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Clinical Case Report

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Successful Outflow Reconstruction to Salvage Traumatic Hepatic Vein-Caval Avulsion of a Normothermic Machine Ex-Situ Perfused Liver Graft

Case Report and Management of Organ Pool Challenges

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Abstract: Donor organ shortage continues to limit the availability of liver transplantation, a successful and established therapy of end-stage liver diseases. Strategies to mitigate graft shortage include the utilization of marginal livers and recently ex-situ normothermic machine perfusion devices.

A 59-year-old woman with cirrhosis due to primary sclerosing cholangitis was offered an ex-situ machine perfused graft with unnoticed severe injury of the suprahepatic vasculature due to road traffic accident.

Following a complex avulsion, repair and reconstruction of all donor hepatic veins as well as the suprahepatic inferior vena cava, the patient underwent a face-to-face piggy-back orthotopic liver transplantation and was discharged on the 11th postoperative day after an uncomplicated recovery.

This report illustrates the operative technique to utilize an otherwise unusable organ, in the current environment of donor shortage and declining graft quality. Normothermic machine perfusion can definitely play a role in increasing the graft pool, without compromising the quality of livers who had vascular or other damage before being ex-situ perfused. Furthermore, it emphasizes the importance of promptly and thoroughly communicating organ injuries, as well as considering all reconstructive options within the level of expertise at the recipient center.

Editor: Henrik Petrowsky.
Received: December 29, 2015; revised: February 6, 2016; accepted: February 25, 2016.
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The authors have no funding and conflicts of interest to disclose.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000003119

(*Medicine* 95(15):e3119)

Abbreviations: DCD = donation after cardiac death, LHV = left hepatic vein, MHV = middle hepatic vein, NMP = normothermic machine perfusion, OLT = orthotopic liver transplantation, PSC = primary sclerosing cholangitis, RHV = right hepatic vein, T_0 = time zero, US = ultrasonography.

INTRODUCTION

As the earliest descriptions of liver transplantation in humans in the 1960s, the technique has propagated to the point where it is considered a routine procedure, reaching excellent outcomes.[1,2] The World Health Organization in fact estimates that >20,000 liver transplantations are undertaken annually across 104 countries.[3] Nevertheless, liver transplantation remains largely limited by a continuing donor shortage.[4]

At the beginning of the 2015 transplant year, the UK liver transplant list consisted of 549 patients.[5] Additionally 1206 new patients were registered. During the same year, liver retrieval from 924 donors generated 812 transplantations, resulting in a net increase of the active list to 611 patients.[6] This represents an 11% active list yearly increase, and a 2-fold increase over 5 years.[5,6] In context, it is now estimated that nearly 18% of adults listed for a first elective liver transplant in the UK will die or deteriorate while waiting for a graft.[2]

Strategies to mitigate the still incumbent graft shortage include the utilization of higher-risk livers, living donation, donation after cardiac death, liver splitting, domino transplantation, and recently ex-situ machine perfusion.[2] In the following report, we describe a case where ex-situ machine perfusion and complex vascular reconstruction techniques were successfully employed and managed the transplantation of a significantly injured, and otherwise unusable, graft.

MATERIALS AND METHODS

Case Presentation

A 59-year-old woman with primary sclerosing cholangitis (PSC) and Child-Pugh Class B cirrhosis was referred to the Royal Free Hospital in London, UK, and following assessment she was listed for liver transplantation. The United Kingdom Model for End-Stage Liver Disease and Model For End-Stage Liver Disease scores were 51 and 18, respectively.

Her medical history was otherwise notable for ulcerative colitis, vitiligo, lichen planus, portal hypertension, incomplete portal vein thrombosis, grade 1 variceal gastropathy, small-volume diuretic-controlled ascites, and 1 episode of low-grade hepatic encephalopathy. The patient was allergic to penicillin, and her regular medication list consisted of propranolol, ursodeoxycholic acid, mesalamine, prednisolone, and therapeutic-dose tinzaparin.

A donation-after-cardiac-death (DCD) graft, retrieved from a 16-year-old male donor of body mass index 25.4 kg/m^2, became available 5 months after listing. The donor did not wear a seatbelt and sustained severe chest compression trauma when his car collided with a campervan. The donor liver function tests were unremarkable. The functional warm ischemic time from asystole to aortic perfusion was 16 minutes. A large hematoma in segment VIII and bluish discoloration at the diaphragmatic caval hiatus were noticed by the retrieving surgeon. Due to the cause of death, only the intra-abdominal organs were considered suitable for procurement.

