka H, Kobayashi T, Watanabe T, Oya H, Sato Y, Hatakeyama K. (2006) Video-assisted living donor hemihepatectomy through a 12-cm incision for adult-to-adult liver transplantation. Surgery, 139: 695-703.

32. Baker TB, Jay CL, Ladner DP, Preczewski LB, Clark L, Holl J, Abecassis MM. (2009) Laparoscopy-assisted and open living donor right hepatectomy: a comparative study of outcomes. Surgery, 146: 817-825.

33. Nagai S, Brown L, Yoshida A, Kim D, Kazimi M, Abouljoud MS. (2012) Mini-incision right hepatic lobectomy with or without laparoscopic assistance for living donor hepatectomy. Liver Transpl, 18: 1188-1197.

34. Soyama A, Takatsuki M, Hidaka M, Muraoka I, Tanaka T, Yamaguchi I, Kinoshita A, Hara T, Eguchi S. (2012) Standardized less invasive living donor hemihepatectomy using the hybrid method through a short upper midline incision. Transplant Proc, 44: 353-355.

35. Zhang X, Yang J, Yan L, Li B, Wen T, Xu M, Wang W, Zhao J, Wei Y. (2014) Comparison of laparoscopy-assisted and open donor right hepatectomy: a prospective case-matched study from china. J Gastrointest Surg, 18: 744-750.

36. Giulianotti PC, Tzvetanov I, Jeon H, Bianco F, Spaggiari M, Oberholzer J, Benedetti E. (2012) Robot-assisted right lobe donor hepatectomy. Transpl Int, 25: e5-e9.

37. McIndoe AH, Counseller VX. (1927) A report on the bilaterality of the liver. Arch Surg, 15: 589.

38. Tung TT. La vascularisation veineuse du foie et ses applications aux resectiones hepatiques. Thése Hanoi, 1939.

39. Tung TT. Les resections majeures et mineures du foie. Masson, Paris, 1979.

40. Hjörtsjö CH. (1931) The topography of the intrahepatic duct systems. Acta Anat, 11: 599-615.

41. Healey JE, Schroy PC. (1953) Anatomy of the biliary ducts within the human liver: analysis of the prevailing pattern of branchings and the major variations of the biliary ducts. Am Med Assoc Arct Surg, 66: 599-616.

42. Goldsmith NA, Woodburne RT. (1957) Surgical anatomy pertaining to liver resection. Surg Gynecol Obstet, 195: 310-318.

43. Couinaud C. Le Foie: Études anatomiques et chirurgicales. Masson, Paris, 1957.

44. Bismuth H, Houssin D, Castaing D. (1982) Major and minor segmentectomies ”réglées” in liver surgery. World J Surg, 6: 10-24.

45. Terminology Committee of the International Hepato-Pancreato-Biliary Association. (2000) The Brisbane 2000 Terminology of Liver Anatomy and Resections. HPB, 2: 333-339.

46. Blumgart LH, Hann LE. Surgical and Radiologic Anatomy of the Liver, Biliary Tract, and Pancreas. In: Blumgart LH. (ed.), Surgery of the Liver, Biliary Tract, and Pancreas. Saunders, Philadelphia, 2007: 3-9.

47. Scheele J, Stang R. Segment orientated anatomical liver resections. In: Blumgart LH. (ed.), Surgery of the Liver and Biliary Tract, 2nd edition. Churchill Livingstone, New York, 1994: 1557-1578

48. Strasberg SM. Hepatic, biliary and pancreatic anatomy. In: Garden OJ, Parks RW. (eds.), Hepatobiliary and Pancreatic Surgery. A companion to specialist surgical practice. Fifth edition. Saunders, Edinburgh, 2014: 17-21.

49. Liu H, Li R, Fu J, He Q, Li J. (2016) Technical Skills Required in Split Liver Transplantation. Ann Transplant, 21:408-415.

50. Yersiz H, Renz JF, Hisatake GM, Farmer DG, Busuttil RW. (2003) The conventional technique in in-situsplit-liver transplantation. J Hepatobiliary Pancreat Surg, 10: 11–15.

51. Dalal AR. (2015) Split liver transplantation: What’s unique? World J Transplant, 5: 89-94.

52. Ogawa K, Kasahara M, Sakamoto S, Ito T, Taira K, Oike F, Ueda M, Egawa H, Takada Y, Uemoto S. (2007) Living donor liver transplantation with reduced monosegments for neonates and small infants. Transplantation, 83: 1337-1340.

