Living liver donor hilar anatomical variations and impact of variant anatomy on transplant outcomes

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Abstract
Donor anatomy is an essential part of donor selection and operative planning in living donor liver transplantation. In this study, variations of hilar structures, and the effects of variant anatomy on donor and recipient outcomes were evaluated. Living donor liver transplantations in a single center between January 2013 and December 2020 were retrospectively reviewed. In total, 203 liver transplantations were analyzed. Type 1 arterial anatomy, type 1 portal vein anatomy and type 1 bile duct anatomy were observed in 144 (70.9%), 173 (85.2%), and 129 (63.5%) donors, respectively. Variant biliary anatomy was observed more frequent in donors with variant portal vein branching than in those with type 1 portal anatomy (60.0% vs 32.3%, P = .004). The overall survival rates calculated for each hilar structure were similar between recipients receiving grafts with type 1 anatomy and those receiving grafts with variant anatomy. When donors with variant anatomy and donors with type 1 anatomy were compared in terms of hilar structure, no significant difference was observed in the frequency of complications and the frequency of serious complications. Biliary variations are more common in individuals with variant portal vein anatomy. Donor anatomic variations are not risk factors for inferior results of recipient survival or donor morbidity.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging.

Keywords: anatomy, liver transplantation, living donor, outcomes

1. Introduction
Variations of hilar structures including hepatic artery, portal vein, and extrahepatic bile ducts of the liver are well defined and classified with the studies of imaging modalities, autopsy series and surgical cases. The clinical implications of hilar variations include technically challenging operations with complex reconstructions, as well as the rejection of potential donors. Evolving experience from variant donor surgery has allowed us to understand the interrelationship of variations and their impact on transplant outcomes. These developments also contributed to nontransplant hepatobiliary surgery. Variant arterial anatomy might result with a graft having 2 arteries requiring 2 arterial anastomosis or variant biliary anatomy might result with a graft having 2 bile duct orifices requiring 2 bile duct anastomoses. Therefore, it can be hypothesized that the post-transplant results of variant hilar anatomy may also be different. The aim of this study was to assess the variations of hilar structures and to evaluate the effect of variant anatomy on donor and recipient outcomes.

2. Materials and methods
2.1. Study design and population
This retrospective study included all living donor liver transplantations which were performed at our institute between January 2013 and December 2020. Donors were selected from up to 4th degree (i.e., cousin) relatives according to national regulations. Exceptionally nonrelative volunteers or relatives with kinship more distant than 4th degree were selected as living donors after approval of Ethical Committee of Ministry of Health as it was compatible with national regulations. Ethical approval was obtained from institutional ethical committee (approval number: 2021/224) and the study protocol was designed in accordance with the Declaration of Helsinki. Informed consents from both donors and recipients were taken before transplantations. All living liver donors were included for analysis to reveal associations between hilar structures while pediatric transplants were excluded from recipient outcomes due to its different characteristics such as indications and graft type (mostly left lobe, left lateral section or monosegment grafts).
2.2. Data collection

Patient and donor files, operation notes, follow up notes were reviewed. Volunteer blood group compatible healthy donors were evaluated with magnetic resonance imaging (MRI) for description of biliary anatomy, evaluation of steatosis and triphasic dynamic multislice computed tomography (CT) for volumetric studies and describing vascular anatomy. Reports of donor MRI and CT studies were also reviewed. Intraoperative cholangiogram was a standard part of donor operation for determining bile duct division level and for confirmation of biliary anatomy which might be different from reported branching according to MRI. Bile duct anatomy was classified according to the classification in the article of Choi et al.[1] Hepatic arterial anatomy was classified according to Michels classification. [2] Portal vein anatomy was classified according to Cheng classification. [3] Variant anatomy for artery, portal vein, or bile duct was described as any anatomical presentation of the hilar structure other than Type 1 presentation according to the anatomical classifications used in the present study. Complications were recorded according to Clavien-Dindo postoperative complications scale. [4] Grade 3a or higher grade complications—requiring intervention or intensive care or resulting with death—were classified as serious complications. Early allograft dysfunction was determined using postoperative laboratory values of bilirubin, prothrombin time, and aminotransferase enzyme levels as described in related publication of the validation study.[5]

2.3. Outcomes

The primary endpoint of this study was patient survival after liver transplant depending on donor hilar variations. Secondary endpoints included donor morbidity depending on hilar variations and relationship of the variations with each other in terms of frequency.

