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Weight trends in United States living kidney donors: Analysis of the UNOS database

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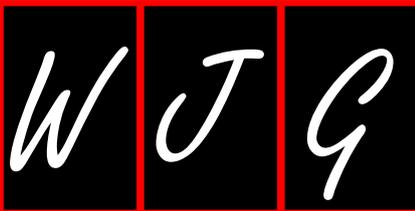
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ORIGINAL ARTICLE

Prospective Study

Risk of venous congestion in live donors of extended right liver graft

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Abstract

AIM: To investigate middle hepatic vein (MHV) management in adult living donor liver transplantation and safer remnant volumes (RV).

METHODS: There were 59 grafts with and 12 grafts without MHV (including 4 with MHV-5/8 reconstructions). All donors underwent our five-step protocol evaluation containing a preoperative protocol liver biopsy Congestive *vs* non-congestive RV, remnant-volume-body-weight ratios (RVBWR) and postoperative outcomes were evaluated in 71 right graft living donors. Dominant *vs* non-dominant MHV anatomy in total liver volume (d-MHV/TLV *vs* nd-MHV/TLV) was constellated with large/small congestion volumes (CV-index). Small for size (SFS) and non-SFS remnant considerations were based on standard cut-off- RVBWR and RV/TLV. Non-congestive RVBWR was based on non-congestive RV.

RESULTS: MHV and non-MHV remnants showed no significant differences in RV, RV/TLV, RVBWR, total bilirubin, or INR. SFS-remnants with RV/TLV < 30% and non-SFS-remnants with RV/TLV ≥ 30% showed

no significant differences either. RV and RVBWR for non-MHV (n = 59) and MHV-containing (n = 12) remnants were 550 ± 95 mL and 0.79 ± 0.1 mL vs 568 ± 97 mL and 0.79 ± 0.13, respectively (P = 0.423 and P = 0.919. Mean left RV/TLV was 35.8% ± 3.9%. Non-MHV (n = 59) and MHV-containing (n = 12) remnants (34.1% ± 3% vs 36% ± 4% respectively, P = 0.148. Eight SFS-remnants with RVBWR < 0.65 had a significantly smaller RV/TLV than 63 non-SFS-remnants with RVBWR ⩾ 0.65 [SFS: RV/TLV 32.4% (range: 28%-35.7%) vs non-SFS: RV/TLV 36.2% (range: 26.1%-45.5%), P < 0.009. Six SFS-remnants with RV/TLV < 30% had significantly smaller RVBWR than 65 non-SFS-remnants with RV/TLV ⩾ 30% (0.65 (range: 0.6-0.7) vs 0.8 (range: 0.6-1.27), P < 0.01. Two (2.8%) donors developed reversible liver failure. RVBWR and RV/TLV were concordant in 25%-33% of SFS and in 92%-94% of non-SFS remnants. MHV management options including complete MHV vs MHV-4A selective retention were necessary in n = 12 vs n = 2 remnants based on particularly risky congestive and non-congestive volume constellations.

CONCLUSION: MHV procurement should consider individual remnant congestive- and non-congestive volume components and anatomy characteristics, RVBWR-RV/TLV constellation enables the identification of marginally small remnants.

Key words: Living donor liver transplantation; Liver volume; Remnant volume; Small-for-size; Small-for-size syndrome

Core tip: Prevention of liver failure in middle hepatic vein (MHV) inclusive right graft donors involves consideration of both congestive and non-congestive remnant volumes. MHV management should be individually based on MHV anatomy characteristics. Non-congestive volumes represent an important safety parameter in MHV management, especially in the setting of small for size remnants. The remnant-volume-body-weight ratios - remnant volumes/total liver volume constellation seems to have a synergistic (complementary) capacity for the identification of marginally small remnants with the highest risk potential of postoperative liver failure.

INTRODUCTION

The precise determination of graft and remnant volumes constitutes the most important parameter to prevent postoperative donor and recipient liver failure in adult live donor liver transplantation (ALDLT)[1-3]. Middle hepatic vein (MHV)-containing grafts are associated with small remnants whose function may be further impaired by early postoperative venous congestion of their medial sector (segment 4A/B)[1,4,5]. The occurrence of small-for-size syndrome (SFSS) in donors as a result of inadequate functional remnant volume is a constant reminder of the controversy surrounding venous congestion and MHV management. The commonly accepted definitions for small-for-size-(SFS)-remnants do not even consider remnant volume values[4,6-11]. To date, there are no published reports correlating the extent of functional impairment and parenchymal congestion in non-MHV containing remnants, and remnant volume limits for safe MHV inclusion with the right graft are still undefined.

