Anatomical Variations in Living Donors for Liver Transplantation – Prevalence and Correlation

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Abstract

Purpose:
Living donor liver transplantation (LDLT) is a widely accepted option to address the lack of a deceased liver program for transplantation. Understanding vascular and biliary anatomy and their variants is crucial for successful and safe graft harvesting. Anatomic variations are common, particularly in the right hepatic lobe. To provide evidence for screening potential liver transplant donors, the presence of vascular and biliary anatomic variations in the preoperative assessment of transplantation donor candidates in Pakistan were explored.

Methods:
The was a retrospective cross-sectional study to evaluate the hepatic artery, portal vein, hepatic vein, and biliary variations in living liver donors. The study included 400 living liver donors, and data was collected from March 2019 to March 2023. We used a CT scan and MRCP to assess the anatomical variations.

Results:
The study examined 400 liver donors aged 18 to 53 years. Conventional arterial anatomy was the most common (65.8%), followed by replaced right hepatic artery (16%) and replaced left hepatic artery (10.8%). Conventional type 1 biliary anatomy was seen in 65.8% of cases. The dominant right hepatic vein was found in 13.3% donors. There was a significant association between the prevalence of variant portal venous anatomy with variant biliary anatomy.

Conclusion:
There was high variability in hepatic venous anatomy and a similar prevalence of variant hepatic arterial anatomy to other studies. A strong relationship between variant portal venous and biliary anatomy was found. These findings can aid in selecting suitable candidates and improving surgical planning for liver transplantation.

INTRODUCTION

Living donor liver transplant (LDLT) has become a generally accepted therapeutic alternative for alleviating the continuing shortage of cadaveric livers for deceased donor liver transplant (DDLT) [1]. With enhanced surgical procedures and immunological advances, LDLT recipient survival rates are equivalent to those of full-sized organ DDLT [2]. LDLT allows healthy individuals to donate a significant portion of their liver to suitable recipients. LDLT has numerous benefits over cadaveric liver transplants, including readily available donors, improved morbidity and mortality rates, and better graft quality [3].

Removing part of the donor's liver is a profoundly personal and surgical endeavor; therefore, enhanced knowledge of the biliary and vascular anatomy and its variations is essential for safe and successful
graft harvest and transplantation [4]. In LDLT, donor mortality risk is estimated at 0.5%, and postoperative morbidity reaches up to 21% [5].

Regarding the biliary and vascular anatomy of the liver, anatomic variations are frequent observations. In adult LDLT, right lobe graft has been widely preferred as it provides sufficient graft volume to the recipient and solves the issue of small for-size grafts. [6]. Vascular and biliary anatomy variations are more prevalent in the right lobe. Awareness of variant anatomy is essential to assuring the safety of the donors. It assists in selecting suitable donor candidates, even though anomalous anatomy is not always a contraindication for liver donation.[6, 7] Technical issues and a failure to recognize aberrant anatomy are to blame for most early postoperative vascular and biliary complications in donors and recipients.

Semi-invasive techniques such as endoscopic retrograde cholangiopancreatography (ERCP) and catheter angiography were utilized to clarify vascular and biliary anatomy. A liver biopsy was performed routinely to rule out diffuse parenchymal changes such as fibrosis or steatosis. Thanks to the advances in computed tomography (CT) and magnetic resonance imaging techniques, the same information can now be obtained noninvasively. By transitioning to preoperative evaluation using CT and MRI, several key drawbacks of conventional invasive procedures, such as high cost, morbidity and mortality, high radiation exposure, and an inadequate demonstration of venous anatomy, have been overcome [7].

Vascular and biliary variants are well sought after in literature; however, fewer publications emphasize their coexistence in surgical patients and their associated surgical importance in preoperative planning. We attempted to investigate the occurrence and concurrence of hepatic arterial, portal venous, and biliary anatomic abnormalities in the assessment of transplantation donor candidates as there is some considerable debate in the literature. We hypothesized that our population might have an association between specific vascular and biliary anatomic variants. This finding would have considerable implications for assessing liver transplant donor candidates. There is a shortage of relevant published evidence in Pakistan.

