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Michel Rayar, Giovanni B. Levi Sandri, Caterina Cusumano, Clara Locher, Pauline Houssel-Debry, et al.. Benefits of temporary portocaval shunt during orthotopic liver transplantation with vena cava preservation: A propensity score analysis. *Liver Transplantation*, 2017, 23 (2), pp.174-183. 10.1002/lt.24650 . hal-01447066

HAL Id: hal-01447066

<https://univ-rennes.hal.science/hal-01447066>

Submitted on 10 Apr 2017

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Benefits of temporary portocaval shunt during orthotopic liver transplantation with vena cava preservation: A propensity score analysis

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Running title: Benefits of TPCS during OLT

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article', doi: 10.1002/lt.24650

During orthotopic liver transplantation (OLT), clamping of the portal vein induces splanchnic venous congestion and accumulation of noxious compounds. These adverse effects could increase ischemia-reperfusion injury and subsequently the risk of graft dysfunction, especially for grafts harvested from extended criteria donors (ECD). Temporary portocaval shunt (TPCS) could prevent these complications. Between 2002 and 2013, all OLT performed in our center were retrospectively analyzed and a propensity score matching analysis was used to compare the effect of TPCS in 686 patients (343 in each group).

Patients in the TPCS group required fewer intraoperative transfusions (median packed red blood cell: 5 vs. 6, $p = 0.02$; fresh frozen plasma: 5 vs. 6, $p = 0.02$), had improvement of postoperative biological parameters (prothrombin time, Factor V, INR, alkaline phosphatase and GGT levels) and showed significant reduction of biliary complications (4.7% vs. 10.2%, $p=0.006$). Survival analysis revealed that TPCS improved 3-month graft survival (94.2% vs. 88.8%, $p = 0.01$) as well as long-term survival of elderly (i.e. age >70 years) donor grafts ($p = 0.02$). In conclusion, the use of TPCS should be recommended especially when considering an ECD graft.

Abbreviations: ALAT: alanine aminotransferase; ASAT: aspartate aminotransferase; EAD: early allograft dysfunction; ECD: extended criteria donor; IRI: Ischemia-reperfusion injuries; IVC: Inferior vena cava; OLT: Orthotopic liver transplantation; POD: postoperative days; PNF: primary non function; PV: Portal vein; TPCS: temporary portocaval shunt

Accepted Article

Introduction

The success of orthotopic liver transplantation (OLT) has increased the waiting time for patients to receive transplantations (1). In order to reduce the number of deaths of patients on the waiting list, transplant teams have expanded the donor pool by increasing the use of grafts harvested from extended criteria donors (ECD) (2, 3). However, ECD grafts are known to be more vulnerable to ischemia-reperfusion injury (IRI), resulting in a higher rate of early allograft dysfunction (EAD) (4, 5).

During OLT, the clamping and sectioning of the portal vein (PV) from the native liver induces splanchnic venous congestion, intestinal edema, bacterial translocation and accumulation of noxious elements (6, 7), which can eventually lead to graft dysfunction.

First described by Tzakis et al. in 1993 (8), temporary portocaval shunt (TPCS) performed during the anhepatic phase of OLT with inferior vena cava (IVC) preservation, enables preservation of splanchnic blood outflow. Retrospective studies have shown that TPCS was associated with better intraoperative hemodynamic parameters, decreased incidence of reperfusion syndrome (9, 10) and better graft survival (11), especially for ECD grafts (12). However, these beneficial effects were not found in the only prospective randomized trial (13) in which no special attention was paid to ECD grafts. Therefore, whether TPCS is useful or not is still debated (14, 15) and its use remains limited (16).

The aim of our study was to evaluate the interest of TPCS using a matched population analysis based on a propensity score, with special focus on ECD graft survival since we hypothesized that TPCS could reduce ECD liver graft vulnerability to IRI.

Methods

Patient selection (figure 1)

All transplanted patients in our department between January 2002 and December 2013 were retrospectively analyzed. In all case, the graft came from a brain death donor and was usually conserved with Celsior®. In order to specifically evaluate the interest of TPCS, only patients for whom the decision to perform TPCS or not depended on the surgeon's preference were included. We therefore excluded from the study patients with complete portal vein thrombosis associated with portal cavernoma (n = 10) since these patients could not possibly have TPCS as well as patients who had permanent surgical portocaval shunt prior to transplantation (n = 5). We also excluded patients transplanted for acute liver failure (n=41) since TPCS was always performed for these patients. Ultimately, the patients transplanted with a split graft (n = 39) or a living donor graft (n=4) and retransplanted patients (n = 126) were also excluded since their outcomes were at significantly higher risk regardless of the use of TPCS or not.

Surgical procedure and medical care

All of the patients had OLT with IVC preservation. Briefly, after standard wound incision and exposition, the hepatoduodenal ligament was first dissected with portal vein divided prior to liver mobilization and TPCS (i.e. end-to-side running suture between the anterior surface of the suprarenal IVC and the portal vein) was performed or not, according to the surgeon's habits. Indeed, some surgeons are used to systematically performed TPCS while others never performed it, regardless of recipient's characteristic (i.e. degree of portal hypertension or history of liver surgery). Native liver was then removed and careful hemostasis was performed. Graft implantation started with a side-to-side caval anastomosis (17). When performed, the

TPCS was then ligated distally with vascular stapler. Portal vein anastomosis was performed end-to-end. The graft was then vascularized prior to artery and then biliary anastomosis. The biliary reconstruction was usually a duct-to-duct anastomosis between the 2 main bile ducts, except in case of transplantation for sclerosing cholangitis or perihilar cholangiocarcinoma (which systematically required an hepaticojejunostomy). Biliary drainage was done according to surgeon preference.

After the procedure, patients were transferred to the intensive care unit (ICU) until graft function was satisfactory. Routine immunosuppression associated low-dose calcineurine inhibitor, mycophenolatemofetil and a short course of corticosteroids (18). No significant modification regarding the surgical procedure or the postoperative medical care was observed during the study period.