In the present series, we evaluated our experience with liver failure in right graft donors. Our goal was to analyse the impact of MHV-containing right grafts on remnant volume (RV) and function. We considered the ratios remnant-volume-body-weight-ratio (RVBWR) and remnant volume percentage of total liver volume (RV/TLV) as a way to discriminate between SFS- and non-SFS remnants based on commonly accepted cut off values[4,8]. The following queries were addressed: (1) How concordant are these ratios in assessing SFS-remnants and determining their volume limits? (2) Is MHV procurement with right grafts associated with substantial loss of remnant volume? (3) Does inclusion of the MHV in right grafts impact remnant liver function and donor morbidity as a result of venous congestion? and (4) Does MHV anatomy affect venous outflow (= congestive volume) and thereby influence MHV management?

We finally considered "reasonable" criteria for procurement of right grafts with/without complete MHV vs selective MHV-4A preservation in remnants based both on our own experience with donors without evidence of steatosis as well as on that of others[4,6-8,11-16].

MATERIALS AND METHODS

Study population

From January 2003 to October 2007, 71 consecutive live donors (36 females and 35 males, mean age 37 ± 10.1 years) underwent right graft hepatectomy at the University Hospital Essen, Germany. There were 59 grafts with and 12 grafts without MHV (including 4 with MHV-5/8 reconstructions). All donors underwent our

Table 1 Etiology of liver disease among right graft recipients (*n* = 71)

Parameter	Number
Total	71
Male	43
Female	28
Autoimmune hepatitis	5
Hepatitis B	4
Hepatitis B associated with hepatocellular carcinoma (HCC)	7
Hepatitis C	8
Hepatitis C associated with HCC	10
Alcoholic	7
Alcoholic + associated with HCC	6
Morbus Wilson	2
Primary biliary sclerosis (PBC)	2
Primary sclerosing cholangitis (PSC)	7
HCC	4
Cryptogenic	6
Others[1]	3

[1]Neuroendocrine lever metastases (*n* = 2), liver metastases from insulinoma.

five-step protocol evaluation containing a preoperative protocol liver biopsy as previously described[14,17]. Biopsy results in all resected donors showed less than 10% steatosis and no evidence of hepatopathologic changes.

Recipient indications for liver transplantation

Sixty eight out of 71 right graft recipients (28 females and 43 males, mean age 50 ± 11.0 years) suffered from liver cirrhosis classified for Child-A score; *n* = 22, Child-B score; *n* = 33, Child-C score; *n* = 13, while in the remaining *n* = 3 cases with no cirrhosis the indication for liver transplantation were neuroendocrine liver metastases (*n* = 2) as well as liver metastases from insulinoma (*n* = 1, Table 1). The overall "Model of End-Stage Liver Diesease"-score (MELD) was of mean of 14 ± 8 (range: 11-40).

All-in-one protocol of multiphasic computed tomography scan

Computed tomography (CT) imaging was performed using a 16-row-Multidetector-CT-Scanner (Sensation16®, Siemens, Erlangen, Germany) as originally published by our group[18].

3D-CT-imaging analysis and -volumetry

CT images were analyzed with the software assistant HepaVision® (MeVis institute, Bremen, Germany)[19,20].

Liver volume definitions

RV: Congestive and non-congestive volumes.

Congestive volume: Venous congestion volume resulting from the detachment of left sided MHV-(4A/B) tributaries draining the left medial sector.

Non-congestive volume: Volume safely drained by the left hepatic vein (LHV) tributaries.

Congestive volume-index: Percentage of volume with venous congestion.

Donor RV/TLV: Remnant volume percentage of total liver volume considering the remnant volume with intact bi-sectorial venous outflow *via* the middle (MHV)- and LHV tributaries.

Donor RVBWR: (Safely drained by MHV and LHV) *vs* non-congestive *RVBWR* (safely drained by LHV) were calculated according to the Heinemann formula[9].

3-D virtual liver partition

The "carving" transection plane followed the course of the MHV, exposing it on the resection surface of either graft (MHV-procurement) or remnant (MHV-retention) livers[21]. The MHV trunk served as a reproducible surgical landmark for the exact extrapolation (by means of color doppler scanning, IOUS) of the 3-D liver model onto the operative field.