**MATERIALS AND METHODS**

The study was conducted in the Department of Hepatobiliary and Liver Transplantation, Pakistan Kidney and Liver Institute and Research Centre (PKLI&RC), from March 2019 to March 2023. This study was performed in line with the principles of the Declaration of Helsinki. Approval from the institutional review board (IRB) of PKLI&RC was taken (IRB approval no. 0106). The study design was a retrospective cross-sectional study, and the sample size consisted of the first 400 consecutive living liver donors selected through non-probability successive sampling.

Living donors ranged in age from 18 to 53 years. All donors were in good health and were initially evaluated for ABO blood type compatibility. The initial evaluation included a thorough history, physical examination, and laboratory tests. The computed tomography (CT) scan comprised an unenhanced sequence, followed by arterial and portal venous phases. The complete evaluation took between 75 and 90 seconds. Two radiologists with over ten years of experience reconstructed and evaluated the images
using the Picture Archiving and Communication System (PACS) workstation. The right and left lobe liver volumes were measured using the middle hepatic vein (MHV) as the cut plane.

Magnetic resonance cholangiopancreatography (MRCP) with 3D reconstruction delineated biliary architecture. The standard minimum donor future liver remnant at our center is 30%. We do not use traditional angiography on our patients. An independent physician as a donor advocate examined all donors. Donors provided informed consent, acknowledging the voluntary nature of the gift and their freedom to withdraw consent at any moment.

Patients of both genders aged 18–53 who were otherwise healthy and willing to donate their liver without any external pressure or coercion were included in the study. The study exclusion criteria were patients with active HBV or HCV infection or autoimmune etiology, patients with liver fibrosis or marked steatosis, those who were overweight with BMI > 30, and those with comorbidities.

The data were classified using Michels' classification for hepatic artery variants and Nakamura's classification for portal venous variations [7]. Hepatic veins were classified according to Varotti et al. [9], as shown below (Fig. 1), and a six-subtype classification was employed for bile duct variations (Fig. 2) according to Nakamura and Varotti et al. [8, 9].

Data analysis was conducted using Statistical Packages for Social Sciences (SPSS) v27.0. Frequencies and percentages were used for qualitative data such as gender, while quantitative data like age were presented using Mean ± S.D. Gender, hepatic arterial, portal venous, biliary, and hepatic venous types were all characterized qualitatively in frequency and percentages. A correlation was used to determine the relationship between the two variables. In all statistical tests, a P value < 0.05 was considered significant.

This study's findings aimed to improve the selection and management of living liver donors, ultimately leading to better outcomes for both donors and recipients.

RESULTS

The study comprised 400 liver donors; 228 (57%) males and 172 (43%) females. Donors varied in age from 18 to 53 years. The average age of the donors was 27 years old. From all 400 procedures, 341 (85.3%) had right donor hepatectomy surgery, 28 (7%) had left hepatectomy surgery, 16 donors (4%) had left lateral donor segmentectomy, and 4 (1%) had an auxiliary liver transplant. Only one donor underwent a deceased donor liver transplant.

The frequencies for variation in hepatic arterial, portal venous, and biliary anatomy are given in Table 1. Arterial Anatomy-Michel Classification shows the different types of arterial anatomy observed in living donors [10]. The conventional arterial anatomy was the most common, accounting for 65.8% of cases, followed by the replaced RHA (right hepatic artery) at 16% and the replaced LHA (left hepatic artery) at 10.8%. Both replaced RHA/LHA accounted for only 3% of cases, while accessory LHA and accessory RHA
were seen in 1.5% and 1% of cases, respectively. The remaining 1% of patients showed replaced RHA/ACC LHA or LHA/ACC RHA. CHA originated from SMA in 0.3% and LGA in 0.8% of cases.

Table 1
Anatomical Variations in the Hepatic Arterial, Biliary, and Portal Venous Anatomy.

<table>
<thead>
<tr>
<th>Hepatic Arterial Anatomy - Michel Classification</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional (Type I)</td>
<td>263</td>
<td>65.8</td>
</tr>
<tr>
<td>Replaced LHA from LGA (Type II)</td>
<td>43</td>
<td>10.8</td>
</tr>
<tr>
<td>Replaced RHA from SMA (Type III)</td>
<td>64</td>
<td>16</td>
</tr>
<tr>
<td>Both RHA and LHA replaced (Type IV)</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Accessory LHA from LGA (Type V)</td>
<td>6</td>
<td>1.5</td>
</tr>
<tr>
<td>Accessory RHA from SMA (Type VI)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Replaced RHA/ ACC LHA or replaced LHA/ACC RHA (Type VII &amp; VIII)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>CHA from SMA (Type IX)</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>CHA from LGA (Type X)</td>
<td>3</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Biliary Anatomy (Fig. 2)

