DONOR-RECIPIENT BODY SURFACE AREA MISMATCH AND THE OUTCOME OF LIVER TRANSPLANTATION IN THE UK

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ABSTRACT

Introduction: Transplanting too small or too big liver grafts for recipient's size has detrimental effects on transplant outcomes. Liver size is correlated with body surface area (BSA).

Research Questions: The purpose was to correlate We investigated whether the donor-recipient body surface area (BSA) ratio or BSA index (BSAi) correlates with liver transplant outcomesrecipient survival, graft survival, hepatic artery or /portal vein or vena cava thrombosis. High and low BSAi cut-off points were determined.

Design: There were We included 11, 245 adult recipients of first deceased donor whole liver-only grafts liver-only transplants of whole liver graft from deceased donors performed in adult recipients in the UK from (January 2000 until–June 2020). The transplants were grouped according to the ratio of donor to recipient BSA or [BSA index (BSAi)] BSAi and compared to complications, graft and recipient survival.

Results: The BSAi ranged from 0.491 to 1.691 with a median of 0.988. The BSAi > 1.3 was associated with a higher rate of portal vein thrombosis within the first 3 months (5.5%). This risk was higher than size-matched transplants (OR: 2.878, 95% CI: 1.292-6.409, pP=0.01). Overall graft survival was worse in transplants with BSAi ≤ 0.85 (HR: 1.254, 95% CI: 1.051-1.497, pP=0.012) or BSAi > 1.4 (HR: 3.704, 95% CI: 2.029-6.762, pP<0.001) than those with intermediate values. The graft survival rates were reduced by only 2% for cases with BSAi ≤ 0.85, but they were decreased by 20% for cases with BSAi > 1.4. These findings were confirmed by bootstrap internal validation. No statistically significant differences were detected in terms of for hepatic artery thrombosis, occlusion of hepatic veins/inferior vena cava or recipient survival.

Conclusions: Donor-recipient size mismatch affects the rates of portal vein thrombosis within the first 3 months and overall graft survival in deceased-donor liver transplants.

INTRODUCTION

In the face of organ shortage, it is essential that the available donor organs are matched correctly to the candidate recipients. Multiple parameters must be considered with each transplant. A parameter that is especially important in liver transplantation is choosing a liver graft that has the right size for the intended recipient. There is evidence that transplanting a liver graft too small or too large for the recipient's size can have detrimental short-term and long-term effects through multifactorial underlying pathophysiological mechanisms.[1] Transplanting a relatively small liver graft results in a lack of enough hepatic parenchymal mass for recipient's metabolic needs. It also results in a relatively high portal blood flow for the liver graft size, causing increased shear stress at the level of microcirculation, sinusoidal endothelial cell injury, hepatocyte oedema, compensatory decrease in the arterial blood flow, and cholestasis. All these contribute to liver graft injury.[1-4] Transplanting a relatively large liver graft leads to compression of the graft, mismatch in portal venous flow and poor graft perfusion. It can also lead to haemodynamic instability during reperfusion, kinking and thrombosis of the reconnected blood vessels, and respiratory complications due to high intra-abdominal pressure after closing the abdomen.[1,4]

To avoid these effects, most studies concluded that a liver graft needed to have at least 0.8% of recipient's weight or 35% of his/her ideal liver volume,[5] but not more than 2.5% of recipient's weight or 125% of his/her ideal liver volume.[6,7] The difficulty with avoiding this problem is that the actual liver graft weight or volume is not available at the time of an offer for a potential deceased donor. Therefore, transplant surgeons must rely on estimating liver graft size indirectly. Liver size strongly correlates with body size as measured by body surface area (BSA), which can be calculated by using height and weight,[8,9] parameters that are available for

every potential donor and candidate recipient. One can get a good idea of the liver graft size relative to the recipient's ideal liver size by dividing donor's BSA by recipient's BSA, a ratio characterized as BSA index (BSAi).[10]

