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Original article

Surgical anatomy of segment four of liver and its implications in hepato-biliary surgery and liver transplantation

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ABSTRACT

Liver anatomy has been extensively studied throughout the evolution of surgical techniques for the liver including transplantation. With the advent of split and living donor transplantation, there has been an obligation for a more detailed re-evaluation of liver anatomy. Though the anatomy of individual lobes of the liver has been described meticulously, the anatomy of segment 4 has never been explained previously. We have aimed to describe in detail, the anatomy of segment 4 with its implications in hepato-biliary surgery and liver transplantation with the notion that a sound understanding of the anatomy will give rise to technical innovations during surgery and thereby decrease the morbidity and mortality associated with these complex surgical procedures.

1. Introduction

A comprehensive knowledge of liver anatomy is essential for safe liver surgery. Post-operative vascular and biliary complications in liver resections and transplantation are often due to a failure in recognising anomalous anatomy. In liver resections, an intimate understanding of liver anatomy allows for an equipoise to be achieved between oncological clearance and adequate functional reserve. A thorough knowledge of liver anatomy is also of paramount importance in liver transplantation (LT), especially in split-LT (SLT), paediatric LT and live donor LT (LDLT), where minimizing complications is closely associated with anatomical and technical competence. Among the various description of segmental liver anatomy, those by Couinaud and the International Hepato-Pancreatico-Biliary Association (IHPBA) - Brisbane committee are most commonly used classifications [1,2]. More recently, the "New World Terminology" has been introduced to describe hepatic resection thereby emphasising the importance of segmental anatomy [3].

An often overlooked yet anatomically, physiologically and surgically important part of the liver is segment 4. Also known as the left medial segment, its vascular and biliary anatomy are of immense significance in liver regeneration following resections and in niche areas of segmental LT. Though the anatomy of this unique section of the liver has previously been elucidated, descriptions from a surgical perspective are lacking. In this review, we describe the anatomy of the segment 4 of liver highlighting its anatomical and physiological importance to various aspects of liver surgery including resection and LT.

1.1. *Defining segment 4*

The Couinaud and the IHPBA classifications characterise segment 4 as being part of the left hemi-liver [1,2]. It is divided into superior (4a) and inferior (4b) parts by a transverse plane passing through the bifurcation of the main portal vein (MPV) (Fig. 1). Anatomists often label segment 4b as the quadrate lobe. This lobe is externally bounded by the gallbladder fossa on the right, the umbilical fossa on the left, the anterior border of the liver below and the porta hepatis above. Radiologically, segment 4 is identified as being between the middle hepatic vein (MHV) and the origin of left hepatic vein (4a) superiorly or the umbilical fissure (4b) inferiorly.

1.2. *Embryology [1,4]*

A brief description of segment 4's embryological development helps provide an insight into its unique vasculo-biliary anatomy and its variations which may often be encountered. The liver primordium appears as an outgrowth from the caudal end of the endoderm of

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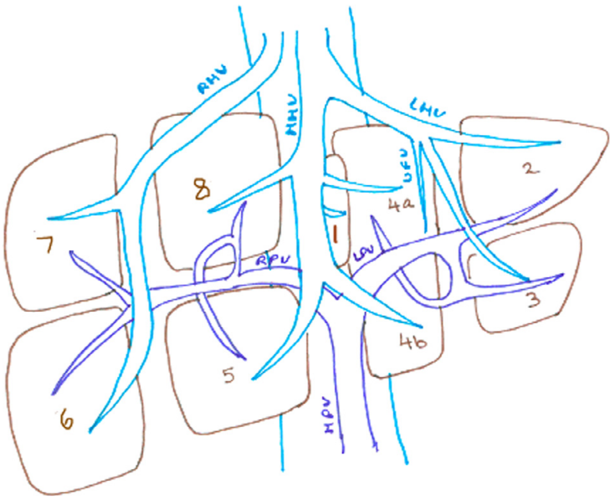

Fig. 1. Schematic representation of Couinaud's segments of the liver with distribution of the hepatic and portal venous branches. [Abbreviations: Right hepatic vein (RHV), Middle hepatic vein (MHV), Left hepatic vein (LHV), Right portal vein (RPV), Left portal vein (LPV), Main portal vein (MPV)].

ventral foregut during the third week of gestation. The proliferation of epithelial cells of this primordium give rise to the future liver and the intra-hepatic biliary tree, whereas the persistent communication with the foregut forms the extra-hepatic portion of the biliary tree. The mesenchymal structures of the septum transversum into which the liver bud proliferates give rise to the vasculature of the liver.