Clinical and biological parameter definitions

Clinical and biological data were retrospectively gathered from a prospective database. The following parameters were analyzed: donor and recipient demographics, underlying liver disease and OLT indication, Child-Pugh and MELD scores (retrospectively calculated for patients transplanted before 2007, date at which a MELD score based graft allocation system was instituted in France), cold ischemia time, intraoperative transfusion (packed red blood cells, fresh frozen plasma and platelet count), post-transplant liver and renal function (estimated by CKD-EPI value (19), arterial complications (i.e. thrombosis and stenosis) and biliary complications (i.e. biliary leakage and stenosis).

An extended criteria graft was considered when the donor matched at least one of the following criteria: Age > 65 years; BMI > 30; ICU stay > 7 days prior to harvesting; natremia > 155 mmol/L; liver enzymes 3 times higher the normal value i.e. aspartate aminotransferase (ASAT) blood level >150 IU/mL, alanine aminotransferase (ALAT)

blood level > 170 IU/mL.

Early allograft dysfunction was defined according to Olthoff et al. (20) criteria (i.e. presence of one or more of the following criteria: bilirubin level \geq 10mg/dL on postoperative day (POD) 7; INR \geq 1.6 on POD7; ALAT or ASAT level > 2000 IU/L within the 7 POD).

Patient and graft survival at 3 and 12 months and overall survival were calculated.

Statistical analysis and propensity score matching

In order to minimize bias owing to the heterogeneity of recipient or graft characteristics, we performed propensity score matching (1/1 ratio). The variables included in the calculation of the propensity score were: recipient age, gender, indication for transplantation (included as factorial variable), MELD score, Child Pugh grade and use of ECD graft. Exact match was prioritized and the maximum distance allowed between two matched patients was set at 0.1 (i.e. caliper restriction).

Quantitative variables were expressed as mean \pm standard deviation or by median with extreme values and compared using Student's *t*-test or Wilcoxon test as appropriate. Qualitative variables were expressed as number and percentage and compared using Chi-squared or Fisher's exact test, as appropriate.

Survival analysis was made with Kaplan-Meier curve and compared with log-rank test. Analysis and comparison of longitudinal data (i.e. evolution of biological parameters during postoperative time) was made with a linear mixed model with random intercept (21).

A $p < 0.05$ value was considered to be statistically significant.

All statistical analyses were made with R software version 3.1.3. The matching procedure was performed with the “Matching” package version 4.9-2. The linear mixed model was made and analyzed with the “nlme” package version 3.1.

Results

Propensity score matching procedure

A total of 954 patients were analyzed among whom 567 patients had TPCS and 387 patients did not. Owing to missing data, propensity scores could only be calculated for 830 patients: 480 who had TPCS and 350 who did not. After the matching procedure, seven patients did not have appropriate matching due to the caliper restriction. Finally, 343 patients in TPCS group were matched with 343 patients in the non-TPCS group (Figure 1). No statistical difference was found between the two groups regarding demographic or preoperative data (Table 1).

Impact of TPCS on intra and postoperative course (Table 2)

Intraoperative parameters

Cold ischemia time was similar in the two groups while the duration of the procedure was significantly higher in the TPCS group compared with the non-TPCS group (388 min vs. 362 min respectively, $p = 0.03$) as well as anhepatic duration (120 min vs 102 min respectively, $p=0.001$).

The median number of intraoperative transfusions was significantly lower in the TPCS group vs. the non-TPCS group regarding packed red blood cells (5 [range: 0-36] vs. 6 [range: 0-40] respectively, $p = 0.02$) as well as fresh frozen plasma (5 [range: 0-37] vs. 6 [range: 0-40] respectively, $p = 0.02$). There were also more patients in the TPCS group requiring no transfusion of packed red blood cells (20.1%

vs 12.8%, $p=0.01$) or of fresh frozen plasma (21% vs 14.6%, $p=0.04$). However, there was no significant difference regarding platelet count transfusion.

Postoperative course

There was no significant difference between the 2 groups regarding postoperative ASAT ($p=0.20$) and ALAT ($p=0.38$) levels (Figure 2). However, the INR and prothrombin time were significantly improved ($p=0.047$ and $p=0.04$, respectively) in the TPCS group while it nearly reached significance for factor V level ($p=0.09$) (Figure 3). Incidence of biliary complications was also significantly lower in the TPCS group compared with the non-TPCS group (4.7% vs. 10.2% respectively, $p=0.006$), resulting in an improvement of alkaline phosphatase level ($p<0.001$) and gamma-glutamyltransferase level ($p=0.07$) in the TPCS group. However, postoperative bilirubin level was similar between the 2 groups ($p=0.53$) (Figure 4).

There was no difference between the TPCS and the non-TPCS groups regarding the incidence of arterial complications (10.8% vs. 11.1% respectively, $p >0.99$), rate of EAD (21.9% vs. 23%, $p = 0.80$) and renal function represented by postoperative CKD-EPI values ($p=0.29$). The incidence of severe postoperative complications (i.e. Clavien-Dindo classification ≥ 3) rate (24.2% vs. 28.3% respectively, $p = 0.41$) as well as ICU- (4 [1-73] vs. 4 [1-76], $p = 0.15$) and hospital-stay (20 [1-232] vs. 20 [1-102], $p = 0.49$) were similar between the TPCS and the non-TPCS.

Survival analysis

The 3-month graft survival rate was significantly improved in the TPCS group compared with the non-TPCS group (94.2% vs. 88.6%, $p = 0.01$), especially when considering the subgroup of patients transplanted with ECD grafts (95.2% vs. 89%, $p = 0.04$), while this difference did not reach significance in the subgroup of patients

transplanted with non-ECD grafts (92.9% vs. 88.2%, $p = 0.23$). The main causes of 3-month graft losses are reported in Table 3.

Regarding the overall graft survival, there was no significant difference ($p = 0.21$) between the two groups (Figure 5a) even when specifically considering ECD grafts ($p = 0.31$) (Figure 5b). However, subgroup analysis revealed that TPCS significantly improved overall graft survival from elderly (age > 70) donors ($p = 0.02$) (Figure 6).

Discussion

Orthotopic liver transplantation is the most effective treatment for end-stage liver diseases. Owing to the limited number of donors, this success has led to an increase in the discrepancy between the number of candidate and transplanted patient and has forced transplant teams to increase the use of ECD grafts. This strategy has reduced the deaths of patients on waiting list (22) but has increased the rate of graft dysfunction (5).