SFS vs non-SFS remnants

We evaluated the correlation between RVBWR and RV/TLV as a way to distinguish between SFS- and non-SFS remnant status based on the following cut off values: SFS-remnant: RVBWR < 0.65 *vs* non-SFS-remnant RVBWR ≥ 0.65[8]. SFS-remnant: RV/TLV< 30% *vs* non-SFS-remnant RV/TLV ≥ 30%[4].

SFSS definition

SFSS was defined as either poor initial remnant function or prolonged remnant dysfunction as a result of inadequate functional liver mass in the absence of other causative factors. This definition was based on criteria for both LDLT donors and recipients likewise tumor hepatectomy patients[22,23]. SFSS was characterised by the presence of at least two of the following symptoms within the first four post-operative weeks: encephalopathy (stage ≥ 2), progressive intrahepatic cholestasis [Bilirubin > 5.0 (reference value: 0.2-1.2)], prolonged severe coagulopathy (INR > 2.2), excessive intractable ascites (> 3 L/d).

Hepatic vein dominance in total liver

Hepatic vein with the largest percentage of total liver volume (TLV) as originally classified by our group[20].

Statistical analysis

The non-parametric Sign test was used for two variables lacking normal distribution. The non-parametric Wilcoxon matched pairs test was applied to test the hypothesis that two variables (lacking normal distribution) were drawn from the same distribution.

Table 2 Concordant *vs* non-concordant interrelation between remnant volume (donor) body weight ratio and remnant volume percentage of total liver volume in discriminating small-for-size from non-small-for-size remnants according to two different cut-off values

Remnant status defined by Rvbwr		Remnant status defined by Rv/tlv	
SFS RVBWR < 0.65 $n = 8$	Non SFS RVBWR $\geqslant$ 0.65 $n = 63$	SFS RV/TLV < 30% $n = 6$	Non SFS RV/TLV $\geqslant$ 30% $n = 65$
RV/TLV < 30% Concordant	RV/TLV < 30% Non-concordant	RVBWR < 0.65 Concordant	RVBWR < 0.65 Non-concordant
2/8	4/63	2/6[1]	5/65[2]
25%	6%	33%	8%
RV/TLV $\geqslant$ 30% Non-concordant	RV/TLV $\geqslant$ 30% Concordant	RVBWR $\geqslant$ 0.65 Non-concordant	RVBWR $\geqslant$ 0.65 Concordant
6/8	59/63	4/6	60/65
75%	94%	67%	92%

[1]incl. 2 remnants with RVBWR = 0.60; [2]incl. 1 remnant with RVBWR = 0.60. SFS: Small-for-size; RV/TLV: Remnant volume percentage of total liver volume; RVBWR: Remnant volume (donor) body weight ratio.

The Mann-Whitney *U* Test was used to test the significance of the difference between two independent samples of an ordinal variable as well as differences in the shape of the distributions (not just the location of the ranks) of the two groups. Significance was considered at a level < 0.05. Statistical release 7 (Statsoft) was used for statistical analysis.

RESULTS

RV and RVBWR
Mean overall RV and RVBWR were 565 ± 97 mL and 0.79 ± 0.12, respectively. RV and RVBWR for non-MHV ($n = 59$) and MHV-containing ($n = 12$) remnants were 550 ± 95 mL and 0.79 ± 0.1 mL *vs* 568 ± 97 mL and 0.79 ± 0.13, respectively ($P = 0.423$ and $P = 0.919$, Mann Whitney *U* test).

RV/TLV
Mean left RV/TLV was 35.8% ± 3.9%. Non-MHV ($n = 59$) and MHV-containing ($n = 12$) remnants (34.1% ± 3% *vs* 36% ± 4% respectively, $P = 0.148$ Mann Whitney *U* test) showed no significant differences.

Correlation between donor RVBWR *vs* RV/TLV in defining SFS-remnants
We assessed the concordance between RVBWR < 0.65 and RV/TLV < 30% in all 71 right graft donors (Table 2).

