

ORIGINAL ARTICLE

Use of middle hepatic vein in right lobe living donor liver transplantation

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Keywords

donor complications, living donor liver transplantation, middle hepatic vein.

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Received: 25 February 2009
Revision requested: 20 March 2009
Accepted: 10 September 2009

doi:10.1111/j.1432-2277.2009.00978.x

Summary

The harvesting of the middle hepatic vein (MHV) with the right lobe graft for living-donor liver transplantation allows an optimal venous drainage for the recipient; however, it is an extensive operation for the donor. This is a prospective, nonrandomized study evaluating liver functions and early clinical outcome in donors undergoing right hepatectomy with or without MHV harvesting. From August 2005 to July 2007, a total of 100 donor right hepatectomies were performed with ($n = 49$) or without ($n = 51$) the inclusion of the MHV. The decision to take MHV was based on an algorithm that considers various donor and recipient factors. There was no donor mortality in donors in either group. Overall complication rate was higher in MHV (+) donor group, however when remnant liver volume was kept above 30%, complication rates were similar between the groups. The results of this study show that right hepatectomy including the MHV neither affects morbidity nor impairs early liver function in donors when remnant volume is kept above 30%. The decision, therefore, of the extent of right lobe donor hepatectomy should be tailored to the particular conditions considering the graft quality and metabolic demand of the recipient.

Introduction

When procurement of middle hepatic vein (MHV) with the right lobe graft was first described by Lo *et al.* [1] in 1997, technique for living donor liver transplantation (LDLT) was still being developed and only few institutions in the world were successfully practicing right lobe LDLT [2]. After a decade, LDLT has developed into an essential part of treatment for end-stage liver disease in countries where cadaveric liver grafts are scarce. Despite extensive experience in donor right hepatectomy, which has become the common practice in adult-to-adult LDLT, the use of MHV in right lobe LDLT is still a controversial issue [3]. In the center of the controversy are the donor safety issues related to difficulty in the procurement technique and disturbance of venous drainage of the anterior sector, which could potentially jeopardize remnant liver

regeneration, the donor disadvantages outweighing the advantages accruing to the recipients [4,5].

In recent years, there have been reports either emphasizing the importance of venous drainage in anterior sector of the right lobe grafts [6–10], or confirming the safety of MHV harvest in right liver donors [11,12]; however reports that address the short- and long-term results of both donors and recipients are lacking. Our group, which performed the first right lobe LDLT in Turkey in 1999, utilizes MHV procurement selectively. We have developed an algorithm based on preoperative imaging studies, intraoperative findings, and the metabolic need of recipient in the decision making process. The aim of this prospective, nonrandomized study was to evaluate our results in right lobe LDLT in donors and their recipients when MHV is procured with the right liver lobe.

Methods

Between August 2005 and July 2007, we have performed 100 adult-to-adult right lobe LDLTs. Data were obtained from medical record review. Data on preoperative and postoperative biochemical, hematologic tests, coagulation profiles, intraoperative and postoperative transfusion requirements, postoperative complications, hospital stay and readmission data of all donors and recipients were collected. Follow-up was complete as of December 2008.

Preoperative donor evaluation

Once the indication for liver transplant is established, the recipients are placed in our cadaveric liver transplantation list and a work-up is started for their living donors as low number of cadaveric organs limits our practice. Donor evaluation includes biochemical and serologic tests, medical and social/psychiatric evaluation, and anatomical imaging studies. All donors are evaluated by a hepatologist, a transplant surgeon and a psychiatrist before arriving at a decision concerning eligibility.

Acceptance criteria for living donors include age between 18 and 65 years, relation to the recipient within the fourth degree of consanguinity, negative results of serologic tests for hepatitis B and C viruses, and normal hematologic, liver and renal functions. We consider only ABO-identical or ABO-compatible donors to be acceptable.

All eligible donors undergo imaging studies, including chest radiography, abdominal ultrasonography, computerized tomography (CT), and magnetic resonance imaging to exclude any unrecognized diseases, evaluation of the

degree of hepatosteatosis, and delineation of vascular and biliary anatomy. All potential donors with grade II–III hepatosteatosis are eliminated from evaluation. Liver biopsy is performed selectively: potential donors with grade I hepatosteatosis or BMI>28 or those testing positive for hepatitis B core antibody undergo liver biopsy. The liver volume of the donor is calculated by an experienced radiologist using contrast-enhanced multi detector CT (MDCT) through the Cavalieri method as described previously by our group [13]. The remnant liver volume is calculated from the volumetric study and expressed as the percentage of the total liver volume.