<table>
<thead>
<tr>
<th>Biliary Anatomy</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional (Type 1)</td>
<td>264</td>
<td>66.0</td>
</tr>
<tr>
<td>Trifurcation (Type 2)</td>
<td>37</td>
<td>9.3</td>
</tr>
<tr>
<td>RAHD into LHD (Type 3a)</td>
<td>27</td>
<td>6.8</td>
</tr>
<tr>
<td>RPHD into LHD (Type 3b)</td>
<td>55</td>
<td>13.8</td>
</tr>
<tr>
<td>RAHD into CHD (Type 4a)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RPHD into CHD (Type 4b)</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>ACC Duct into CHD</td>
<td>16</td>
<td>4</td>
</tr>
</tbody>
</table>

Portal Venous Anatomy – Nakamura Classification

<table>
<thead>
<tr>
<th>Portal Venous Anatomy</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A</td>
<td>354</td>
<td>88.5</td>
</tr>
<tr>
<td>Type B</td>
<td>17</td>
<td>4.3</td>
</tr>
<tr>
<td>Type C</td>
<td>29</td>
<td>7.2</td>
</tr>
</tbody>
</table>

LHA = left hepatic artery, RHA = right hepatic artery, SMA = superior mesenteric artery, ACC = accessory, RAHD = Right Anterior Hepatic Duct, RPHD = Right Posterior Hepatic Duct, LHD = Left Hepatic Duct, CHD = Common Hepatic Duct, ACC = accessory.

Regarding frequencies in biliary anatomy, conventional biliary anatomy (Type 1) was observed in most cases, i.e., 65.8%, while trifurcation (Type 2) was seen in 9.3% of cases. Type 3a, where the right anterior
hepatic duct (RAHD) joins the left hepatic duct (LHD), was observed in 6.8% of cases, while Type 3b was the most observed variant (13.8%), where the right posterior hepatic duct (RPHD) joins the LHD. Type 4b, where the RPHD joins the common hepatic duct (CHD), was seen in only one case, and accessory duct into CHD was seen in 4% of cases.

Type A portal venous anatomy was most commonly observed in 88.5% of cases, while Type B and Type C were seen in 4.3% and 7.2% of cases, respectively.

With hepatic venous anatomy, there was a more widespread prevalence of different variations. The results we found from our donors are illustrated in Table 2. As described below, eight types of drainage patterns are categorized based on the presence or absence of particular veins. Dominant RHV was present in 15.1% of cases. 27.3% of subjects had inferior hepatic vein (RIHV). 36% of patients had a single adequately sized anterior sector vein, while 46% had two veins draining both segments 5 & 8 into the middle hepatic (MHV). A total of 45 cases (11.3%) underwent left lobe or left lateral graft; all showed a common insertion of the left hepatic vein/middle hepatic vein (LHV/MHV).

<table>
<thead>
<tr>
<th>Hepatic Venous Drainage (Fig. 1)</th>
<th>Description</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1a</td>
<td>Dominant right hepatic vein (RHV) with an absent fifth and eighth segmental hepatic vein (S5/8)</td>
<td>53</td>
<td>15.1</td>
</tr>
<tr>
<td>Type 1b</td>
<td>Dominant RHV and a right inferior hepatic vein (RIHV) present</td>
<td>10</td>
<td>2.8</td>
</tr>
<tr>
<td>Type 2a</td>
<td>RHV presents with an S5</td>
<td>32</td>
<td>9.0</td>
</tr>
<tr>
<td>Type 2b</td>
<td>RHV with a S5 and RIHV present</td>
<td>13</td>
<td>3.7</td>
</tr>
<tr>
<td>Type 3a</td>
<td>RHV with an S8 present</td>
<td>55</td>
<td>15.6</td>
</tr>
<tr>
<td>Type 3b</td>
<td>RHV with a S8 and RIHV present</td>
<td>27</td>
<td>7.7</td>
</tr>
<tr>
<td>Type 4a</td>
<td>RHV with both S5 and S8 present</td>
<td>116</td>
<td>32.9</td>
</tr>
<tr>
<td>Type 4b</td>
<td>RHV with S5, S8, and RIHV present</td>
<td>46</td>
<td>13.1</td>
</tr>
</tbody>
</table>

RHV = right hepatic vein, RIHV = right inferior hepatic vein, V5 = fifth segmental hepatic vein, V8 = eighth segmental hepatic vein.

