Application of various surgical techniques in liver transplantation: a retrospective study

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Introduction

Liver transplantation (LT) is considered the only curative treatment for end stage liver diseases (ESLD) (1). The surgical techniques of LT have continually evolved and have been modified (2). In 1963, Starzl et al. initiated a technique for LT in which the superior (SHVC) and inferior hepatic vena cava (IHVC) and portal vein (PV) were completely blocked, and the retrohepatic inferior vena cava (RHIVC) was removed as a part of the diseased liver; it was named classic OLT (3). However, the hemodynamics in the anhepatic phase is not stable, and reflux of the renal vein is blocked, causing renal dysfunction (4,5). In 1989, Tzakis et al. described a novel technique called classic piggy-back liver transplantation (CPBLT) (6). In this technique, the PHVC is preserved, the SHVC of the donor liver is anastomosed with

Background: Surgical techniques of liver transplantation have continually evolved and have been modified. We retrospectively analyzed a single-center case series and compared the advantages and disadvantages of each method.

Methods: Six-hundred and seventy-four recipients’ perioperative data were assessed and analyzed stratified by different surgical technics [modified classic (MC), modified piggyback (MPB) and classic piggyback (CPB)].

Results: MELD score and Child-Pugh scores was significantly higher in CPB groups (P=0.008 and 0.003, respectively). Anhepatic time in MPB group was longer than those in CPB group (P<0.05). The operation duration in MPB group was significantly longer than those in MC group and CPB group (P=0.003). Three patients had outflow obstruction (P=0.035). The overall survival in MPB group were better than those in MC group and CPB group in general comparison (P<0.001). In patients with preoperative creatine >120 μmol/L, the overall survival in MC group was worst (P<0.001). In patients with a high MELD score (>24), the overall survival in MPB group tended to be the best (P<0.001).

Conclusions: The advantages and disadvantages are different for these three surgical techniques. A reasonable operation technique should be adopted considering the patient’s unique condition to ensure the stability of hemodynamics.

Keywords: Surgical techniques; liver transplantation (LT); classic piggyback; early allograft dysfunction; outflow venous obstruction

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a common opening formed by the left and middle hepatic veins of the recipient liver, and the IHVC of the donor liver is ligated. The flow during the anhepatic period and hemodynamic stability are maintained during the operation. The technique can also reduce the occurrence of renal failure after liver transplantation and is more beneficial to patients with cardiac insufficiency or a poor general condition. However, specific complications related to CPB, such as outflow obstruction, can cause liver congestion, swelling and even delayed graft function (DGF) or transplanted liver failure. In 1992, Belghiti et al. (7) developed the modified piggy-back (MPB) technique in which side-to-side cavocaval anastomosis is performed at the anterior face of the recipient RHIVC to minimize outflow obstruction. Wu et al. (8) also reported another MPB technique, which has the advantages of simplifying the steps of hepatectomy and separation, and the anastomosis of the vena cava is large, thereby avoiding outflow tract obstruction. However, this operation requires a complete blockade of the inferior vena cava, and the anhepatic period is long, thereby leading to intraoperative hemodynamic instability and renal dysfunction.

The CPB and MPB techniques are limited when the caudate lobe of the recipient liver is hypertrophied (9,10). Particularly, in some patients with Budd-Chiari syndrome, the RHIVC is surrounded in the caudate lobe of the liver, making it difficult to preserve the inferior vena cava during hepatectomy (11,12). Additionally, in patients with large liver cancers, the RHIVC tends to be dissected, and classic LT is recommended (13,14). To simplify the operation process and shorten the anhepatic period, we developed a modified classic LT technique (15). In this technique, it is not necessary to isolate the IVC neither dissect the posterior space of the IVC and right adrenal vein. The IVC would be clamped directly from front to back and sutured continually from front to back after dissection of the liver. Compared with conventional classic LT, it is easy to expose and convenient for the surgeon to anastomose.