53. Azouz SM, Diamond IR, Fecteau A. (2011) Graft type in pediatric liver transplantation. Curr Opin Organ Transplant, 16: 494-498.

54. Yersiz H, Renz JF, Hisatake G, Reichert PR, Feduska NJ Jr, Lerner S, Farmer DG, Ghobrial RM, Geevarghese S, Baquerizo A, Chen P, Busuttil RW. (2001) Technical and logistical considerations of in situ split-liver transplantation for two adults: Part I. Creation of left segment II, III, IV and right segment I, V–VIII grafts. Liver Transpl, 7: 1077-1080.

55. Yersiz H, Renz JF, Hisatake G, Reichert PR, Feduska NJ Jr, Lerner S, Farmer DG, Ghobrial RM, Geevarghese S, Baquerizo A, Chen P, Busuttil RW. (2002) Technical and logistical considerations of in situ split-liver transplantation for two adults: Part II. Creation of left segment I–IV and right segment V–VIII grafts. Liver Transpl, 8: 78-81.

56. Cintorino D, Spada M, Gruttadauria S, Riva S, Luca A, Volpes R, Vizzini G, Arcadipane A, Henderson K, Verzaro R, Foglieni CS, Gridelli B. (2006) In situ split liver transplantation for adult and pediatric recipients: An answer to organ shortage. Transplant Proc, 38: 1096-1098.

57. Giacomoni A, Lauterio A, Donadon M, De Gasperi A, Belli L, Slim A, Dorobantu B, Mangoni I, De Carlis L. (2008) Should we still offer split-liver transplantation for two adult recipients? A retrospective study of our experience. Liver Transpl, 14: 999-1006.

58. Azoulay D, Astarcioglu I, Bismuth H, Castaing D, Majno P, Adam R, Johann M. (1996) Split-liver transplantation. The Paul Brousse policy. Ann Surg, 224: 737-748.

59. Yersiz H, Renz JF, Farmer DG, Hisatake GM, McDiarmid SV, Busuttil RW. (2003) One hundred in situ split-liver transplantations: A single-center experience. Ann Surg, 238: 496-507.

60. Broering DC, Mueller L, Ganschow R, Kim JS, Achilles EG, Schäfer H, Gundlach M, Fischer L, Sterneck M, Hillert C, Helmke K, Izbicki JR, Burdelski M, Rogiers X. (2001) Is there still a need for living-related liver transplantation in children? Ann Surg, 234: 713-722.

61. Rogiers X, Bismuth H, Busuttil RW, Broering DC, Azoulay D. Split Liver Transplantation. Springer, Darmstadt, 2002.

62. Broering DC, Wilms C, Lenk C, Schulte am Esch J 2nd, Schönherr S, Mueller L, Kim JS, Helmke K, Burdelski M, Rogiers X. (2005) Technical refinements and results in full-right full-left splitting of the deceased donor liver. Ann Surg, 242: 802–813.

63. Liver Transplantation: Selection criteria and recipient registration. Liver Selection Policy. in: http://odt.nhs.uk/transplantation/guidance-policies/

64. Azoulay D, Castaing D, Adam R, Savier E, Delvart V, Karam V, Ming BY, Dannaoui M, Krissat J, Bismuth H. (2001) Split-liver transplantation for two adult recipients: Feasibility and long-term outcomes. Ann Surg, 233: 565-574.

65. Ramcharan T, Glessing B, Lake JR, Payne WD, Humar A. (2001) Outcome of other organs recovered during in situ split-liver procurements. Liver Transpl, 7: 853-857.

66. Humar A, Ramcharan T, Sielaff TD, Kandaswamy R, Gruessner RW, Lake JR, Payne WD. (2001) Split liver transplantation for two adult recipients: an initial experience. Am J Transplant, 1: 366-372.

67. Gridelli B, Perico N, Remuzzi G. (2001) Strategies for a greater supply of organs for transplantation. Recent Prog Med, 92: 9–15.

68. Rogiers X, Malago M, Habib N, Knoefel WT, Pothmann W, Burdelski M, Meyer-Moldenhauer WH, Broelsch CE. (1995) In situ splitting of the liver in the heart-beating cadaver organ donor for transplantation in two recipients. Transplantationn, 59: 1081-1083.

