How to Deal with Non-Extractable TIPS Complicating Liver Transplantation.

Nicholas Gilbo^{1,2} , Laurens J Ceulemans^{1,2}, Geert Maleux³, Frederik Nevens⁴, Wim Laleman⁴,
Ina Jochmans^{1,2}, Diethard Monbaliu^{1,2} and Jacques Pirenne^{1,2}

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ORCIDs: Nicholas Gilbo: 0000-0001-6456-7071; Ina Jochmans: 0000-0003-4592-2810

1. Abdominal Transplantation Surgery, University Hospitals of Leuven, Leuven, Belgium
2. Laboratory of Abdominal Transplant Surgery, Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium
3. Radiology, University Hospitals Leuven, Herestraat 49, B-3000 Leuven (Belgium).
4. Hepatology, University Hospitals Leuven, Herestraat 49, B-3000 Leuven (Belgium).

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Footnote page**Abbreviations:**

CIT, Cold Ischemia Time

CT-scan, Computed Tomography scan

DCD, Donor after Circulatory Death

LTx, Liver Transplantation

MELD, Model for End stage Liver Disease

PH, Portal Hypertension

PV, Portal Vein

SMV, Superior Mesenteric Vein

SV, Splenic Vein

TIPS, Transjugular Intrahepatic Portosystemic Shunt

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Corresponding author:

Jacques Pirenne, MD, PhD, MSc

Abdominal Transplant Surgery, University Hospitals Leuven, Herestraat 49, B-3000 Leuven

(Belgium). Phone: +32 16 348727, Fax: +32 16 348743, E-mail: jacques.pirenne@uzleuven.be

To the editor:

Liver Transplantation (LTx) is the definitive and successful treatment of end-stage-liver-disease of many etiologies. The demand for LTx outweighs organ availability, thereby lengthening waiting time of listed patients and increasing the risk of pre-transplant complications, such as those related to Portal Hypertension (PH). Transjugular Intrahepatic Portosystemic Shunt (TIPS) is a well-established option for treatment and prevention of sequelae of PH, such as variceal bleeding, refractory ascites, hepatic hydrothorax, hepato-renal syndrome, and is frequently performed as a bridging therapy towards LTx.

A underestimated complication potentially posing a threat to the success of LTx after TIPS is an non-extractable stent. After a systematic search performed on February 27th 2018 using the MeSH terms 'portosystemic shunt, transjugular intrahepatic' AND 'liver transplantation' AND ('intraoperative complication' OR 'side effects') we identified only two cases in which TIPS-stents placed beyond the PV confluence could not be extracted during hepatectomy^{1,2}. However, only in one a fragment of TIPS-stent was left *in situ*¹, while in the second an extended tract of the PV-mesenteric system was excised to remove the TIPS². Nevertheless, the literature remains very scant concerning intraoperative and post-transplant management of such complication and we report two cases in which stents placed in the PV beyond the confluence of splenic (SV) and superior mesenteric vein (SMV) could not be extracted completely, discussing challenges and consequences that might derive from the obliged choice of leaving a (fragment of) TIPS-stent *in situ*.

Cases presentation

Case 1

On April 2008, a 56 yo male affected by post-alcoholic liver cirrhosis underwent TIPS for refractory ascites (MELD 13, Child C11) using a ePTFE-covered endo-prosthesis (Viator, W.L. Gore&Associates, Flagstaff, AZ, USA). The procedure was uncomplicated but recurrence of ascites required three revisions, including two balloon dilatations and the insertion of an extra bare metal stent due to thrombosis in the extrahepatic PV despite the TIPS-shunt. Decompensation occurred and the patient underwent LTx with MELD 27 (five years after TIPS). The liver graft was procured in a 63 yo male Donor-after-Circulatory-Death (DCD). The LTx was rendered difficult by the unexpected displacement of the TIPS-stent beyond the spleno-mesenteric confluence into the SV. The PV could not be safely dissected distally due to severe adhesions. Hence, the PV was clamped and divided as distally as possible and the TIPS transected. Despite several attempts, the fragment of TIPS located in the SV could not be safely extracted and had to be left *in situ*. It occupied only the medial/splenic side of the lumen of the PV and adequate PV blood flow was observed. The lateral wall of the PV was used for an end-to-side anastomosis of the graft-PV onto the recipient-PV (Figure 1A). Cold Ischemia Time (CIT) was 6h45min.

