

ORIGINAL ARTICLE

Conventional versus piggyback technique of caval implantation; without extra-corporeal veno-venous bypass. A comparative study

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Summary

Conventional orthotopic liver transplantation (CON-LT) involves resection of recipient cava, usually with extra-corporeal circulation (veno-venous bypass, VVB), while in the piggyback technique (PC-LT) the cava is preserved. Along with a temporary portacaval shunt (TPCS), better haemodynamic maintenance is purported with PC-LT. A prospective, consecutive series of 384 primary transplants (2000–2003) were analysed, 138 CON-LT (with VVB) and 246 PC-LT (54 without TPCS). Patient/donor characteristics were similar in the two groups. PC-LT required less usage of fresh-frozen plasma and platelets, intensive care stay, number of patients requiring ventilation after day 1 and total days spent on ventilator. The results were not different when comparing, total operating and warm ischaemia time (WIT), red cell usage, requirement for renal support, day 3 serum creatinine and total hospital stay. TPCS had no impact on outcome other than WIT ($P = 0.02$). Three patients in PC-LT group (three of 246;1.2%) developed caval outflow obstruction ($P = 0.02$). There was no difference in short- or long-term graft or patient survival. PC-LT has an advantage over CON-LT using VVB with respect to intraoperative blood product usage, postoperative ventilation requirement and ITU stay. VVB is no longer required and TPCS may be used selectively in adult transplantation.

Introduction

Conventional orthotopic liver transplantation (CON-LT) with resection of the native liver of the recipient, together with the retro hepatic inferior vena cava (IVC) and interposition of the donor IVC attached to the new graft, has been the common surgical approach in liver transplantation [1]. This usually requires extra-corporeal veno-venous bypass (VVB), with the potential hazard of large bore venous cannulation in the setting of coagulopathy. In addition to requiring trained personnel and equipment, disadvantages of VVB include thromboembolic events, hypothermia and significant complications, related to line removal (lymph leaks, neuropraxia, bleeding).

Application of the supra-hepatic caval clamp can cause right phrenic nerve paresis resulting in right-sided pleural effusions [2,3].

Although reported by pioneers in liver transplantation in the early 1960s [4], Tzakis *et al.* in 1989, were the first to adopt the novel technique of piggyback cavocavoplasty (PC-LT) [5,6]. During total hepatectomy, the full-length of the recipient IVC is preserved. Subsequently, a side-to-side or end-to-side anastomosis of the donor IVC to the preserved recipient IVC provides venous continuity. The advantages reported for piggyback techniques are a shorter operation time [7], shorter anhepatic phase [7], shorter warm ischaemia time (WIT) and a reduction of blood loss [8,9]. By the preservation of caval blood flow to the

heart, patient haemodynamics are also kept more stable and kidney function is better preserved. Also there is a reduction in cost of the operative procedure [8,9]. Additionally, many centres currently using PC-LT technique consider VVB redundant. The potential problem of occlusion of splanchnic flow without VVB can be overcome by creating a temporary portocaval shunt (TPCS) to maintain portal flow [6,10]. Consequently the PC-LT has become increasingly popular among liver transplantation centres all over the world. The potential disadvantage of PC-LT is a higher risk of venous outflow obstruction (piggyback syndrome, PBS) [11].

There have been many reports on the use of PC-LT and its benefits over the use of CON-LT, especially if concurrent VVB was used, including two small randomized-controlled trials (RCTs) comparing the two methods [8]. Some of these reports resulted in conflicting outcomes and were all on cohorts <100 liver transplants each [15]. Between 1982 and 2001 the preferred method of caval reconstruction in our unit was CON-LT. In February 2002, in the light of emerging reports, the practice was changed to PC-LT. The aim of this study was to report a single centre's larger experience with PC-LT compared with our previous experience with CON-LT. In particular, we analysed the impact of this change on perioperative parameters, renal function, ventilatory support, complications and outcome, with a view to resolving some of the controversies that exist.