69. Broering DC, Rogiers X, Malagó M, Bassas A, Broelsch CE. (1998) Vessel loop guided technique for parenchymal transection in living donor or in situ split-liver procurement. Liver Transpl Surg, 4: 241.

70. Ghobrial RM, Yersiz H, Farmer DG, Amersi F, Goss J, Chen P, Dawson S, Lerner S, Nissen N, Imagawa D,Colquhoun S, Arnout W, McDiarmid SV, Busuttil RW. (2000) Predictors of survival after in vivo split liver transplantation: analysis of 110 consecutive patients. Ann Surg, 232: 312-323.

71. Busuttil RW, Goss JA. (1999) Split liver transplantation. Ann Surg, 229: 313-321.

72. Emre S, Umman V. Split liver transplantation: an overview. (2011) Transplant Proc, 43: 884-887.

73. Kim JS, Broering DC, Tustas RY, Fischer L, Ganschow R, Burdelski M, Rogiers X. (2004) Split liver transplantation: Past, present and future. Pediatr Transplant, 8: 644-648.

74. Hong JC, Yersiz H, Farmer DG, Duffy JP, Ghobrial RM, Nonthasoot B, Collins TE, Hiatt JR, Busuttil RW. (2009) Longterm outcomes for whole and segmental liver grafts in adult and pediatric liver transplant recipients: A 10- year comparative analysis of 2,988 cases. J Am Coll Surg, 208: 682-691.

75. Broering DC, Topp S, Schaefer U, Fischer L, Gundlach M, Sterneck M, Schoder V, Pothmann W, Rogiers X. (2002) Split liver transplantation and risk to the adult recipient: analysis using matched pairs. J Am Coll Surg, 195: 648-657.

76. Rela M, Vougas V, Muiesan P, Vilca-Melendez H, Smyrniotis V, Gibbs P, Karani J, Williams R, Heaton N. (1998) Split liver transplantation: King's College Hospital experience. Ann Surg, 227: 282-288.

77. Bismuth H, Morino M, Castaing D, Gillon MC, Descorps Declere A, Saliba F, Samuel D. (1989) Emergency orthotopic liver transplantation in two patients using one donor liver. Br J Surg, 76: 722-724.

78. Gundlach M, Broering D, Topp S, Sterneck M, Rogiers X. (2000) Split-cava technique: Liver splitting for two adult recipients. Liver Transpl, 6: 703-706.

79. Colledan M, Segalin A, Andorno E, Corno V, Lucianetti A, Spada M, Gridelli B. (2000) Modified splitting technique for liver transplantation in adult-sized recipients. Technique and preliminary results. Acta Chir Belg, 100: 289-291.

80. Sommacale D, Farges O, Ettorre GM, Lebigot P, Sauvanet A, Marty J, Durand F, Belghiti J. (2000) In situ split liver transplantation for two adult recipients. Transplantation, 69: 1005–1007.

81. Kilic M, Seu P, Goss J. Maintaining the Celiac Trunk with the Left Graft for In-Situ Split Liver Transplantation, Joint Meeting of the International Liver Transplantation Society, European Liver Transplantation Association and Liver Intensive Care Group of Europe, 11-13 July, 2001, Berlin, Germany.

82. Broelsch CE, Whitington PF, Emond JC, Heffron TG, Thistlethwaite JR, Stevens L, Piper J, Whitington SH, Lichtor JL. (1991) Liver transplantation in children from living related donors. Surgical techniques and results. Ann Surg, 214: 428-439.

83. Emond JC, Heffron TG, Kortz EO, Gonzalez-Vallina R, Contis JC, Black DD, Whitington PF. (1993) Improved results of living related liver transplantation with routine application in a pediatric program. Transplantation, 55: 835– 840.

84. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, Sawada H, Shirahase I, Kim HJ, Yamaoka Y. (1993) Surgical techniques and innovations in living related liver transplantation. Ann Surg, 217: 82–91.

85. Houssin D, Couinaud C, Boillot O, Laurent J, Habib N, Matmar M, Vigouroux C, Devictor D, Chapuis Y. (1991) Controlled hepatic bipartition for transplantation for children. Br J Surg, 78: 802-804.

86. Broelsch CE, Emond JC, Whitington PF, Thistlethwaite JR, Baker AL, Lichtor JL. (1990) Application of reduced-size liver transplants as split grafts, auxiliary orthotopic grafts, and living related segmental transplants. Ann Surg, 212: 368-377.