In general, the selection of surgical techniques depends on the patient’s conditions. In this study, we retrospectively analyzed a single-center case series (674 cases) at our center and compared the advantages and disadvantages of each method. We present the following article in accordance with the STROBE checklist (available at https://dx.doi.org/10.21037/atm-21-1945).

Methods

All procedures were performed in accordance with the ethical standards of the IEC for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University for human experimentation (institutional and national) and with the Declaration of Helsinki (as revised in 2013). All the organs used in our study were acquired by organ donation, and none were from executed prisoners. The study was approved by the Institutional Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University [Ethical approval ID: [2021]434], and an informed consent waiver was granted by the IEC given the retrospective, minimal-risk nature of the study.

In total, 803 patients had undergone transplantation at our department from January 2015 to December 2019. After excluding 112 other types of transplantations (combined liver and kidney transplantation, combined pancreas kidney transplantation, combined liver pancreas transplantation and combined upper abdominal organ transplantation), 686 patients underwent LT were taken into consideration. During the follow-up period, 12 patients were lost to follow up (Figure 1A). Therefore, 674 patients were enrolled in this retrospective study (Figure 1B). The recipient pretransplantation data, including demographics, the results of preoperative laboratory examinations, model for end-stage live disease (MELD) score, Child-Pugh score, history, and diagnosis were collected. The perioperative data, including the anhepatic time, cold ischemia time, duration of operation, blood loss and transfusion of red blood cells (RBCs), fresh frozen plasma (FFP), and platelets, were recorded. Additionally, postoperative surgical complications, length of stay in the intensive care unit (ICU), and the mortality rates and cause of death within the postoperative 30 days were assessed and analyzed.

Surgical techniques

In general, venous-venous bypass (VVBP) techniques were not used during operation in all groups. The selection of surgical techniques depends on the patient’s conditions, including diagnosis, MELD score, pretransplant imaging and laboratory test results.

Modified classic (MC) technique

The classical surgical technique has been used in our center since 2009. And after that, we developed a modified classic technique which is an improvement of classical orthotopic LT. First, the common bile duct, hepatic artery and portal vein were dissociated in turn for dissection of the first hepatic hilum.
Thereafter, the left triangular ligament, hepatogastric ligament and right triangular ligament were separated and the RHIVC was dissociated. The differences from the conventional method are that dissociating the IVC is unnecessary, and the blocking direction was from front to back. The donor’s and recipient’s IVC were fixed together at 0 and 6 o’clock using two 4-0 prolene lines. The suture was continuous from back to front. The patients who had undergone this technique were enrolled in MC group (Figure 2A).

**MPB technique**

The dissection of the first hepatic hilum and peri-hepatic ligaments was the same as that in the conventional technique. Subsequently, the SIVC and PIVC were dissociated and then immediately blocked. The diseased liver was resected close to the anterior wall of the IVC, and all short hepatic veins were ligated. Thereafter, the openings of the three hepatic veins were cut and reshaped, and the anterior wall of the IVC was cut longitudinally to form a large triangular outlet. Anastomosis was performed between the outlet of the recipient IVC and matched the opening of the SVC in the donor liver. The IHVC of the donor liver was ligated before reperfusion. VVBP techniques were not used during operation. The patients who had undergone this technique were enrolled in MPB group (Figure 2B).

**CPB technique**

This technique was described as the standard back-table procedure for the liver. The dissection of the first hepatic hilum and peri-hepatic ligaments was the same as that in the conventional technique. The short hepatic veins in the third hepatic hilum were ligated so the right, left and middle hepatic veins (RHV , LHV and MHV) were exposed. The diseased liver was then resected after ligation of the RHV and blockade of the LHV as well as the MHV. Anastomosis was performed between the recipient SVC and the reshaped common trunk of the LHV and MHV of the donor liver. During the entire operation, the blood flow in the IVC was maintained. The patients who had undergone this technique were enrolled in CPB group (Figure 2C).

**Postoperative management**

Routine Doppler ultrasound of the liver graft blood flow

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**Figure 1** Information about recipient in our study. (A) The study flowchart. (B) Components of participants in our study.
and biliary tract was performed once every 2 days for 7 days. Thereafter, imaging studies were performed based on the patients’ clinical status or laboratory findings.