Methods

Data for this nonrandomized study was prospectively collected and analysed retrospectively. Consecutive primary liver transplants between April 2000 and March 2003, were analysed. From February 2002, the majority of transplants were carried out using PC-LT in accordance with change of unit practice. These resulted in the PC-LT group. It was considered comparing consecutive series within a relatively short space of 3 years would reduce the confounding error of improvement of surgical techniques with time. All surgical procedures were either performed by consultant surgeons or under their direct supervision. Surgical technique utilized for CON-LT and PC-LT have previously been described [1,12]. All PC-LT were side-to-side cavocavostomies. Reperfusion of the graft was achieved sequentially (portal followed by arterial). Venovenous bypass was utilized in all of the CON-LT procedures. TPCS (end-to-side) was used in all acute liver failure recipients and those without established chronic collateral porto-caval shunts, judged intraoperatively. All grafts were procured from heart-beating brain-dead ABO compatible donors using standard donor procurement techniques. The grafts were flushed and preserved

in University of Wisconsin (UW) preservation solution. All recipients included in this study were followed up until death or 30 June 2004, whichever occurred first.

Data collected for the donors included: age, body mass index (BMI) and hepatic biochemistry. Recipients parameters studied were: age, prognostic markers of survival – Child-Pugh grade/score [13] and its individual parameters, Model for End-stage Liver Disease (MELD) score [14], serum creatinine, hepatic biochemistry and indication for transplantation. Perioperative factors analysed were, total operating time, cold and WIT and blood product usage (packed allogeneic and autologous red blood cells were transfused to maintain haematocrit between 0.25 and 0.30). Data collected for postoperative parameters were, number of days in the intensive care unit (ITU), requirement for ventilatory/renal support and inpatient stay. Day 3 serum creatinine and highest aspartate aminotransferase (AST) were also studied postoperatively. Long-term survival and graft function (primary nonfunction, failure, histological chronic rejection and episodes of hepatic artery thromboses) were documented.

Cumulative patient and graft survival rates were calculated using Kaplan–Meier's plots with log-rank test. Categorical variables were analysed using the Pearson's chi-square test or the Fisher's exact test. Comparison of medians and mean values between two groups were performed using the Mann–Whitney *U*-test and the independent sample *t*-test or the Spearman rank correlation test (as appropriate). The level of significance was set at $P = 0.05$. Statistical analysis was performed using the SPSS/PC+ Advanced Statistics Package, version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

During the 3-year study period a total of 384 consecutive liver transplants were carried out. These included 138 CON-LT and 246 PC-LT. In the PC-LT group 192 patients (78%) underwent a perioperative TPCS. Patients were followed up for 17.2 months (median; interquartile range: 0.5–35 months).

Donor characteristics are represented in Table 1. There was no significant statistical difference between the groups except for serum alkaline phosphatase (ALP) and AST. The median values were within the normal range for both of these parameters.

The two groups were also comparable with regard to recipient Child-Pugh grade/score, MELD score, renal biochemistry (Table 2) and indications for transplantation (Table 3). However, serum bilirubin was significantly higher in the CON-LT group and more patients had ascites in the PC-LT group.

Table 1. Donor characteristics.

Median (interquartile range)	CON-LT	PCT-LT	P-value
Donor age (years)	45.5 (20–65)	48 (35–66)	NS
Donor body mass index (BMI)	25 (19–31)	25.1 (20–30)	NS
Donor aspartate aminotransferase (AST; IU/l)	29 (3–110)	31.5 (2–115)	0.06
Donor bilirubin (mm)	10 (2–20)	11 (3–22)	NS
Donor alkaline phosphatase (ALP; U/l)	75 (2–145)	65 (3–110)	0.03
Donor albumin (g/l)	27 (18–39)	28 (10–40)	NS

Table 2. Patient characteristics.