Our study aimed at evaluating if TPCS, performed during the anhepatic phase of the transplant procedure, could improve graft function and survival. Using a propensity score matching analysis, we showed that TPCS significantly improved ECD grafts survival in the early postoperative outcomes represented by a significant improvement of the 3-month survival rate. Moreover, this beneficial effect was even more pronounced when considering the sub-group of elderly graft (i.e. >70 years) with an improved long-term survival in the TPCS group.

Liver parenchyma injuries related to IRI, which could be represented by transaminase levels in the early POD, were not improved by the use of TPCS. However, the incidence of biliary complications and cholestasis enzymes were significantly reduced in the TPCS group during the postoperative course, which could reflect the reduction

of IRI injury in the biliary tree. We also found that TPCS significantly reduced intraoperative transfusions and improved postoperative liver function. However, this effect only prevailed in the early POD and faded progressively since POD3, which could explain the similar rate of EAD observed between the 2 groups since the definition of EAD is based on biological parameters that are collected on POD7 for the most part. These observations revealed that TPCS only improve initial graft recovery and its effects may then disappear due to the potential incidence of other complications (i.e. immunologic, infectious and vascular complications). We found a significant increase in operative time, which may be explained by the time to performed and removed TPCS. Even if this impact is moderate compared to the average 6 hours of the procedure, our finding and explication are questionable as TPCS could make easier native liver removal and then reducing operative time as previously reported.(23)

During OLT, the clamping and sectioning of the portal vein from the native liver induces portal hypertension and splanchnic venous congestion (7) which leads to intestinal edema and mucosal barrier dysfunction, with subsequent bacterial translocation, endotoxemia and secretion of pro-inflammatory cytokines (interleukin 6, Tumor Necrosis Factor (TNF) alpha) (8). This accumulation of noxious products is directly released into the graft on revascularization, resulting in activation of Kupffer cells, thereby exacerbating IRI lesions (24), especially since endotoxemia clearance, which is supported by the liver, is not functional in early post-OLT (25).

By avoiding portal hypertension during the anhepatic phase, TPCS could enable significant reduction in blood transfusion. By the same mechanism, it could reduce the production of cytotoxic elements and provide a better and safer hemodynamic situation after revascularization (10). We believe that taken together, these

phenomenon participate in improving initial graft function and survival, especially in ECD grafts which are known to be more vulnerable to hemodynamic status and IRI lesions (26).

The interest of TPCS has been previously studied by Figueras et al.(13) in the only prospective randomized study on the subject. They found an improvement of cardiac output, renal function and reduced blood transfusion in the TPCS group especially for patients with severe portal hypertension prior to LT. However, that study failed to show an improvement in graft function in the TPCS group, probably due to the limited sample size (40 patients in each group) with almost no ECD grafts. Other studies have confirmed the benefit of TPCS on blood transfusion, intraoperative hemodynamic status and reduction of reperfusion syndrome incidence (10, 23, 27-29). As for graft outcome and function, Ghinolfi et al. (11) reported their series of 148 OLT and found a significant reduction in 30-day mortality in the TPCS group and in 3-month mortality when the patients received high-risk donor grafts. However, improvement in graft function was not demonstrated. Pratscke et al. (12) also found that TPCS, using a prosthetic shunt between the portal and femoral veins, significantly reduced liver enzyme level on POD1, 2 and 7 as well as bilirubin level on POD1 and significantly improved graft survival. However, despite a large study population (448 OLT) over a 13-year study period, these results suffered from the absence of a selection process. Indeed, the patients in the shunt group were significantly younger ($p < 0.001$), had lower MELD scores ($p = 0.1$) and fewer emergency transplantations ($p = 0.05$).

With more than 600 matched patients, our study is the largest to evaluate the benefit of TPCS. The size of the study population and the use of advanced statistical method (i.e. propensity matched analysis with a caliper restriction of 0.1 and linear mixed

model) highly reduced bias owing to heterogeneity of the study population and therefore enhanced the strength of our results.

However, our results must be interpreted with caution since this is a retrospective study with potential bias. Indeed, the decision to perform or not TPCS, which was dependent to the surgeon habits, could still have induced a selection bias despite the matching process. Moreover, in our study, the portal vein was divided prior to liver mobilization in all cases while it could have been done later (i.e. just before liver removal) in the non-TPCS group in order to reduce splanchnic congestion duration and then occurrence of IRI. However, most authors reported the same procedure as us. (9, 11, 13) Indeed, delaying the portal vein division may make the liver mobilization, the detachment of the caudate lobe from the IVC and the section of the retrohepatic accessory veins harder and consequently increase bleeding during the liver mobilization. Therefore, our results must be confirmed by a prospective randomized trial with enough power. This awaited study (29), is currently being performed by our team (clinical trial: NCT02784119).

Conclusion

During OLT, TPCS should be recommended especially when considering the use of an ECD graft which now represents the majority of situations. These results should be confirmed by a prospective randomized trial.

References

1. biomedecine Adl. **Le rapport médical et scientifique de l'Agence de la biomédecine**. 2013.
2. Busuttil RW, Tanaka K. The utility of marginal donors in liver transplantation. *Liver Transpl*2003 Jul;9(7):651-63.
3. Merion RM, Goodrich NP, Feng S. How can we define expanded criteria for liver donors? *J Hepatol*2006 Oct;45(4):484-8.
4. Maluf DG, Edwards EB, Kauffman HM. Utilization of extended donor criteria liver allograft: Is the elevated risk of failure independent of the model for end-stage liver disease score of the recipient? *Transplantation*2006 Dec 27;82(12):1653-7.
5. Feng S, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punch JD, DeBroy MA, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. *Am J Transplant*2006 Apr;6(4):783-90.
6. Filos KS, Kirkilesis I, Spiliopoulou I, Scopa CD, Nikolopoulou V, Kouraklis G, et al. Bacterial translocation, endotoxaemia and apoptosis following Pringle manoeuvre in rats. *Injury*2004 Jan;35(1):35-43.
7. Unno N, Uchiyama T, Yamamoto N, Inuzuka K, Sagara D, Konno H. Portal triad occlusion induces endotoxin tolerance: role of portal congestion. *J Surg Res*2006 Oct;135(2):213-7.
8. Tzakis AG, Reyes J, Nour B, Marino IR, Todo S, Starzl TE. Temporary end to side portacaval shunt in orthotopic hepatic transplantation in humans. *Surg Gynecol Obstet*1993 Feb;176(2):180-2.
9. Arzu GD, De Ruvo N, Montalti R, Masetti M, Begliomini B, Di Benedetto F, et al. Temporary porto-caval shunt utility during orthotopic liver transplantation. *Transplant Proc*2008 Jul-Aug;40(6):1937-40.

