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ORIGINAL ARTICLE

Comparison of surgical methods in liver transplantation: retrohepatic caval resection with venovenous bypass (VVB) versus piggyback (PB) with VVB versus PB without VVB

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Summary

Use of piggyback technique (PB) and elimination of venovenous bypass (VVB) have been advocated in adult liver transplantation (LT). However, individual contribution of these two modifications on clinical outcomes has not been fully investigated. We performed a retrospective review of 426 LTs within a 3-year period, when three different surgical techniques were employed per the surgeons' preference: retrohepatic caval resection with VVB (RCR + VVB) in 104 patients, PB with VVB (PB + VVB) in 148, and PB without VVB (PB-Only) in 174. The primary outcomes were intraoperative blood transfusion and the patient and graft survivals. Demographic profiles were similar, except younger recipient age in RCR + VVB and fewer number of grafts with cold ischemic time over 16 h in PB-Only. PB-Only required lesser intraoperative red blood cells ($P = 0.006$), fresh frozen plasma ($P = 0.005$), and cell saver return ($P = 0.007$); had less incidence of acute renal failure ($P = 0.001$), better patient survival ($P = 0.039$), and graft survival ($P = 0.003$). The benefits of PB + VVB were only found in shortened total surgical time ($P = 0.0001$) and warm ischemic time ($P = 0.0001$), and less incidence of acute renal failure ($P = 0.001$) than RCR + VVB. PB-Only method seemed to provide the best clinical outcome. The benefit of PB was not fully achieved when it was used with VVB.

Introduction

The pros and cons of venovenous bypass (VVB) in adult liver transplantation (LT) have often been debated [1], especially when comparing the classic retrohepatic caval resection technique (RCR) [2] with VVB to the retrohepatic caval preservation technique, or 'piggyback' technique (PB) [3] without VVB. A recent comprehensive review of the reported benefits and drawbacks of VVB in modern adult LT confirms the existence of the controversy, which is testified by the great diversity among centers in their use of VVB [4]. The reported advantages of PB without VVB include: shorter surgical time [5], shorter anhepatic phase [5], shorter warm ischemic time [6,7], reduction in blood products transfused [6,7], and lower total cost of the operative procedure [6,7].

The question remains whether these reported benefits are attributed solely to the difference in the implantation technique (PB versus RCR) or due to the elimination of VVB. The main goal of this retrospective analysis was to elucidate the individual clinical impact of PB and that of the elimination of VVB, respectively, on the outcomes of adult patients who underwent LT.

Methods

After the approval of the local institutional review board (IRB), the prospectively recorded clinical and laboratory data was reviewed and analyzed in a retrospective fashion.

The requirement for written informed consent was waived by the IRB.

Study population

We studied adult patients who underwent LT at our institution within a 3-year period (January 1, 2001–December 31, 2003). Only primary, isolated, deceased donor, adult (age ≥18 years) LTs were included. Patients were excluded if they had fulminant hepatic failure, were undergoing retransplantation, or required LT with combined cardiac procedures or combined organ transplantations.

Surgical methods and selection

Three different surgical techniques were used for LT during the study period: (i) the classic retrohepatic caval resection technique with VVB (RCR + VVB), (ii) the PB technique with VVB (PB + VVB), and (iii) the PB technique without VVB (PB-Only). None of the case was performed with RCR without VVB. No patient received a temporary portocaval shunt [8] during the period.

The choice of surgical technique depended on the surgeon's preference in each case. The relative contraindications to perform PB technique during this period were: (i) the main hepatic veins were obliterated; (ii) no suitable retrohepatic vena cava remained for PB technique due to previous surgeries; (iii) extremely dense adhesion to the vena cava. All PB anastomoses were performed based on the technique reported by Tzakis *et al.* [3] The donor suprahepatic inferior vena cava was anastomosed to the confluence of the recipient's hepatic veins with ligation of the donor infrahepatic inferior vena cava. None of the modified PB techniques including infrahepatic vena cavocavostomy [9] or the side-to-side inferior vena cava anastomosis by Belghiti [10–13] were used. During the study period, 12 attending transplant surgeons, each with more than 5 years of transplantation experience, participated in the LT program. All of the attending surgeons performed the majority of the surgeries. Among them, eight surgeons who performed all three surgical techniques were included in the study. The other four surgeons with a total of 21 LTs were excluded from the analysis because they only performed one or two of the three surgical techniques.

Revascularization of the grafts was achieved sequentially (the portal venous flow first, followed by the hepatic arterial flow).

Anesthetic management and intraoperative monitoring

Eight designated attending transplant anesthesiologists were involved in the intraoperative management of LT during the study period. Packed red blood cell (PRBC) was administered to keep hematocrit between 26% and 30%. A cell saver was routinely used throughout LT, except on recipients with hepatocellular carcinoma or other hepatic malignant lesions. Fresh frozen plasma (FFP), platelets, and cryoprecipitate were indicated based on thromboelastography (TEG) and findings on the surgical field. TEG was performed in the standardized schedule including the baseline (after the induction of the general anesthesia); 15 min prior to the graft reperfusion; and 5, 30, 90 min after the reperfusion. Antifibrinolytics were indicated only when fibrinolysis was confirmed by TEG. In such cases, epsilon-aminocaproic acid 100–500 mg intravenously or continuous intravenous infusion of aprotinin (Trasylol®; Bayer Pharmaceuticals Co., West Haven, CT, USA) at 10 ml (100 000 KIU)/h was used. The choice between the two regimens depended on the attending transplant anesthesiologists' preference. No patients received a prophylactic dose of aprotinin.

For VVB, after induction of general anesthesia of the recipient, the anesthesiology team inserted a percutaneous return cannula in the internal jugular vein. The surgical team inserted a venous blood drainage cannula in the femoral vein and a portal blood drainage cannula in the stump of the portal vein. The details of the cannula insertion techniques and anesthesia care were described in our previous report [14,15]. Transesophageal echocardiography (TEE) and a pulmonary artery catheter with continuous thermodilution cardiac output monitoring were included as standard intraoperative monitors in all recipients.

Preoperative factors

All clinical data were prospectively collected, recorded, and maintained in the transplantation center. The recipients' preoperative data included age, gender, model for end-stage liver disease (MELD) score [16], etiology of end-stage liver disease, other co-morbidities include diabetes mellitus, coronary arterial disease, hypertension, chronic obstructive pulmonary disease, end-stage renal disease requiring hemodialysis, baseline serum creatinine, and hematocrit. The donor data were summarized to identify the number of extended criteria donor (ECD) grafts in each group. The quality of the liver graft is classified as an ECD with the following criteria: (i) donation after cardiac death, (ii) age >65 years, (iii) serum sodium level >155 mEq/l, (iv) donor liver macrosteatosis ≥30% on biopsy, (v) cold ischemia time >16 h, or (vi) warm ischemia time >90 min [17].