Median (interquartile range)	CON-LT (n = 138)	PC-LT (n = 246)	P-value
Age (years)	52.6 (35–60)	52 (37–59)	NS
Gender	76 (males)	144 (males)	NS
Creatinine (μm)	90 (55–125)	92.5 (60–128)	NS
Bilirubin (μm)	68 (2–130)	53 (3–115)	0.008
Albumin (g/l)	30 (20–40)	32 (22–41)	NS
International normalized ratio	1.3 (0.7–1.4)	1.3 (0.7–1.3)	NS
Ascites	74 (53.6%)	104 (42.2%)	0.03
Encephalopathy	29 (40%)	57 (23.1%)	NS
Child-Pugh score	9	8	NS
MELD score	15 (11.5)	13.8 (9.7)	NS

CON-LT, Conventional orthotopic liver transplantation; MELD, Model for End-stage Liver Disease.

Table 3. Indications for transplantation.

Indication for transplantation	CON-LT (n = 138)	PC-LT (n = 246)
Cholestatic liver disease/AICAH	63 (46%)	106 (43%)
Viral hepatitis B/C	17 (12%)	29 (12%)
Alcoholic liver disease	11 (8%)	22 (9%)
Acute/subacute liver failure	33 (24%)	46 (19%)
Hepatocellular carcinoma	14 (10%)	43 (17%)
Cholestatic liver disease/AICAH	3	11
Viral hepatitis B/C	10	24
Alcoholic liver disease	1	8

Comparison of operative data between CON-LT and PC-LT is shown in Table 4. Amongst the perioperative factors, significantly less fresh-frozen plasma and platelets were utilized in the PC-LT group, although red cell usage was similar. Cold ischaemia time was shorter in PC-LT group but the total operating time was not different between the two. Patients who underwent PC-LT required a significantly shorter stay in the ITU and a shorter period of ventilatory support. Number of patients requiring ventilation after day 1 was also significantly less in the PC-LT group (Table 4). There was no difference between the two groups in relation to postoperative renal and liver biochemistry.

A subgroup analysis was carried out for patients that underwent PC-LT. Patients who underwent the TPCS ($n = 192$) were compared against those who did not ($n = 54$). No difference was seen in any of the variables compared, except the WIT, which was significantly lower in those who did not receive the shunt ($P = 0.02$). Statistically significant association was noted when cold ischaemia time, WIT and total theatre time were compared with total days spent on ITU and total inpatient days ($P < 0.0001$). Equally, when the blood product usage (red cells, FFP and platelets) were individually compared with days spent in ITU and total in-patient stay, all comparisons were found to be significantly related ($P < 0.0001$). Sixteen patients in the CON-LT group developed a haematoma at the site of VVB in the axilla. These varied from simple bruising to large haematoma formation. Ten of these patients had haematomas at the site of the axillary incision of which two required evacuation. The remaining six had bruising in the region of the axilla close to the site of cannulation. None had compromised limb perfusion or needed radiological intervention.

Four patients in the PC-LT group were investigated for the PBS. All four recipients presented with refractory ascites and lower limb oedema. One recipient additionally had a large right-sided pleural effusion, due to pleuro-peritoneal connections, causing respiratory distress requiring chest drainage. Three were confirmed to have PBS using imaging (venography) and required percutaneous placement of stents. The fourth recipient did not have demonstrable PBS following investigation. This patient too was eventually stented resulting in a reduction of ascites. No venous outflow complications were noted in the CON-LT group ($P = 0.02$). The 30-day mortality rate for this cohort was 8.1%. Survival and graft function (failure and chronic rejection) were not different between the two groups (Table 5). None of the deaths was related to surgical technique.