10. Paugam-Burtz C, Kavafyan J, Merckx P, Dahmani S, Sommacale D, Ramsay M, et al. Postreperfusion syndrome during liver transplantation for cirrhosis: outcome and predictors. *Liver Transpl*2009 May;15(5):522-9.
11. Ghinolfi D, Marti J, Rodriguez-Laiz G, Sturdevant M, Iyer K, Bassi D, et al. The beneficial impact of temporary porto-caval shunt in orthotopic liver transplantation: a single center analysis. *Transpl Int*2011 Mar;24(3):243-50.
12. Pratschke S, Meimarakis G, Bruns CJ, Kaspar M, Prix N, Zachoval R, et al. Temporary intraoperative porto-caval shunt: useless or beneficial in piggy back liver transplantation? *Transpl Int*2012 Jan;26(1):90-8.
13. Figueras J, Llado L, Ramos E, Jaurrieta E, Rafecas A, Fabregat J, et al. Temporary portocaval shunt during liver transplantation with vena cava preservation. Results of a prospective randomized study. *Liver Transpl*2001 Oct;7(10):904-11.
14. Audet M, Piardi T, Panaro F, Cag M, Habibeh H, Gheza F, et al. Four hundred and twenty-three consecutive adults piggy-back liver transplantations with the three suprahepatic veins: was the portal systemic shunt required? *J Gastroenterol Hepatol*2010 Mar;25(3):591-6.
15. Muscari F, Suc B, Aguirre J, Di Mauro GL, Bloom E, Duffas JP, et al. Orthotopic liver transplantation with vena cava preservation in cirrhotic patients: is systematic temporary portacaval anastomosis a justified procedure? *Transplant Proc*2005 Jun;37(5):2159-62.
16. Kluger MD, Memeo R, Laurent A, Tayar C, Cherqui D. Survey of adult liver transplantation techniques (SALT): an international study of current practices in deceased donor liver transplantation. *HPB (Oxford)*2011 Oct;13(10):692-8.

17. Belghiti J, Panis Y, Sauvanet A, Gayet B, Fekete F. A new technique of side to side caval anastomosis during orthotopic hepatic transplantation without inferior vena caval occlusion. *Surg Gynecol Obstet*1992 Sep;175(3):270-2.
18. Boudjema K, Camus C, Saliba F, Calmus Y, Salame E, Pageaux G, et al. Reduced-dose tacrolimus with mycophenolate mofetil vs. standard-dose tacrolimus in liver transplantation: a randomized study. *Am J Transplant*2011 May;11(5):965-76.
19. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*2009 May 5;150(9):604-12.
20. Olthoff KM, Kulik L, Samstein B, Kaminski M, Abecassis M, Emond J, et al. Validation of a current definition of early allograft dysfunction in liver transplant recipients and analysis of risk factors. *Liver Transpl*2010 Aug;16(8):943-9.
21. Cnaan A, Laird NM, Slasor P. Using the general linear mixed model to analyse unbalanced repeated measures and longitudinal data. *Stat Med*1997 Oct 30;16(20):2349-80.
22. Barshes NR, Horwitz IB, Franzini L, Vierling JM, Goss JA. Waitlist mortality decreases with increased use of extended criteria donor liver grafts at adult liver transplant centers. *Am J Transplant*2007 May;7(5):1265-70.
23. Suarez-Munoz MA, Santoyo J, Fernandez-Aguilar JL, Sanchez-Perez B, Perez-Daga JA, Ramirez-Plaza C, et al. Transfusion requirements during liver transplantation: impact of a temporary portacaval shunt. *Transplant Proc*2006 Oct;38(8):2486-7.
24. Bilzer M, Roggel F, Gerbes AL. Role of Kupffer cells in host defense and liver disease. *Liver Int*2006 Dec;26(10):1175-86.

25. Abdala E, Baia CE, Mies S, Massarollo PC, de Paula Cavalheiro N, Baia VR, et al. Bacterial translocation during liver transplantation: a randomized trial comparing conventional with venovenous bypass vs. piggyback methods. *Liver Transpl*2007 Apr;13(4):488-96.
26. Ghinolfi D, De Simone P, Lai Q, Pezzati D, Coletti L, Balzano E, et al. Risk analysis of ischemic-type biliary lesions after liver transplant using octogenarian donors. *Liver Transpl*2016 Jan 19.
27. Margarit C, de Cenarruzabeitia IL, Lazaro JL, Cancino JD, Rojas LH, Escartin A, et al. Portacaval shunt and inferior vena cava preservation in orthotopic liver transplantation. *Transplant Proc*2005 Nov;37(9):3896-8.
28. Hesse UJ, Berrevoet F, Troisi R, Mortier E, Pattyn P, de Hemptinne B. Liver transplantation by preservation of the caval flow with temporary porto-caval shunt or veno-venous bypass. *Transplant Proc*1997 Dec;29(8):3609-10.
29. Davila D, Bartlett A, Heaton N. Temporary portocaval shunt in orthotopic liver transplantation: need for a standardized approach? *Liver Transpl*2008 Oct;14(10):1414-9.