Cut-off points for BSAi have been suggested in 4 published studies but were calculated based only on graft survival. Fukazawa et al.[10] found that a BSAi lower than 0.6 or higher than 1.4 were associated with shorter graft survival, based on a single-centre cohort of 1228 deceased-donor liver transplants. Two other studies, conducted by Fukazawa et al.[11] and Reyes et al.,[12] were based on the United Network for Organ Sharing (UNOS) registry and included 24 509 and 71 365 deceased-donor liver transplants, respectively. They found graft survival was improved when BSAi was between 0.78 and 1.24, and between 0.68 and 1.25, respectively. In the 2 studies conducted by Fukazawa et al., a higher risk of vascular complications and primary non-function was detected in liver transplants with small donor's size relative to recipient's size.[10,11] Kubal et al[13] used the cut-off points recommended by Reyes et al[12] in their single-centre cohort of 1694 deceased-donor liver transplants. They detected higher rates of early allograft dysfunction in patients receiving large livers for their size, but this difference did not reach statistical significance. They also did not find any difference between matched and mismatched cases for overall recipient survival and 1-year graft survival. Interestingly, they observed an advantage of the transplants with BSAi > 1.25 for overall graft survival.

Specific aim

The purpose was to correlate donor-recipient body surface area ratio with recipient survival, graft survival, hepatic artery or portal vein or vena cava thrombosis. A secondary purpose was to define the cut-off points beyond which these

outcomes are significantly affected, and thus determine a safety range for BSAi when transplant surgeons decide about an offer of a liver graft from a deceased donor.

METHODS

Design

This descriptive comparative study retrospectively reviewed all liver-only transplants performed in the UK over a 20-year period (January 2000 – June 2020) were. Anonymised data of the UK Transplant Registry were provided by the National Health Service Blood and Transplant (NHSBT) organization. This study was approved by the Liver Advisory Group of the NHSBT organization.

Population

There were 15660 liver-only transplants were performed in the UK between January 2000 and June 2020, including 1920 paediatric and 13740 adult transplants. These corresponded to 15190 deceased-donor liver transplants and 470 living-donor or domino liver transplants. The mean age of the entire population was 45.3 years (SD: 19.1), with 9323 male and 6337 female recipients. The two most common indications for liver transplantation in the entire population were alcohol-related liver cirrhosis (2410 cases) and hepatocellular carcinoma with underlying liver cirrhosis (2345 cases).

Sampling

Cases were excluded if they were living-donor and domino liver transplants, liver transplants in paediatric and adolescent recipients (less than 18 years old), split

or reduced liver grafts, retransplants, as well as those transplants without data concerning donor's and recipient's weight and height.

Data collection

Data were collected retrospectively in June 2020 from the prospectively maintained database of the UK Transplant Registry about the following parameters.

Donor characteristics

Type (donation after brain death or donation after circulatory death), age, gender, weight at donation, height at donation, liver graft steatosis, cold ischaemia time (time period between aortic cross-clamp with initiation of donor's cold perfusion and liver reperfusion with recipient's blood).

Recipient characteristics

Age, gender, weight at transplant, height at transplant, ethnicity, underlying liver disease, urgency for transplant (urgent or elective).

Transplant outcomes

Primary non-function, vascular thrombosis of liver graft within the first 3 months after liver transplant (hepatic artery thrombosis, portal vein thrombosis or inferior vena cava/hepatic vein occlusion), overall graft survival (time period between transplantation and death, re-transplantation or end of follow-up with working liver graft), overall recipient survival (time period between transplantation and death or end of follow-up).

Body surface area

Donors' BSA at donation and recipients' BSA at transplant were calculated using the Du Bois' equation:[14,15] BSA = 0.007184 x Weight $(kg)^{0.425}$ x Height $(cm)^{0.725}$. BSAi was defined as the ratio of donor's BSA to recipient's BSA: BSAi = Donor BSA / Recipient BSA.