Intraoperative factors

Intraoperative data included the total duration of the transplantation, cold ischemic time, warm ischemic time,

Table 1. Choice of the surgical techniques.

Surgeons	Total number of LT performed	RCR + VVB	PB + VVB	PB-Only
A	111	68 (61.3)	38 (34.2)	5 (4.5)
B	90	8 (8.9)	13 (14.4)	69 (76.7)
C	76	6 (7.9)	20 (26.3)	50 (65.8)
D	58	8 (13.8)	27 (46.6)	23 (39.7)
E	50	4 (8.0)	30 (60.0)	16 (32.0)
F	16	5 (31.3)	3 (18.8)	8 (50.0)
G	15	1 (6.7)	13 (86.7)	1 (6.7)
H	10	4 (40.0)	4 (40.0)	2 (20.0)
Total	426	104 (24.5)	148 (34.7)	174 (40.8)

Values in parenthesis are expressed in percent (%) of total cases per surgeon.

LT, liver transplantation; RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass.

units of transfused blood products (PRBC, FFP, platelet, and cryoprecipitate, respectively) and the amount of cell saver return. The total units of blood products transfused during the perioperative period, which was defined as the period from the induction of anesthesia to 24 h post-LT, were also analyzed. The result of the TEG was summarized as coagulation index (CI) and the incidence of lysis. The CI was calculated as follows:

$$\mathrm{CI} = -0.3258 \times R - 0.1886 \times K + 0.1224 \times \alpha + 0.0759 \times \mathrm{MA} - 7.7922,$$

where R is the reaction time (minutes), K is the time to reach 10 mm in amplitude (minutes), α is the alpha angle (degree), MA is the maximum amplitude (mm). The lysis was determined by more than 8% fibrinolysis at 30 min after the TEG achieved the maximum amplitude.

The incidence of postreperfusion syndrome [18,19], systemic hypotension (defined as systolic blood pressure <80 mmHg), and administration of catecholamines (epinephrine and dopamine) were recorded. The collective values of central venous pressure (measured by Swan–Ganz catheter) were recorded in the three stages (stage I, II, and III).

Intraoperative complications were collected and summarized. Cardiac arrest was defined as such when closed or open cardiac massage was required. Pulmonary embo-

Table 2. Preoperative data of recipients.

	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	ANOVA	Chi-square test
Recipient age (years)	50.9 ± 10.1‡§	55.4 ± 9.3	54.0 ± 9.1	0.0009	–
Recipient male/female (%)	70.2/29.8	64.9/35.1	57.8/42.2	–	0.09
MELD Score	16.1 ± 6.7	14.5 ± 5.7	15.5 ± 6.4	0.2	–
Postnecrotic cirrhosis	76.0% (79)	81.1% (120)	84.5% (147)	–	0.2
Hepatitis C	(38)	(45)	(65)	–	–
Alcoholic	(20)	(41)	(40)	–	–
Cryptogenic	(5)	(14)	(19)	–	–
Other	(16)	(20)	(23)	–	–
Cholestatic liver disease	14.4% (15)	12.8% (19)	12.1% (21)	–	0.9
Other liver disease	9.6% (10)	6.1% (9)	3.4% (6)	–	–
Budd-Chiari	2	0	0	–	–
Malignant lesions*	5.8% (6)	6.8% (10)	4.6% (8)	–	0.7
Diabetes mellitus	22.1% (23)	27.0% (40)	24.1% (47)	–	0.7
Coronary arterial disease	14.4% (15)	19.6% (29)	18.4% (32)	–	0.6
Hypertension	21.2% (22)	28.4% (42)	22.4% (39)	–	0.3
COPD	12.5% (13)	10.1% (15)	6.9% (12)	–	0.3
Hemodialysis	4.8% (5)	1.4% (2)	2.9% (5)	–	0.3
Creatinine (mg/dl)	0.8 (0.4, 5.3)	0.8 (0.5, 4.2)	0.9 (0.4, 6.2)	0.4†	–
Hematocrit (%)	30.6 ± 5.6	30.7 ± 5.3	31.0 ± 5.9	0.8	–

Data is presented as mean ± SD, percentage per the group (number of cases), or median (minimum, maximum).

RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; ANOVA, analysis of variance (Bonferroni); MELD, the model for end-stage liver disease; COPD, chronic obstructive pulmonary disease.

*Malignant lesions included both hepatocellular carcinoma (HCC), which co-existed in the other liver disease, and non-HCC.

†Kruskal–Wallis test was used.

‡Significantly less than PB + VVB.

§Significantly less than PB-Only.

Table 3. Demographic data of donors.

	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	ANOVA	Chi-square test
Age (years)	47.1 ± 16.6	49.3 ± 17.7	45.3 ± 18.0	0.1	–
Age >65 years	17.3% (18)	20.3% (30)	15.5% (27)	–	0.5
DCD status	4.8% (5)	9.5% (14)	8.0% (14)	–	0.4
Serum sodium (mEq/l)	147 ± 7	147 ± 9	145 ± 9	0.1	–
Serum sodium >155	13.5% (14)	14.9% (22)	14.9% (26)	–	0.9
Macrosteatosis ≥30%	3.9% (3)	3.4% (5)	2.3% (4)	–	0.8
CIT >16 h	16.3% (17)	8.1% (12)	5.2% (9)*	–	0.006
WIT >90 min	0	0	0.6% (1)	–	n/a
ECD status	46.2% (48)	46.6% (69)	35.6% (62)	–	0.09

Data is presented as mean ± SD or percentage per the group (number of cases).
RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; ANOVA, analysis of variance (Bonferroni); DCD, donation after cardiac death; CIT, cold ischemic time; WIT, warm ischemic time; ECD, extended criteria donor.
*Significantly less than RCR + VVB.

lism was diagnosed clinically with (i) sudden onset of systemic hypotension with elevated pulmonary arterial pressures, and (ii) identification of blood clots in the right atrium and/or the right ventricle or acutely dilated right ventricle with empty left ventricle by TEE. Acute lung injury was defined as $PaO_2/F_IO_2 < 60$ mmHg. A liver graft function was defined as 'poor' if bile production was not detected during LT.

Postoperative factors

Postoperative outcomes included the length of stay in intensive care unit (ICU), the length of stay in hospital, the incidence of re-intubation for mechanical ventilation, the incidence of acute renal injury (increase of postoperative serum creatinine ≥2 times more than the preoperative serum creatinine) and acute renal failure (increase of

Table 4. Intraoperative data: duration of the surgery, blood transfusion.