The umbilical vein enters the liver along the cholecystic axis and comes to lie within the left portion of the primitive middle lobe. This entrance marks the future plane between segments 4 and 3, both arising from the middle lobe. As the liver increases in mass, the middle lobe containing the umbilical vein rapidly enlarges in size forming a larger segment 4 and a smaller segment 3, while the primitive left lobe regresses to become segment 2. This rapid growth of segment 4 also results in a long extra-hepatic course of the left portal vein (LPV) and its displacement to a more lateral position in the Rex recess. Since segment 4 develops from the embryological middle lobe, it is predominantly drained by the MHV.

The liver is embryologically supplied by 3 principle arteries which develop around the 8th week of gestation. The left gastric artery supplies segment 2, an artery from the coeliac axis supplies the paramedian sectors (segments 5,8,4 and 3) and the superior mesenteric artery supplies the right lateral sectors (segments 6,7). Subsequently, these 3 arteries fuse, to form a single artery originating from the coeliac axis. However, any of the other arteries may persist as aberrant hepatic arteries. On this embryological basis the segment 4 artery has traditionally been labelled as the the middle hepatic artery (MHA). The ductal plate arises from periportal hepatoblasts and segment 4's bile ductules unite variably with those of segments 3 and 2 to form the left hepatic duct (LHD).

1.3. Hepatic veins

Anatomically MHV is the chief conduit of segment 4's venous drainage (Fig. 1). Moreover, the hepatic vein draining segment 4b (V4inf) joins the segment 5 vein to form the main trunk of MHV. The MHV also receives tributaries from segment 8 on its right and segment 4a (V4sup) on the left before draining into the inferior vena cava (IVC) with left hepatic vein (LHV) as a common trunk. In 15-30% of the cases, the MHV and LHV may drain individually into the IVC [5,6]. The intersegmental zone between segment 4 and the left lateral segment (segments 2 & 3) is a watershed between the drainage areas of the MHV and LHV. While segment 4 predominantly drains into the MHV, a variably sized umbilical fissural vein (UFV) also drains segments 3 and 4 into the LHV [7,8]. In addition, small veins draining segment 4a (V4a) may directly open into the suprahepatic cava close to the main trunk of MHV-LHV.

Implications: The venous drainage of segment 4 is of importance in deciding the plane of surgical transection in hepatectomies for malignancy as well as in split-LT and LDLT. Castaing et al showed that after a formal right hepatectomy (H5678-MHV) where the MHV is removed with the specimen, segment 4 regenerates proportionally less when compared to segments 2 and 3 [3,9]. They highlighted the impact of MHV anatomy on congestion and consequently, regeneration of the remnant liver (segment 4). The real-world importance of a congested segment of the liver, is that it can potentially lead to a gross disparity in the calculated and the actual functional liver remnant (FLR). Hence, compounded of various other factors which adversely affect liver regeneration (age, diabetes etc.), it could have catastrophic implications in major liver resections and donor outcomes in LDLT. Due to the shared drainage of segments 5, 8 & 4, one of the biggest dilemmas in LDLT is that of the MHV, and the anatomy of the MHV holds the key to right lobe (RL) living donation. Given that donor safety is paramount and for the reasons cited above, there is a decisive shift towards retaining the MHV with the donor. This has implications on volume and functionality of the retained segment 4 which is drained by the MHV [10]. As a result, several studies have been published which have tailored donor hepatectomy based on segment 4 anatomy to reduce morbidity in liver transplantation [11,12].

A conventional split-LT involves division of the liver into a LLS (H23) graft based on the LHV, and an extended right lobe (H45678) graft based on the MHV & RHV [3]. The line of splitting passes through the venous watershed zone between segment 4 and H23, and tributaries of the left and middle hepatic veins draining this zone are invariably encountered. These can be ligated without compromising the outflow of the H23 graft or segment 4. The UFV can also be an unexpected source of major bleeding during H23 resections, LLS-LDLT donor operations and *in-situ* split LT. The UFV may also play an important role in the post-RH venous drainage of segment 4, and is a factor in the decision making with regards to MHV in right lobe LDLT. A relatively large calibre UFV allows for a bolder decision-making with regards to retaining the MHV with the right lobe graft during the donor operation.

1.4. Portal vein

The LPV is divided into a transverse part which lies at the base of segment 4 and a vertical segment that runs in the umbilical fissure [5,6]. The branches from the umbilical portion of the LPV supply segment 4. The portal branches to segment 4a arise at right angles along the upper right border of the umbilical portion whereas those to segment 4b arise posteriorly and from the lower part (Fig. 2) [13]. A rare variant is the presence of a single portal venous trunk that gives off branches to the right and left lobes as it courses into the liver through the umbilical fissure.