Data analysis

To identify the cut-off points of BSAi above and below which transplant outcomes were significantly affected by donor-recipient size mismatch, BSAi values were divided into the following 16 groups in intervals of 0.05 and in ascending order: ≤0.7, (0.7, 0.75], (0.75, 0.8], (0.8, 0.85], (0.85, 0.9], (0.9, 0.95], (0.95, 1], (1, 1.05], (1.05, 1.1], (1.1, 1.15], (1.15, 1.2], (1.2, 1.25], (1.25, 1.3], (1.3, 1.35], (1.35, 1.4], >1.4. (Parenthesis means that the value is not included, whereas bracket means that the value is included). The groups were compared to the numbers of episodes of primary non-function and vascular thrombosis within the first 3 months after transplantation (hepatic artery thrombosis, portal vein thrombosis or inferior vena cava/hepatic vein occlusion) using the Chi-squared test or the Fisher's exact test. They were also compared to the overall graft survival and the overall recipient survival using Kaplan-Meier curves and the log-rank test. For each of the aforementioned outcomes (primary non-function, hepatic artery thrombosis, portal vein thrombosis, inferior vena cava/hepatic vein occlusion, overall graft survival, overall recipient survival) that provided statistically significant results in the initial comparison of the 16 groups, cases were further categorized into 3categories according to the BSAi values that resulted in the largest increase/decrease between adjacent intervals, namely the small for size (SFS) group for cases with low BSAi (size mismatch with smaller donor than recipient), the large for size (LFS) group for cases with high BSAi

(size mismatch with bigger donor than recipient), and the normal for size (NFS) group for cases between (size matched donor and recipient). Subsequently, the SFS, NFS and LFS groups were compared with each other.

Multivariable logistic regression analysis was performed to evaluate the BSAi effect on the risk for binary outcomes, taking also into consideration donor and recipient characteristics and cold ischaemia time. Multivariable Cox regression analysis was performed to evaluate the BSAi effect on time-dependent outcomes, taking also into consideration donor and recipient characteristics and cold ischaemia time. Internal validation was performed using bootstrap resampling (100 data sets) for the multivariable models that resulted from logistic and Cox regression.16,17 All the tests were two-tailed. The level of statistical significance was set at P-value <0.05. All analysis was performed using IBM SPSS Statistics version 26 (IBM Corporation, Armonk, NY, USA).

RESULTS

Included cases

After assessing for exclusion criteria, 11245 adult recipients of first deceased donor whole liver-only graft with no previous history of liver transplant during the study time period. Out of the 11245 included transplants, the liver grafts were from donors after brain death in 9504 (84.5%) transplants and from donors after circulatory death in 1741 (15.5%) transplants. The median donor BSA was 1.871 m^2 (min-max: 0.892-2.991), the median recipient BSA was 1.894 m^2 (min-max: 1.093-2.92), and the median BSAi was 0.988 (min-max: 0.491-1.691). Table 1 summarizes donor, recipient, and transplant characteristics and outcomes. Table 2 summarizes primary non-function rates, rates of vascular thrombosis within the first 3 months after liver

transplant (hepatic artery thrombosis, portal vein thrombosis or inferior vena cava/hepatic vein occlusion), and the 75th percentile graft survival and the 75th percentile recipient survival for each BSAi group.

Primary non-function of liver graft

The primary non-function rate for the entire cohort was 0.5% (52/11245), with this ranging between 0% and 2.7% among the 16 BSAi groups. There was no statistically significant variation in the primary non-function rates among these groups (P=0.101), and there were no higher primary non-function rates in the groups at the top or the bottom of the BSAi spectrum.

Hepatic artery thrombosis within 3 months post-transplant

The 3-month rate of hepatic artery thrombosis for the entire cohort was 1.6% (170/10 858), with this ranging between 0% and 3.5% among the 16 BSAi groups. The differences concerning the 3-month rates of hepatic artery thrombosis among these groups were not statistically significant (P=0.783).

Portal vein thrombosis within 3 months post-transplant

The 3-month rate of portal vein thrombosis for the entire cohort was 2.5% (271/10857), with this ranging between 0% and 8.6% among the 16 BSAi groups (P=0.013). Due to the increase in the rate of portal vein thrombosis from 1.5% to 2.6% at the BSAi value of 0.85 and the increase in the rate of portal vein thrombosis from 1.4% to 5.1% at the BSAi value of 1.3, transplants were divided into the following 3 categories for portal vein thrombosis: $SFS_{PVT} \leq 0.85$ (donor's size 85% of recipient's size or less), $0.85 < NFS_{PVT} \leq 1.3$ (donor's size more than 85%, but up to

130% of recipient's size), LFS_{PVT}>1.3 (donor's size more than 130% of recipient's size). The rates in these 3categories were as follows: SFS_{PVT}: 16/1087 (1.5%), NFS_{PVT}: 248/9642 (2.6%), LFS_{PVT}: 7/128 (5.5%), with the lowest ones in the SFS_{PVT} category and the highest ones in the LFS_{PVT} category (P=0.007).