Total	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	ANOVA [Kruskal–Wallis]
Total operation time (h)	8.9 ± 2.2	7.5 ± 1.8*	7.6 ± 1.8*	0.0001
Cold ischemic time (h)	11.8 ± 3.5	11.3 ± 3.1	10.4 ± 3.0*†	0.005
Warm ischemic time (min)	43.4 ± 7.9	30.2 ± 7.0*‡	35.1 ± 10.0*	0.0001
PRBC (units)				
Intraop.	9 (0, 80)	8.5 (0, 91)	7 (0, 40)*†	[0.006]
Periop.	10 (0, 86)	10 (0, 93)	8 (0, 45)*†	[0.002]
FFP (units)				
Intraop.	8 (0, 79)	8 (0, 80)	6 (0, 40)*	[0.005]
Periop.	9 (0, 79)	9 (0, 82)	6 (0, 46)*	[0.005]
Platelet (units)				
Intraop.	11.5 (0, 40)	6 (0, 71)	7 (0, 36)	[0.4]
Periop.	11.5 (0, 48)	12 (0, 77)	8 (0, 42)	[0.5]
Cryo. (units)				
Intraop.	0 (0, 42)	0 (0, 36)	0 (0, 30)	[0.2]
Periop.	0 (0, 42)	0 (0, 54)	0 (0, 30)*	[0.03]
Cell Saver (L)	2.2 (0, 61.0)	1.5 (0, 48.6)	1.1 (0, 16.0)*	[0.007]

Data is presented as mean ± SD or median (minimum, maximum).
RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; ANOVA, analysis of variance (Bonferroni); RPBC, packed red blood cell; LT, liver transplantation; FFP, fresh frozen plasma; Cryo., cryoprecipiate; Intraop., the intraoperative period; Periop., the perioperative period (from the induction of the anesthesia to 24 h post-transplantation).
*Significantly less than RCR + VVB.
†Significantly less than PB + VVB;
‡Significantly less than PB-Only.

Table 5. Intraoperative data: thromboelastography.

	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	ANOVA	Chi-square test
Base					
CI	−1.6 ± 4.5	−1.0 ± 3.6	−2.1 ± 3.9*	0.04	–
Lysis	1.0% (1)	2.7% (4)	2.3% (4)	–	0.6
III − 15					
CI	−3.2 ± 5.8	−3.6 ± 7.3	−3.0 ± 4.9	0.6	–
Lysis	8.7% (9)	16.3% (24)	4.6% (8)*	–	0.002
III + 5					
CI	−10.2 ± 8.3	−8.4 ± 9.4	−8.8 ± 8.4	0.3	–
Lysis	33.7% (35)	27.0% (40)	22.4% (39)	–	0.2
III + 30					
CI	−11.1 ± 9.6*	−8.0 ± 7.7	−9.5 ± 10.4	0.04	–
Lysis	14.4% (15)	8.1% (12)	11.5% (20)	–	0.23
III + 90					
CI	−7.2 ± 7.3	−5.4 ± 8.8	−6.3 ± 6.0	0.2	–
Lysis	4.8% (5)	4.1% (6)	2.3% (4)	–	0.5

Data is presented as mean ± SD or percentage per the group (number of cases).

RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; ANOVA, analysis of variance (Bonferroni); CI, coagulation index; III-15, 15 min prior to reperfusion; III + 5, 5 min after the onset of stage III; III + 30, 30 min after the onset of stage III; III + 90, 90 min after the onset of stage III.

*Significantly less than PB + VVB.

postoperative serum creatinine ≥3 times more than the preoperative serum creatinine) which were defined by RIFLE (risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function and end-stage kidney disease) criteria [20]. The requirement of re-exploration of the abdominal wound and the incidence of hepatic arterial thrombosis were recorded. Recipients who failed to survive at 30-days after LT were identified and the main cause of death was determined. Also, the causes of death of the patients from 1 month to 1 year post-LT and those from 1 year to 3 years post-LT were analyzed respectively.

The patient and graft survivals were recorded. Loss of a graft due to death of the recipient was included in the failure of graft survival.

Subset analysis of the non-ECD

To examine the effect of the three surgical techniques in the non-ECD population, the subset analysis was performed excluding ECD donors from each group. Patient and graft survivals, requirement of intraoperative and perioperative blood transfusions, total operation time, cold ischemic time, and warm ischemic time were compared.

Data analysis

Categorical variables were analyzed using Pearson's chi-square test or Fisher's exact test as appropriate. Comparison of continuous values among three groups was performed using the analysis of variance with *post hoc* test using Bonferroni method, or Kruskal–Wallis test with *post hoc* test using Dunn's multiple comparison method for the data with non-parametric distribution. The overall survival of the patients and the grafts were compared using Log-rank (Mantel-Cox) test among the three groups. The 30-day, 1-year, and 3-year survivals of patients and grafts were also compared using Pearson's chi-square test. The level of significance was set at $P < 0.05$. Statistical analysis was performed using GRAPHPAD PRISM 5 (GraphPad Software, Inc., La Jolla, CA, USA). Continuous data were presented as mean ± SD or median with range (minimum, maximum).

Results

Study population and selection of the surgical techniques

Of the patients receiving LT, 426 recipients fulfilled the inclusion criteria and were therefore used for further analysis. Of these patients, 104 (24.5%) underwent LT with RCR + VVB, 148 (34.7%) with PB + VVB, and 174 (40.9%) with PB-Only. The eight attending transplant surgeons performed these three techniques based on their preference (Table 1).

Preoperative factors

Three groups were similar in preoperative recipient demography, except the recipients were significantly younger in RCR + VVB (Table 2). Only two cases of Budd-Chiari syndrome were found in the entire series; both of them underwent LT using RCR + VVB. No other recipients who were retrospectively considered to be relatively contraindicated for PB technique were found. In the donor demographic data (Table 3), the incidence of the long cold ischemic time (>16 h) was significantly less in PB-Only compared to RCR + VVB, however, ECD status were similar ($P = 0.09$).

Intraoperative factors

Use of PB technique (PB + VVB and PB-Only) demonstrated significantly shorter operation time, cold ischemic time, and warm ischemic time compared to RCR + VVB (Table 4).

Elimination of VVB (PB-Only) led to the decrease of both the intraoperative and the perioperative transfusions of PRBC and FFP, and cell saver return (Table 4).

Table 6. Intraoperative data: hemodynamic parameters and usage of catecholamines.