Figure and table legends

Figure 1: Flow chart

PCS: portocaval shunt; PVT: portal vein thrombosis; TPCS: temporary portocaval shunt

Figure 2: Evolution of aminotransferase level in the early post-operative days

ALAT: alanine aminotransferase; ASAT: aspartate aminotransferase; TPCS: temporary portocaval shunt

Figure 3: Evolution of hemostasis parameters level in the early post-operative days

PT :prothrombin time; FV :Factor V; TPCS: temporary portocaval shunt

Figure 4: Evolution of biliary parameters level in the early post-operative days

GGT : gamma-glutamyltransferase; PAL: alkaline phosphatase; TPCS: temporary portocaval shunt

Figure 5: Overall graft survival after propensity score matching

A: graft survival of the whole matched population

B: graft survival of matched patients transplanted with extended criteria donor (ECD) graft

Figure 6: Elderly (> 70 years old) graft survival

Graft survival of matched patients transplanted with elderly (i.e. >70 year) graft

Table 1: Preoperative data

Table 2: Per and postoperative data

Table 3: Causes of 3-month graft loss

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Table 1: Preoperative data

	Entire population n= 954 (%)	Propensity matching		p- value
		Non-TPCS Group n=343 (%)	TPCS group n=343 (%)	
Gender				
Male	718 (75.3)	269 (78.4)	270 (78.7)	0.99
Female	236 (24.7)	74 (21.6)	73 (21.3)	
Age	56 [15-73]	55 [17-73]	56 [17-68]	0.47
BMI	26.2 [16-47]	26.5 [17-47]	26 [16-44]	0.75
Diagnosis				0.87
HCC	279 (29.2)	110 (32.1)	111 (32.4)	
Alcohol	407 (42.7)	157 (45.8)	157 (45.8)	
Biliary and immunologic	77 (8.1)	24 (7)	19 (5.5)	
Viral hepatitis	101 (10.6)	35 (10.2)	34 (9.9)	
Other	90 (9.4)	17 (5)	22 (6.4)	
Child Pugh class				0.18
A	340 (35.6)	91 (26.5)	106 (30.9)	
B	251 (26.3)	102 (29.7)	82 (23.9)	
C	363 (38.1)	150 (43.7)	155 (45.2)	
MELD score (median value)	14.1 [5-40]	15.9 [5-40]	16.1 [5-40]	0.76
<30	865 (93.6)	311 (90.7)	316 (92.1)	
≥30	59 (6.4)	32 (9.3)	27 (7.9)	
Creatinine level (preoperative)	77 [8-486]	77 [35-371]	77.5 [8-356]	0.74
Types of preservation solution				0.64
Celsior	767 (80.4)	279 (81.3)	270 (78.7)	
UW	54 (5.7)	13 (3.8)	13 (3.8)	
Other/Unknown	133 (13.9)	51 (14.9)	60 (17.5)	
Cause of donor's death				0.14
Traumatic	277 (29)	100 (29.2)	100 (29.2)	
Vascular	551 (57.8)	188 (54.8)	208 (60.6)	
Anoxic	92 (9.6)	41 (12)	27 (7.9)	
Other	34 (3.6)	14 (4.1)	8 (2.3)	
Donor Gender				0.35
Male	578 (60.6)	207 (60.3)	220 (64.1)	
Female	376 (29.4)	136 (39.7)	123 (35.9)	
Donor age (median value)	52 [1-90]	52 [1-90]	55 [10-86]	0.48
< 65	713 (74.7)	250 (72.9)	243 (70.8)	
≥65	241 (25.3)	93 (27.1)	100 (29.2)	
Donor BMI (median value)	24.4 [12-54]	24.4 [12-49]	24.7 [14-54]	0.84
< 30	845 (88.6)	301 (87.8)	304 (88.6)	
≥30	109 (11.4)	42 (12.2)	39 (11.4)	
ECD graft	522 (54.7)	191 (55.7)	189 (55.1)	0.94

ECD: extended criteria donor; TPCS: temporary portocaval shunt

Table 2: Intra- and postoperative data

	Entire population n= 954 (%)	Propensity matching		
		Non-TPCS Group n=343 (%)	TPCS group n=343 (%)	p-value
Cold ischemia time (min)	577 [183-1393]	558 [194-938]	572 [196-1148]	0.52
Warm ischemia time (min)	45 [16-190]	48 [20 – 190]	44 [16-125]	0.1
Anhepatic duration (min)	110 [24-310]	102 [24 – 280]	120 [25-310]	0.001
TPCS				
Yes	567 (59.4)	0 (0)	343 (100)	-
No	387 (40.6)	343 (100)	0 (0)	
Biliary reconstruction				>0.99
Duct-to-duct	902 (94.5)	330 (96.2)	329 (95.9)	
Hepaticojejunostomy	52 (5.5)	13 (3.8)	14 (4.1)	
Biliary drainage*				0.18
none	181 (20.1)	84 (25.5)	64 (19.5)	
T-Tube drain	523 (58)	169 (51.2)	182 (55.3)	
Trans-cystic drain	198 (22)	77 (23.3)	83 (25.3)	
Operative duration (min)	365 [160-1020]	362 [160-665]	388.5 [175-665]	0.03
Intra operative transfusion				
Packed Red blood cell (median)	5 [0-47]	6 [0-40]	5 [0-36]	0.02
none transfused	161 (17.4)	44 (12.8)	69 (20.1)	0.01
Fresh frozen plasma (median)	6 [0-60]	6 [0-40]	5 [0-37]	0.02
none transfused	189 (20.5)	50 (14.6)	72 (21)	0.04
Platelet count (median)	0 [0-64]	0 [0-10]	0 [0-8]	0.11
none transfused	561 (60.7)	185 (53.9)	209 (60.9)	0.08
EAD incidence	229 (24.4)	79 (23)	75 (21.9)	0.80
Arterial complications	106 (11.1)	38 (11.1)	37 (10.8)	>0.99
Thrombosis	32 (3.4)	13 (3.8)	7 (2)	0.26
Stenosis	74 (7.8)	25 (7.3)	30 (8.7)	0.57
Biliary complications	65 (6.8)	35 (10.2)	16 (4.7)	0.006
leak	43 (4.5)	21 (6.1)	11 (3.2)	0.1
Stenosis	22 (2.3)	14 (4.1)	5 (1.5)	0.06
ICU stay	4 [1-180]	4 [1-76]	4 [1-73]	0.15
hospitalization duration	20 [1-368]	20 [1-102]	20 [1-232]	0.49
Clavien-Dindo\geq3	246 (25.8)	97 (28.3)	83 (24.2)	0.41
Outcomes				
Median follow up (months)	48.61 [0-157]	48.36 [0-143]	41.44 [0-156]	0.42
3-months graft's survival	860 (90.1)	304 (88.6)	323 (94.2)	0.01
1-year graft's survival	810 (84.9)	287 (83.7)	304 (88.6)	0.08
3-months patient's survival	893 (93.6)	319 (93)	329 (95.9)	0.13
1-year patient's survival	848 (88.9)	306 (89.2)	313 (91.3)	0.44