These findings were confirmed by the multivariable logistic regression analysis, which showed that when compared with the NFS_{PVT} category, the LFS_{PVT} category had a higher risk of portal vein thrombosis within 3 months after transplant (OR: 2.878, 95% CI: 1.292-6.409, P=0.01), whereas the SFS_{PVT} category had a lower risk (OR: 0.509, 95% CI: 0.297-0.871, P=0.014) (Table 3). The LFS_{PVT} category had also a higher risk of portal vein thrombosis within 3 months after transplant than the SFS_{PVT} category (OR: 5.656, 95% CI: 2.171-14.739, P<0.001). The findings of the multivariable analysis were confirmed by bootstrap internal validation.

Occlusion of inferior vena cava or hepatic veins within 3 months posttransplant

The 3-month rate of inferior vena cava/hepatic vein occlusion for the entire cohort was 0.8% (83/10854), with this ranging between 0% and 2.4% among the 16 BSAi groups. There was no statistically significant variation in the 3-month rates of inferior vena cava/hepatic vein occlusion among these groups (P=0.919).

Overall graft survival

As shown in Table 2, there was significant variation in the 75th percentile graft survival among the 16 BSAi groups (P=0.005). Due to the increase in the 75th percentile graft survival from 4104 days to 6789 days at the BSAi value of 0.85 and the decrease in the 75th percentile graft survival from a 75th percentile survival not reached yet to just 569 days at the BSAi value of 1.4, transplants were divided into the

following 3 categories for overall graft survival: SFS_{GS} ≤0.85 (donor's size 85% of recipient's size or less), 0.85 <NFS_{GS} ≤1.4 (donor's size more than 85%, but up to 140% of recipient's size), LFS_{GS} >1.4 (donor's size more than 140% of recipient's size). There were statistically significant differences for overall graft survival among these 3 categories (P<0.001). See Figure 1 for graft survival up to 20 years posttransplant.

The SFS_{GS} category had shorter overall graft survival (75th percentile: 4514 days) than the NFS_{GS} category (75th percentile: 5721 days), while the LFS_{GS} category had much shorter overall graft survival than both of them (75th percentile: 569 days). This was reflected in the graft survival rates of these 3 groups. The 1-year, 5-year and 10-year graft survival rates were 94.9%, 89.4%, and 82.8%, respectively, for the NFS_{GS} category, 93.1%, 88.3%, and 80.6%, respectively, for the SFS_{GS} category, and 77.5%, 69.6% and 61.9%, respectively, for the LFS_{GS} category.

The multivariable Cox regression analysis confirmed these results, showing that both the SFS_{GS} category (HR: 1.254, 95% CI: 1.051-1.497, P=0.012) and the LFS_{GS} category (HR: 3.704, 95% CI: 2.029-6.762, P<0.001) have higher risk of graft failure when compared with the NFS_{GS} category (Table 4). The multivariable Cox regression analysis showed that the LFS_{GS} category had higher risk of graft failure than the SFS_{GS} category (HR: 2.953, 95% CI: 1.58-5.518, P=0.001). The findings of the multivariable analysis were confirmed by bootstrap internal validation.

Overall recipient survival

As shown in Table 2, there was no statistically significant variation in the 75th percentile recipient survival among the 16 BSAi groups (P=0.147).

DISCUSSION

The purpose of this study was to correlate BSAi with recipient survival, graft survival, hepatic artery or portal vein or vena cava thrombosis. A secondary purpose was to define the cut-off points beyond which these outcomes are significantly affected, and thus determine a safety range for BSAi when transplant surgeons decide about an offer of a liver graft from a deceased donor.

This was a large study based on a comprehensive national dataset collected rigorously by the transplant regulatory organization NHSBT. The study used internal validation techniques to support the recommended cut-off points. Although previous studies have analysed BSAi in assessing the donor-recipient size mismatch in liver transplantation,[10-13] there have only been 2 studies based on national data.[11,12]

To identify BSAi thresholds beyond which transplant outcomes were affected, the included transplants were placed in ascending order of BSAi and divided in multiple BSAi groups, ranging from cases with donor's size less than 70% of recipient's size up to cases with donor's size more than 140% of recipient's size. Based on these groups, BSAi cut-off points beyond which transplant outcomes were affected were identified and determined when a liver transplant was considered size matched or mismatched based on vascular regarding each outcome. Unlike the rest of the studies on this subject,10-13 this was done for every outcome separately to ensure that the BSAi thresholds were relevant to each of the outcomes analysed.