The decision for the procurement of MHV involves a complex and stepwise process (Fig. 1). In the CT, venous anatomy of the liver is examined; venous tributaries of MHV, right hepatic vein (RHV) and their drainage areas are found. In order to prevent any donor morbidity, MHV is not included in grafts when anterior segment of remnant liver (segment IVb) lacks a separate drainage vein. Preoperative CT findings of RHV and MHV anatomy, as well as the presence and caliber of segment IVb vein are confirmed intraoperatively with ultrasonography before proceeding with parenchymal division.

Operative procedure

The donor- and recipient-related operative procedures are same as our previous description [14]. In brief: The donors and recipients are admitted to hospital the night before the planned transplantation. A J-shaped or bilateral subcostal incision with upper midline extension is used. Intraoperative ultrasound is used for evaluation of the MHV, RHV, segment IVb, segment V, segment VIII and

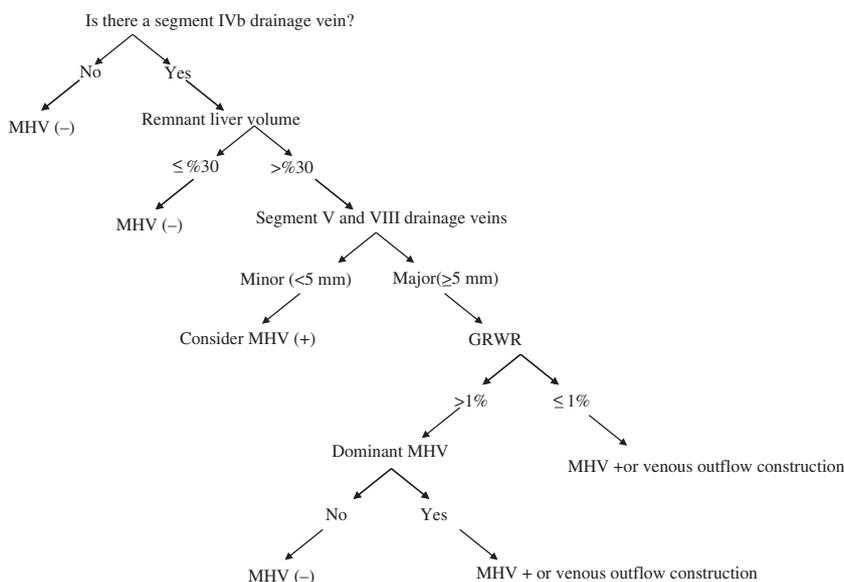


Figure 1 Middle hepatic vein (MHV) decision-making algorithm in living liver donors.

accessory inferior hepatic vein branches. After cholecystectomy, cholangiography through cystic duct stump for evaluation of the biliary tree is performed. After complete right lobe mobilization, hepatocaval ligament and all the direct vein branches from caudate to inferior vena cava (IVC) are ligated and divided. Accessory venous branches larger than 5 mm in diameter are temporarily clamped for testing their drainage capacities; if no congestion is observed in segment VI and segment VII after clamp trial, these branches are sacrificed. Right hepatic artery (RHA) and right portal vein (RPV) are then temporarily clamped to mark the parenchymal border between right and left lobes. A cavitron ultrasonic surgical aspirator (CUSA System 200 Macrodissector; Cavitron Surgical Systems, Stamford, CT, USA) is used for parenchymal division. In MHV (-) grafts, segment V venous branch is ligated and divided, and parenchymal dissection is performed on the right border of the MHV. When MHV is procured with the graft [MHV (+)], segment V vein is preserved and parenchymal dissection is performed on the left border of the MHV. Heparin sodium 2000 units i.v. is given before clamping the vessels after transection of the parenchyma. In MHV (+) grafts, MHV and RHV openings are combined with continuous 5-0 polypropylene suture in order to create a common orifice.

On the recipient side, cava-sparing total hepatectomy is performed. Once the graft is ready, IVC is clamped, middle/left hepatic vein opening is suture-closed and right hepatic vein stump is tailored to a larger triangular opening. Graft right/middle hepatic vein is anastomosed to this opening. Any inferior hepatic veins in the graft are anastomosed to a separate opening in the IVC. Portal vein, hepatic artery, and biliary anastomoses are performed as described previously [14].