87. Rogiers X, Malagó M, Gawad K, Jauch KW, Olausson M,Knoefel WT, Gundlach M, Bassas A, Fischer L, Sterneck M,Burdelski M, Broelsch CE. (1996) In situ splitting of cadaveric livers: the ultimate expansion of the donor pool. Ann Surg, 224: 331–336.

88. Goss JA, Yersiz H, Shackleton CR, Seu P, Smith CV, Markowitz JS, Farmer DG, Ghobrial RM, Markmann JF, Arnaout WS, Imagawa DK, Colquhoun SD, Fraiman MH, McDiarmid SV, Busuttil RW. (1997) In situ splitting of the cadaveric liver for transplantation. Transplantation, 64: 871– 877.

89. Otte JB, de Ville de Goyet J, Sokal E, Alberti D, Moulin D, de Hemptinne B, Veyckemans F, van Obbergh L, Carlier M, Clapuyt P. (1990) Size reduction of the donor liver is a safe way to alleviate the shortage of size-matched organs in pediatric liver transplantation. Ann Surg, 211: 146 –157.

90. Ryckman FC, Flake AW, Fisher RA, Tchervenkov JI, Pedersen SH, Balistreri WF. (1991) Segmental orthotopic hepatic transplantation as a means to improve patient survival and diminish waiting-list mortality. J Pediatr Surg, 26: 422-428.

91. Emond JC, Heffron TG, Whitington PF, Broelsch CE. (1993) Reconstruction of the hepatic vein in reduced size hepatic transplantation. Surg Gynecol Obstet, 176: 11–15.

92. Kuang AA, Renz JF, Ferrell LD, Ring EJ, Rosenthal P,Lim RC, Roberts JP, Ascher NL, Emond JC. (1996) Failure patterns of cryopreserved vein grafts in liver transplantation. Transplantation, 62: 742–747.

93. Millis JM, Seaman DS, Piper JB, Alonso EM, Kelly S, Hackworth CA, Newell KA, Bruce DS, Woodle ES, Thistlethwaite JR, Whitington PF. (1996) Portal vein thrombosis and stenosis in pediatric liver transplantation. Transplantation, 62: 748-753.

94. Kuang AA, Rosenthal P, Roberts JP, Renz JF, Stock P, Ascher NL, Emond JC. (1996) Decreased mortality from technical failures improves results in pediatric liver transplantation. Arch Surg, 131: 887-893.

95. Fan ST, Lo CM, Liu CL, Tso WK, Wong J. (2002) Biliary reconstruction and complications of right lobe live donor liver transplantation. Ann Surg, 236: 676–683.

96. Lee KW, Joh JW, Kim SJ, Choi SH, Heo JS, Lee HH, Park JW, Lee SK. (2004) High hilar dissection: new technique to reduce biliary complication in living donor liver transplantation. Liver Transpl, 10: 1158–1162.

97. Fulcher AS, Turner MA, Ham JM. (2002) Late biliary complications in right lobe living donor transplantation recipients: imaging findings and therapeutic interventions. J Comput Assist Tomogr, 26: 422-427.

98. Reichert PR, Renz JF, D'Albuquerque LA, Rosenthal P, Lim RC, Roberts JP, Ascher NL, Emond JC. (2000) Surgical anatomy of the left lateral segment as applied to living-donor and split-liver transplantation: a clinicopathologic study. Ann Surg, 232: 658–664.

99. Wadhawan M, Kumar A, Gupta S, Goyal N, Shandil R, Taneja S, Sibal A. (2013) Post-Transplant Biliary Complications - An Analysis from a Predominantly Living Donor Liver Transplant Centre. J Gastroenterol Hepatol, 28: 1056-1060.

100. Kishi Y, Imamura H, Sugawara Y, Sano K, Kaneko J, Kokudo N, Makuuchi M. (2010) Evaluation of donor vasculobiliary anatomic variations in liver graft procurements. Surgery, 147: 30-39.

101. Cho A, Asano T, Yamamoto H, Nagata M, Takiguchi N, Kainuma O, Soda H, Mori M, Narumoto S, Okazumi S, Makino H, Ochiai T, Ryu M. (2007) Relationship between right portal and biliary systems based on reclassification of the liver. Am J Surg, 193: 1-4.

102. Varotti G, Gondolesi GE, Goldman J, Wayne M, Florman SS, Schwartz ME, Miller CM, Sukru E. (2004) Anatomic variations in right liver living donors. J Am Coll Surg, 198: 577-582.