The findings demonstrated that donor-recipient size mismatch affected the risk of developing portal vein thrombosis within the first 3 months after liver transplant and reduced the overall graft survival. A BSAi >1.3 (donor's size more than 130% of recipient's size) was an independent risk factor for portal vein thrombosis within the first 3 months after transplant with the rate of portal vein thrombosis reaching 5.5%.

A BSAi ≤0.85 (donor's size 85% of recipient's size or less) resulted in a lower risk for portal vein thrombosis within the first 3 months after transplant, even though the actual difference in the portal vein thrombosis rate with the size-matched transplants was only 1.1%. Both a BSAi ≤0.85 (donor's size 85% of recipient's size or less) and a BSAi >1.4 (donor's size more than 140% of recipient's size) were independent risk factors for shorter overall graft survival. Although a BSAi ≤0.85 (donor's size 85% of recipient's size or less) resulted in a reduction of graft survival rates at 10 years after transplant by approximately 2% only in comparison with those of the size-matched transplants, a BSAi >1.4 (donor's size more than 140% of recipient's size) led to a great decrease of graft survival rates by approximately 20% when compared with size-matched cases. These outcomes beyond the cut-off points of BSAi were confirmed by bootstrap internal validation.

The combination of lower risk for portal vein thrombosis and slightly higher risk for graft loss in case of BSAi ≤0.85, could be something to take into consideration when choosing a donor for a recipient with risk factors for posttransplant portal vein thrombosis, eg, a pre-existing portal vein thrombosis that would require thrombectomy during transplant, a known hypercoagulable condition, etc. Perhaps in these recipients, a slightly higher risk of long-term graft loss could be acceptable to reduce the risk of posttransplant portal vein thrombosis. No statistically significant impact on primary non-function rates, 3-month rates of hepatic artery thrombosis, 3-month rates of inferior vena cava/hepatic vein occlusion or overall recipient survival was detected.

The analysis was adjusted for the time period (2000-2005, 2006-2010, 2011-2015, 2016-2020) by adding it as variable in multivariable analyses. There was higher risk of portal vein thrombosis in the 2 latter periods, which could depict a tendency to

perform an increasing number of liver transplants in surgically more complex recipients with preexisting portal vein thrombosis, as more experience was accumulated in transplant centres. However, high BSAi (big donor for recipient's size) was still an independent risk factor for early portal vein thrombosis after transplant. There was a lower risk of graft loss in the 2 latter periods, which could be a result of advances in immunosuppression regimens to prevent or treat rejection episodes, as well as advances in endoscopic and percutaneous techniques to deal with biliary and vascular complications post liver transplant, prolonging graft survival. Nevertheless, low BSAi (small donor for recipient's size) and high BSAi (big donor for recipient's size) were still independent risk factors for liver graft loss.

There were some limitations to the current study. There were no data available in the UK Transplant Registry for some additional potential confounding factors, such as recipient comorbidities apart from these related to the liver, prothrombotic conditions, anticoagulation protocols, and the surgical technique. There were no data about transplant outcomes that could be affected by donor-recipient size mismatch, such as the ability for primary closure of abdominal wall or the need for mesh placement in case of a significantly large liver graft for recipient's size. In addition, the clinical practice of choosing livers from donors as size matched as possible to the intended recipients to avoid significant size mismatch resulted inevitably in relatively few truly mismatched cases. The cases of extreme donor-recipient size mismatch, such as BSAi <0.6 or BSAi >1.5 were very few, not letting us extract conclusions about both extreme edges of the BSAi spectrum. Primary non-function rates, 3-month rates of hepatic artery thrombosis, 3-month rates of inferior vena cava/hepatic vein occlusion and/or overall recipient survival could be still affected in cases of extreme

donor-recipient size mismatch that extends beyond the levels that we were able to study.