Discussion

As the first description of the PC-LT technique [6], it has increasingly been adopted as a preferred approach of venous outflow reconstruction at OLT. The anastomosis

Median (interquartile range)	CON-LT (n = 138)	PC-LT (n = 246)	P-value
Perioperative factors			
Operating time (h)	5.3 (3.5–7.3)	5.1 (3.6–7)	NS
Cold ischaemia (h)	11.5 (4–11.2)	10.7 (4–9.2)	0.01
Warm ischaemia (min)	44 (35–48)	43 (34–46)	NS
RBCs (units)	5 (0–9)	4 (0–9)	NS
Platelets (units)	10 (2–12)	10 (2–8)	0.01
FFP (units)	10 (2–12)	9 (2–9)	0.03
Postoperative factors			
Ventilatory support (days)	2 (1–4)	1 (1–3)	0.04
Patients requiring ventilation >1 day	69 (50%)	96 (39%)	0.03
ITU stay (days)	4 (1–14)	3 (1–7)	0.005
Total hospital stay (days)	13 (8–21)	11.5 (7–19)	0.15
Day 3 creatinine (μm)	116 (35–135)	112 (32–129)	NS
Number of patients with renal failure	43 (31.3%)	62 (25%)	NS
Renal support – continuous veno-venous hemofiltration (days)	6.5 (1–9)	4.1 (2–7)	0.26
Highest aspartate aminotransferase (AST; IU/l)	691 (88–750)	641 (59–680)	NS

Table 4. Perioperative and postoperative factors.

Table 5. Median survival and graft function/complications (the differences were not statistically significant; $P > 0.05$; NS).

	CON-LT (n = 138)	PC-LT (n = 246)
30 day mortality	15 (10.8%)	16 (6.5%)
Long-term mortality	34 (24.6%)	39 (15.8%)
Graft failure	5	10
Chronic rejection	0	1
Hepatic artery thrombosis	4	6
Primary nonfunction	1	3

is technically easier to perform and reduces the need for VVB equipment and personnel. A literature review of publications over the last decade identified several key studies (Table 6). There included two RCTs, one prospective and nine retrospective studies. Although the outcomes analysed were highly variable, most of the retrospective studies have found PC-LT to have significant advantages over the conventional technique with respect to operating time, blood product usage and postoperative intensive care support. No differences were reported in graft function or short-term patient survival. However, in the two RCTs, the outcomes were conflicting. Jovine *et al.* recruited 39 patients and found the piggyback procedure to be superior in operating time only. Isern *et al.* [15] (Table 6) randomized 67 patients into conventional VVB and piggyback with interest in pulmonary outcomes. No difference was observed in operative factors, blood product usage and intensive care support. In particular, there was no difference in recovery of pulmonary function. These RCTs were probably not adequately powered due to the small numbers involved [8]. The benefits and drawbacks of either procedure remaining unclear.

This study is a large single centre prospective study that compares the outcome of CON-LT and PC-LT. In our experience, the graft survival, patient morbidity and overall survival were similar with both techniques. Additionally unlike in previous reports, VVB was utilized in all of the CON-LT. Temporary portacaval shunt was used selectively. The study also offers the largest comparisons, addressing key haemodynamic, operative and postoperative parameters in relations to these two techniques.

The two patient groups (CON-LT versus PC-LT) are comparable in relation to patient, donor and graft characteristics with only minor differences. These differences (marginally elevated serum bilirubin in the CON-LT group and more patients with ascites in the PC-LT group) may not have affected outcome.

Veno-venous bypass was used in CON-LT primarily to preserve renal perfusion and function and to prevent portal hypertension with engorgement of the splanchnic circulation. Using such a VVB avoids haemodynamic instability and metabolic alterations with low renal flow. Haemodynamic measurements have, however, confirmed that in most instances, CON-LT can be carried out without VVB. When VVB was used in conjunction with CON-LT, it was associated with a higher rate of bleeding complications in our series. This could also explain the additional use of FFP and blood products in this group. In our series, CON-LT could in many instances have been performed without VVB. Therefore, the use of VVB may be limited to selected cases of CON-LT with haemodynamic instability or failed trial of caval clamping [16]. Therefore, it is likely that CON-LT performed without VVB may not require as much blood products than when performed with VVB.