2.4. Statistical analysis

SPSS 20.0 (IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp.) package program was used for statistical analysis. Continuous variables were reported with means and standard deviation while categorical variables were reported with frequency and percentages. Associations between categorical variables were calculated with Pearson Chi-Square test or Fisher exact test. Continuous variables were compared between groups with Student’s t test. Kaplan–Meier survival curves were created for survival analysis and survival rates were compared with Log-rank test. Two-sided significance level was chosen as 0.05. Power analysis was performed at the end of the procedure for appropriate evaluation of the results.

3. Results

3.1. Descriptive statistics

Totally 203 living donor liver transplantations were evaluated retrospectively. Median age was 32.3 ± 8.6 years, 62.1% were male. Mean donor body mass index was 25.0 ± 3.4 kg/m² and donor operation time was 386 ± 70 minutes. Right, left, left lateral, and other types of grafts were utilized in 154 (75.9%), 32 (15.8%), 12 (5.9%), and 5 (2.5%) liver transplantations, respectively. Mean graft to recipient weight ratio was 1.2 ± 0.5 g liver tissue/(kg recipient body weight × 10) (Table 1). Michels type 1 arterial anatomy was observed in 144 (70.9%) donors. Type 2 and type 3 variants were observed in 23 (7.9%) and 23 (11.3%) cases, respectively (Table 2). Type 1, type 2, and type 3 portal vein branching was observed in 173 (85.2%), 7 (3.4%) and 23 (11.3%) donors, respectively (Table 3). Type 1 bile duct branching was observed in 129 (63.5%) donors. Second most frequent variant was type 3a which was reported in 38 (18.7%) donors (Table 4).

| Table 1 | Donor characteristics. |
|---------|------------------------|
| n (%) or mean ± SD |
| n | 203 |
| Age, yr | 32.3 ± 8.6 |
| Female gender, n (%) | 77 (37.9%) |
| Donor body mass index, kg/m² | 25.0 ± 3.4 |
| Donor operation time, min | 386 ± 70 |
| Grafts, n (%) |
| Right | 154 |
| Type 1 artery | (75.9%) |
| | Type 1 portal vein | (71.4%) |
| Type 1 bile duct | (89.6%) |
| Left | 110 |
| Type 1 artery | (55.5%) |
| | Type 1 portal vein | (71.9%) |
| Type 1 bile duct | (65.6%) |
| Left lateral | 12 (5.9%) |
| Type 1 artery | 9 (75.0%) |
| | Type 1 portal vein | 9 (75.0%) |
| Type 1 bile duct | 8 (66.7%) |
| Other | 5 (2.5%) |
| Graft recipient weight ratio, g liver mass/(kg recipient body weight × 10) | 1.2 ± 0.5 |

SD = standard deviation.

*Percentages were the ratio of frequencies of type 1 hilar structure within each graft type.

| Table 2 | Anatomic presentations of hepatic artery. |
|---------|-----------------------------------------|
| Type | n |
| 1 | 144 (70.9%) |
| 2 | 16 (7.9%) |
| 3 | 23 (11.3%) |
| 4 | 4 (2.0%) |
| 5 | 6 (3.0%) |
| 6 | 4 (2.0%) |
| 7 | 1 (0.5%) |
| 8 | 2 (1.0%) |
| 9 | 1 (0.5%) |
| 10 | 2 (1.0%) |

| Table 3 | Anatomic presentations of portal vein. |
|---------|----------------------------------------|
| Type | n |
| 1 | 173 (85.2%) |
| 2 | 7 (3.4%) |
| 3 | 23 (11.3%) |

| Table 4 | Anatomic presentations of bile duct. |
|---------|-------------------------------------|
| Type | n |
| 1 | 129 (63.5%) |
| 2 | 12 (5.9%) |
| 3a | 38 (18.7%) |
| 3b | 14 (6.9%) |
| 3c | 2 (1.0%) |
| 4 | 1 (0.5%) |
| 5 | 5 (2.5%) |
| 6 | 2 (1.0%) |
3.2. Anatomical associations