103. Balderramo D, Sendino O, Miquel R, de Miguel CR, Bordas JM, Martinez-Palli G, Leoz ML, Rimola A, Navasa M, Llach J, Cardenas A. (2013) Prospective evaluation of single-operator peroral cholangioscopy in liver transplant recipients requiring an evaluation of the biliary tract. Liver Transpl, 19: 199-206.

104. Ribeiro JB, Martins Fde S, Garcia JH, Cunha AC, Pinto RA, Satacaso MV, Prado-Júnior FP, Pessoa RR. (2012) Endoscopic management of biliary complications after liver transplantation. Arq Bras Cir Dig, 25: 269-272.

105. Kurita A, Kodama Y, Minami R, Sakuma Y, Kuriyama K,Tanabe W, Ohta Y, Maruno T, Shiokawa M, Sawai Y,Uza N, Yazumi S, Yoshizawa A, Uemoto S, Chiba T. (2013) Endoscopic stent placement above the intact sphincter of Oddi for biliary strictures after living donor liver transplantation. J Gastroenterol, 48: 1097-1104.

106. Rodriguez-Davalos MI, Arvelakis A, Umman V, Tanjavur V, Yoo PS, Kulkarni S, Luczycki SM, Schilsky M, Emre S. (2014) Segmental grafts in adult and pediatric transplantation improving outcomes by minimizing vascular complications. JAMA Surg, 149: 63-70.

107. Deshpande RR, Heaton ND, Rela M. (2002) Surgical anatomy of segmental liver transplantation. Br J Surg, 89: 1078-1088.

108. Yazumi S, Chiba T. (2005) Biliary complications after a right-lobe living donor liver transplantation. J Gastroenterol, 40: 861–865.

109. Seehofer D, Eurich D, Veltzke-Schlieker W, Neuhaus P. (2013) Biliary complications after liver transplantation: Old Problems and new challenges. Am J Transplant, 13: 253-265.

110. Anderson CD, Turmelle YP, Darcy M, Shepherd RW, Weymann A, Nadler M, Guelker S, Chapman WC, Lowell JA. (2010) Biliary strictures in pediatric liver transplant recipients – early diagnosis and treatment results in excellent graft outcomes. Pediatr Transplant, 14: 358-363.

111. Tannuri AC, Gibelli NE, Ricardi LR, Santos MM, Maksoud-Filho JG, Pinho-Apezzato ML, Silva MM, Velhote MC, Ayoub AA, Andrade WC, Leal AJ, Miyatani HT, Tannuri U. (2011) Living related donor liver transplantation in children. Transplant Proc, 43: 161-164.

112. Salvalaggio PR, Whitington PF, Alonso EM, Superina RA. (2005) Presence of multiple bile ducts in the liver graft increases the incidence of biliary complications in pediatric liver transplantation. Liver Transpl, 11: 161-166.

113. Hounsfield GN. (1980) Computed medical imaging. Nobel lecture, December 8, 1979. J Comput Assist Tomogr, 4: 665-674.

114. Törő K, Kiss M, Szarvas V, Nemeskéri A, Kristóf I, Magyar L, Keller E. (2007) Post mortem introduction of corrosion cast method after coronary stent implantation. Forensic Sci Int, 171(2-3): 208-211.

115. Nemeskéri A, Matlakovics B, Dudás I, Molnár B, Bartykowski A, Kiss M, Kristóf I, Törő K, Karlinger K. (2009) Combination of post mortem coronary angiography, corrosion cast method and multi-slice computed tomography (MSCT) for diagnostic improvement in pathology and forensics. Interv Med Appl Sci, 1: 20-34.

116. Törő K, Matlakovics B, Dudás I, Karlinger K, Kiss M,Molnár A, Nemeskéri A. (2014) The utility of the combination of the corrosion cast method and post mortem MSCT scans. Leg Med (Tokyo), 6: 283-289.

117. Rosero O, Nemeth K, Turoczi Z, Fulop A, Garbaisz D, Gyorffy A, Szuak A, Dorogi B, Kiss M, Nemeskeri A, Harsanyi L, Szijarto A. (2014) Collateral circulation of the rat lower limb and its significance in ischemia - reperfusion studies. Surg Today, 44: 2345-2353.