Table 6. Literature review of studies comparing conventional liver transplantation (CON-LT, with or without veno-venous bypass VVB) versus piggyback (PC-LT) technique in the last 10 years.

Author (year)	Type of study	Number of CON-LT/PC-LT	VVB used CON-LT/PC-LT	Outcomes studied	Results
Isern <i>et al.</i> (2004) [15]	Randomized -controlled trial	34/33	34 CON-LT	Pulmonary static compliance PaO ₂ /FiO ₂ *	No difference noted, PC-LT ↑ pulmonary infiltrates
Jovine <i>et al.</i> (1997) [8]	Randomized -controlled trial	19/20	20 CON-LT	Operating, ischaemia times, renal parameters	PC-LT, ↓ warm ischaemia time and ↓ incidence of renal failure
Shokouh-Amiri <i>et al.</i> (2000) [24]	Prospective	56/34	56 CON-LT	Operating time, blood product usage, ITU stay, hospital stay, cost	PC-LT, ↓ anhepatic phase, which was directly related to ↓ blood product usage, ↓ ITU stay, ↓ hospital stay, ↓ cost
Miyamoto <i>et al.</i> (2004) [20]	Retrospective ×2 reperfusion protocols in PC-LT group	96/71	96 CON-LT	Survival, blood product usage, complications, operating time, liver and renal function	PC-LT, ↓ blood product usage, ↓ warm ischaemia time, ↓ incidence of cholangitis and sepsis
Cabezuelo <i>et al.</i> (2003) [17]	Retrospective	84/80	20 CON-LT	Renal function, blood product usage, vasopressor usage, complications	PC-LT significantly ↓ risk of renal failure. VVB in patients who do not tolerate IVC clamping has no effect on postoperative renal complications
Hesse <i>et al.</i> (2000) [18]	Retrospective	75/87	50/14	Operating, ischaemia times, re-laparotomy, renal failure, blood product usage	PC-LT - ↓ blood products, ↓ VVB, ↑ early renal dysfunction, ↑ technical failure
Reddy <i>et al.</i> (2000) [25]	Retrospective	40/36	40/8	Blood product usage, operating time, ITU and hospital stay, cost	PC-LT, ↓ blood product usage, ↓ need for VVB, ↓ operating time, trend towards ↓ ITU stay and cost
Busque <i>et al.</i> (1998) [21]	Retrospective (all CON-LT patients had a failed PC-LT)	98/33	20 CON-LT	Blood product usage, operating time, ITU stay	PC-LT, ↓ blood product usage, ↓ operating time, ↓ ITU stay, and facilitates re-transplantation
Gonzalez <i>et al.</i> (1998) [26]	Retrospective	70/52	35 CON-LT	Operating time, blood product usage, renal function, complications	PC-LT, ↓ operating time, ↓ blood product usage
Lerut <i>et al.</i> (1997) [9]	Retrospective	38/39	38/17	Implantation time, blood product usage, morbidity	PC-LT - ↓ implantation time, ↓ blood product usage, earlier extubation, ↓ need for VVB
Koveker <i>et al.</i> (1996) [23]	Retrospective	19/12	12 CON-LT	Flow velocity, resistance and flow in hepatic veins using Duplex scan	No difference noted
Stieber (1995) [27]	Retrospective	66/128	62/128	Survival, blood product usage, ITU and hospital stay	PC-LT, ↓ blood product usage, absence of brachial plexus injury

*Partial pressure of oxygen/inspired oxygen concentration.

ITU, intensive therapy unit; IVC, inferior vena cava; VVB, veno-venous bypass; CON-LT, Conventional orthotopic liver transplantation.