	RCR + VVB (n = 104)s	PB + VVB (n = 148)	PB-Only (n = 174)	ANOVA	Chi-square test
Stage I					
CVP mmHg (start)	7.6 ± 2.9	7.7 ± 2.7	7.1 ± 2.8	0.1	–
CVP mmHg (end)	13.8 ± 3.5	14.2 ± 3.4	14.2 ± 3.4	0.6	–
CVP mmHg (mean)	10.4 ± 3.0	11.0 ± 2.9	10.6 ± 2.7	0.2	–
Hypotension	10.6% (11)	14.2% (21)	17.8% (31)	–	0.3
Epinephrine	0% (0)	0% (0)	0% (0)	–	–
Dopamine	5.8% (6)	9.5% (14)	8.6% (15)	–	0.6
Stage II					
CVP mmHg (start)	5.5 ± 3.0	5.3 ± 3.3	5.6 ± 3.0	0.6	–
CVP mmHg (end)	13.1 ± 3.0	11.5 ± 3.4*	11.2 ± 3.6*	0.001	–
CVP mmHg (mean)	8.8 ± 2.9	8.1 ± 3.3	8.3 ± 2.9	0.2	–
Hypotension	20.2% (21)	12.8% (19)*	6.9% (12)*	–	0.005
Epinephrine	14.4% (15)	4.7% (7)*	2.3% (4)*	–	0.0002
Dopamine	30.8% (32)	37.8% (56)	37.9% (66)	–	0.4
Stage III					
CVP mmHg (start)	7.8 ± 2.9	7.7 ± 2.5	7.2 ± 2.5	0.1	–
CVP mmHg (end)	13.7 ± 3.5	14.3 ± 3.2	13.6 ± 3.1	0.1	–
CVP mmHg (mean)	10.5 ± 3.0	10.8 ± 2.7	10.3 ± 2.6	0.2	–
PRS	51.9% (54)	45.9% (68)	47.7% (83)	0.14	–
Epinephrine	39.4% (41)	48.0% (71)	35.6% (62)	–	0.08
Dopamine	48.1% (50)	44.6% (66)	55.7% (97)	–	0.1

Data is presented as mean ± SD or percentage per the group (number of cases).
RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; ANOVA, analysis of variance (Bonferroni); CVP, central venous pressure; PRS, postreperfusion syndrome.
*Significantly less than RCR + VVB.

Reduction of cryoprecipitate became statistically significant in the perioperative period in PB-Only group (Table 4).

In terms of CI in TEG (Table 5), the baseline was significantly hypocoagulable in PB-Only compared to PB + VVB; however, it was RCR + VVB which became significantly more hypocoagulable than PB + VVB at 30 min after the reperfusion. The incidence of fibrinolysis was significantly high in PB + VVB compare to PB-Only at 15 min before the graft reperfusion.

Hemodynamic data revealed that PB techniques (PB + VVB and PB-Only) had significantly less incidence of hypotension and less use of epinephrine in stage II (Table 6). No statistically significant difference was found in the intraoperative complications among the three groups (Table 7).

Table 7. Intraoperative complications.

Total	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	Chi-square test
Death	2.9% (3)	1.4% (2)	0% (0)	0.09
Cardiac arrest	4.8% (5)	2.7% (4)	4.6% (8)	0.6
Pulmonary embolism	3.8% (4)	0.7% (1)	0.6% (1)	0.053
Acute lung injury	1.9% (2)	1.4% (2)	0.6% (1)	0.6
Poor graft function	8.7% (9)	11.5% (17)	7.5% (13)	0.5

Data is presented as percentage per the group (number of cases).
RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass.

Postoperative factors

Among the transplantation surgery survivors, PB-Only had significantly shorter ICU stay, less incidence of re-intubation due to respiratory failure, and less incidence developing acute renal failure compared to the VVB groups (RCR + VVB and PB + VVB), while PB + VVB had a less incidence of acute renal failure compared to RCR + VVB (Table 8). PB-Only also had significantly less 30-day graft loss and a trend toward less 30-day mortality compared to those in the VVB groups (Table 9). The main causes of death of the recipients in 30 days after the transplantation were pulmonary complications and multi-organ failure (Table 9). After 1-month post-transplantation, the main causes of death of the recipients including sepsis, multi-organ failure, recurrent hepatitis C infection, and cardiovascular disease (Table 10). There was no significant difference in the causes of death among the three

Table 8. Postoperative data.

	RCR + VVB (n = 100)*	PB + VVB (n = 147)*	PB-Only (n = 174)	ANOVA [Kruskal–Wallis]	Chi-square test
ICU stay (days)	5 (2, 128)	6 (2, 105)	4 (2, 70)†	[0.004]	–
Hospital stay (days)	15 (7, 185)	15 (7, 126)	13 (7, 98)	[0.3]	–
Re-intubation	30.0% (30)	26.7% (39)	16.1% (28)¶**	–	0.002
Post/pre creatinine	2.6 ± 1.8	2.5 ± 1.9	1.9 ± 0.9¶**	0.0007	–
Acute renal injury	21.1% (20)†	23.4% (34)‡	17.8% (30)§	–	0.5
Acute renal failure	34.7% (33)†	24.8% (36)‡§	15.4% (26)§¶**	–	0.001
Re-exploration	21.0% (21)	28.1% (41)	17.8% (31)	–	0.08
Hepatic artery thrombosis	2.0% (2)	3.4% (5)	0% (0)	–	0.06

RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass.

*Only the intraoperative survivors were included. Data is presented as median (minimum, maximum), percentage per the group (number of cases) or mean ± SD.

†Include only 95 recipients, due to exclusion of five recipients with preoperative hemodialysis.

‡Include only 145 recipients, due to exclusion of one recipients with preoperative hemodialysis.

§Include only 169 recipients, due to exclusion of five recipients with preoperative hemodialysis.

¶Significantly less than RCR + VVB.

**Significantly less than PB + VVB.

groups (Table 10). Overall recipient survival and graft survival were significantly better in PB-Only than in the two VVB groups (Figs 1 and 2).

Subset analysis of the non-ECD

Exclusion of the ECD population yielded the subset of the recipients with non-ECD grafts in RCR + VVB (n = 56), in PB + VVB (n = 79), and in PB-Only (n = 112). Significant reductions in duration of the total operation time, the cold ischemic time, and the warm ischemic time were demonstrated in usage of PB (Table 11). In terms of blood transfusion, a significant reduction was found only in the perioperative PRBC transfusion in PB-Only compared to that in PB + VVB. Although the overall patient survival did not have any significant difference, the same trend of significantly improved survival in PB-Only was found in 1 year and 3-year patient survivals as in the ECD combined population (Fig. 3). The overall graft survival was significantly better in PB-Only as in the ECD combined population (Fig. 4).

Discussion

Over the last decade, the effects of retrohepatic caval preservation – or PB technique – on patient outcomes have been reported from observational studies [7,21–31] and by two small prospective randomized studies [6,32]. These results generally indicate that PB technique has advantages over the classic retrohepatic caval resection (RCR) technique, including shorter operating time, lower transfusion requirement, and shorter intensive care unit stay.