Implications: During a H45678 resection, the portal venous branches to segment 4 are identified and ligated in the umbilical fissure. In a conventional SLT, where the liver is split into H45678 and H23 grafts, the portal supply to segment 4 is interrupted with resultant ischemia. Embolisation of segment 4 portal venous branches in addition to RPV embolization is a useful technique to enhance the extent of hypertrophy when the FLR is inadequate, a principle also applied surgically in the ALPPS (Associating Liver Partition and Portal vein ligation for Staged hepatectomy) procedure [14]. Monosegment ALPPS preserving only segment 4 has also been reported, emphasizing the importance of this segment in the future of liver surgery for extensive malignancy [15]. Similarly, staged hepatectomy for bilobar colo-rectal liver metastasis (CRLM) with multiple staged resections

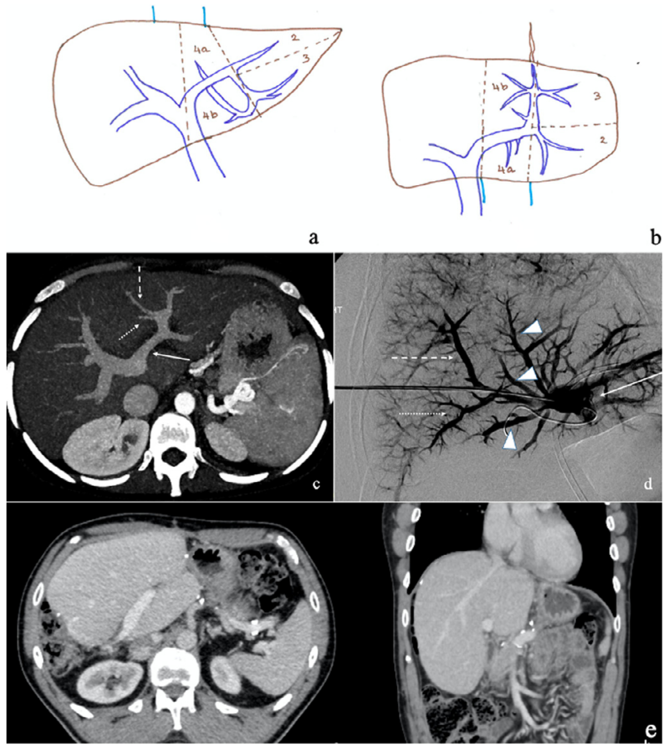

Fig. 2. Top panel: Schematic representation of left portal vein branches, dotted lines represent the plane between individual segments (a) anterior view (b) inferior view. Bottom panel: (c) axial reformatted computed tomography scan of left portal vein (solid arrow) with branches to segment 4a (dashed arrow) and segment 4b (dotted arrow) and (d) direct portography of left portal vein (solid arrow) with branches to segment 4a (dashed arrow), segment 4b (dotted arrow) and segment 3 (arrow heads), (e) Computed tomography scans showing liver remnant formed by segment 4 with surgical clips visible at both margins after multiple metastasectomies.

and intra-operative ablations leaving only segment 4 of liver to hypertrophy (Fig. 2e) have shown remarkable disease-free survival.

1.5. Hepatic artery

The MHA or the artery to segment 4 (A4) arises from the LHA in a majority of cases (54–61.5%) either intra or extrahepatically [16]. MHA with an extrahepatic origin, usually (83.8%) courses on the ventral surface of the LPV in the hilar plate [17]. Hence, if the MHA is not found ventral to the LPV at the hilum, it is safe to assume that it originates intrahepatically or is a branch of an aberrant LHA. A4 may also arise from the RHA or the aberrant LHA (Fig. 3). Other variations include origin directly from the proper hepatic artery as a trifurcation (Fig. 3g) and the presence of dual MHA.

Implications: The origin of A4 is of importance in the donor operation of a right lobe LDLT [18]. Preserving A4 while dividing the RHA for the right lobe graft is crucial, as this may lead to an ischemic segment 4, compromising the FLR in a donor. In a H23 LDLT/ SLT graft, preserving the A4 prevents total ischemia to segment 4. However, due to persistence of functioning hepatocytes in this relatively ischemic segment 4b, there may be an increased incidence of bile leaks. In SLT, it is not uncommon to excise segment 4b from the H45678 graft to prevent this complication. MHA thrombosis was once commonly seen in SLT; however, it is now seldom seen due to adoption of various microsurgical techniques for its reconstruction. In the ALPPS procedure, prevention of complete ischemia and hence improved outcomes and superior regeneration can be achieved by preserving the A4 [19].