Twenty-five percent ($n = 2/8$) of SFS-remnants had RVBWR < 0.65 with RV/TLV < 30%. 94% ($n = 59/63$) of non-SFS-remnants had RVBWR $\geqslant$ 0.65 and RV/TLV $\geqslant$ 30%. Eight SFS-remnants with RVBWR < 0.65 had a significantly smaller RV/TLV than 63 non-SFS-remnants with RVBWR $\geqslant$ 0.65 [SFS: RV/TLV 32.4% (range: 28%-35.7%) *vs* non-SFS: RV/TLV 36.2% (range: 26.1%-45.5%), $P < 0.009$, Mann Whitney *U* test] Figure 1A.
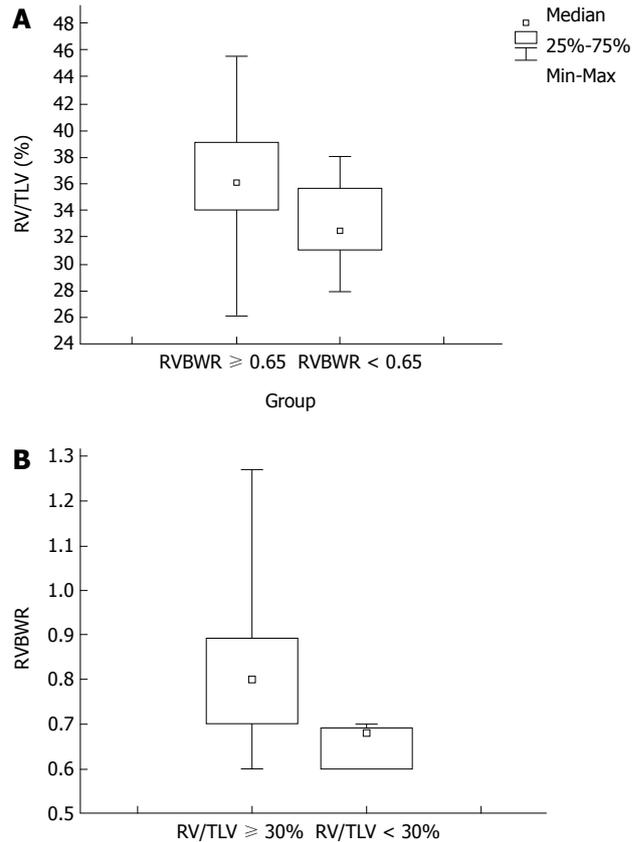

Figure 1 Correlation between remnant-volume-(donor) body-weight ratio (< 0.65 *vs* $\geqslant$ 0.65) and remnant volume percentage of total liver volume in left remnants of 71 right graft donors (A) and correlation between remnant volume percentage of total liver volume (< 30% *vs* $\geqslant$ 30%) and remnant-volume-(donor) body-weight ratio in the left remnants of 71 right graft donors (B). RV/TLV: Remnant volume percentage of total liver volume; RVBWR: Remnant-volume-(donor) body-weight ratio.

Thirty-three percent ($n = 2/6$) of SFS-remnants had RV/TLV < 30% with RVBWR < 0.65. 92% ($n = 60/65$) of non-SFS-remnants had RV/TLV $\geqslant$ 30% and RVBWR $\geqslant$ 0.65. Six SFS-remnants with RV/TLV < 30% had significantly smaller RVBWR than 65 non-SFS-remnants with RV/TLV $\geqslant$ 30% [0.65 (range: 0.6-0.7) *vs* 0.8 (range: 0.6-1.27), $P < 0.01$, Mann Whitney *U* test] Figure 1B.

Congestive volume-index and non-congestive RVBWR
Mean overall congestive volume (CV) was 209.2 ± 77.6 mL (range: 40-459 mL) with a CV-index of 36.9 ± 11.6 %RV (range: 6.1-70.2 %RV). Mean non-congestive [safely drained by the left hepatic vein (LHV)] donor RVBWR (0.48 ± 0.12, range: 0.2-0.79) was significantly smaller than the corresponding donor RVBWR (safely drained by both MHV and LHV) (0.79 ± 0.12, range: 0.6-1.27, $P < 0.0001$, Wilcoxon's signed ranks test).

Liver function laboratory markers
Non-MHV containing remnants had a higher (although *P* values were very close) peak total bilirubin and INR

Peak (mean ± SD)	Remnants MHV	Remnants Non-MHV	Remnants RV/TLV ≥ 30%	Remnants RV/TLV < 30%
	n = 12	*n* = 59	*n* = 65	*n* = 6
Bilirubin (0.2-1.2)	4.26 ± 2.86	5.54 ± 7.89	4.39 ± 3.92	5.1 ± 2.9
	P = 0.544		*P* = 0.27	
INR (1.0)	1.99 ± 0.52	2.15 ± 0.83	1.87 ± 0.44	2.02 ± 0.57
	P = 0.9		*P* = 0.587	

Table 3 Comparison of early postoperative biochemical liver function markers among right graft donors (*n* = 71)

RV/TLV: Remnant volume percentage of total liver volume; MHV: Middle hepatic vein; INR: International normalized ratio; Bili: Total bilirubin (reference value 0.2-1.2).

than MHV-containing remnants (potentially suggesting a "negative effect" of venous congestion in the early postoperative liver function) (Table 3).