The limitation of the previous studies was the use of VVB in both surgical techniques. In seven retrospective studies, the use of VVB was not regulated (20–100% in the RCR group vs. 0–44% in the PB group) [7,22–27]. In another six studies, including two small prospective randomized trials [6,32], RCR + VVB was compared to PB-Only [6,28–32]. In these studies, the reported benefits of the PB technique over the RCR technique could be partially attributed to the elimination of VVB in the PB group. One retrospective report by Stieber *et al.* [27] compared 66 cases with the RCR + VVB (although four cases underwent LT without VVB) versus 128 cases with PB + VVB. In this study, PB + VVB showed reduced usage of blood products.

Our report is the largest single center study that evaluated the three major surgical methods of LT: RCR + VVB, PB + VVB, and PB-Only. This study was not a randomized one and the choice of surgical technique depended solely on the eight participating transplant surgeons. We excluded fulminant hepatic failure and retransplantation from this study because these conditions could potentially dictate the surgical method of choice. All of the 426 LTs were performed in a relatively short period of time (in a period of 3 years) under the care of the same providers, which minimized the potential variability of the patients' management.

Under the use of VVB, PB + VVB had significantly shorter duration of total operation time and the warm ischemic time than RCR + VVB. These findings are consistent with other reports of the benefits of the PB

Table 9. Summary of 30-day mortality and graft loss, the causes of death after liver transplantation.

Total	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	Chi-square test
30-day patient mortality (%)	8.7	6.8	2.3	0.051
30-day graft loss (%)	12.5	11.5	3.4†‡	0.008

ID	Age/Sex	MELD	DX	Date of death*	Date of redo LT*	Cause of death	Intraoperative complications
RCR + VVB							
1	67 M	20	PNC-E	0	–	PE	PE (CA)
2	53 F	11	PNC-E	0	–	PE	PE (CA)
3	70 M	17	PNC-NASH	0	–	PRS	PRS (CA)
4	54 F	11	PBC	1	–	ALI	PRS, PNF, ALI
5	48 M	16	PNC-C	2	1	PE/ALI	PE (CA), ALI (ECMO), PNF
6	51 M	13	PNC-C	7	3	PNF/PE	None
7	56 F	11	PNC-E	9	–	Intracranial bleeding	None
8	49 F	16	PNC-E	10	–	MOF (rejection)	PRS, Severe fibrinolysis
9	45 F	15	PNC-C	17	–	MOF	Poor graft function
PB + VVB							
1	59 F	9	PBC	0	–	PE	PE (CA)
2	52 M	7	PNC-drug	1	1	ALI	ALI (ECMO), PNF
3	54 M	15	PNC-E	1	–	ALI	PNF, Severe fibrinolysis, ALI
4	56 M	15	PNC-E	3	–	MOF	Poor graft function
5	64 M	17	Metabolic	3	–	Sudden Death	None
6	47 F	6	PNC-E	6	1	ALI	PRS (CA), PNF
7	71F	22	PBC	13	–	MOF	Myocardial infarction
8	44 F	12	PNC-C	19	1	MOF (sepsis)	PNF
9	38 F	18	Biliary complication	19	–	MOF (sepsis)	None
10	56 M	14	PNC-E	24	–	MOF (sepsis)	None
PB-Only							
1	50 M	18	PNC-C	2	2	ALI	PRS (CA), ALI (ECMO), PNF
2	49 F	6	Primary malignancy	6	6	MOF	PNF
3	47 M	11	PNC-C	20	–	MOF (sepsis)	PE (CA)
4	54 M	13	PNC-E	29	–	MOF (sepsis)	None

MELD, model for end-stage liver disease; DX, diagnosis of the liver disease; LT, liver transplantation; RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; M, male; F, female; PNC-E, postnecrotic cirrhosis due to alcohol; PNC-NASH, postnecrotic cirrhosis due to nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PNC-C, postnecrotic cirrhosis due to hepatitis C; PE, pulmonary embolism; PRS, postreperfusion syndrome; ALI, acute lung injury; PNF, primary nonfunctioning liver graft; MOF, multiple organ failure; CA, cardiac arrest; ECMO, extracorporeal membrane oxygenation.

*Date after the initial liver transplantation.

†Significantly less than RCR + VVB.

‡Significantly less than PB + VVB.

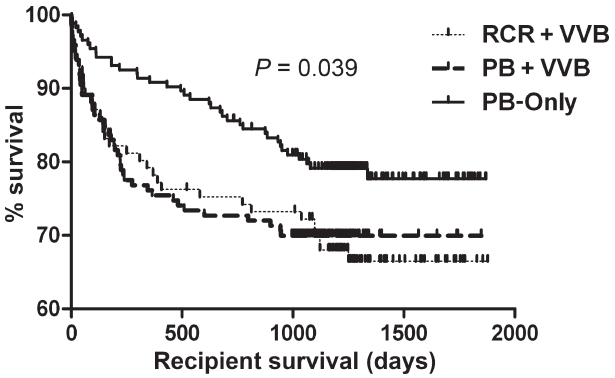
technique [6,28]. This is likely explained by the elimination of one anastomosis (between the infra-hepatic vena cava of the graft to the inferior vena cava of the recipient). We did not find a difference in the blood transfusion requirement or the patient and graft survival between these two methods, although the incidence of acute renal failure in RCR + VVB was significantly higher than PB + VVB. There were some modest clinical benefits in PB + VVB over RCR + VVB: lesser hypo-coagulable state at III + 30, lesser incidence of hypotension and use of epinephrine in stage II. However, our study indicated that the use of PB + VVB offered only a few clinical benefits for the outcome of LT compared with RCR + VVB.

On the other hand, under the use of the PB method, elimination of VVB (PB-Only versus PB + VVB) demonstrated shorter cold ischemic time, less requirement of PRBC, and shorter ICU stay, less incidence of re-intubation and acute renal failure. As the result, PB-Only demonstrated improved overall survivals of the recipients and the grafts than those of the use of VVB (PB + VVB and RCR + VVB). These survival trends were also confirmed in the non-ECD groups in the subset analysis.

Table 10. Causes of a longer term mortality.