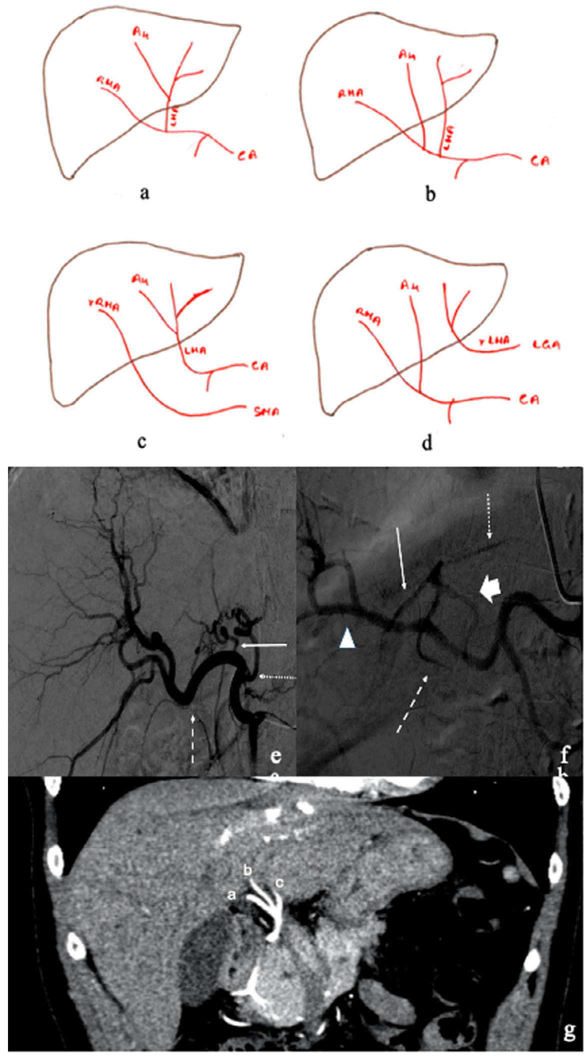

Fig. 3. Top panel: Schematic representation of common variations in the origin of middle hepatic artery (A4) (a) origin from LHA (b) origin from RHA (c) origin from replaced LHA (d) origin from replaced RHA; Middle panel: Coeliac angiogram showing (e) MHA (solid arrow) arising from RHA (dashed arrow), LHA (dotted arrow) is separate (f) LHA (thick solid arrow) giving rise to segment 2 artery (dotted arrow), segment 3 artery (dashed arrow) and MHA (thick solid arrow); Bottom panel: (g) Arterial phase computed tomography scan showing trifurcation of hepatic artery into right (a), middle (b) and left (c) hepatic artery. [Abbreviations: Right hepatic artery (RHA), replaced Right hepatic artery (rRHA), Left hepatic artery (LHA), replaced Left hepatic artery (rLHA), Celiac artery (CA), Superior mesenteric artery (SMA)].

1.6. Bile ducts

The pattern of biliary drainage remarkably follows that of the portal vein. The segment 4 duct joins ducts from segments 2 & 3 in various configurations to form the LHD. Among the several classifications proposed for biliary drainage patterns of the left lobe, those described by Okhubo et al and Reichert et al are the most commonly used ones [20,21]. Both these classifications suggest the dominant (55%-78%) pattern of drainage is where the segment 4 duct joins a single common channel from segments 2 and 3 between the umbilical fissure and the hilum (Fig. 4a).

Implications: A thorough knowledge of segment 4 biliary anatomy is necessary before planning a hepatectomy or LT. In patients with a variant segment 4 biliary drainage into the segment 3 duct, a left lateral segmentectomy risks the exposure of the segment 4 duct at the umbilical fissure, resulting in a post-operative bile leak (Fig. 4b). Anomalous drainage of segment 4 duct into the RHD in right lobe LDLT or right-left SLT may result in its injury, leading to