**Statistical analysis**

All the statistical analyses of the data were performed using SPSS version 26.0. All the data were expressed as means ± standard deviation or numbers and percentages of patients. For comparison between groups, chi-square and the ANOVA test were performed for frequencies and continuous data, respectively. Overall survival was compared using the Kaplan-Meier method with a log-rank test. The Cox proportional hazards model was used for multivariate analysis. A P value <0.05 was significant.

**Results**

**Baseline data comparison**

Preoperative data of 674 patients were presented in Figure 1B and Table 1. In general, 54.6% patients were diagnosed with tumors and 74.8% patients were diagnosed with cirrhosis. Two-hundred and eighty-two, 291 and 101 patients underwent LT in MC group, MPB group and CPB group, respectively. In comparison, MELD score and Child-Pugh score were significantly higher in CPB group (P=0.008 and 0.003, respectively). Except these, the results of other preoperative baseline data including demographic indicators, laboratory test results and past medical history were similar.

**Perioperative data comparison**

Intraoperative and postoperative data comparison among different groups were presented in Table 2 and Figure 3. We found that the anhepatic time in MPB group was 57.43±1.20 minutes, longer than those in CPB group with 52.88±1.76 minutes (P<0.05). During operation, the volume of blood loss in CPB group was significantly larger than those in MC group (2,753.66±289.65 vs. 2,116.70±127.12 mL; P<0.05, Figure 3B).

The median ventilation time, duration of oral in-take,
ICU stay time and hospital stay time of all patients was 14 hours, 34.5 hours, 100 hours and 24 days, respectively. During comparison, the ventilation time and ICU stay time in CPB group was both significantly longer than those in MC group (P<0.05; Figure 3C). The most frequent postoperative complications within 30 days in all patients was abdominal bleeding (n=35, 5.2%), followed by HAT (n=30, 4.5%) and portal vein thrombosis (PVT; n=7, 1.0%). Notably, 3 patients had outflow obstruction (MPB group: n=2, 0.33%; CPB group: n=1, 0.84%; P=0.035).

No significantly differences were observed in other complications (Figure 3D). Ten patients developed primary non-function (PNF) and 131 patients developed early allograft dysfunction (EAD). The 30- and 90-day mortality rate was 8.0% and 11.3%, respectively. Comparisons among groups showed that the results were similar and without significantly different (Figure 3E).

**Survival and multivariable analysis**

Kaplan-Meier survival analyses were performed among groups and presented in Figure 4. In total, one-year survival rates in three groups were similar (79.7%, 83.1% and 81.1% in MC, MPB and CPB group, respectively). However, the comparison of 3-year survival rate showed that the overall survival in MPB group were better than those in MC group and CPB group (3-year: 59%, 66% and 60% in MC, CPB and MPB group, respectively; P<0.001, Figure 4A). Kaplan-Meier survival analyses for clinical subgroups were also performed and shown in Figure 4B-4G, 4I. In patients with preoperative creatine >120 μmol/L, the overall survival in MC group was worst (1-year: 61.7%; 3-year: 28.6%; P<0.001, Figure 4G). In patients with high MELD score (>24), the overall survival in MPB group tended to be the best compared with those in MC group and CPB group (1-year: 74.4%; 3-year: 60.8%; P<0.001, Figure 4E). In other subgroups, the results showed that the overall survival were similar in MC group and MPB group and worse in CPB group (Figure 4B-4F, 4H). In multivariable analysis, we found that tumor and EAD were both independent factors impacting survival within 30 days and within 90 days, respectively (Table 3).