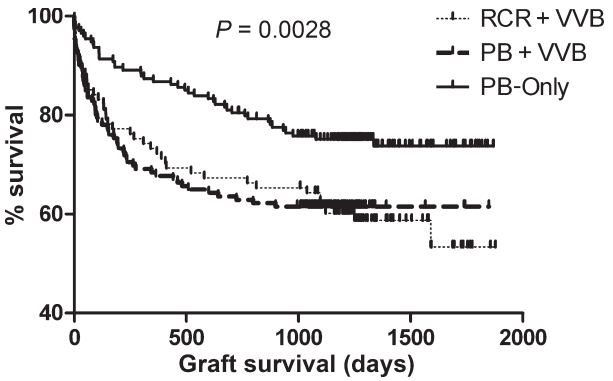
No. patients at risk (1 month–1 year; 1 year-3 years)	RCR + VVB (95; 80)	PB + VVB (138; 111)	PB-Only (170; 158)	Chi-square test
Total number of death	15; 7	27; 8	12†‡; 20	0.04; 0.3
Sepsis	4; 2	12; 1	4; 4	0.5; 0.7
MOF	2; 2	5; 2	3; 3	0.7; 0.7
Recurrent HCV	1; 0	5; 0	0; 4	0.2; 0.2
CVD	2; 2	1; 3	0; 2	0.3; 0.2
Hemorrhage	2; 0	3; 0	1; 1	0.9; 0.7
HCC	1; 0	0; 1	1; 1	0.3; 0.6
Graft failure	1; 0	0; 0	2; 1	0.1; 0.7
Renal failure	0; 0	0; 1	0; 1	n.a.; 0.6
Trauma	0; 0	0; 0	1; 1	0.2; 0.6
Other malignancy	0; 0	0; 0	0; 1*	n.a.; 0.2
HAT	1; 0	0; 0	0; 0	0.3; n.a.
GVHD	1; 0	0; 0	0; 0	0.3; n.a.
PTLD	0; 0	1; 0	0; 0	0.6; n.a.
Suicide	0; 1	0; 0	0; 0	n.a.; 0.1
Unknown	0; 0	0; 0	0; 1	n.a.; 0.2

RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; HCV, hepatitis C virus; CVD, cardiovascular disease; MOF, multiple organ failure; HCC, hepatocellular carcinoma; HAT, hepatic arterial thrombosis; GVHD, graft-versus-host disease; PTLD, post-transplant lymphoproliferative disease; n.a., not available.
*Lung cancer.
†Significantly less than RCR + VVB.
‡Significantly less than PB + VVB.



	RCR + VVB (n = 56)	PB + VVB (n = 79)	PB-Only (n = 112)	X^2 test
30-day patient survival (%)	92.9%	93.5%	96.4%	0.4
1-year patient survival (%)	76.8%*	79.2%*	93.6%	0.003
3-year patient survival (%)	71.4%*	74.0%*	88.2%	0.01

Figure 1 The overall patient survival after liver transplantation. RCR+VVB, retrohepatic caval resection technique with venovenous bypass; PB+VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass. *Significantly less than PB-Only.



	RC R+ VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	X^2 test
30-day patient survival (%)	91.3%	93.2%	97.7%	0.05
1-year patient survival (%)	76.0%*	79.7%*	93.1%	0.0001
3-year patient survival (%)	71.2%*	76.4%*	85.1%	0.02

Figure 2 The overall graft survival after liver transplantation. RCR+VVB, retrohepatic caval resection technique with venovenous bypass; PB+VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass. *Significantly less than PB-Only.

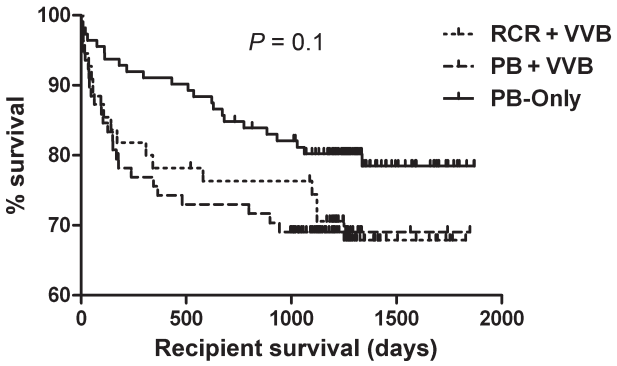
Taken together, elimination of VVB seems to have more clinical benefits over the use of the PB technique *per se*. In other words, the potential clinical benefits of the PB technique could be best achieved by elimination of VVB. With the modern refinement of surgical technique [10,11], majority of the adult LTs can nowadays be performed using retrohepatic caval preservation techniques without the use of VVB [12,13].

This is the first study to show statistically significant survival benefits using PB-Only technique compared with RCR + VVB [6,28–32] or PB + VVB [27]. The elucidation of the mechanisms for the clinical benefits of elimination of VVB was beyond the scope of this study; however, VVB has been known to activate complement system [33–36], inflammatory cytokines, and adhesion molecules [37], which lead to hemodynamic derangement [36,38], and to activate hemostatic factors [39], which may contribute to thromboembolism, acute lung injury, and multiple-organ failure [38,40]. Indeed, the major causes of deaths of the recipients in 30 days in all groups were characterized by pulmonary thromboembolism, cardiac arrest after graft reperfusion, acute lung injury, and multiple organ failure (Table 9); therefore, elimination of VVB might further prevent activation of the above mentioned molecular pathways and may result in an improved clinical outcome. Although a recent small randomized study failed to demonstrate any significant difference between RCR + VVB ($n = 16$) versus PB-Only ($n = 16$) in the level of endotoxin in the artery, in the portal vein, or in the hepatic vein samples during LT

Table 11. Subset analysis of non-ECD population: duration of the surgery, blood transfusion.

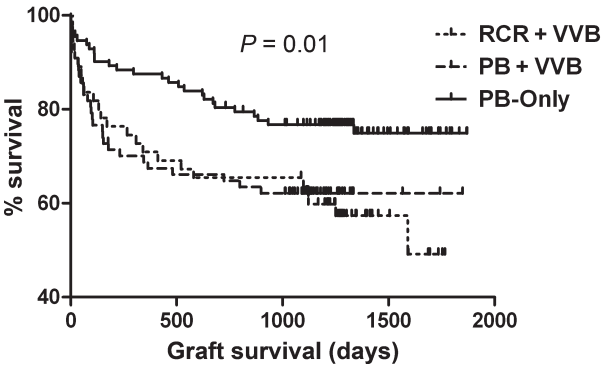
Total	RCR + VVB (n = 56)	PB + VVB (n = 79)	PB-Only (n = 112)	ANOVA [Kruskal–Wallis]
Total operation time (h)	9.0 ± 2.2	7.6 ± 1.6*	7.6 ± 1.9*	0.0001
Cold ischemic time (h)	10.5 ± 2.7	10.8 ± 2.9	9.7 ± 2.6†	0.04
Warm ischemic time (min)	43.8 ± 7.9	30.5 ± 6.9*‡	36.0 ± 11.1*	0.0001
PRBC (units)				
Intraop.	8 (0, 80)	8 (0, 55)	7 (0, 40)	[0.08]
Periop.	9 (0, 86)	9 (0, 64)	8 (0, 45)†	[0.03]
FFP (units)				
Intraop.	7 (0, 79)	7 (0, 45)	6 (0, 40)	[0.2]
Periop.	8 (0, 79)	8 (0, 45)	6 (0, 46)	[0.06]
Platelet (units)				
Intraop.	12 (0, 40)	6 (0, 30)	7 (0, 36)	[0.4]
Periop.	12 (0, 48)	12 (0, 44)	8 (0, 42)	[0.3]
Cryo. (units)				
Intraop.	0 (0, 42)	0 (0, 24)	0 (0, 30)	[0.3]
Periop.	0 (0, 42)	0 (0, 24)	0 (0, 30)	[0.06]
Cell saver (L)	1.5 (0, 48.0)	1.2 (0, 10.0)	1.1 (0, 16.0)	[0.1]