Correlations between variance of hilar structures were analyzed. Variant arterial anatomy was found to be significantly more common in patients with Type 1 portal branching (32.2% vs 13.3%, \( P = .037 \)). Variant portal anatomy showed negative correlation with arterial variant anatomy. Variant biliary anatomy was observed more frequent in donors with variant portal vein branching than in donors with Type 1 portal anatomy (60.0% vs 32.3%, \( P = .004 \)) showing variant portal vein anatomy is in correlation with variant bile duct anatomy. There was no significant association between variant arterial anatomy and variant biliary anatomy (\( P = .162 \)).

3.3. Anatomic variations and recipient outcomes

Kaplan–Meier survival curves of: recipients whose donors had Type 1 arterial anatomy and recipients whose donors had variant arterial anatomy; recipients whose donors had Type 1 portal vein anatomy and recipients whose donors had variant portal vein anatomy; recipients whose donors had Type 1 bile duct anatomy and recipients whose donors had variant bile duct anatomy were and compared with Log-rank test. However, no statistical difference between abovementioned subgroups was observed in terms of overall survival (\( P \)) being 0.676, 0.166, and 0.255, respectively (Fig. 1). The closest \( P \) value of Log-rank test to the significance was for portal vein. Thus, a power analysis performed for survival analysis between patients having Type 1 and variant portal vein anatomy. A 2-sided Log-rank test with an overall sample size of 203 subjects (172 in the control group and 31 in the treatment group) achieves 50.1% power at a 0.05 significance level to detect a hazard ratio of 1.63 and an overall sample size of 461 subjects (391 in the control group and 70 in the treatment group) are required to achieve 80.0% power.

3.4. Anatomic variations and donor outcomes

Complicated case was determined with report of any grade of complication in the follow-up. Clavien-Dindo Grade 4a, Grade 4b, and Grade 5 complications were not observed among donors. Donors with Type 1 arterial anatomy and donors with variant arterial anatomy had complication rates of 20.8% and 11.9%, respectively (\( P = .133 \)). Serious complication rates were 6.2% for Type 1 and 3.4% for variant arterial anatomy (\( P = .414 \)). Donors with Type 1 portal vein anatomy and donors with variant portal vein anatomy had complication rates of 18.5% and 17.6%, respectively (\( P = .102 \)). There is no significant difference in terms of serious complication rates between donors with Type 1 and those with variant portal vein anatomy (5.8% vs 3.3%, \( P = .585 \)). Donors with Type 1 bile duct anatomy and donors with variant bile duct anatomy had complication rates of 18.6% and 17.6%, respectively (\( P = .613 \)). There is no significant difference in terms of serious complication rates between donors with Type 1 portal anatomy and 4.1% for variant portal anatomy (\( P = .515 \)) (Table 6).

Donors were grouped into 2; having at least 1 variant hilar structure and having Type 1 arterial, portal and bile duct

![Figure 1](image-url).

**Table 5**

| Bile leak | P | Biliary stricture | P | Hepatic artery thrombosis | P | Postoperative portal vein thrombosis | P | Early allograft dysfunction | P | Grade 3a or higher complication | P |
|-----------|---|------------------|---|--------------------------|---|-------------------------------------|---|-------------------------------|---|-------------------------------|---|
| Hepatic artery | .497 | .900 | .213 | .820 | .916 | .579 |
| Portal vein | | | | | | |
| Type 1 | 24 (18.6%) | 14 (10.9%) | 4 (3.1%) | 2 (1.6%) | 36 (25.8%) | 52 (40.3%) |
| Variant | 7 (14.3%) | 5 (10.2%) | 0 (0.0%) | 1 (2.0%) | 12 (25.0%) | 22 (44.9%) |
| Bile duct | | | | | | |
| Type 1 | 27 (17.8%) | 17 (11.2%) | 2 (1.3%) | 2 (1.3%) | 36 (24.0%) | 61 (40.1%) |
| Variant | 4 (15.4%) | 2 (7.7%) | 2 (7.7%) | 1 (3.8%) | 9 (34.6%) | 13 (50.0%) |
| Type 1 | 19 (17.0%) | 9 (8.0%) | 3 (2.7%) | 2 (1.8%) | 24 (21.8%) | 43 (38.4%) |
| Variant | 12 (18.2%) | 10 (15.2%) | 1 (1.5%) | 1 (1.5%) | 21 (31.8%) | 31 (47.0%) |
4. Discussion
The current study showed association between portal vein variation and bile duct variations. This kind of relationship was reported in prior studies with a variant biliary anatomy rate of 58.3%–89.1% in individuals with variant portal anatomy while variant biliary anatomy rate was being reported <40% in the whole cohort of same studies.[6–11] Tan and Vijayan[12] hypothesized that embryological contact between the portal vein and progenitor cells which will develop intrahepatic bile ducts may result formation of the bile ducts and the portal vein in the same manner. The current study failed to show a positive association between variant portal anatomy and variant arterial anatomy similarly with the large series probably because of later development of arterial circulation in the liver during gestation.[6,8,9,13] Moreover, this study showed that patients having variant portal anatomy had lower rate of variant arterial anatomy than those having type 1 portal anatomy.