**Discussion**

Many factors play an important role in the outcome of LT and technique-related factors, including operative duration, intraoperative bleeding, and complications, are the most important. In China, majority of patients are complicated with portal hypertension, causing extensive...
collateral circulation between the PV and vena cava (16,17). Therefore, hemodynamic instability, such as bleeding during the operation, higher PV pressure during the anhepatic period and lower peripheral vascular resistance, more commonly occur and affect the success of the operation and posttransplant survival. Over the decades, the surgical techniques of LT have continually evolved and have been modified. In summary, the difference among the techniques mainly concerns whether to block the RIHVC, which is the main factor affecting the hemodynamics in the anhepatic phase. In this study, we retrospectively analyzed the data of patients who had undergone LT at our center and compared the advantages and disadvantages of each method.

Many patients are diagnosed with liver cirrhosis in China, and the annual incidence is 2–10% (18,19). The annual incidence of HCC in patients with liver cirrhosis is 3% to 6% (20). In our study, 54.6% patients were diagnosed with tumors and 74.8% patients were diagnosed with cirrhosis. MPB would be the optimal choice for patients with nontumor-related ESLD. A large proportion of the tumors in the advanced-stage patients tend to undergo surgical resection or conservative treatment due to economic or ideological reasons, even if the tumors are detected early. LT would be considered only when other treatments were ineffective or if the tumor progressed (21). Thus, the modified classic LT would be more radical.

The median operation duration at our center was

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=674)</th>
<th>MC (n=282)</th>
<th>MPB (n=291)</th>
<th>CPB (n=101)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anhepatic time (min)</td>
<td>56.16±0.76</td>
<td>56.01±1.17</td>
<td>57.43±1.20</td>
<td>52.88±1.76</td>
<td>0.136</td>
</tr>
<tr>
<td>Cold ischemia time (min)</td>
<td>416.88±6.96</td>
<td>409.63±11.43</td>
<td>431.53±9.35</td>
<td>394.91±20.19</td>
<td>0.146</td>
</tr>
<tr>
<td>Operation duration (min)</td>
<td>466.16±4.36</td>
<td>455.04±6.64</td>
<td>483.08±6.98</td>
<td>448.46±9.28</td>
<td>0.003</td>
</tr>
<tr>
<td>RBC volume (mL)</td>
<td>1,375.46±57.14</td>
<td>1,262.22±73.38</td>
<td>1,416.29±99.71</td>
<td>1,574.00±143.31</td>
<td>0.0159</td>
</tr>
<tr>
<td>FFP volume (mL)</td>
<td>0.75±2.16</td>
<td>9.93±4.41</td>
<td>5.88±2.37</td>
<td>5.88±3.19</td>
<td>0.653</td>
</tr>
<tr>
<td>Blood loss (mL)</td>
<td>2,368.07±95.54</td>
<td>2,116.70±127.12</td>
<td>2,477.84±153.03</td>
<td>2,753.66±289.65</td>
<td>0.052</td>
</tr>
<tr>
<td>Ventilation time (hr)</td>
<td>44.99±8.00</td>
<td>36.22±4.18</td>
<td>40.11±4.32</td>
<td>84.36±51.46</td>
<td>0.120</td>
</tr>
<tr>
<td>Duration of oral in-take (hr)</td>
<td>130.06±5.51</td>
<td>133.44±9.30</td>
<td>127.13±8.42</td>
<td>128.06±8.88</td>
<td>0.099</td>
</tr>
<tr>
<td>ICU stay time (hr)</td>
<td>77.63±8.67</td>
<td>66.18±6.30</td>
<td>73.53±7.45</td>
<td>121.11±50.45</td>
<td>0.862</td>
</tr>
<tr>
<td>Abdominal bleeding, n (%)</td>
<td>35 (5.2)</td>
<td>17 (2.5)</td>
<td>14 (2.1)</td>
<td>14 (2.1)</td>
<td>0.552</td>
</tr>
<tr>
<td>HAT, n (%)</td>
<td>30 (4.5)</td>
<td>14 (2.1)</td>
<td>14 (2.1)</td>
<td>2 (0.3)</td>
<td>0.425</td>
</tr>
<tr>
<td>PVT, n (%)</td>
<td>7 (1.0)</td>
<td>1 (0.1)</td>
<td>4 (0.6)</td>
<td>2 (0.3)</td>
<td>0.290</td>
</tr>
<tr>
<td>Outflow obstruction, n (%)</td>
<td>3 (0.4)</td>
<td>0</td>
<td>1 (0.1)</td>
<td>2 (0.3)</td>
<td>0.035</td>
</tr>
<tr>
<td>AKI, n (%)</td>
<td>27 (4.0)</td>
<td>11 (1.6)</td>
<td>11 (1.6)</td>
<td>5 (0.7)</td>
<td>0.869</td>
</tr>
<tr>
<td>PNF, n (%)</td>
<td>10 (1.5)</td>
<td>5 (0.7)</td>
<td>4 (0.6)</td>
<td>1 (0.1)</td>
<td>0.838</td>
</tr>
<tr>
<td>EAD, n (%)</td>
<td>131 (19.4)</td>
<td>58 (8.6)</td>
<td>49 (7.3)</td>
<td>24 (3.6)</td>
<td>0.260</td>
</tr>
<tr>
<td>Hospital stays (d)</td>
<td>29.07±21.01</td>
<td>30.52±1.65</td>
<td>28.82±1.01</td>
<td>25.71±1.38</td>
<td>0.166</td>
</tr>
<tr>
<td>Death in 30 days, n (%)</td>
<td>54 (8.0)</td>
<td>22 (3.3)</td>
<td>22 (3.3)</td>
<td>10 (1.5)</td>
<td>0.746</td>
</tr>
<tr>
<td>Death in 90 days, n (%)</td>
<td>76 (11.3)</td>
<td>31 (4.6)</td>
<td>32 (4.7)</td>
<td>13 (1.9)</td>
<td>0.860</td>
</tr>
</tbody>
</table>