Postoperative care

Donors are extubated in the operating room (OR) and remain in the surgical intensive care unit (ICU) overnight. Donors are started on ambulation and clear liquid diet on postoperative day 2. Diet is advanced slowly on postoperative days 3 and 4. For recipients, ICU stay depends on their recovery from the anesthesia. Postoperative diet and ambulation regimen are similar to those in the donors. Immunosuppression is established using corticosteroids, tacrolimus, and mycophenolate mofetil. Postoperative complications were defined as any event satisfying the classification of Clavien *et al.* [15].

For statistical analysis, continuous parameters in each group were compared by independent sample *t*-test, and categorical parameters were compared using the chi-squared test. All analyses were performed using SPSS 14.0 for Windows (SPSS, Chicago, IL, USA), and differences

were considered significant at a *P* value of <0.05. Values of measured variables were expressed as means \pm standard deviation or range.

Results

Demographic characteristics of donors and operative data are summarized in Table 1. There were 51 patients in MHV (-) and 49 patients in MHV (+) group. There were no differences in age, gender, and BMI between the two groups. Although parenchymal dissection time was significantly longer in MHV (+) group, intraoperative estimated blood loss and total graft ischemic time were similar. None of the donors in either group received blood transfusion. No interposition graft was used in this cohort.

Demographic characteristics of recipients and operative data are summarized in Table 2. There were no differences in age, gender, and BMI between MHV (-) and MHV (+) groups. None of the recipients received a small-for-size graft (GRWR < 0.8%). There were no differences in GRWR between the groups. A comparison of laboratory data in the first postoperative week showed that, MHV (-) graft recipients showed significantly higher peak aspartate transaminase (AST) (421 ± 453 U/lvs. 263 ± 146 U/l, *P* = 0.02) and alanine transaminase (ALT) (477 ± 528 U/l vs. 307 ± 214 U/l, *P* = 0.03) levels (Fig. 2a, b). Peak total bilirubin level was also higher in this group; however it did not reach statistical significance.

Table 1. Demographic characteristics and operative data of 100 donors undergoing right hepatectomy with or without middle hepatic vein (MHV) procurement.

	MHV (-) (n = 51)	MHV (+) (n = 49)	<i>P</i>
Age	38.6 \pm 10.9	38.1 \pm 9.6	ns
Gender (F/M)	22/29	27/22	ns
BMI	25.1 \pm 4.1	25.0 \pm 3.2	ns
Parenchymal dissection time (minutes)	69.9 \pm 34.2	85.3 \pm 28.7	0.02
Estimate blood loss (ml)	444 \pm 173	385 \pm 240	ns
Graft weight (g)	859 \pm 152	836 \pm 135	ns
Ratio of remnant volume (%)	34.3 \pm 3.6	35.8 \pm 4.1	ns
Postoperative day 0-7			
Maximum AST (U/l)	227 \pm 127	223 \pm 169	ns
Maximum ALT (U/l)	242 \pm 136	243 \pm 187	ns
Maximum total bilirubin (mg/dl)	4.5 \pm 2.7	4.8 \pm 2.1	ns
Maximum INR	1.7 \pm 0.2	1.8 \pm 0.1	ns
Hospital stay (days)	9.7 \pm 2.6	10.2 \pm 3.2	ns
Mean follow-up (months)	24.4 \pm 11.3	26.3 \pm 12.4	ns

Table 2. Demographic characteristics and operative data in 100 recipients undergoing right lobe LDLT.

	MHV (–) grafts (n = 51)	MHV (+) grafts (n = 49)	P
Age	49.0 ± 11.4	51.3 ± 9.8	ns
Gender (F/M)	10/41	16/33	ns
BMI	25.5 ± 4.4	26.4 ± 3.6	ns
MELD	18.0 ± 5.9	16.0 ± 6.3	ns
Graft total ischemia (minutes)	81.4 ± 26.2	80.2 ± 17.7	ns
GRWR (%)	1.19 ± 0.2	1.15 ± 0.2	ns
Postoperative days 0–7			
Maximum AST (U/l)	421 ± 453	263 ± 146	0.02
Maximum ALT (U/l)	477 ± 528	307 ± 214	0.03
Maximum bilirubin (mg/dl)	11.8 ± 7.9	10.1 ± 6.9	ns
Maximum INR	2.2 ± 0.6	2.0 ± 0.4	ns
Hospital stay (days)	21.6 ± 10.9	21.7 ± 14.2	ns

None of the donors in either group had steatosis more than 20%; therefore steatosis did not play a role in decision making process for MHV inclusion in grafts. An important safety parameter, donor remnant liver volume was similar between the groups: mean remnant volume to total liver volume was $34.3 \pm 3.6\%$ (range 28–42%) in

MHV (–) donors and $35.8 \pm 4.1\%$ (range 27–46%) in MHV (+) donors.