The liver was enrolled to a multicenter randomized controlled trial comparing the efficacy of ex-vivo normothermic machine perfusion (NMP) with static cold storage in human liver transplantation. The graft was randomized to the machine protocol arm, and underwent 17 hours 28 minutes of perfusion with the OrganOx metra (OrganOx Ltd, Oxford, UK) normothermic perfusion device (total preservation time was 19 hours 32 minutes). Standard liver backtable preparation was performed by an experienced retrieval surgeon as part of the cannulation process. Before commencing NMP the suprahepatic cava was closed, as usual, with a vascular stapler preserving as much of the inferior vena cava (IVC) length as possible to cannulate the vessel.

The severe traumatic avulsion of the liver outflow was not immediately recognized by the time the organ was machine perfused. However, the organ tolerated the NMP well, due to the low blood pressure via the OrganOx device. The physiological flows were satisfactory during perfusion and no parenchymal compromise was recorded. An initial lactate was measured at 9.1 mmol/L, which by 1 hour had fallen to 0.5 mmol/L. The lactate remained <0.7 mmol/L for the rest of the perfusion. The hepatic arterial flow was consistently between 200 and 400 mL/min, the portal vein flow was maintained 1.0 to 1.2 L/min, and the IVC flow was kept at the level of 1.2 to 1.6 L/min. The pH normalized to 7.3 after ~60 minutes of perfusion. This pH was maintained unaided for the duration of the perfusion. Bile production was consistently 12 to 20 mL/hour. The liver appeared soft, healthy, and homogeneously perfused throughout the ex-situ process. At the end of the NMP, the liver was flushed on the device.

Operative Approach

On benchtop inspection at the recipient hospital, the graft appeared to be of excellent quality, with a weight of 1390 g, smooth contours, and conventional biliovascular anatomy. The infrahepatic IVC was noted to be quite long, and it was divided above the renal veins. As already mentioned, the suprahepatic IVC was stapled and excised about 5 mm below the staple line. At this point, the following 3 issues were identified by the implanting surgeon on the backtable:

(1) The trauma to the hepatic veins, with their ostia, was evaluated as follows: the right hepatic vein (RHV) was fully avulsed from the cava, the middle hepatic vein (MHV) was separated at the anterior hemicircumference, the left hepatic vein (LHV) suffered intimal tear at the confluence with the vena cava. The pericaval diaphragmatic connective tissue was however still intact.

(2) After removing the staple line, the suprahepatic IVC was very short: 1 mm at the LHV, 2 mm at the MHV, and 3 to 4 mm at the RHV. Although no thoracic organ was retrieved, unfortunately an expected cuff of right atrium was not present in continuity with the suprahepatic IVC (Figure 1).

(3) The hepatic vein avulsion was not noticed and not communicated to the implanting team.
General anesthesia was induced intravenously with fentanyl, propofol, and rocuronium, followed by cannulation of the right internal jugular vein with a central venous and rapid infusor catheter. Additional monitoring took place via a right radial arterial catheter. Peritoneal access was achieved through an inverse "L"-shaped incision, and the liver was completely mobilized. A total hepatectomy was performed with caval preservation.

The graft was flushed with 4 L of histidine–tryptophan–ketoglutarate solution. Given the reasonable concerns that the liver would not have been implantable due to the vascular damage, a complex venous reconstruction was undertaken before implantation in order to repair the avulsion and restore the length of the suprahepatic IVC. Part of the long suprarenal infrahepatic IVC was resected and used as an interposition homograft to re-establish continuity between the suprahepatic IVC and the hepatic veins ostia (Figure 2). A 6–0 polydioxanone venoplasty between the LHV and MHV, and between the MHV and RHV respectively was performed to reconstruct the continuity of the 3 ostia and to improve the outflow, avoiding stenosis. The remainder of the traumatized junction, between the hepatic veins and the suprahepatic IVC, was completely taken down and the suprarenal segment of IVC was used to reconfigure the liver outflow into a single common ostium (Figure 2). Continuous 5–0 polypropylene sutures were used. Subsequently, the donor IVC was spatulated posteriorly (Figure 3) and the recipient IVC was spatulated anteriorly as part of face-to-face cavo-cavostomy, performed with 3–0 running polypropylene suture. Attention was then turned to the donor and recipient portal veins, which were anastomosed in end-to-end fashion with 5–0 polypropylene sutures. On completion of the above venous inflow and outflow anastomoses, the IVC clamps were released and the liver assumed a normal appearance of satisfactory reperfusion.

Following liver reperfusion, the donor and recipient common hepatic arteries were anastomosed end-to-end using 6–0 polypropylene sutures. Finally, an end-to-end anastomosis between the donor common hepatic duct and the recipient common bile duct was formed with 6–0 polydioxanone sutures.