Anti-thrombotic prophylaxis was administered post-transplant and the post-operative course was uneventful. The PV anastomosis and the SV were repeatedly found patent on post-transplant imaging (Figure 1B). The recipient is doing well after four years.

Case 2

On April 2013, a 67 yo male affected by post-alcoholic liver cirrhosis underwent TIPS for refractory ascites (MELD 12, CHILD B7). During TIPS, a newly-formed PV thrombus extending

into the SV was discovered (grade 3 according to Yerdel et al.³), for which no anticoagulant therapy was ongoing. An ePTFE-covered endo-prosthesis (Viator, W.L. Gore&Associates, Flagstaff, AZ, USA) from the main PV up to the IVC and two additional bare metal-stents (Zilver nitinol-stent, Cook Medical, Bloomington, KT, USA) from the main PV down to the SV were used as a bail-out procedure after failed balloon angioplasty of the thrombosed SV. A post-procedural CT-scan showed early thrombosis of both stents. Low-Molecular-Weight-Heparin therapy was started. The thrombus persisted after two months extending from the SV until the right supra-hepatic vein (Figure 1C). Due to progressive hepatic failure (MELD 15), the patient was transplanted in June 2013 (65 yo male controlled-DCD). The nitinol-stent extending in the SV could not be safely removed; the second one extending into the SMV could be entirely removed but adequate PV flow could not be achieved despite several attempts to release the occlusion with Fogarty. Portal inflow to the graft was established by a 'jump graft' between the recipient-SMV and the graft-PV. The non-extractable SV-stent was left in its original position (Figures 1D, E). CIT was 6h45min. Post-operative course was complicated by hepatic artery thrombosis requiring re-LTx at day twenty-five. The 'jump graft' was open and re-used for a new PV-reconstruction. CIT was 8h48min.

Post-operative course was complicated by recurrent bacteraemia, the origin of which remained unknown after thorough microbiological investigation. Since gram-negative bacteria of gastrointestinal origin were repeatedly isolated (*Enterococcus Faecium*, *Brevimonas*, *Granulicatella*, *Klebsiella Oxytoca*) infection of the tips, or endotipsitis, was suspected. The recipient eventually succumbed to sepsis fifty-three days post-LTx.

Discussion

TIPS represents a major advancement in the management of PH-related complications and many LTx are performed in patients in whom a TIPS has been placed. The most commonly used stents are expanded-polytetrafluoroethylene (PTFE)-covered, and particular care is paid to position the covered part of the TIPS within the hepatic vein upwards and not too distally in the PV downwards, so that stents can be easily removed en-bloc with the liver during LTx.

Embedding leading to impossible removal of the TIPS is a threat of which transplant surgeons might be less aware as the real incidence of this complication, although expectedly low, is yet not known probably due to underreporting. Indeed, leaving a fragment of a TIPS *in situ* might be perceived as a low-risk situation since these are in fact vascular stents designed for long-term use and post-operative anti-coagulation can mitigate thrombotic events. However, as showed by our experience, a remnant stent in the PV poses both surgical and medical challenges that might compromise results after transplant.