* : reported only for duct-to-duct anastomosis ; EAD: early allograft dysfunction; ICU: intensive care unit; TPCS: temporary portocaval shunt

Table 3: Causes of 3-month graft loss

Causes of 3-month graft loss	Non-TPCS Group n=343 (%)	TPCS group n=343 (%)	p-value
Vascular complication	10 (2.9)	3 (0.9)	0.09
Graft and/or multivisceral failure	15 (4.3)	8 (2.3)	0.20
Infection	6 (1.7)	2 (0.6)	0.29
Surgical bleeding	1 (0.3)	0 (0)	>0.99
Cardiovascular disease	6 (1.7)	6 (1.7)	>0.99
Other	1 (0.3)	1 (0.3)	>0.99
Total	39 (11.4)	20 (5.8)	0.014

TPCS: temporary portocaval shunt

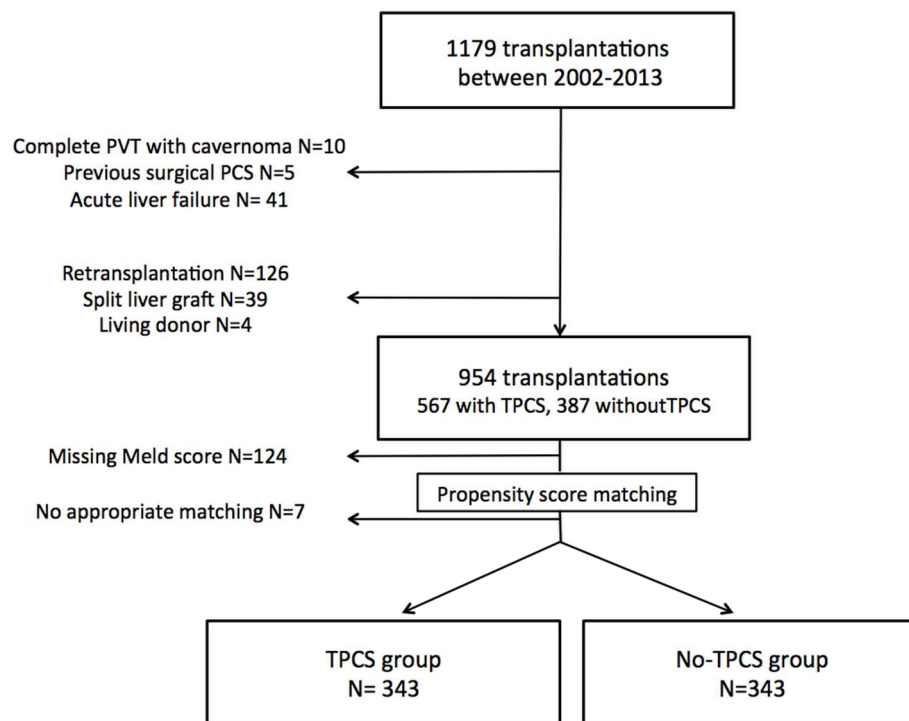


Figure 1 : Flow chart

94x70mm (300 x 300 DPI)

Accept

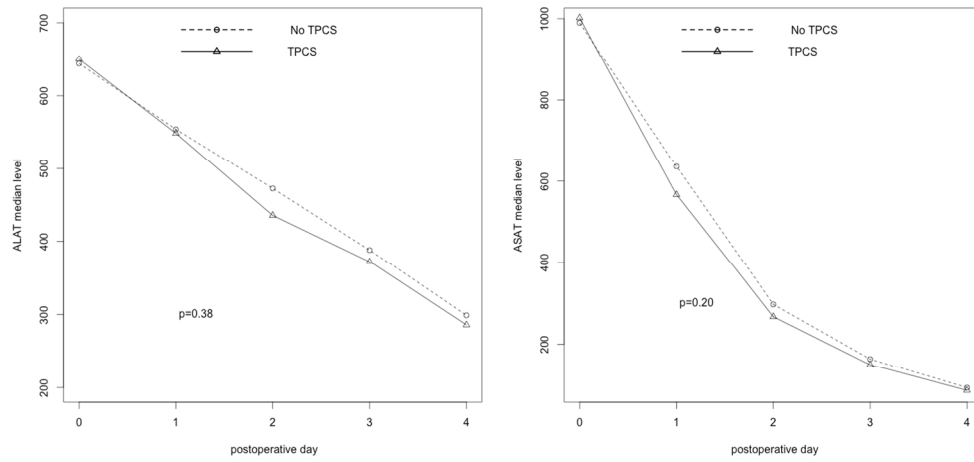


Figure 2 : Evolution of aminotransferase level in the early post-operative days

122x63mm (300 x 300 DPI)

Accepted

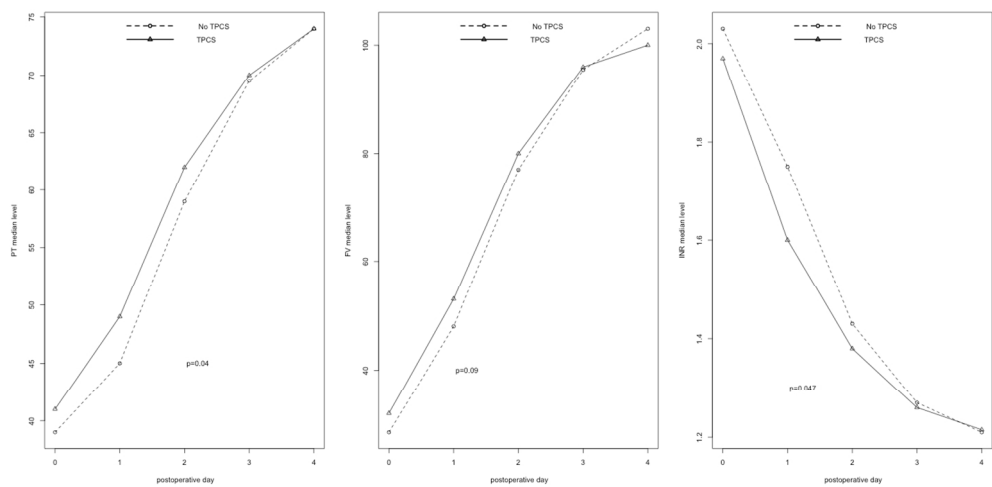


Figure 3 : Evolution of hemostasis parameters level in the early post-operative days