Ductal variations were not found to be associated with arterial variations probably because of the same reason. Donors usually underwent both MR cholangiography and contrast enhanced computed tomography scans preoperatively and direct cholangiograms intraoperatively in most modern liver transplant centers, hence most reports are coming from these centers showing detailed anatomical relations. Donor safety deserves detailed anatomical mapping preoperatively. Clinical importance of current study in terms of anatomical relations is informing and alerting surgeons about patients undergoing major resections for liver tumors without bile duct imaging studies. The patients with portal vein variations may need intraoperative cholangiogram, preoperative MR cholangiogram or intraoperative bile duct visualization with indocyanine to prevent jeopardizing the bile ducts to be preserved. Donor and recipient outcomes are main endpoints of the study.

We compared recipient survival rates. Recipient survival rates did not differ between those with and without variant artery, portal vein, and bile duct anatomy. We can attribute this to the preoperative demonstration of the recipient and donor anatomy in detail and the preoperative planning of appropriate technical preparation. For example, since the portal vein of a right lobe donor with a type 3 portal vein may be short or may need to be unified with a vein graft in the backtable, it may be necessary to provide a cadaveric Y vein graft before surgery. Or, in another example, hepatectomy of a donor with a type 3a bile duct may result in 2 separate bile ducts. In this case, if a duct-to-duct anastomosis is planned, the recipient bile duct should be cut to obtain 2 orifices from an upper level while maintaining circulation. In the presence of a left lobe donor where the segment 4 artery originates from the right hepatic artery and the left hepatic artery comes from the left gastric artery, the technique required to combine these 2 arterial orifices in the backtable and the preparation of a vein graft or preparation of 2 healthy feeder arteries in the recipient should be planned in advance.

In a retrospective analysis of 323 transplants, authors failed to show an association between variant donor arterial anatomy and complications or survival.[14] In another retrospective analysis of 200 transplantations authors concluded that both recipient vascular complications and donor complications were not associated with donor vascular variations.[15] Similar studies with cadaveric grafts showed no difference between variant and normal donor arterial anatomy in terms of recipient survival.[16,17] Recipient arterial complications were reported to be associated with recipient arterial variations in a retrospective analysis of 325 deceased donor liver transplantations. In the same study donor arterial variations were not reported to be associated with arterial complications or recipient survival rates.[18]

In the present study, we did not observe significant difference between donors with type 1 bile duct anatomy and variant bile duct anatomy in terms of recipient survival and donor morbidity. However, in terms of effect of anatomical variation on recipient survival, our results could not be sufficiently free of type 2 error due to sample size and consistent with the survival trends of recipients in comparisons. In a detailed study of 71 right lobe donors and recipient outcomes authors concluded that variant central bile duct (type C to E bile duct according to Smadja/Blumgart classification) and arterial anatomy (other than type 1 according to Michels classification) were predictors of recipient morbidity.[19] In a recent study, supraportal right posterior bile duct anatomy or shorter right bile duct trunk were found to be related with increase in recipient biliary complications.[20] Variant bile duct anatomy was reported to marginally increase recipient biliary complications while not threatening donor safety in another study.[11] However, authors reported that they could not find an association between variant donor bile duct anatomy and recipient biliary complications in a recent retrospective study of 127 right lobe living donor liver transplantations.[21] Blood supply of bile ducts is the main point of interest hence ischemia may lead to the biliary complications. In a radiologic study of 44 donors and their recipients, variant anatomy was not found to be a risk factor for recipient complications. Although in the same study grafts with variant biliary anatomy requiring separate sectoral bile duct anastomosis and whose recipients experienced biliary complications had significantly increased second order bile duct-second order artery distance on imaging. Donor second order bile duct-second order artery distance of 10 mm was found to be a cut-off for recipient biliary complications.[22] The last study may be an explanation of different results of the studies on relationship of variant bile duct anatomy and recipient outcomes.