CONCLUSIONS

Donor-recipient size mismatch following adult liver transplant affected the risk of early postoperative portal vein thrombosis and was associated with reduced graft survival. The BSAi may be useful for predicting mismatch prior to transplant and an additional important parameter for transplant surgeons to consider when choosing deceased donors for liver transplants, along with the patient-specific clinical context.

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Table 1 Donor, Recipient, And Transplant Characteristics

Characteristic	**N (%)**
Time period	
2000-2005	2584 (23%)
2006-2010	2310 (20.5%)
2011-2015	3054 (27.2%)
2016-2020	3297 (29.3%)
Donor characteristics	
Donor BSA (m^2)	
Mean (SD)	1.873 (0.209)
Median [min-max]	1.871 [0.892-2.991]
Age (years)	
Mean (SD)	49 (15.7)
Median (min-max)	51 (5-86)
Type	
Donation after brain death	9504 (84.5%)
Donation after circulatory death	1741 (15.5%)
Male gender	5844 (52%)
Liver graft steatosis	4895 (45.1%)
Recipient characteristics	
Recipient BSA (m^2)	
Mean (SD)	1.897 (0.229)
Median (min-max)	1.894 (1.093-2.92)
Age (years)	
Mean (SD)	51.6 (12.2)
Median [min-max]	54 [18-76]
Male gender	7066 (62.8%)
Ethnicity	
White	9739 (86.9%)
Asian	848 (7.6%)
Black	311 (2.8%)
Chinese/Oriental	93 (0.8%)
Mixed/Other	219 (2%)
Underlying liver disease	
Alcoholic liver disease	2075 (18.5%)
Acute liver failure	1052 (9.4%)
Autoimmune hepatitis	339 (3%)
Primary biliary cirrhosis	919 (8.2%)
Primary sclerosing cholangitis	945 (8.4%)
Chronic hepatitis B	215 (1.9%)

Characteristic	**N (%)**
Chronic hepatitis C	920 (8.2%)
Hepatocellular carcinoma	1984 (17.6%)
Non-alcoholic steatohepatitis	521 (4.6%)
Metabolic disease	366 (3.3%)
Other disease	1495 (13.3%)
Cryptogenic cirrhosis	414 (3.7%)
Urgency for liver transplant	
Elective	9788 (87%)
Urgent	1457 (13%)
Transplant characteristics	
BSAi	
Mean (SD)	0.995 (0.119)
Median (min-max)	0.988 (0.491-1.691)
Cold ischaemia time (hours)	
Mean (SD)	8.94 (2.79)
Median (min-max)	8.68 (0.42-25.65)
Transplant outcomes	
Primary non-function	52 (0.5%)
Hepatic artery thrombosis within 3 months	170 (1.6%)
Portal vein thrombosis within 3 months	271 (2.5%)
Inferior vena cava/hepatic vein occlusion within 3 months	83 (0.8%)
Graft survival rates	
1-year	94.7%
3-year	91.7%
5-year	89.2%
10-year	82.5%
Recipient survival rates	
1-year	91.2%
3-year	85.7%
5-year	80.2%
10-year	67.2%

BSA: body surface area, BSAi: body surface area index

Table 2. Transplant Outcomes According To BSAi Group

BSAi groups	**Number of transplants**	**Primary non-function rates**	**3-month hepatic artery thrombosis rates**	**3-month portal vein thrombosis rates**	**3-month inferior vena cava/hepatic vein occlusion rates**	**75th percentile graft survival (days)**	**75th percentile recipient survival (days)**
≤0.7	41	0%	2.4%	0%	2.4%	4179	2281
(0.7, 0.75]	88	2.3%	3.5%	1.2%	0%	4011	1906
(0.75, 0.8]	313	0.6%	2.6%	1.7%	1%	Not reached yet	2459
(0.8, 0.85]	684	0.6%	1.5%	1.5%	0.6%	4104	2522
(0.85, 0.9]	1204	0.4%	1.3%	2.6%	0.7%	6789	2801
(0.9, 0.95]	1730	0.5%	1.5%	2.6%	0.6%	5685	2640
(0.95, 1]	2025	0.3%	1.3%	3.7%	1.1%	5514	2634
(1, 1.05]	1771	0.3%	1.3%	1.7%	0.6%	5175	2541
(1.05, 1.1]	1438	0.3%	1.8%	2.4%	0.9%	5495	2706
(1.1, 1.15]	896	0.6%	1.6%	2.6%	0.7%	5483	2427
(1.15, 1.2]	506	1%	2.3%	1.6%	1%	Not reached yet	3091
(1.2, 1.25]	262	1.1%	1.6%	2.7%	0.4%	6589	1755
(1.25, 1.3]	144	0%	2.2%	1.4%	0.7%	5721	3069
(1.3, 1.35]	64	1.6%	0%	5.1%	0%	Not reached yet	1702
(1.35, 1.4]	37	2.7%	2.9%	8.6%	0%	Not reached yet	2266
>1.4	42	0%	2.9%	2.9%	0%	569	166
***P*-value**		0.101	0.783	**0.013**	0.919	**0.005**	0.147