122x63mm (300 x 300 DPI)

Accepted

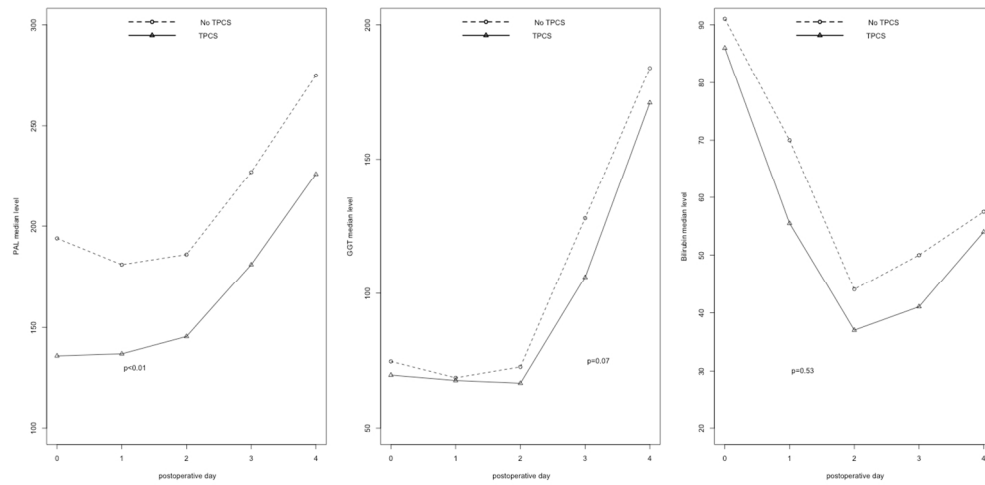


Figure 4 : Evolution of biliary parameters level in the early post-operative days

122x63mm (300 x 300 DPI)

Accepted

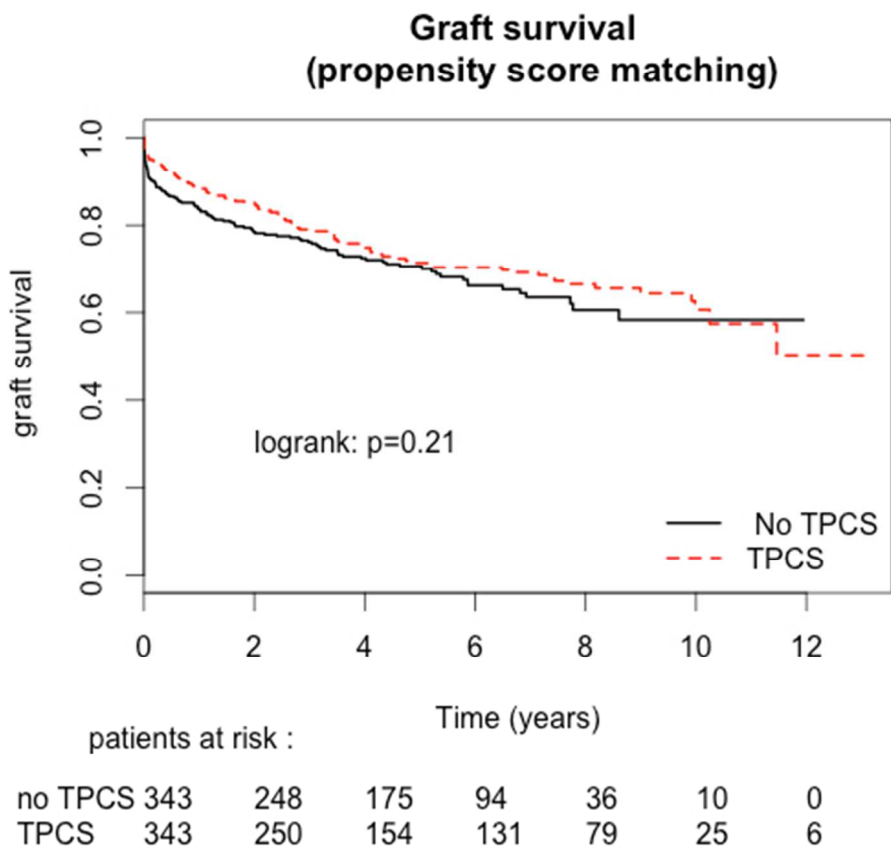


Figure 5 : Overall graft survival after propensity score matching
 † A: Graft survival of the entire matched population

46x44mm (300 x 300 DPI)