Postoperative donor recovery between the two groups was comparable. Inclusion of MHV in grafts did not increase peak transaminase, total bilirubin or international normalized ratio (INR) levels in donors during the first postoperative week. Donors in MHV (+) group had somewhat higher transaminases on postoperative day 1; however this did not reach statistical significance. In both groups, total bilirubin level peaked around postoperative day 3; this gradually decreased to normal levels by the end of postoperative week 2. Two donors in MHV (+) group experienced prolonged hyperbilirubinemia beyond postoperative week 2, both of them had liver remnant volume <30%.

None of the donors in either group had mortality or life-threatening (grade IV) complication requiring ICU management (Table 3). Long-term follow-up in donors in either group (median, 28 months) did not reveal any additional complications. Overall complication rate was higher in donors in MHV (+) group (22.4% vs. 7.8%, $P = 0.05$). However, subgroup analysis showed that the complication rates were similar [7.3% in MHV (–) group vs. 10% in MHV (+) group] between two study groups when remnant liver volume was more than 30%. The

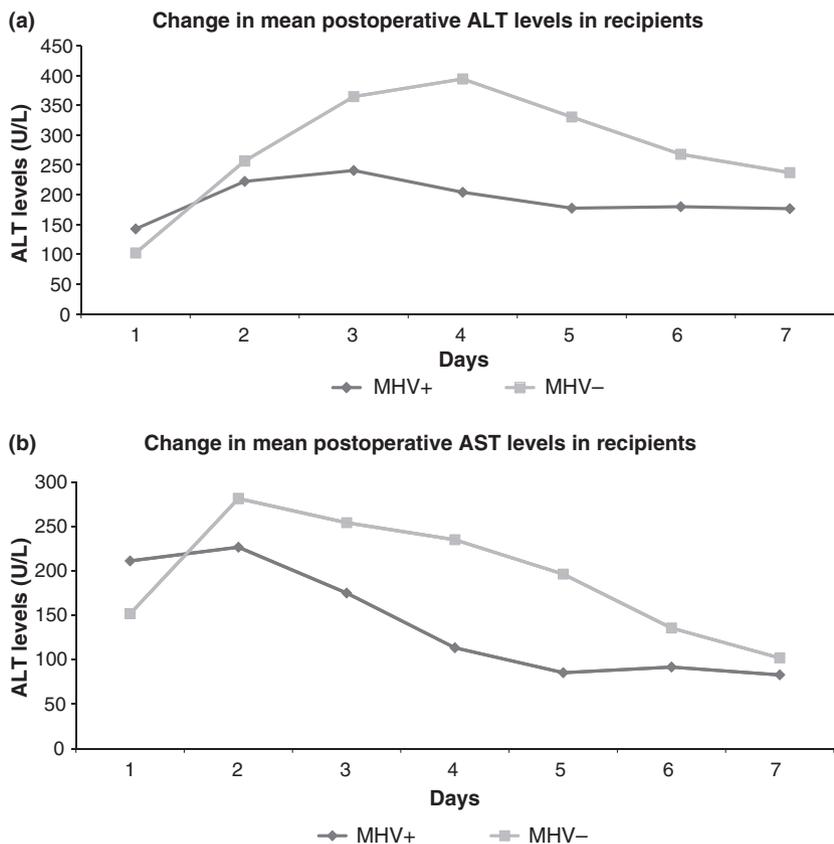
**Figure 2** Change in mean ALT (2a), AST (2b) levels during the first post-transplant week in recipients of middle hepatic vein (MHV) (+) vs. MHV (–) right liver grafts.

Table 3. Donor complications according to modified Clavien classification.

	MHV (-) donors (n = 51)	MHV (+) donors (n = 49)
Grade 1	Surgical site infection§, n = 1	Pleural effusion, n = 1 Surgical site infection§, n = 1 Prolonged hyperbilirubinemia, n = 2
Grade 2		Pneumonia§, n = 1 Pulmonary embolism***, n = 1 Retroperitoneal hematoma, n = 1
Grade 3	Postoperative hemorrhage†, n = 1 Incisional hernia‡, n = 1 Bile leak**, n = 1	Postoperative collection**, n = 1 Incisional hernia‡, n = 1 Biliary stricture¶, n = 2 Bile leak¶, n = 1
Grade 4	None	None
Total	4/51 (7.8%)	11/49 (22.4%)*

* $P = 0.05$, RR = 3.4 (1.0–11.5, % 95 CI). †Re-operation; ‡Hernioplasty; §Antibiotic treatment; ¶Endoscopic biliary stenting; **Ultrasound guided percutaneous drainage; ***Re-hospitalization and short term LMW heparin treatment.

highest complication rate (57.1%) was experienced in donors in MHV (+) group when liver remnant volume was < 30% [RR = 12.0 (0.9–153.8), 95% confidence interval] (Table 4).