The *P*-value shows whether there was at least one statistically significant difference among at least two of the included groups.

Table 3 Multivariable analysis for portal vein thrombosis in the original cohort and after bootstrap internal validation

Characteristic	**Original cohort**			**Validation samples**		
	OR	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
BSAi (reference: 0.85<BSAi≤1.3)						
BSAi≤0.85	0.509	0.297-0.871	**0.014**	0.509	0.246-0.826	**0.01**
BSAi>1.3	2.878	1.292-6.409	**0.01**	2.878	1.024-5.732	**0.008**
Time period (reference: 2000-2005)						
2006-2010	1.398	0.844-2.316	0.193	1.398	0.817-2.393	0.192
2011-2015	2.499	1.587-3.936	**<0.001**	2.499	1.586-3.865	**0.001**
2016-2020	2.995	1.914-4.686	**<0.001**	2.995	1.865-4.773	**0.001**
Donor type (reference: donation after brain death)						
Donation after circulatory death	0.861	0.609-1.218	0.398	0.861	0.594-1.218	0.401
Donor gender (reference: male)						
Female	1.194	0.921-1.548	0.181	1.194	0.923-1.568	0.187
Donor age (years)	0.992	0.984-1.001	0.067	0.992	0.984-1.001	0.067
Liver graft steatosis (reference: no)						
Yes	1.06	0.82-1.371	0.656	1.06	0.818-1.361	0.647
Recipient gender (reference: male)						
Female	0.826	0.616-1.107	0.201	0.826	0.611-1.109	0.205
Recipient age (years)	1.001	0.989-1.014	0.808	1.001	0.991-1.013	0.797
Recipient ethnicity (reference: White)						
Asian	1.096	0.679-1.769	0.709	1.096	0.623-1.74	0.722
Black	0.862	0.346-2.147	0.749	0.862	0.177-1.915	0.74
Chinese/Oriental	1.933	0.684-5.46	0.213	1.933	0.402-4.288	0.168
Mixed/Other	0.69	0.217-2.199	0.531	0.69	0.254-1.675	0.47
Underlying liver disease (reference: Alcoholic liver						

Characteristic	Original cohort			Validation samples		
	OR	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
disease)						
Acute liver failure	0.124	0.035-0.44	**0.001**	0.124	0.017-0.411	**0.001**
Autoimmune hepatitis	0.986	0.49-1.981	0.968	0.986	0.405-1.873	0.967
Primary biliary cirrhosis	0.609	0.346-1.072	0.085	0.609	0.296-1.019	0.097
Primary sclerosing cholangitis	0.509	0.295-0.878	**0.015**	0.509	0.267-0.86	**0.018**
Chronic hepatitis B	0.962	0.402-2.304	0.931	0.962	0.257-1.986	0.93
Chronic hepatitis C	0.602	0.343-1.057	0.077	0.602	0.32-1.018	0.069
Hepatocellular carcinoma	0.571	0.381-0.857	**0.007**	0.571	0.382-0.851	**0.006**
Non-alcoholic steatohepatitis	1.51	0.966-2.361	0.071	1.51	0.95-2.308	0.065
Metabolic disease	0.62	0.281-1.369	0.237	0.62	0.199-1.232	0.242
Other	0.699	0.436-1.12	0.136	0.699	0.43-1.112	0.123
Cryptogenic cirrhosis	0.746	0.367-1.515	0.417	0.746	0.275-1.376	0.394
Urgency for liver transplant (reference: elective)						
Urgent	0.969	0.459-2.046	0.935	0.969	0.366-1.997	0.936
Cold ischaemia time (hours)	1.007	0.961-1.056	0.771	1.007	0.955-1.059	0.763