Intraoperative Doppler ultrasonography (US) confirmed satisfactory arterial, portal venous, and hepatic venous flow. Subsequently, a time-zero (T_0) biopsy was taken from the left lateral section.

The operative duration was 4 hours 40 minutes, requiring the transfusion of 1 unit of packed red blood cells.

RESULTS AND FOLLOW-UP

Postoperatively, an intravenous epoprostenol (Flolan) infusion was maintained in addition to 5000 units of unfractionated heparin twice daily, and the patient was monitored in the Intensive Care Unit. Postoperative peak serum values were as follows: INR = 1.6; Bilirubin = 24 μmol/L; ALT = 373iu/L; AST = 395iu/L; ALP = 193iu/L; creatinine = 100 μmol/L; urea = 13.6 mmol/L. Doppler US revealed patent inflow and

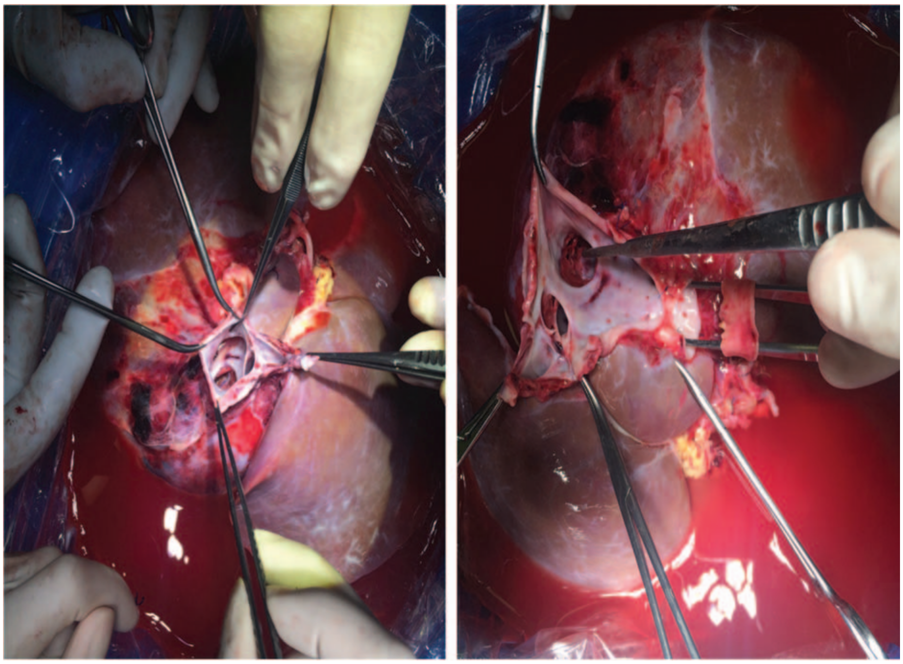

FIGURE 1. Short suprahepatic IVC (left) and areas of severe injury (right). IVC = inferior vena cava.

outflow hepatic vessels, with turbulent antegrade portal vein flow, biphasic hepatic vein flow, and a hepatic arterial resistive index of 0.6. Histopathological analysis confirmed cirrhosis in the native liver, with features consistent with PSC. Examination of the T_0 graft biopsy revealed artifactual degeneration with normal liver architecture, mild mixed portal inflammation, and minimal reperfusion injury. Furthermore, there was no graft steatosis, cholestasis, siderosis, or alpha-1-antitrypsin deposition.

On the first postoperative day, extubation took place and inotropic support was weaned. On the second postoperative day the nasogastric tube was removed, the patient was transferred to ward, and the normal diet was recommenced. On the 5th postoperative day, both drains were removed and bowel