Data is presented as mean ± SD or median (minimum, maximum).
RCR + VVB, retrohepatic caval resection technique with venovenous bypass; PB + VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass; ANOVA, analysis of variance (Bonferroni); RPBC, packed red blood cell; LT, liver transplantation; FFP, fresh frozen plasma; Cryo., cryoprecipiate; Intraop., the intraoperative period; Periop., the perioperative period (from the induction of anesthesia to 24 h post-transplantation).
*Significantly less than RCR + VVB.
†Significantly less than PB + VVB.
‡Significantly less than PB-Only.



	RCR + VVB (n = 56)	PB + VVB (n = 79)	PB-Only (n = 112)	X^2 test
30-day graft survival (%)	89.3%	89.6%	94.5%	0.3
1-year graft survival (%)	76.8%*	75.3%*	90.9%	0.009
3-year graft survival (%)	71.4%*	71.4%*	84.5%	0.0002

Figure 3 The patient survival in nonextended criteria donor population after liver transplantation. RCR+VVB, retrohepatic caval resection technique with venovenous bypass; PB+VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass. *Significantly less than PB-Only.



	RCR + VVB (n = 104)	PB + VVB (n = 148)	PB-Only (n = 174)	X^2 test
30-day graft survival (%)	87.5%*	88.5%*	96.6%	0.008
1-year graft survival (%)	75.0%*	73.6%*	89.7%	0.0004
3-year graft survival (%)	70.2%	70.2%	80.5%	0.06

Figure 4 The graft survival in nonextended criteria donor population after liver transplantation. RCR+VVB, retrohepatic caval resection technique with venovenous bypass; PB+VVB, piggyback technique with venovenous bypass; PB-Only, piggyback technique without venovenous bypass. *Significantly less than PB-Only.

[41], such transient increases of endotoxin in the systemic circulation, as was demonstrated in the study [41], may affect more in the outcome of VVB groups. Of note, VVB and its cannula insertion also carry potential risks including air embolization, wound infection, lymphorrhea, and peripheral nerve damage, although the wound

complications can be minimized with the use of percutaneous cannula insertion technique [14].

There are several important limitations in this study. First, and most importantly, it was a nonrandomized, retrospective observational study, therefore, the potential of selection bias of the procedures cannot be excluded. However, given the logistic difficulty of performing a prospective, randomized study to compare all three procedures, we believe this study was the best possible attempt to propose a meaningful hypothesis of the benefits of the PB method and elimination of VVB in LT. Second, we acknowledge that we only employed three of the four potential methods. The fourth important technique, RCR without VVB, was not performed during the period; therefore, it was not included in the comparison. RCR without VVB is employed as a standard technique in several centers. Third, the average MELD score in this particular study period was lower than the other era in this institution, which was the average MELD of 20 in 2004–2006 [14]. This seems to be due to the change of the practice in this particular era. However, this particular period had to be chosen for this study due to relatively balanced distribution of the three techniques to achieve the three-way comparison of the techniques. Fourth, a 30-day morality of 5% in our series appears rather high, despite relatively low MELD score of the study population. This seemed due to the aggressive usage of the ECDs in this particular period; therefore, we employed the subset-analysis excluding all the ECDs in our study.

In summary, this retrospective, observational study suggests that the combination of retrohepatic caval preservation (PB) with elimination of VVB has clinical benefits over the classic RCR with VVB or the PB technique with VVB in adult primary isolated deceased donor LT. We found that the benefit of the PB technique was decreased when it was combined with VVB.

Authorship

TS and RMP: designed study. TS, TM and JWM: collected data. TS: wrote paper. TM, JWM and IAH: reviewed paper.

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References

1. Hilmi IA, Planinsic RM. CON: venovenous bypass (VVB) use in orthotopic liver transplantation (OLT). *J Cardiothorac Vasc Anesth* 2006; **20**: 744.
2. Starzl TE, Iwatsuki S, Van Thiel DH, *et al.* Evolution of liver transplantation. *Hepatology* 1982; **2**: 614.
3. Tzakis A, Todo S, Starzl TE. Orthotopic liver transplantation with preservation of the inferior vena cava. *Ann Surg* 1989; **210**: 649.
4. Fonouni H, Mehrabi A, Soleimani M, Müller SA, Büchler MW, Schmidt J. The need for venovenous bypass in liver transplantation. *HPB (Oxford)* 2008; **10**: 196.
5. Hosein Shokouh-Amiri M, Osama Gaber A, Bagous WA, *et al.* Choice of surgical technique influences perioperative outcomes in liver transplantation. *Ann Surg* 2000; **231**: 814.
6. Jovine E, Mazziotti A, Grazi GL, *et al.* Piggy-back versus conventional technique in liver transplantation: report of a randomized trial. *Transpl Int* 1997; **10**: 109.
7. Lerut JP, Molle G, Donataccio M, *et al.* Cavocaval liver transplantation without venovenous bypass and without temporary portocaval shunting: the ideal technique for adult liver grafting? *Transpl Int* 1997; **10**: 171.
8. Davila D, Bartlett A, Heaton N. Temporary portocaval shunt in orthotopic liver transplantation: need for a standardized approach? *Liver Transpl* 2008; **14**: 1414.
9. Khanmoradi K, Defaria W, Nishida S, *et al.* Infrahepatic vena cavocavostomy, a modification of the piggyback technique for liver transplantation. *Am Surg* 2009; **75**: 421.
10. Belghiti J, Panis Y, Sauvanet A, Gayet B, Fékété F. A new technique of side to side caval anastomosis during orthotopic hepatic transplantation without inferior vena caval occlusion. *Surg Gynecol Obstet* 1992; **175**: 270.
11. Navarro F, Le Moine MC, Fabre JM, *et al.* Specific vascular complications of orthotopic liver transplantation with preservation of the retrohepatic vena cava: review of 1361 cases. *Transplantation* 1999; **68**: 646.
12. Mehrabi A, Mood ZA, Fonouni H, *et al.* A single-center experience of 500 liver transplants using the modified piggyback technique by Belghiti. *Liver Transpl* 2009; **15**: 466.
13. Lerut J, Ciccarelli O, Roggen F, *et al.* Cavocaval adult liver transplantation and retransplantation without venovenous bypass and without portocaval shunting: a prospective feasibility study in adult liver transplantation. *Transplantation* 2003; **75**: 1740.
14. Sakai T, Planinsic RM, Hilmi IA, Marsh JW. Complications associated with percutaneous placement of venous return cannula for venovenous bypass in adult orthotopic liver transplantation. *Liver Transpl* 2007; **13**: 961.