Postoperative donor morbidity
There were no donor deaths. Overall postoperative donor morbidity was 15.5% (*n* = 11), including 6 (8.4%) grade III-IV Dindo-Clavien complications[23]. There was no significant difference among remnants with (*n* = 3, 25%) or without (*n* = 8, 13.6%) MHV under their diverse volume conditions (*P* = 0.4077, chi-square). Five medical complications included: 2 pleural effusions (1 in an MHV- and 1 in a non-MHV remnant) requiring drainage (D-II), 1 pneumonia in a non-MHV remnant (D-II), and 2 reversible liver failures (D-IVA). Six surgical morbidities included 2 bile leaks (1 in a non-MHV- and 1 in an MHV remnant) associated with bilomas and treated with percutaneous drainage (D-IIIA), 1 IVC thrombosis treated surgically in a non-MHV remnant (D-IIIB), 1 subphrenic abscess drained operatively in a non MHV remnant (D-IIIB), and 2 superficial wound infections (D-IA).

Association of MHV management and remnant liver failure in donors
Two (2.8%) donors developed reversible liver failure (see SFSS definition). Neither of them had a history of liver disease, experienced any adverse intraoperative events, or developed surgical/medical complications. Postoperative color doppler ultrasonography confirmed intact porto-arterial inflow and hepatic venous outflow.

Case-1: 40 year old female, BMI 26, liver biopsy < 10% steatosis, normal preoperative LFTs. MHV-containing remnant with safely (MHV + LHV)-drained-RVBWR of 0.63 (RV = 434 mL, RV/TLV = 35%). Postoperatively developed grade 2° encephalopathy, with peak Bilirubin of 26.5mg/dl and INR of 3.7. Recovered completely after two courses of plasmapheresis.

Case 2: 44-year-old male, BMI 27, liver biopsy < 10% steatosis, normal preoperative LFTs. Non-MHV-containing remnant with RVBWR of 0.65 (RV = 584

mL = RV/TLV 31%). RV safely drained by LHV of 344 mL (CV-index = 40.2%), with safely (LHV)-drained-RVBWR of 0.39. Postoperatively developed grade 2° encephalopathy, with peak bilirubin of 19.8 mg/dL and INR of 2.5. Recovered spontaneously after a hospital stay of 26 d.

MHV management in remnants with liver failure vs without liver failure
Our stepwise 3D-CT volumetry combined estimated left remnant congestive- and non-congestive volumes following virtual liver partition (Figure 2). Based on the experience of the Kyoto and Nagoya groups[12,13], the extremely low (25%-33%) concordance between donor RVBWR and RV/TLV, and the two reversible remnant liver failures in our series, we differentiated between right grafts inclusive of complete MHV and left remnants with selective MHV-4A retention by considering individual MHV anatomy patterns[16].

In 12 donors, the MHV was completely retained with the left remnants, providing an intact two-sectorial venous (MHV + LHV) drainage. In 10 cases, a risky dominant (d)-MHV type was preserved because of its particularly large congestive volume when compared to the non-dominant (nd)-MHV (d-MHV mean CV-index 41.2 ± 6.6 %RV *vs* nd-MHV mean CV-index 36.1 ± 12.2 %RV, *P* = 0.07, Mann-Whitney *U* test). In 2 donors with nd-MHV, the decision to retain the MHV with the left remnant was based on their small donor RVBWR-RV/TLV constellation (0.6/28.2% and 0.63/35%, Table 4).

The left sided MHV-4A drainage territory was preserved in 4 of 59 donors who underwent procurement of MHV-containing grafts as originally described by our group[15]. This decision was based on an extremely small non-congestive-RVGWR (0.2-0.27) (safely drained by LHV) in 2 cases (Table 4) and on the anatomical characteristics of the MHV-4A/MHV-8 confluence into the MHV trunk in the other 2 instances.

Two (20%) of ten donors with estimated very small RVBWR ≤ 0.65 (inclusive of two with RV/TLV < 30%) developed reversible liver failure. The MHV was retained in two remnants (one with liver failure). Eight remnants (one with liver failure) had no MHV. In three non-liver failure remnants with extremely low non-congestive-RVBWR < 0.3 (safely drained by LHV), the MHV was completely retained or the MHV-4A drainage was preserved in the remnant liver (Table 4).