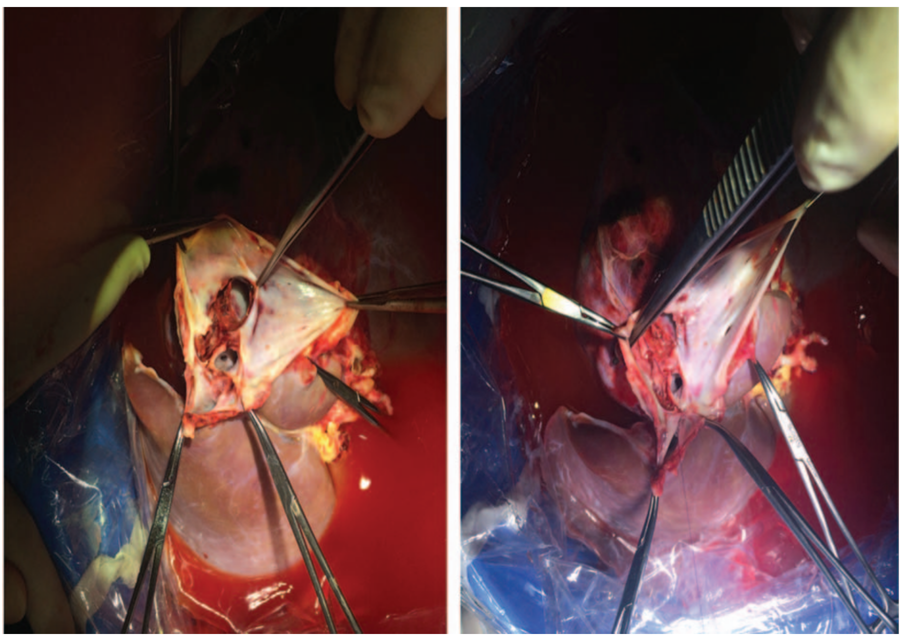

FIGURE 2. Septoplasty of the middle and left hepatic veins septum (left). Division and septoplasty of the middle and right hepatic veins, in anticipation of further reconstruction (right).

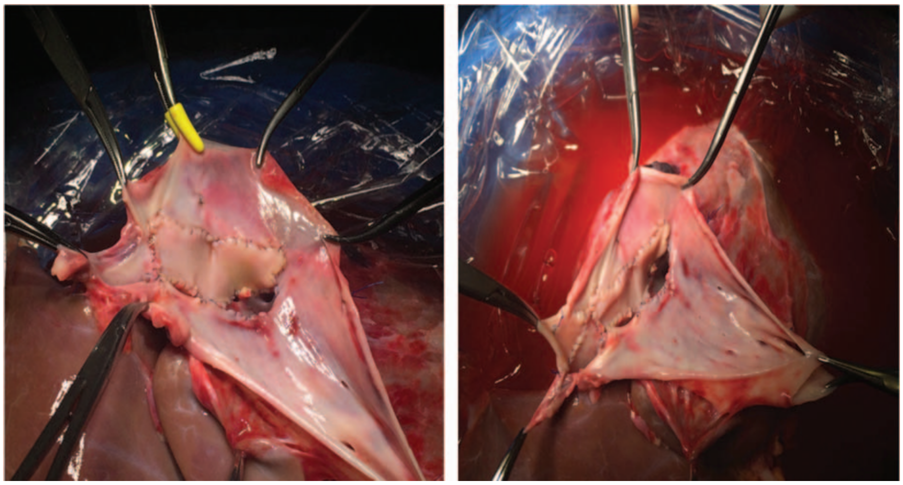

FIGURE 3. Completion of the septoplasty/reconstruction of hepatic veins and suprahepatic IVC. The right side illustrates the elongation of the LHV by 1 mm, using a patch to cover the gap. Creation of neo-lumen of the hepatic veins and repair of their junction with the IVC. Spatulation of the posterior IVC wall.IVC = inferior vena cava, LHV = left hepatic vein.

function resumed. On the 11th postoperative day, the patient was discharged home asymptomatic with aspirin, azathioprine, lactulose, senokot, co-trimoxazole, ranitidine, prednisolone, and tacrolimus. At seventy days postoperatively the patient remained well and the graft function was satisfactory, with good venous outflow and without sign of thrombosis of the hepatic veins or IVC. At that point, the prospect of publishing this case was discussed with the patient, who gave his full consent to proceed.

DISCUSSION

This case illustrates how the application of technological innovation and operative expertise can achieve a successful outcome with a suboptimal, yet scarce and therefore extremely valuable graft. The growing relative shortage of donors discussed earlier is compounded by a downward trend in graft utilization. Orman et al conducted a discrete event simulation using the United Network for Organ Sharing database to predict that liver utilization will fall in the United States from the current 78% level to 44% by 2030, and that utilization of marginal grafts would only influence this trend toward 48%.[7] Factors implicated in declining graft utilization and quality include an ageing donor pool with an increasing reliance on DCD organs, and a rise in comorbidities such as diabetes mellitus, obesity, and nonalcoholic fatty liver disease. The authors conclude that transplant surgeons will find themselves compromising with inferior grafts and outcomes, unless they develop new strategies to increase donation and utilization.[7]

An additional threat to graft quality is of course injury, either during the mechanism of trauma/death, or during organ procurement. As Nijkamp et al demonstrate in their study of 241 donor livers, anatomical injuries occur in up to 34%, with parenchymal and vascular injuries occurring more commonly.[4] Their analysis revealed that injuries led to complications in 6.6% of all grafts, but that many injuries were clinically insignificant. Venous injuries specifically accounted for 10% of all injuries and presented in 3% of all grafts. Their implications however were not discussed. Alarmingly, only 20 (21%) of these 96 injuries were reported by retrieval teams.[4] Nicolini et al agree that hepatic injuries are underestimated, and state: ''in our experience the surgical expertise achieved during living donor and domino liver transplantation was essential to rescue 2 severely damaged liver grafts.''[8] In our case, however, the graft had been severely damaged prior to procurement, due to road accident, and was fortunately repaired by a complex caval reconstruction at the recipient center.