First, it is usually an unexpected intraoperative finding since pre-transplant imaging rarely predicts embedding^{1,2}. In many cases TIPS placed eccentrically in the PV can be safely extracted after more extensive dissection of the vessel below the stent; therefore, extraction of the stent should always be attempted and 'eversion thromboendovenectomy' of the PV might be needed to complete it. In case of non-successful extraction, alternative strategies might include exenteratio of long tracts of the porto-mesenteric venous system containing the TIPS² or leaving a (fragment of) stent *in situ* and including the remnant TIPS in the PV-anastomosis¹. Nevertheless, extended exeresis of the PV-mesenteric system increases the risk of major bleeding (especially in presence of varices) and is technically challenging since

requires multiple and complex vascular reconstructions². Therefore, leaving a (segment of) TIPS-stent *in situ* might be, in our opinion, the safest intraoperative rescue option in the presence of adequate portal inflow (Figure 2). However, when a TIPS-stent is transected and its metal wires are exposed to the bloodstream the risk of thrombosis can theoretically increase. In our two cases, attention was paid on avoiding the presence of the stent at the suture line. In these situations, alternative techniques for PV inflow might be required, including an end-to-side PV anastomosis as we performed in one LTx. This technique might have been implemented already in experienced centers dealing i.e. with PV thrombosis; however, it was never described before and we report for the first time its feasibility, simplicity, safety, and efficacy on achieving liver reperfusion in presence of a remnant stent and patent PV. Additionally, anticoagulant prophylaxis might concur on the mitigation of post-transplant PV thrombotic events when balanced against the risk of post-operative bleeding.

The possibility to combine PV recanalization during TIPS in presence of complete obliterative PV thrombosis pre-transplant⁴ might reduce the number of stents used, thereby diminishing the risk of distally (dis)placed and non-extractable TIPS during LTx.

Finally, leaving a fragment of TIPS *in situ* might increase the risk of perioperative contamination of the stent, which may progress to infection of the TIPS, or endotipsitis, and fatal sepsis in immunocompromised patients, as in our second case. Despite its low incidence (1-2%), endotipsitis in a *native* liver is a life-threatening complication and if refractory to antibiotics may represent *per se* an indication for TIPS removal through LTx⁵.

The pathogenesis is multifactorial, but colonization of the stent by bacteria of

gastrointestinal origin seems to play a major role. Early onset endotipsitis (<3 months after TIPS placement) is likely due to microbial seeding at the time of insertion, whereas late onset (>3 months after TIPS placement) endotipsitis is usually associated with thrombosis or revision/manipulation of the TIPS-stent⁵. Recipients that underwent TIPS revisions or developed thrombosis of the stent might be at even higher risk of endotipsitis post-LTx if a (fragment of) stent is left *in situ*.

In conclusion, leaving a segment of TIPS-stent *in situ* may be the only possible strategy in rare cases of non-extractable TIPS. However, transplant surgeons should not underestimate the impact of this obliged rescue strategy, which might impair results after transplantation.

Revascularization of the graft may require alternative venous reconstructions and the simple end-to-side PV anastomosis should be part of the surgical armamentarium in these situations if PV remains patent. More importantly, the risk of infection of a remnant TIPS-stent after LTx should be taken into account.

Figures legend

Figure 1. Panel A shows case 1 per-operative view of the end-to-side portal vein anastomosis leaving the splenic part of the TIPS *in situ* (arrow indicates the graft-PV, arrow-heads indicate the recipient-PV); panel B shows the post-transplantation CT-scan with the wide open end-to-side portal vein anastomosis (arrow) and the remnant TIPS-stent (arrowheads). Panel C depicts case 2 pre-transplant CT-scan showing the thrombosis of the TIPS-stent; the post-operative CT-scan in panel D shows the presence of the remnant TIPS-stent in the SV, an open jump graft and extended areas of parenchymal necrosis due to hepatic artery thrombosis. Finally, panel E shows the intraoperative view of the open 'jumping graft' in case 2 at the time of re-transplantation for hepatic artery thrombosis and secondary biliary necrosis.

Figure 2. Proposal of a decision algorithm for the intraoperative management of a distally displaced TIPS-stent.

*The decision to perform extended excision of the PV-mesenteric system² should be based on the risk of intraoperative bleeding (especially in presence of signs of portal hypertension) and local expertise.

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Figure 2

Proposal of a decision algorithm for the intraoperative management of a distally displaced TIPS-stent.

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