Table 4. Multivariable Analysis Regarding Graft Failure In The Original Cohort And After Bootstrap Internal Validation

Characteristic	**Original cohort**			**Validation samples**		
	HR	**95% CI**	***P*-value**	**HR**	**95% CI**	***P*-value**
BSAi (reference: 0.85<BSAi≤1.4)						
BSAi ≤0.85	1.254	1.051-1.497	**0.012**	1.254	1.04-1.491	**0.013**
BSAi >1.4	3.704	2.029-6.762	**<0.001**	3.704	1.643-7.14	**0.001**
Time period (reference: 2000-2005)						
2006-2010	0.871	0.753-1.008	0.064	0.871	0.757-1.014	0.064
2011-2015	0.611	0.515-0.726	**<0.001**	0.611	0.51-0.724	**<0.001**
2016-2020	0.457	0.363-0.576	**<0.001**	0.457	0.36-0.572	**<0.001**
Donor type (reference: donation after brain death)						
Donation after circulatory death	1.195	0.994-1.438	0.059	1.195	0.981-1.441	0.068
Donor gender (reference: male)						
Female	0.951	0.846-1.069	0.4	0.951	0.848-1.062	0.408
Donor age (years)	1.008	1.004-1.012	**<0.001**	1.008	1.004-1.012	**0.001**
Liver graft steatosis (reference: no)						
Yes	1.153	1.027-1.296	**0.016**	1.153	1.016-1.304	**0.026**
Recipient gender (reference: male)						
Female	1.012	0.888-1.155	0.854	1.012	0.887-1.167	0.876
Recipient age (years)	1.011	1.005-1.016	**<0.001**	1.011	1.005-1.017	**0.001**
Recipient ethnicity (reference: White)						
Asian	1.142	0.937-1.392	0.188	1.142	0.904-1.38	0.184
Black	1.467	1.086-1.982	**0.013**	1.467	1.067-1.955	**0.012**
Chinese/Oriental	1.155	0.649-2.054	0.624	1.155	0.536-1.913	0.651
Mixed/Other	1.043	0.652-1.667	0.862	1.043	0.555-1.553	0.869
Underlying liver disease (reference: Alcoholic liver disease)						
Acute liver failure	0.994	0.692-1.427	0.973	0.994	0.697-1.425	0.969

Characteristic	**Original cohort**			**Validation samples**		
	HR	**95% CI**	***P*-value**	**HR**	**95% CI**	***P*-value**
Autoimmune hepatitis	0.842	0.558-1.271	0.413	0.842	0.542-1.237	0.411
Primary biliary cirrhosis	0.652	0.488-0.871	**0.004**	0.652	0.486-0.842	**0.003**
Primary sclerosing cholangitis	1.309	1.027-1.667	**0.029**	1.309	1.029-1.653	**0.025**
Chronic hepatitis B	0.741	0.459-1.197	0.221	0.741	0.43-1.161	0.232
Chronic hepatitis C	1.552	1.245-1.935	**<0.001**	1.552	1.243-1.941	**0.001**
Hepatocellular carcinoma	1.465	1.209-1.776	**<0.001**	1.465	1.225-1.797	**0.001**
Non-alcoholic steatohepatitis	1.227	0.837-1.798	0.295	1.227	0.807-1.741	0.284
Metabolic disease	1.182	0.847-1.65	0.326	1.182	0.821-1.607	0.326
Other	1.826	1.47-2.269	**<0.001**	1.826	1.451-2.317	**0.001**
Cryptogenic cirrhosis	0.966	0.699-1.334	0.832	0.966	0.673-1.331	0.844
Urgency for liver transplant (reference: elective)						
Urgent	1.127	0.864-1.471	0.376	1.127	0.846-1.486	0.396
Cold ischaemia time (hours)	1.014	0.993-1.037	0.192	1.014	0.992-1.037	0.205

BSAi: body surface area index

Figure 1. Graft Survival According To BSAi Category