DISCUSSION
Although a RV/TLV of at least 30%-35% is usually required to avoid small-for-size syndrome (SFSS)[1,4,8], successful outcomes with RV/TLV < 30% have been reported in the setting of optimal liver quality[6,7,11,24]. Inclusion of the MHV with right grafts, which has been reported to optimize graft function[1,4,7,25] but to potentially impair remnant recovery[1,26-28], has both
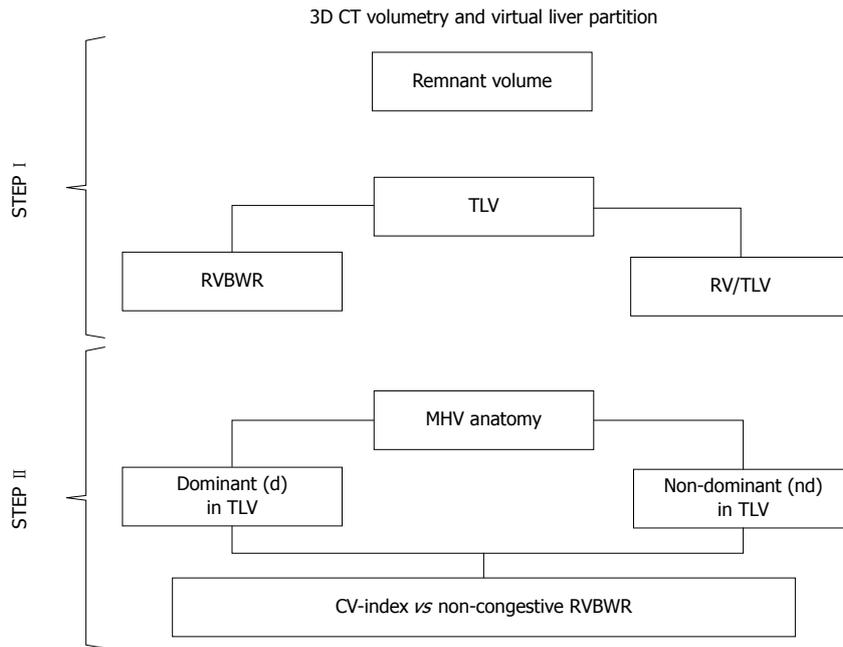
3D CT volumetry and virtual liver partition

Figure 2 Stepwise 3D-computed tomography volumetry and virtual liver partition assessing congestive- and non-congestive (remnant) volumes. CV-index: Congestive volume percentage of remnant liver volume; 3-D: Three-dimensional; d: Dominant; MHV: Middle hepatic vein; nd: Non-dominant; RV/TLV: Remnant volume percentage of total liver volume; RVBWR: Remnant-volume-(donor) body-weight ratio; non-congestive-RVBWR: Safely LHV drained remnant-volume-body-weight ratio; TLV: Total liver volume.

Table 4 Middle hepatic vein management in small-for-size -remnants with remnant-volume (donor) body-weight-ratio ≤ 0.65

Donor n = 71	Remnant Total MHV preserved	Remnant MHV-4A preserved	Remnant volume	Remnant RV/TLV	Remnant RVBWR	Remnant CV-index	Remnant nc-RVBWR (LHV)	SFSS
1	Yes	Yes	434 mL	35%	0.63	37.9%	0.38	Yes
2	No	No	584 mL	31%	0.65	40.2%	0.39	Yes
3	No	No	512 mL	32.9%	0.62	40.0%	0.40	No
4	No	No	500 mL	31.7%	0.64	37.2%	0.38	No
5	No	Yes	429 mL	35.1%	0.60	67.9%	0.20	No
6	No	No	506 mL	38%	0.65	14.8%	0.57	No
7	No	Yes	536 mL	35.6%	0.62	43.4%	0.27	No
8	No	No	505 mL	32%	0.63	39.4%	0.49	No
9	No	No	389 mL	28%	0.60	24.4%	0.41	No
10	Yes	Yes	464 mL	28.2%	0.60	55.4%	0.20	No

SFS: Small-for-size; SFSS: Small-for-size syndrome; LDLT: Live donor liver transplantation; MHV: Middle hepatic vein; MHV-4A: Branch of MHV draining left medial sector; LHV: Left hepatic vein; RVBWR: Remnant-volume (donor) body-weight-ratio; Non-congestive-(nc)-RVBWR: Volume safely drained by LHV; RV/TLV: Remnant volume percentage of total (donor) liver volume; CV-index: Potential congestion volume percentage of remnant liver volume.

supporters and detractors[2,7,8,27,29-34]. Currently, many centres encourage a selective MHV management policy based on individual graft/remnant characteristics[4,7,12].