We found a significant association between the prevalence of variant portal venous anatomy and variant biliary anatomy (p-value = 0.009), as described in Table 3. Although most cases showed Type A portal venous anatomy in all biliary subtypes (89.1%), there was a strong association of type C portal vein with variant biliary anatomy (4.3%). Furthermore, type 3a biliary anatomy was most associated with Type C portal vein (22%).
Table 3  
Correlation between variations in biliary anatomy and portal venous anatomy.

<table>
<thead>
<tr>
<th>Biliary Anatomy</th>
<th>Portal Venous Anatomy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type A</td>
</tr>
<tr>
<td>Conventional (Type 1)</td>
<td>242 (60.5%)</td>
</tr>
<tr>
<td>Nonconventional</td>
<td>Trifurcation (Type 2)</td>
</tr>
<tr>
<td>RAHD into LHD (Type 3a)</td>
<td>18 (4.5%)</td>
</tr>
<tr>
<td>RPHD into LHD (Type 3b)</td>
<td>47 (11.8%)</td>
</tr>
<tr>
<td>RAHD into CHD (Type 4a)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>RPHD into CHD (Type 4b)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>ACC Duct into CHD</td>
<td>16 (4.5%)</td>
</tr>
</tbody>
</table>

RAHD = Right Anterior Hepatic Duct, RPHD = Right Posterior Hepatic Duct, LHD = Left Hepatic Duct, CHD = Common Hepatic Duct, ACC = accessory.

**DISCUSSION**

Before embarking on a liver transplantation surgery, it is imperative to understand and correlate the donor’s segmental hepatic vascular and biliary anatomy. Through this description, surgeons have developed skills and modifications to the traditional liver transplant, including living donor or split liver transplantations [11, 12]. Although variant vascular and biliary anatomy is not usually a contraindication to liver donation, their understanding is essential for guaranteeing the safety of donors and recipients alike [9, 13].

Our results among 400 living donors who successfully underwent a living donor liver transplantation (LDLT) reported 65.8% (n = 263) with conventional hepatic arterial anatomy, 66% (n = 264) with conventional biliary anatomy, and an overwhelming 88.5% (n = 354) with conventional portal venous anatomy. In accordance with the literature, variation in hepatic venous anatomy was relatively high in our population [14].

The prevalence of variant hepatic arterial anatomy we found (34.2%), as classified by Michel classification, was similar to what has been reported in other studies (25–46%) [15–17]. Although it has been hypothesized that variant hepatic arterial anatomy may be associated with variant biliary anatomy, we could not find a significant correlation. Our finding was supported by Cheng et al. and Lee et al., who were also unable to find any meaningful relationship between these two variables [17, 18].
Portal vein variation was found in 11.5% of our population. According to Nakamura's classification, normal anatomy was defined as the right portal vein originating from the main portal vein and subsequently dividing into right anterior and right posterior portal branches within the right lobe [9]. Varotti et al., who analyzed a population of 96 individuals, reported nonconventional anatomy in 13.6% of the patients [16], while Lee et al. discovered 11% (12 out of 108) patients with variation in their patients' portal venous anatomy [17]. Atri et al. described that 10.8% of patients exhibited intrahepatic portal venous system trifurcation [19]. Thus, our findings are similar to the literature, bolstering the abundant prevalence of conventional portal venous anatomy in the general population.

Regarding variations in biliary anatomy, we reported a prevalence of 34% among the 400 living donors who underwent MRCP preoperatively. Our result was similar to numerous other studies [15, 20], including a regional study on 342 patients using MRCP [21]. In this study, Naeem et al. revealed a frequency of 34.2% for nonconventional biliary anatomy, thus strengthening our data [21].