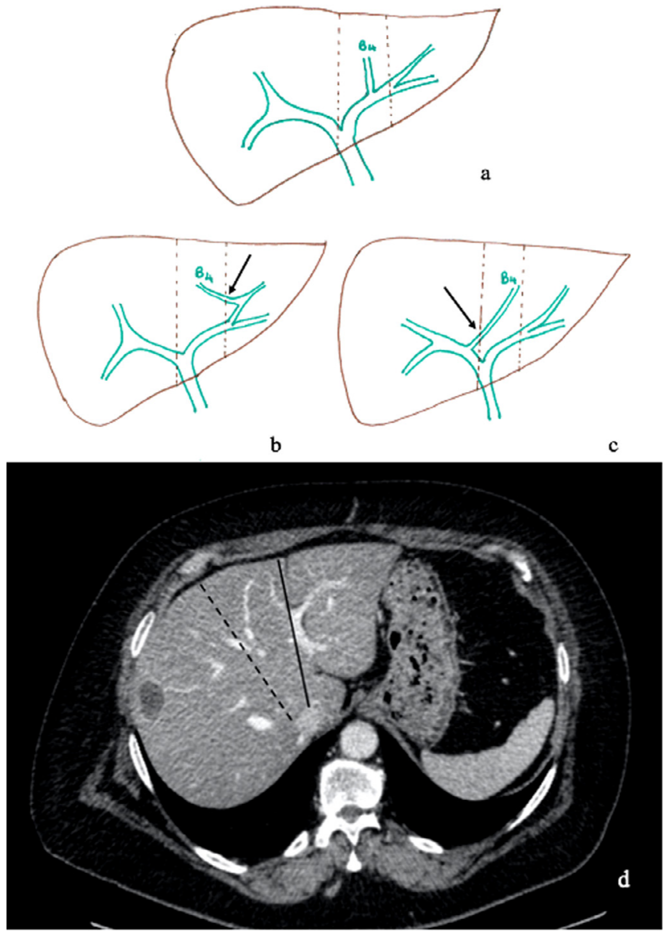

Fig. 4. Top panel: Schematic representation: (a) the most common pattern of biliary drainage of segment 4 (B4) draining into left hepatic duct; (b,c) the possible sites of bile leak (black arrows) due to anomalous drainage of segment 4 bile duct (B4) into segment 3 duct and right hepatic duct; dotted lines show the plane of transection of the liver for right hepatectomy and left lateral segmentectomy; Bottom panel: (d) Computed tomography scan showing the plane of transection for splitting the liver into a left lateral segment for an adult and a pediatric recipient (solid black line) and into right and left lobes for two adult recipients (dotted black line).

morbidity in the LDLT donor and the recipient or the two recipients in SLT (Fig. 4c). Recent studies have reported biliary complications related to segment 4 in SLT to be an important contributor for post-operative morbidity [22,23].

1.7. The King's technique of splitting the liver

Expanding indications for LT combined with the shortage of organs led to the development of techniques such as SLT and LDLT. In the conventional SLT, the plane of transection lies 1cm to the right of the falciform ligament. Whereas, in right-left SLT for 2 adults and in right lobe LDLT, the plane of transection lies just to the right of the MHV (Fig. 4d). As described above, segment 4 plays an important role, forming a part of the cut surface in both types of SLT, and consequently a major contributor to post-operative complications.

The technical details of performing the split and our experience have been described previously [24]. Briefly, in SLT for 2 adults, the MHV is retained with the left lobe to maintain the venous outflow from segment 4 (H5678 and H234-MHV grafts). The division of the hepatic artery is based on the origin of the MHA. A left lobe with 2 arteries (MHA and LHA) may be encountered when the MHA arises from the RHA and reconstruction of both the arteries remains a matter of debate. To avoid this scenario, the RHA is divided distal to the origin of A4, allowing for a single anastomosis in both the split liver grafts. In the standard SLT, the inflow to segment 4 is invariably compromised and may result in ischemic necrosis of segment 4. Previously, segment 4 was resected as a standard. However, with evolving experience this bench resection is no longer performed. In an attempt to reduce bile leaks, a meticulous hilar dissection in the bench, along with a gentle probing of bile ducts helps to identify biliary anomalies. When uncertain, flushing the bile duct with saline or methylene blue helps reliably identify cut surface bile leaks. Bench cholangiograms are rarely performed.

Our center has also pioneered in harvesting viable hepatocytes from segment 4 obtained from split livers and transplanting them into a one-day old recipient with pre-natal diagnosis of ornithine transcarbomylase deficiency [25]. This technique had a successful short-term outcome for managing metabolic derangements in the newborn and thereby further expanded the use of a single organ to benefit three different recipients. Thus, segment 4 may revolutionize the future of liver transplantation.

2. Conclusion

The planes of transection in hepatectomies, SLT and LDLT often involve segment 4. Hence a sound knowledge of its anatomy is necessary to avoid major post-operative complications. Apart from improving outcomes of these complex procedures it would also pave the way for development of novel surgical techniques.

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