In 29 of 49 of study patients who received a right lobe graft with MHV, we were able to find the long-term MHV status. MHV patencies were evaluated retrospectively according to the radiologic findings which included either Doppler Ultrasound ($n = 13$) or contrast enhanced CT/MRI scans ($n = 16$) performed at least more than 3 months after the transplantation. Not only was the flow pattern/contrast enhancement in the MHV, but also the parenchymal appearance of the medial sector considered [16]. In a median of 12 months (range 3–51 months), the MHV patency rate was 93% [only two of the 29 MHV (+) recipients were found with an occluded MHV, accompanied by a heterogenous appearance of the medial sector showing a venous drainage problem].

Furthermore, retrospective analysis of the postoperative day 7 remnant regeneration was performed in 23 available donors [11 MHV(+) and 12 MHV (-)] whose data was extracted from the overlapping data of our current prospective liver regeneration study in living donor liver transplantation [17]. Average preoperative estimated

remnant (left liver) volumes and percentages were almost identical [490 ± 66 ml and $35.0 \pm 4.4\%$ in MHV(+) group vs. 572 ± 119 ml and $35.2 \pm 4.7\%$ in MHV (-) group] in both groups. Although, MHV (+) donors had slightly higher average postoperative liver regeneration rate [94.9% in MHV (+) donors vs. 80.7% in MHV (-) donors], which resulted in a slightly higher average day 7 remnant to original total liver volume [67.4% in MHV (+) donors vs. 62.5% in MHV (-) donors], the differences were not statistically significant between the groups.

On the other hand, graft regeneration data was also analysed in the recipients of these 23 donors. Having similar average radiologic graft volumes in MHV (+) (920 ± 188 ml) and MHV (-) (1056 ± 223 ml) recipients, the average day 7 regeneration rate was significantly higher (76% in MHV (+) grafts vs. 50% in MHV (-) grafts, $P = 0.02$) in the extended RL grafts.

Discussion

This prospective, nonrandomized study in right lobe LDLT demonstrates that donor complication rates in MHV (-) and MHV (+) groups are similar as long as remnant volume is above 30%. More important, a comparison of laboratory data reveals a significantly better functional recovery in MHV (+) grafts. To the best of our knowledge, this is the largest study systematically comparing MHV (-) and MHV (+) groups in right lobe grafts.

Unique vascular anatomy of the liver is the basis of the discussion in surgery of liver. As opposed to right and left division of the arterial and portal venous inflow, the outflow is provided by three hepatic veins. In the anterior sector, MHV drains both right and left lobes. Therefore, this vein can be left in the remnant or included in the

Table 4. Correlation between middle hepatic vein (MHV) procurement and remnant liver volume in donor complications after right hepatectomy.

	MHV (-) donors (n = 51)	MHV (+) donors (n = 49)
Remnant $\geq 30\%$	3/41 (7.3%)	7/42 (16.7%)
Remnant <30%	1/10 (10%)	4/7 (57.1%)*

*RR = 12.0 (0.9–153.8), 95% confidence interval.

graft. The portion of the liver that is devoid of this drainage vein then can have problems related to congestion. However, our data showed that inclusion of MHV in the graft did not cause significant increase overall in transaminases in donors. This could be indirect evidence that in the MHV (+) group, parenchymal congestion and/or injury of the remnant liver is comparable to that of MHV (-) group, provided that venous drainage in the paramedian sector of the liver remnant is well preserved.