ACCEPT

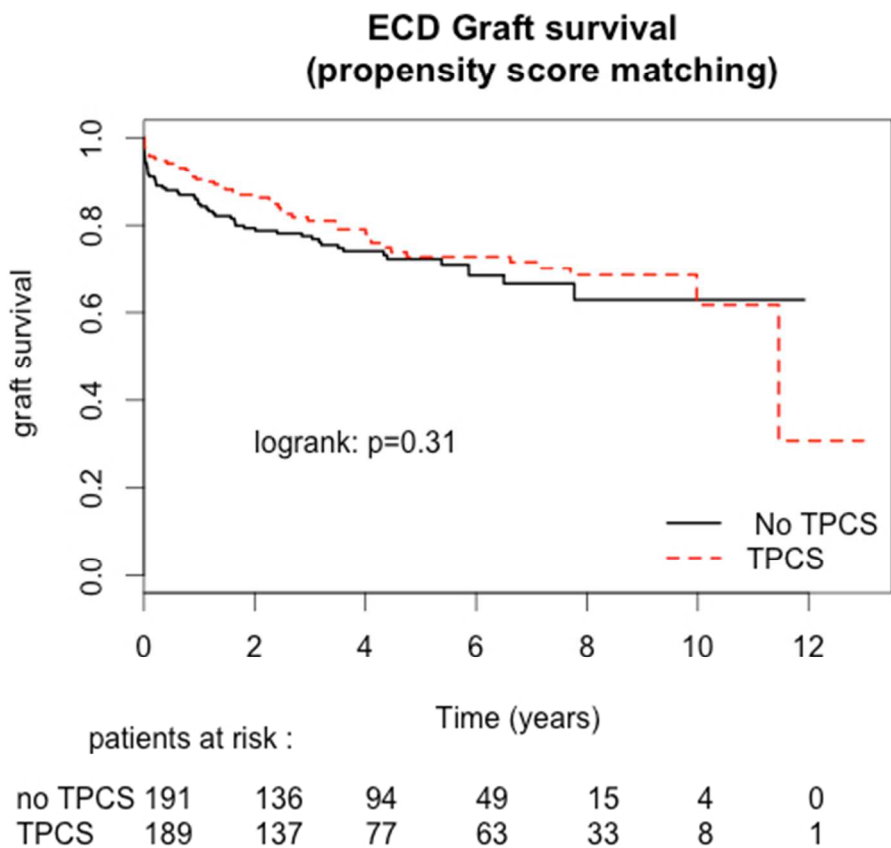


Figure 5: Overall graft survival after propensity score matching B: graft survival of matched patients transplanted with extended criteria donor (ECD) graft

46x44mm (300 x 300 DPI)

ACCEPT

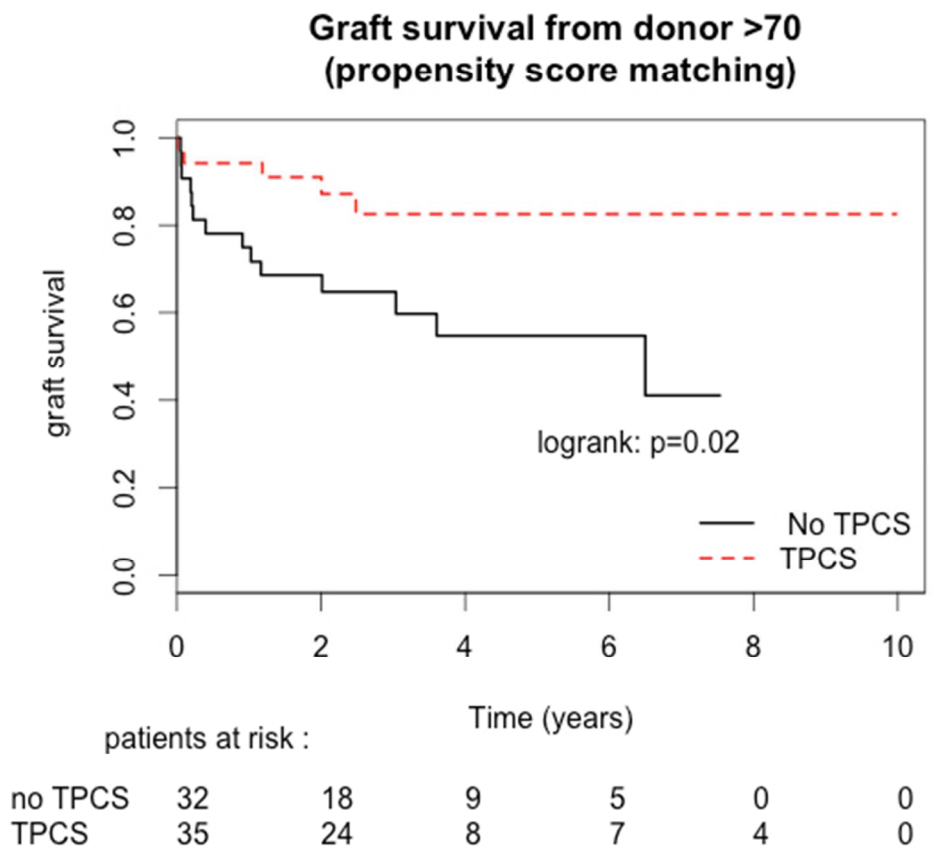


Figure 6: Elderly (> 70 years old) graft survival

46x44mm (300 x 300 DPI)

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Table S1: Interest of TPCS in supposed low portal tension group

	Supposed Low Portal tension group*		
	Non-TPCS Group n=100 (%)	TPCS group n=145 (%)	p-value
Gender			
Male	93 (93)	131 (90.3)	0.62
Female	7 (7)	14 (9.7)	
Age	59 [47-69]	59 [17-71]	0.85
Child Pugh class			0.003
A	66 (66)	121 (83.4)	
B	34 (34)	24 (16.6)	
C	0	0	
MELD score (median value)	10.2 [5.4-24.5]	8.8[5.4-20.4]	0.03
Donor age (median value)	55.5 [12-90]	56 [10-86]	0.67
< 65	73 (73)	101 (69.7)	
≥65	27 (27)	44 (30.3)	
ECD graft	58 (58)	79 (55.5)	0.94
Cold ischemia time (min)			
Operative duration (minutes)			
Intra operative transfusion			
Packed Red blood cell (median)	4 [0 ; 20]	3 [0 ; 27]	0.02
Fresh frozen plasma (median)	5 [0 ; 18]	3 [0 ; 19]	0.02
Platelet count (median)	0 [0 ; 8]	0 [0 ; 3]	0.03
EAD incidence	21 (21%)	37 (25.5%)	0.51
Arterial complications	18 (18)	20 (13.8)	0.49
Biliary complications	9 (9)	9 (6.2)	0.57
ICU stay	3 [1 ; 24]	3 [0 ; 73]	0.54
hospitalization duration	17 [2 ; 368]	17 [0 ; 75]	0.96
Clavien-Dindo≥3	17 (17)	34 (23.4)	0.05
Outcomes			
Median follow up (months)	47.3 [0 ; 168]	40.2 [0 ; 156]	0.88
3-months graft's survival	90 (90)	131 (90.3)	> 0.99
1-year graft's survival	86 (86)	125 (86.2)	> 0.99
3-months patient's survival	95 (95)	135 (93.1)	0.74
1-year patient's survival	94 (94)	130 (89.7)	0.34

* : defined as patient transplanted for HCC with Child-Pugh grade A or B.

EAD: early allograft dysfunction; ICU: intensive care unit; TPCS: temporary portocaval shunt

Supplementary Figure 1 : Distribution of standardized mean differences before and after matching process