It has been long debated whether there is any strong correlation between variation in biliary anatomy with portal venous anatomy [22]. If we trace the development of these structures back to their embryological state, the science behind their origin and growth postulates a possible common ground. Intrahepatic bile ducts, or “ductal plates,” form from liver progenitor cells in conjunction with the portal vein mesenchymal cells. The ductal plate remodels to form a bile duct in the periportal mesenchymal cells, which later becomes the portal canal. As a result, the formation of the portal vein and biliary system are linked. Other examples of biliary abnormalities coupled with portal vein malformations include a subgroup of biliary atresia patients with coexisting preduodenal portal veins or a nonexistent portal vein [23, 24].

A few other studies have also reported a significant connection between the prevalence of variant portal venous system with variant biliary anatomy. Lee et al. found a substantial association between portal venous and biliary variants (p = 0.012) but not between hepatic arterial and biliary variants [17]. Chen et al. studied that while there was a statistically significant concordance between second-order portal venous and biliary tract anatomies, several patients with conventional portal venous anatomy had variant biliary anatomy [25]. Schmidt and colleagues discovered that portal vein variations enhanced the likelihood of bile duct anatomical variation. These variations must be identified prior to undergoing a complicated hepatectomy, split or living donor transplantation, or advanced interventional treatments such as portal vein embolization [26]. Similarly, our significant finding (p-value = 0.009) between the existence of portal venous anatomy and biliary anatomy relates to the need for stringent contemporaneous examination to characterize biliary anatomy if variant portal venous anatomy is discovered on CT Triphasic. Prompt detection and intervention can help to reduce the high prevalence of biliary complications after LDLT, which presently stands at 7–10% of procedures [27].

The study's findings, i.e., the prevalence of anatomic variations, significantly emphasize screening potential liver transplant donor candidates using non-invasive techniques like CT and MRCP. The knowledge of the majority and coexistence of vascular and biliary variants in living liver donors can aid in selecting suitable candidates, identifying variations, and appropriate surgical planning accordingly. A
donor with significant anatomic variations may be unsuitable for donation or require a modified surgical approach. In 2022, our institution rejected 364 potential living donors for an LDLT. Of these, eight donors (2.2%) were denied based on complex biliary anatomy, and five each (1.4%) were due to complex arterial or venous anatomy. Therefore, this study's results help educate donors about the risks and benefits of LDLT and obtaining informed consent.

This study has several limitations. Although the sample size we included was adequate to draw meaningful conclusions, all the patients were consecutively sampled from a single Pakistan-based center. As such, the results may not be generalizable to other populations. Second, the study used computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) to evaluate the vascular and biliary anatomy. Although these non-invasive methods have several advantages over invasive procedures, they may have some limitations. The reported accuracy of MRCP for successfully defining biliary anatomy is between 81–84% [28]. Hence, using an intraoperative cholangiogram, considered the gold standard [15], may have been more beneficial.

CONCLUSION

In conclusion, our study has highlighted the importance of preoperative imaging evaluation of living liver donors. Anatomic variations of the hepatic arterial, portal venous, and biliary systems are common and should be carefully evaluated to ensure a safe and successful LDLT. Our results have shown a high prevalence of anatomic variations in the Pakistani population, including a significant correlation between portal venous and biliary anatomy. Our findings emphasize the need for a detailed preoperative evaluation. A multidisciplinary approach involving radiologists, hepatobiliary surgeons, and anesthesiologists is necessary to reduce donor morbidity and mortality. The study supports the notion that preoperative imaging using non-invasive techniques such as CT and MRCP can provide a detailed evaluation of vascular and biliary anatomy, allowing for improved selection of suitable candidates for LDLT. The study is valuable to the literature and can help guide clinical decision-making in selecting potential LDLT donors.

Declarations

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: None.

Ethics approval and consent to participate: The study was approved by the Institutional Review Board at Pakistan Kidney and Liver Institute & Research Center.

Availability of data and materials: Data can be provided upon reasonable request.

Acknowledgments: None
Authors’ Contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Abdullah Khalid and M. Asad Saleem. The first draft of the manuscript was written by Abdullah Khalid and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References


Figures

Figure 1.

Classification of the right liver hepatic venous anatomy. IRHV, inferior right hepatic vein; IVC, inferior vena cava; LHV, left hepatic vein; MHV, middle hepatic vein; RHV, right hepatic vein; S8, Segment VIII vein; S5, Segment V vein.

Figure 2.

Classification of biliary tree anatomy variation. CHD common hepatic duct, LHD left hepatic duct, RAHD right anterior hepatic duct, RPHD right posterior hepatic duct.