Our series allowed us to conclude that procurement of right grafts including complete MHV itself did not cause a significant volume loss in remnants. Indeed, there were no significant RV, RV/TLV and RVBWR differences between remnants with and without MHV. We attributed this result to our "carving" liver partitioning technique, in which the transection plane exposed the MHV trunk on the resection surface of either graft (MHV-harvest) or remnant (MHV-retention) livers. There was no difference in donor morbidity attributable to SFS-remnant-status or MHV inclusion

(even with RVBWR and RV/TLV below the respective marginal limits of < 0.6 and < 30%).

Our overall donor morbidity of 15.5% including 8.4% of Dindo-Clavien Ⅲ-Ⅳ type complications were comparable with the data reported in the literature[5,7,12].

In the Kyoto series overall 10% of donors suffered morbidity with similar incidence of complications who required treatment between (-) MHV (13%) *vs* (+) MHV (9%) remnants[12]. Comparable, in our donors the incidence of postoperative interventions did not considerably differ between the non-MHV (5.1%) and the MHV-contained (8.3%) remnants. In line with the cited reports, all our donors returned to

their pre-donation lifestyles. The subgroup analysis of the Istambul series[7] revealed a much higher overall complication rate in non-MHV (22.4%) *vs* MHV-contained remnants (7.8%) mirroring our own experience with the tendency for (-) MHV remnants to have more complications than (+) MHV ones (25% *vs* 14%).

Furthermore, our experience as well as that of others did not reveal any late complications attributable to remnant size or MHV-status[7,35]. Our virtual data however, showed that the "sacrifice" of the left sided MHV-4A/B drainage in remnants due to MHV inclusion with the graft was associated with large congestive volumes (CV-index of 36.9 ± 11.6 %RV) that resulted in a significant reduction of non-congestive volumes (non-congestive-RVBWR) safely drained by LHV. We also observed a potentially (not statistically significant) detrimental effect of venous congestion in non-MHV remnants as illustrated by their elevated liver function markers (INR, total bilirubin) in the early postoperative period. These observations strongly correlate with previous published reports.

In the study of the Clischy group[5] segment Ⅳ congestion was never seen on the postoperative CT in donors who underwent a standard MHV-exclusive right graft harvest, while in the setting of the extended right graft inclusive of MHV procurements 84% remnants revealed venous congestion with the morbidity rate of 37%. Yaprak *et al*[11] had observed that RV/TLV ⩽ 30% impacted donor outcome (especially postoperative hyperbilirubinemia and major complications) irrespective of donor RVBWR (< 0.6 or > 0.6). In their experience, RVBWR < 0.6 significantly affected liver function but not donor morbidity. In a prospective study by Dayangac *et al*[7], procurement of right grafts inclusive of MHV was not associated with any additional donor risk except in SFS-remnants with RV/TLV < 30% (57% complication rate and prolonged postoperative hyperbilirubinemia). Others showed an association between small remnant volume and donor morbidity[1,11,36,37]. In our series the slightly higher bilirubin and INR levels in SFS-remnants probably resulted from a small RV.

The impact of remnant volume and remnant MHV-status on remnant regeneration has been extensively investigated. Belghiti *et al*[1] observed that a small RV accelerated early tissue regeneration, decreasing the proportion of functional liver tissue and increasing the risk of liver failure. Dayangac *et al*[7] showed that small non-MHV remnants had a significantly higher volume increase after the first postoperative week when compared to MHV remnants (76% and 50%, respectively). Similarly to our data, studies from several other groups showed that the volume regeneration rate of the total remnant liver (TLV) did not significantly differ among extended and regular right graft hepatectomies[7,38,39]. However, the observed compensatory lateral hyper-growth effect attributable to transient venous congestion in the MHV drainage area seems to reflect a competition between sectors, with the lateral one dominating regardless of remnant MHV status[40]. The development of a procoagulant state induced by the intense remnant regeneration as described by the Paris group might help explain the Ⅳ C thrombosis in one of our donors[1].

Our study revealed a very poor concordance between donor RVBWR and RV/TLV cut offs in SFS remnants (25%-33% in our series). Preoperative volume assessment based solely on RV/TLV can be misleading, particularly when compared to RVBWR of remnant volume and donor BMI[41]. RVBWR was also found to be more specific than RV/TLV as a predictor of postoperative outcomes in hepatic resections with SFS remnants[6]. Yigitler *et al*[42] observed a poor correlation between RV/TLV ⩽ 30% and RVBWR < 0.6 for SFS remnants after major hepatic resections. In a retrospective analysis by Yaprak *et al*[11], remnants with marginal RVBWR < 0.6 and RV/TLV ⩽ 30% constellation had the highest (52.2%) donor morbidity. However, their observation was not reproduced in our marginally small remnants.