118. Kiss M, Deshpande RR, Nemeskéri A, Nguyen TT, Kürti Z, Kovács S, Pápai Z, Németh K, Szuák A, Dudás I, Kóbori L. (2015) Optimal line of hepatotomy for left lateral living donor liver transplantation according to the anatomical variations of left hepatic duct system. Pediatr Transplant, 19: 510-516.

119. Nemeth K, Deshpande R, Mathe Z, Szuak A, Kiss M, Korom C, Nemeskéri A, Kóbori L. (2015) Extrahepatic arteries of the human liver - anatomical variants and surgical relevancies. Transpl Int, 28: 1216-1226.

120. Smadja C, Blumgart LH. The biliary tract and the anatomy of biliary exposure. In: Blumgart LH. (ed.), Surgery of the Liver and Biliary Tract. Vol. 1. 2nd ed. Churchill Livingstone, Edinburgh, 1994: 11-24.

121. Elias H, Petty D. (1952) Gross anatomy of the blood vessels and ducts within the human liver. American Journal of Anatomy, 90: 59-111.

122. Lee VS, Morgan GR, Lin JC, Nazzaro CA, Chang JS, Teperman LW, Krinsky GA. (2004) Liver transplant donor candidates: Associations between vascular and biliary anatomic variants. Liver Transplantation, 8: 1049-1054.

123. de Ville de Goyet J. (1995) Split liver transplantation in Europe--1988 to 1993. Transplantation, 59: 1371-1376.

124. Renz JF, Yersiz H, Reichert PR, Hisatake GM, Farmer DG, Emond JC, Busuttil RW. (2003) Split-Liver transplantation: A Review. Am J Transplantation, 3: 1323-1335.

125. Russell E. Yrizzary JM, Montalvo B M, Guerra JJ, Al-Refai F. (1990) Left hepatic Duct Anatomy: Implications. Radiology, 174: 353-356.

126. Yoshida J, Chijiiwa K, Yamaguchi K, Yokohata K, Tanaka M. (1996) Practical classification of the branching types of the biliary tree: an analysis of 1,094 consecutive direct cholangiograms. J Am Coll Surgeons, 182: 37-40.

127. Nakamura T, Tanaka K, Kiuchi T, Kasahara M, Oike F, Ueda M, Kaihara S, Egawa H, Ozden I, Kobayashi N, Uemoto S. (2002) Anatomical variations and surgical strategies in right lobe living donor liver transplantation: Lessons from 120 cases. Transplantation, 73: 1896-1903.

128. Choi JW, Kim TK., Kim KW, Kim AY, Kim PN, Ha HK, Lee ML. (2003) Anatomic variation in intrahepatic bile ducts: an analysis of intraoperative cholangiograms in 300 consecutive donors for living donor liver transplantation. Korean J Radiol, 4: 85-90.

129. Ohkubo M, Nagino M, Kamiya J, Yuasa N, Oda K, Arai T, Nishio H, Nimura Y. (2004) Surgical anatomy of the bile ducts at the hepatic hilum as applied to living donor liver transplantation. Ann Surg, 1: 82-86.

130. Couinaud C. Surgical Anatomy of the Liver Revisited. Couinaud, Paris, 1989.

131. Xu X, Wei X, Ling Q, Wang K, Bao H, Xie H, Zhou L, Zheng S. (2012) Inaccurate preoperative imaging assessment on biliary anatomy not increases biliary complications after living donor liver transplantation. Eur J Radiol, 81: e457-460.

132. Darius T, Rivera J, Fusaro F, Lai Q, de Magnée C,Bourdeaux C, Janssen M, Clapuyt P, Reding R. (2014) Risk factors and surgical management of anastomotic biliary complications after pediatric liver transplantation. Liver Transpl, 20: 893-903.

133. Renz JF, Reichert PR, Emond JC. (2000) Biliary anatomy as applied to pediatric living donor and split-liver transplantation. Liver Transpl, 6: 801-804.

134. Yersiz H, Cameron AM, Carmody I, Zimmerman MA, Kelly BS Jr, Ghobrial RM, Farmer DG, Busuttil RW. (2006) Split liver transplantation. Transpl Proc, 38: 602-603.

135. Florman S, Miller CM. (2006) Live donor liver transplantation. Liver Transpl, 12: 499-510.

136. Jeng KS, Huang CC, Lin CK, Lin CC, Chen KH, Chu SH. (2014) Repeated intraoperative cholangiography is helpful for donor safety in the procurement of right liver graft with supraportal right bile duct variants in living-donor liver transplantation. Transplant Proc, 46: 686-688.