MC, modified classic; MPB, modified piggyback; CPB, classic piggyback; RBC, red blood cell; FFP, Fresh Frozen Plasma. ICU, intensive care unit; HAT, hepatic artery thrombosis; PVT, portal vein thrombosis; PNF, primary nonfunction; EAD, early allograft dysfunction; AKI, acute kidney injury.
450 minutes. Compared with previous national reports (range from 320 to 708 minutes) (22-25), our data for the MPB technique (483.08±6.98 minutes) in MPB group were consistent with the international data and were significantly longer than those in MC group and CPB group. This result is acceptable compared with that in the randomized trial conducted by Jovine et al. (26) in which the operative time was 506±85 minutes and 462±87 minutes in the CPB and conventional groups, respectively.

The cold ischemia time is an inherent and unavoidable factor in LT (27). Ruiz de Azúa-López et al. (28) reported that a long ischemia time (>6 hours) leads to a higher rate of complications after LT. The median cold ischemia time in this study was 416.5 minutes and comparable with that in previous reports (29). The anhepatic phase is defined as the time from the dissection of the recipient liver to reperfusion of the graft. Cleland et al. (30) concluded that the anhepatic phase would increase blood loss because of the absence of hepatic synthesis and clearance. Ijtsma et al. (31) revealed that a long anhepatic phase duration (>100 minutes) is an independent risk factor for graft dysfunction in LT. VVBP (32) was introduced to solve the problems of interruption of venous return, hemodynamic instability, and renal failure (33) caused by a full or partial cross-clamping of the inferior vena cava. In our study, VVBP was not used in all groups. Because of the shortening of anhepatic time therefore the decrease of hemodynamic instability, VVBP is not commonly used in LT with MC; In addition, In MPB and CPB, because inferior vena cava is not blocked, VVBP is not needed, neither. The median and mean anhepatic times were 54 and 56.16±0.76 minutes, respectively. This result may suggest that the modified classic LT technique could achieve comparable anhepatic times as CPB or MPB because of its simplified procedure compared with the classic technique.