Orthotopic liver transplantation was initially described as consisting of complete IVC resection, with interposition of the intrahepatic donor IVC and formation of a cranial and caudal cavo-cavostomies.[9] Although still commonly used, the complete resection technique has made way for the newer piggyback technique, whereby the recipient cava is preserved. Since its original description by Tzakis et al in 1989,[10] the piggyback technique evolved to the point where the recipient IVC is never completely occluded during the operation. Advantages of the piggyback versus the complete resection technique include shorter operative, anhepatic, and warm ischemia times, as well as less hemorrhage.[9] The piggyback technique usually carries a hepatic outflow complication risk of 1.5% to 3.8%, which has been minimized to 0.5% in experienced hands. Hepatic outflow complications in turn have been associated with retransplantation and mortality rates of 40% and 23%.[11]

The face-to-face cavo-cavostomy, where the donor/recipient IVC is spatulated and splayed open wide in a triangular fashion, has the disadvantage of requiring full IVC clamping with potential need for veno-venous bypass. However, it is our preferred technique for the following reasons:

(1) It creates the largest possible opening, which maximizes the venous outflow.
(2) It does not entail a posterior caval anastomosis, so it is quicker to perform and it requires less exposure during the anastomosis allowing also an easier examination of the suture line post reperfusion.
(3) There is no need to meticulously dissect the liver off the IVC, which also shortens the hepatectomy time because the hepatic tributaries to the recipient anterior IVC become part of the incision and can be quickly cut off, once the recipient IVC clamps have been applied.
(4) Bleeding during this phase of hepatectomy is minimized since the IVC is fully controlled.

(5) The aforementioned anastomosis counterbalances any rotational forces, which can cause IVC mechanical occlusion due either to size mismatch (small graft) or to technical fault.[12–15]

To the best of our knowledge, there is no standardized method for the repair of hepatic outflow injuries; the approach frequently requires original thinking, and it must always be tailored to the particular anatomy and surgical experience. In other case reports, Di Francesco et al advocated the use of an infrahepatic IVC segment as a cuff to the suprahepatic IVC.[16] Additionally, Falconer et al describe 3 grafts with suprahepatic IVCs, which had been divided inappropriately close to the hepatic vein ostia during retrieval.[17] The techniques used were as follows:

(1) Transposition of an infrahepatic IVC cuff to elongate the suprahepatic IVC.
(2) Use of a donor common iliac vein as a circumferential collar to the suprahepatic IVC.
(3) The use of an infrahepatic IVC cuff to extend the suprahepatic IVC, followed by end-to-side cavo-cavostomy onto a triangular opening in the anterior wall of the recipient IVC.[17]

Given the scarcity and value of liver grafts, retrieving teams should promptly, openly, and thoroughly report injuries to recipient centers. Conversely, implanting teams should consider all reconstructive options prior to declining any organs. In fact the level of expertise in the recipient center is the major limiting factor, which can define the fate of a marginal liver due to vascular damage.

In the current case, anatomical disruption dictated interposition of a venous homograft, as well as refashioning of the hepatic vein ostia and spatulation of both venae cavae. In doing so, an effective outflow tract was established and a severely injured, otherwise unusable, graft was utilized. The face-to-face cavo-cavostomy guaranteed a safe and functional anastomosis. The role of NMP in yielding a better organ was beneficial. Moreover, NMP was really feasible without causing further harm despite the existing unrecognized vascular damage; this positive finding can be attributed to the low-pressure system in the OrganOx machine, which can be proved advantageous in case of future NMP livers with major vascular or other injury. Regarding the closure of the suprahepatic IVC before starting NMP, the option of oversewing with running polypropylene suture instead of stapling, as done historically, should be seriously considered so as to provide more length to the top IVC. To achieve good length preservation if a stapler has been used, the suprahepatic IVC should be transected directly below the staple line without leaving any margin. Finally, the retrieving surgeon should always make an effort to transect the intrathoracic IVC at the level of the right atrium, accommodating the liver needs appropriately whenever a cardiac donation is taking place as well.

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