The presence of small-caliber intrahepatic collaterals between RHV and MHV has been shown, however, they exist only in 20% of the cases and likely to increase their function with time after the transplantation [7]. Therefore, it is doubtful that the collateral circulation is enough to protect the anterior sector in the first days after transplantation, which is the most critical period for graft regeneration. Intrahepatic collateral circulation between RHV and MHV was previously thought to be enough for compensation of loss of a major drainage vein. RHV only drainage therefore, was deemed optimal for the graft [2]. In fact, initial experience with right lobe grafts without adequate anterior sector drainage through MHV were reported to be successful [18,19]. However, contradictory reports emerged as the experience with the right lobe grafts grew in the recent years. Congestion in the anterior sector was first reported by Lee *et al.* [20]. They reported that five right lobe recipients experienced congestion of the graft in addition to postoperative ascites and sepsis. As a remedy, they proposed that segments V and VIII should be drained into IVC through separate interposition vein grafts [6]. Same group also suggested that this technique should be used in case of small right lobe grafts, when there are large segment V and VIII drainage veins, or when recipient has severe portal hypertension. Another approach to the congestion problem came from Fan *et al.* [7]. They suggested that instead of routine MHV inclusion in the graft, the decision should be made at the time of operation. MHV should be clamped; portal flow should be evaluated with Doppler ultrasound: if a reversal of flow is detected, then reconstruction of the segment V and VIII veins should be performed. However, reconstruction of the veins using interposition vein grafts on the bench increases ischemia time. In addition, this approach has been shown to cause potential unequal drainage in the anterior sector [21]. As additional anastomoses are done, this also increases risk of thrombosis. The long-term MHV patency rate of 93% in the extended RL grafts in our study group is better than any such figure given for the interposition grafts [22,23]. Therefore, whenever anterior sector drainage is required, we prefer to procure MHV trunk in every suitable donor rather than using interposition vein grafts.

Although, this prospective study is not randomized, an objective set of data emerged from our experience as the

groups were similar in terms of patient numbers and demographic characteristics and the same criteria were used for each donor/recipient pair for MHV inclusion in grafts. However, previous publications addressing the MHV controversy suggest that segment IV regeneration is affected adversely but regeneration of segments I-III compensates for this adverse effect [11,12,24]. Liver regeneration data of the last 23 patients which was extracted from the overlapping data of our current prospective liver regeneration study in LDLT showed that, having identical average remnant liver ratios of 35%, day 7 regeneration rate was even higher in the donors with extended RL resection ($94.9 \pm 24.4\%$ in MHV(+) donors vs. $80.7 \pm 25.7\%$ in MHV(-) donors). On the other hand, recipients of MHV (+) grafts showed a significantly higher average day 7 regeneration rate (76% in MHV (+) grafts vs. 50% in MHV (-) grafts). The fact that the highest liver regeneration is observed during the first postoperative week and regeneration rate decreases thereafter, day 7 data should give a reliable idea on remnant liver regeneration. In a recent volumetry study in right lobe donors, Yokoi *et al.* [25]. showed that the residual donor liver increased to 61% and 68% of original total liver volume by week 1 and 2 respectively. Remnant volume increase was gradual afterwards to reach 79% and 97% of original total liver volume by months 6 and 12 respectively. This data is consistent with our findings.

Use of MHV in the right lobe grafts is not an 'all or none' issue. Teams practicing right lobe LDLT should be flexible according to the recipient's graft requirement as well as donor's safety. We believe that development and systematic utilization of algorithms increase the safety margin. As our experience with LDLT has grown since 1999, we developed an algorithm to better select donors and recipients for MHV (-) and MHV (+) groups. Our initial algorithm did not involve criteria for remnant volume. However, four out of seven patients in MHV (+) group with remnant volume <30% experienced prolonged hospital stay and complications [14]. After observing increased morbidity, we have added this crucial criterion to avoid inclusion of MHV in the graft in this subgroup of donors. We propose that MHV should not be included in right liver grafts when remnant liver is <30% of total liver volume.

Donor age should also be an important factor for consideration of the MHV inclusion in the graft. In this series, only one of 11 donors above age of 55 had MHV included in the graft. In the presence of remnant congestion, decreased regeneration capacity of the aged liver can potentially increase morbidity. In this regard, other donor characteristics such as steatosis in the liver should be taken into consideration separately in each case.

In conclusion, the decision as to the extent of donor hepatectomy should be tailored to the particular anatomy of the donor and the metabolic demand of the recipient. The donor safety is the primary concern when considering LDLT. Liver graft is a precious gift; the mission of the transplant surgeon should be to optimize the graft utilization and to protect the remnant from damage. Therefore, anterior sector drainage should be placed in the center of the planning for transplantation.

Authorship

MD: designed study, analysed data, wrote the paper. CBT: analysed data, performed research/study, wrote the paper. DB, IM, OY, BA, CD, RK and OA: collected data, performed research/study. YY and YT: final approval of manuscript.

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