According to our study, the median intraoperative blood loss, transfusion of RBCs, and FFP were 1,500, 1,000 and 1,600 mL, respectively. A significant large volume of blood loss was founded in CPB group and was within an acceptable range compared with the experience at other centers (34,35). In a cohort study of over 5,000 patients in France, Savier et al. (36) found that the median ICU duration after LT was 8 days (5–15 days). Mehrabi et al. (24) reported a 14-day ICU and IMC stay in their experience of 500 LTs using the MPB technique. In our study, the median

Figure 3 Perioperative comparison in three groups. (A) Anhepatic time, cold ischemia time and operation time (B) RBC transfusion, FFP transfusion and blood loss; (C) ventilation time, duration of oral in-take and ICU stay time; (D) abdominal bleeding, HAT, PVT, outflow obstruction and AKI; (E) EAD, PNF, 30- and 90-day death. * means P<0.05. FFP, fresh frozen plasma; ICU, intensive care unit; HAT, hepatic artery thrombosis; PVT, portal vein thrombosis; AKI, acute kidney injury; EAD, early allograft dysfunction; PNF, primary nonfunction.
and mean ICU stay time were 100 and 77.6±8.67 hours, respectively, markedly shorter than previous experiences. Our center promoted the concept of ‘enhanced recovery after surgery’ (ERAS) to achieve early extubation, early functional exercise, and a shortened length of stay at the hospital (37).

Complications in the early postoperative period are important concerns in LT. AKI was a prevalent complication, and its incidence was 4.0% in our study (38,39). The incidence of AKI in previous reports ranged from 0% to 16.7% (40,41). AKI was mainly caused by hemodynamic instability, IVC blockade, and severe intraoperative blood loss. Hesse et al. (40) showed that the incidence of postoperative renal dysfunction was significantly lower in the MPB group. However, no significant difference was found in the incidence of renal failure among the different groups in our study. Although the IVC was blocked during the operation in MC group, the operation process was simplified and the operative time was shortened, leading to little impact on the hemodynamic stability (42). However, in patients with high preoperative creatinine, the overall survival in MC group was worst. The results suggest that piggyback is a better choice for patients with poor preoperative renal function. Notably, outflow obstruction occurred in both MPB and CPB group, with incidences of 0.3% and 2.0%, respectively. Arudchelvam et al. (43) reported that 2.0% of 253 patients with CPB had outflow obstruction. An enlarged caudate lobe, oversized donor graft, abnormalities of the IVC, or adhesions between the liver and the RHIVC may be the main obstacles for the use of the CPB or MPB technique (44). In our center, the donor IVC was trimmed in a triangle-shaped fashion to avoid obstruction of hepatic venous outflow. Additionally, the incision on the IVC should have sufficient distance
from the hepatic veins. The early (within 30 days) and intermediate (within 90 days) mortality rates in all cases were 8.0% and 11.3%, respectively. In a previous report, approximately 10.9% had graft failure within 30 days (45). In another study, Zanetto et al. reported the estimated 30-day mortality rate of over 3,000 LTs was 8.4% (46). For long-term survival analysis, the overall survival in MC group and MPB group were similar and better than those in CPB group in total. From results of subgroups we figured out that in patients with severe ESLD (MELD >24), MPB would be the optimal choice.

Our study has limitations. The study is a retrospective study from a single center. Selection bias exists and may impact the comparison results. A summary of Multi center experience or a randomized clinical trial is needed.

### Conclusions

Our study demonstrates that different surgical techniques have specific advantages and disadvantages and a reasonable operation technique based on the patient’s condition to ensure the stability of hemodynamics during the operation is of considerable significance to improve the prognosis. In brief, in patients with poor pretransplant renal function, the MC technic would not be recommended. In patients with high MELD score (>24), MPB tended to be the best choice. In other conditions, MPB or MC would have similar outcomes.

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**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related
to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures were performed in accordance with the ethical standards of the IEC for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University for human experimentation (institutional and national) and with the Declaration of Helsinki (as revised in 2013). All the organs used in our study were acquired by organ donation, and none were from executed prisoners. The study was approved by the Institutional Ethics Committee for Clinical Research and Animal Trials of the First Affiliated Hospital of Sun Yat-sen University (Ethical approval ID: [2021]434), and an informed consent waiver was granted by the IEC given the retrospective, minimal-risk nature of the study.

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