15. Sakai T, Gligor S, Diulus J, McAffee R, Wallis JM, Planinsic RM. Insertion and management of percutaneous veno-venous bypass cannula for liver transplantation: a reference for transplant anesthesiologists. *Clin Transplant* 2009; DOI: 10.1111/j.1399-0012.2009.01145.x.
16. Kamath PS, Kim WR, Advanced Liver Disease Study Group. The model for end-stage liver disease (MELD). *Hepatology* 2007; **45**: 797.
17. Hilmi I, Horton CN, Planinsic RM, *et al.* The impact of postreperfusion syndrome on short-term patient and liver allograft outcome in patients undergoing orthotopic liver transplantation. *Liver Transpl* 2008; **14**: 504.
18. Aggarwal S, Kang Y, Freeman J, DeWolf AM, Begliomini B. Is there a post-reperfusion syndrome? *Transplant Proc* 1989; **21**: 3497.
19. Aggarwal S, Kang Y, Freeman JA, Fortunato FL Jr, Pinsky MR. Postreperfusion syndrome: hypotension after reperfusion of the transplanted liver. *J Crit Care* 1993; **8**: 154.
20. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2004; **8**: R204.
21. Nishida S, Nakamura N, Vaidya A, *et al.* Piggyback technique in adult orthotopic liver transplantation: an analysis of 1067 liver transplants at a single center. *HPB (Oxford)* 2006; **8**: 182.
22. Hesse UJ, Berrevoet F, Troisi R, *et al.* Hepato-venous reconstruction in orthotopic liver transplantation with preservation of the recipients' inferior vena cava and veno-venous bypass. *Langenbecks Arch Surg* 2000; **385**: 350.
23. Reddy KS, Johnston TD, Putnam LA, Isley M, Ranjan D. Piggyback technique and selective use of veno-venous bypass in adult orthotopic liver transplantation. *Clin Transplant* 2000;**14**:370.
24. Busque S, Esquivel CO, Concepcion W, So SK. Experience with the piggyback technique without caval occlusion in adult orthotopic liver transplantation. *Transplantation* 1998; **65**: 77.
25. González FX, García-Valdecasas JC, Grande L, *et al.* Vena cava vascular reconstruction during orthotopic liver transplantation: a comparative study. *Liver Transpl Surg* 1998; **4**: 133.
26. Koveker G, Viebahn R, Schott U, Judt-Stelzer G, Becker HD, Lauchart W. Does piggy-back liver transplantation have a detrimental effect on venous drainage? – a comparative duplex ultrasound study *Langenbecks Arch Chir Suppl Kongressbd* 1996; **113**: 402.
27. Stieber AC. One Surgeon's experience with piggyback versus the standard technique in orthotopic liver transplantation: is one better than the other? *Hepatogastroenterology* 1995; **42**: 403.
28. Miyamoto S, Polak WG, Geuken E, *et al.* Liver transplantation with preservation of the inferior vena cava. A comparison of conventional and piggyback techniques in adults. *Clin Transplant* 2004; **18**: 686.
29. Shokouh-Amiri MH, Grewal HP, Vera SR, *et al.* Eighteen years of experience with adult and pediatric liver transplantation at the University of Tennessee, Memphis. *Clin Transplant* 2000; **14**: 255.
30. Cabezuelo JB, Ramírez P, Ríos A, *et al.* Risk factors of acute renal failure after liver transplantation. *Kidney Int* 2006; **69**: 1073.
31. Khan S, Silva MA, Tan YM, *et al.* Conventional versus piggyback technique of caval implantation; without extracorporeal veno-venous bypass. A comparative study. *Transpl Int* 2006; **19**: 795.
32. Isern MR, Massarollo PC, de Carvalho EM, *et al.* Randomized trial comparing pulmonary alterations after conventional with venovenous bypass versus piggyback liver transplantation. *Liver Transpl* 2004; **10**: 425.
33. Lew PD, Forster A, Perrin LH, *et al.* Complement activation in the adult respiratory distress syndrome following cardiopulmonary bypass. *Bull Eur Physiopathol Respir* 1985; **21**: 231.
34. Chenoweth DE, Cooper SW, Hugli TE, Stewart RW, Blackstone EH, Kirklin JW. Complement activation during cardiopulmonary bypass: evidence for generation of C3a, C5a anaphylatoxins. *N Engl J Med* 1981; **304**: 497.
35. Hammerschmidt DE, Weaver LJ, Hudson LD, Craddock PR, Jacob HS. Association of complement activation and elevated plasma C5a with adult respiratory syndrome, Pathological relevance and possible prognostic value. *Lancet* 1980; **1**: 947.
36. Segal H, Sheikh S, Kallis P, *et al.* Complement activation during major surgery: the effect of extracorporeal circuits and high-dose aprotinin. *J Cardiothorac Vasc Anesth* 1998; **12**: 542.
37. Tomasdottir H, Bengtson JP, Bengtsson A. Neutrophil and macrophage activation and anaphylatoxin formation in orthotopic liver transplantation without the use of venovenous bypass. *Acta Anaesthesiol Scand* 1996; **40**: 250.
38. Függer R, Hamilton G, Steininger R, Mirza D, Schulz F, Mühlbacher F. Intraoperative estimation of endotoxin, TNFα and IL-6 in orthotopic liver transplantation and their relation to rejection and postoperative infection. *Transplantation* 1991; **52**: 302.
39. Sundsmo JS, Fair DS. Relationship among the complement, kinin, coagulation and fibrinolytic system. *Springer Semin Immunopathol* 1983; **6**: 231.
40. Frank MM. Complement in the pathophysiology of human disease. *N Engl J Med* 1987; **316**: 1525.
41. Abdala E, Baía CE, Mies S, *et al.* Bacterial translocation during liver transplantation: a randomized trial comparing conventional with venovenous bypass vs. piggyback methods. *Liver Transpl* 2007; **13**: 488.