Reversible liver failure occurred in MHV-inclusive as well as in non-MHV remnants with remnant volumes much above the commonly accepted limits (RVBWR 0.63-0.65 and RV/TLV 31%-35%). A retrospective analysis of virtual and clinical data confirming a non-steatosis in all donors on preoperative liver biopsy suggested that extensive venous congestion (CV-index of 40.2% RV) likely accounted for liver failure in case-2 [a non-MHV remnant with a tightly calculated functional reserve (non-congestive-RVBWR) of 0.39]. On the contrary, in case-1 (liver failure in an MHV-inclusive-remnant with intact bi-sectorial venous drainage *via* MHV + LHV, no plausible explanation could be found. A small-for-size syndrome (SFSS) is a multifactorial process primarily associated with insufficient functional liver mass that constitutes a life-threatening condition for both donors and recipients[22]. Although, a "safe" donor RVBWR-RV/TLV constellation seems to be the most effective parameter in donor selection and remnant MHV management, "liver quality" and "remnant volumes" are by no means dogmatic parameters[11,43]. The "venous congestion" and *vice versa* "non-congestive volume" association is potentially a strong additional factor[44].

The main goal of our study was to evaluate MHV management safety parameters to prevent life-threatening liver failure in MHV inclusive-right graft donors. As venous congestion in the drainage territories of MHV-4A/B branches can occur after procurement of right grafts containing MHV, congestive and non-congestive volume characteristics for each remnant should be carefully considered when making a decision on safe MHV management in donors.

Our study also showed that 10 of 12 retained MHV remnants had risky dominant d-MHV anatomy, with

considerably large CV-index when compared to nd-MHV, that required complete preservation of the MHV in the left remnants. Based on our learning curve experience (including two lethal SFSS grafts[14] and two reversible SFSS remnants) and the experiences of other groups[12,13], we followed an "exclusion" scheme aimed at identifying high risk donors unsuitable for MHV-inclusive grafts. The main finding distinguishing our series from previous ones is that MHV inclusion with right grafts is not (by itself) associated with prohibitively small remnant volumes. We individualized MHV management by determining MHV-4A/B drained congestive and safely LHV drained non-congestive volume components.

All donors with (extremely small) non-congestive-RVBWR < 0.3 underwent successfully either complete MHV- or MHV-4A remnant-preserving right graft procurements. The two donors with reversible liver failure in our series portray an enormous risk potential. Further validation of our findings with a systematic prospective clinical study will be required.

Our final conclusions include: (1) prevention of liver failure in MHV inclusive right graft donors involves consideration of both congestive and non-congestive remnant volumes; (2) MHV management should be individually based on MHV anatomy characteristics; (3) non-congestive volumes represent an important safety parameter in MHV management, especially in the setting of SFS remnants; and (4) the RVBWR-RV/TLV constellation seems to have a synergistic (complementary) capacity for the identification of marginally small remnants with the highest risk potential of postoperative liver failure.

COMMENTS

Background
The accurate magnitude of graft and remnant volumes comprises the most critical parameter to preclude postoperative donor and recipient liver failure in adult live donor liver transplantation (ALDLT). Middle hepatic vein (MHV)-containing grafts are correlated with small remnants whose function may be further compromised by immediate postoperative venous congestion of their medial sector (segment 4A/B). The incident of small-for-size syndrome (SFSS) in donors as a result of ineffective functional remnant volume is a steady notice of the dispute encompassing venous congestion and MHV management.

Research frontiers
Current virtual data, disclosed that the "sacrifice" of the left sided MHV-4A/B drainage in remnants due to MHV inclusion with the graft was related with large congestive volumes (CV-index of 36.9 ± 11.6 %RV) that gave rise to a significant reduction of non-congestive volumes (non-congestive-RVBWR) securely drained by LHV. The authors likewise noted a potentially harmful outcome of venous congestion in non-MHV remnants as demonstrated by their elevated liver function tests (INR, total bilirubin) in the early postoperative period.

Innovations and breakthroughs
As yet, there are no published studies connecting the magnitude of functional impairment and parenchymal congestion in non-MHV containing remnants, and remnant volume limits for secure MHV enclosure with the right graft are still indeterminate.

Applications
MHV management in adult live donor liver transplantation should be individually based on MHV anatomy characteristics.

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