Perioperative blood product usage was significantly less with PC-LT. Particularly so for fresh-frozen plasma and platelets. The red cell usage did not reach statistical significance but others have reported such an advantage for PC-LT [7]. The requirement for blood products with this technique has consistently been shown to be less in both prospective and retrospective studies [7,17,18]. From the patient records, it would seem that the use of VVB in these recipients was the main reason for the observed

increased requirement for blood products. The probable explanation is the use of VVB and hence the need for anticoagulation and extra-corporeal circulation. In addition, others have also linked the use of blood products (individually) to ITU and hospital stay, similar to our findings, and also re-intervention rate [7,19]. Techniques like thromboelastography were used to monitor coagulation during the transplant procedure well before the period of our study. The improvement in the utilization of

FFP and platelets due to such techniques therefore should not have had an influence on our findings.

One of the purported benefits of PC-LT is shorter warm ischaemia [8,20] which is not evident in our study. It is also unlikely that the cold ischemia time could have been impacted by the technique of PC-LT. The cold ischemia time being shorter in the PC-LT group therefore has no relevance to the study and is possibly a statistical quirk.

In the postoperative period, the PC-LT group required a shorter time on the ITU and were more likely to be extubated early compared with CON-LT. Similar findings have previously been reported [9,21]. This suggests that pulmonary function after PC-LT may be less affected. However, no specific assessment of pulmonary function was undertaken. Recovery of pulmonary function alone may expedite discharge from intensive care and this did not translate to an earlier hospital discharge. In a recently reported RCT, Isern *et al.* [15] did not show any significant difference in pulmonary function or time of ventilation between the CON-LT patients and the piggyback patients. However, in their 'piggyback' patients, no TPCS was created once portal clamping was initiated. This may have accounted for the increase in pulmonary infiltrates and lack of difference between the two groups.

Renal function is also reported to improve following piggyback techniques compared with CON-LT. Clamping of the vena cava in CON-LT reduces renal perfusion pressure and can precipitate acute renal failure [8]. In our patients, this advantage was not observed (Table 4). None of the postoperative renal parameters studied (Table 4) showed a significant benefit for either technique.

When selectively used, the TPCS is a component of the PC-LT providing decompression of the gut venous drainage and boosting venous return. The only advantage of not using a TPCS in our study was a slightly shorter WIT (median 40 min vs. 44 min). One randomized study has addressed this issue, reporting advantages in intraoperative haemodynamics and postoperative serum creatinine levels [22]. Patient outcome was not different between the two groups in our study.

One of the drawbacks of the PC-LT is the potential for venous outflow obstruction which manifest as PBS. This occurs when the piggyback liver compresses the venous anastomosis similar to a 'ball valve'. It is considered more common when the anastomosis is performed end-to-side to the patch of the mid and left hepatic veins. To overcome this, others have advocated a wide latero-lateral (side-to-side) cavocavostomy. A side-to-side longitudinal cavocavostomy is used at our centre as standard. We encountered three confirmed cases (1.2%) of PBS, all of these were dealt with percutaneous radiological intervention. The presentation was late (1–3 months) with symp-

toms similar to Budd-Chiari Syndrome. Complications and a higher incidence of PBS have been reported previously with PC-LT [18]. Interestingly, duplex flow studies have not shown any postoperative difference in hepatic venous flow [23]. Meticulous technique is imperative (which must ensure a reasonable outflow channel for the transplanted liver without impinging on the inflow or outflow of the native cava) to try and prevent this catastrophe. Patient and graft survival were comparable (both short and long term) in the two groups, as has also been reported previously [20].

In conclusion, we found that the PC-LT technique was safe, and did not impact surgical time, graft or patient survival. We observed a reduced need for the transfusion of fresh-frozen plasma, and platelets perioperatively, which was significantly better than when using the CON-LT technique with VVB. PC-LT resulted in a significantly reduced need for respiratory support and ITU stay. It would also seem that TPCS could be omitted when PC-LT is carried out in selected recipients. PC-LT, however, is associated with the complication of venous outflow obstruction; PBS that occurred in 1.2% of our cases.

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