137. Ragab A, Lopez-Soler RI, Oto A, Testa G. (2013) Correlation between 3D-MRCP and intra-operative findings in right liver donors. Hepatobiliary Surg Nutr, 2: 7-13.

138. Guillaud A, Pery C, Campillo B, Lourdais A, Sulpice L, Boudjema K. (2013) Incidence and predictive factors of clinically relevant bile leakage in the modern era of liver resections. HPB (Oxford), 15: 224-229.

139. Wang HQ, Yang J, Yang JY, Yan LN. (2013) Bile leakage test in liver resection: a systematic review and meta-analysis. World J Gastroenterol, 19: 8420-8426.

140. Deshpande RR, Bowles MJ, Vilca-Melendez H, Srinivasan P, Girlanda R, Dhawan A, Mieli-Vergani G, Muiesan P, Heaton ND, Rela M. (2002) Results of Split Liver Transplantation in children. Ann Surg, 236: 248-253.

141. Seda-Neto J, Godoy AL, Carone E, Pugliese V, Fonseca EA, Porta G, Pugliese R, Miura IK, Baggio V, Kondo M, Chapchap P. (2008) Left lateral segmentectomy for pediatric live-donor liver transplantation: special attention to segment IV complications. Transplantation, 86: 697-701.

142. Sepulveda A, Scatton O, Tranchart H, Gouya H, Perdigao F, Stenard F, Bernard D, Conti F, Calmus Y, Soubrane O. (2012) Split liver transplantation using extended right grafts: the natural history of segment 4 and its impact on early postoperative outcomes. Liver Transpl, 18: 413-422.

12 Bibliography of the candidate's publications

Publications related to the subject

Kiss M, Deshpande RR, Nemeskéri A, Nguyen TT, Kürti Z, Kovács S, Pápai Z, Németh K, Szuák A, Dudás I, Kóbori L. (2015) Optimal line of hepatotomy for left lateral living donor liver transplantation according to the anatomical variations of left hepatic duct system. Pediatr Transplant, 19: 510-516. IF: 1.284

Németh K, Deshpande R, Máthé Z, Szuak A, Kiss M, Korom C, Nemeskéri A, Kóbori L. (2015) Extrahepatic arteries of the human liver - anatomical variants and surgical relevancies. Transpl Int, 28: 1216-1226. IF: 2.835

Törő K, Matlakovics B, Dudás I, Karlinger K, Kiss M, Molnár A, Nemeskéri A. (2014) The utility of the combination of the corrosion cast method and post mortem MSCT scans. Leg Med (Tokyo), 6: 283-289. IF: 1.238

Rosero O, Németh K, Turoczi Z, Fülöp A, Garbaisz D, Gyorffy A, Szuák A, Dorogi B, Kiss M, Nemeskéri A, Harsányi L, Szijárto A. (2014) Collateral circulation of the rat lower limb and its significance in ischemia - reperfusion studies. Surg Today, 44: 2345-2353. IF: 1.526

Nemeskéri A, Matlakovics B, Dudás I, Molnár B, Bartykowski A, Kiss M, Kristóf I, Törő K, Karlinger K. (2009) Combination of post mortem coronary angiography, corrosion cast method and multi-slice computed tomography (MSCT) for diagnostic improvement in pathology and forensics. Interv Med Appl Sci, 1:20-34.

Törő K, Kiss M, Szarvas V, Nemeskéri A, Kristóf I, Magyar L, Keller E. (2007) Post mortem introduction of corrosion cast method after coronary stent implantation. Forensic Sci Int, 171 (2-3): 208-211. IF: 2.015

DOI:10.14753/SE.2018.2104

Other Publications

Dezső K, Rókusz A, Bugyik E, Szücs A, Szuák A, Dorogi B, Kiss M, Nemeskéri Á, Nagy P, Paku S. (2017) Human liver regeneration in the late, irreversible phase of cirrhosis is driven and organized by the portal tree. J Hepatol. 66: 778-786. IF: 10.58

Kóbori L, Máthé Z, Fazakas J, Gerlei Z, Doros A, Fehérvári I, Sárváry E, Hartmann E, Németh A, Mándli T, Tóth S, Szonyi L, Korponay Z, Kiss M, Görög D, Járay J. (2008) Surgical aspects of pediatric liver transplantation. Living donor liver transplant program in Hungary. Orv Hetil, 149: 1271-1275.

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