Frequency of type 1 portal vein anatomy is higher than type 1 arterial or biliary anatomy. Outcomes of utilization of grafts with variant portal anatomy were reported. In our retrospective cohort we used only grafts with Type 1, type 2, and type 3 portal vein anatomy. Fifty-two liver transplantations of liver grafts with variant portal anatomy were reported by Guler et al with acceptable outcomes.[23] None of the recipients experienced postoperative portal vein thrombosis and 1-year recipient survival was 91%. In the same study, overall donor morbidity rate consisting of Grade 2 to 4 complications was reported as 29%. No recipient portal complication was reported among 10 transplantation of portal variant right lobe grafts.[24] Ninety-one portal variant graft transplantations in which portal reconstruction was performed with a funnel shaped fence was reported to have nearly 85% 1-year recipient survival rate.[25] Excision of an oval shaped patch

### Table 6

| Complication         | P   | Serious complication | P   |
|----------------------|-----|----------------------|-----|
| Hepatic artery       |     |                      |     |
| Type 1 (20.8%)       | .133| 9 (6.2%)             | .414|
| Variant              | 7 (11.9%) |                      | 2 (3.4%) |
| Portal vein (18.5%)  | .811| 10 (5.8%)            | .585|
| Type 1 (16.7%)       | 5   | 1 (3.3%)             |     |
| Variant              | 1   |                      |     |
| Bile duct (18.6%)    |     | 8 (6.2%)             |     |
| Type 1 (17.6%)       | 13  | 3 (4.1%)             |     |

Table 6: Donor complications according to hilar variations.

Having any variant structure was found to have no correlation with complication (P = .649) or serious complication (P = .622).
from the main portal vein to unify 2 sector portal branches and reconstruction in the donor operation may risk the donor for postoperative portal vein thrombosis in the setting of variant donor portal anatomy.[26] Utilization of a right lobe graft with type 4 portal anatomy was reported, although rejection of donor or usage of right posterior sector grafts were recommended in presence of type 4 donor portal vein anatomy in the earlier ages of living donor liver transplantation.[23,26–28] Posterior wall unification, extension with Y grafts or quill plasty are easily applicable back table procedures for grafts with variant portal anatomy. Recipient right anterior and right posterior portal vein stumps can be used for separate anastomoses as well.[24]

Portal variant graft use has also spilled over into the field of laparoscopic donor hepatectomy. In a recent propensity score matched analysis of 444 living donor liver transplants including 171 laparoscopic donor hepatectomies concluded that Type 1 donor portal vein anatomy is superior than other types in terms of recipient portal vein thrombosis free survival. In the same article, laparoscopic 18 right lobe procurements with type 2 or 3 portal anatomy were reported.[23] This study has several limitations. Results in this study should not be compared with those in an anatomical or radiological study. Since only donors suitable for transplantation were selected, the presence of individuals excluded from the study due to extreme variations, volumetric issues, newly diagnosed donor disease or ceasing to be donors should not be ignored. However, donor anatomical variations are rarely a contraindication in our center. Therefore, we think that correlation analysis reflects the general population. Another important limitation was the sample size of the study due to the retrospective single center design. This condition had negative effect on the power of the study in survival analysis.

In conclusion, biliary variations are more common in individuals with variant portal vein anatomy. This relation is more important in liver resections other than donors due to less detailed preoperative imaging studies. Donor anatomical variations are not major risk factors for worse recipient survival or donor morbidity.

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