Transplantation Publish Ahead of Print

DOI: 10.1097/TP.0000000000002673

DELAYED KIDNEY TRANSPLANTATION AFTER 83 HOURS OF COLD ISCHEMIA TIME IN COMBINED LIVER-KIDNEY TRANSPLANT

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Authorship: BE and AMC finalized the draft. All authors participated in the patient care and gave important feedback. All authors approved the final version.

Disclosure: None.

The field of kidney transplantation (KTx) has evolved with hypothermic machine perfusion (HMP) to extend the time between procurement and transplant expanding the shipping distance (e.g. East-to-West coast in the U.S.). HMP also enabled to limit the harmful effect of cold ischemia time (CIT), therefore, decreased the rate of delayed graft function (DGF).[1] Studies on long-term effects of CIT showed proportional increase in DGF and graft failure with each hour of CIT.[2] In case of combined liver-kidney transplantation (CLKTx), the recipient is critically ill with coagulopathy, hyperbilirubinemia, and on pressor(s) support immediately after liver transplantation (LTx), creating an unfavorable hostile environment for the kidney allograft. Therefore, it is preferable that KTx is delayed with the support of HMP.[3] We previously showed a novel approach of delaying the kidney portion of CLKTx in a cohort of 61 patients with a mean CIT of 50 hours (range 20-81 hours) with excellent outcomes in patient survival.[3,4] Our studies confirmed that DGF is the most important negative predictor of patient survival in this complex group of patients.

Here, we are reporting a delayed KTx in CLKTx with a CIT of 83.3 hours (longest reported in the literature). The recipient was a 54-year-old male with a history of chronic liver failure secondary to alpha1-antitrypsin deficiency, hepatitis C cirrhosis, and chronic kidney disease on hemodialysis starting 3 months prior to transplant. His MELD score was 33. He was very frail, sarcopenic, and required biweekly paracenteses for significant ascites. He was frequently admitted for encephalopathy and required esophageal variceal banding and underwent fixation for a femoral neck fracture from a fall.

In November 2017, he underwent LTx from a 47-year-old male donor who died of stroke (Figure 1). The patient was supported by continuous veno-venous hemodialysis intra-operatively until delayed KTx (routine for our CLKTx patients). Donor calculated kidney donor profile index was

71% with a positive crossmatch. Due to the requirement of significant vasopressor support post-LTx, KTx was delayed for 83.3 hours. The patient developed acute tubular necrosis post-KTx, confirmed by renal biopsy. Six months after CLKTx, the patient came off of hemodialysis. In order to confirm the residual function of native kidneys, a renal scan was performed and confirmed the sole function of the transplanted kidney (Figure 1). At 1-year follow up, his both liver and kidney have good function. This case demonstrates the amazing capacity of renal allograft to recover its function despite multiple insults in a hostile environment, even 6 months after CLKTx. We believe that most likely mechanism of delayed graft recovery was the significant initial insult due to (i) high bilirubin which crystalized in the renal tubules, (ii) high pressor needs, and (iii) overall weak and sarcopenic status of the recipient. With the recent advancement in normothermic machine perfusion,[5] future studies comparing hypothermic and normothermic machine perfusions in KTx will be valuable not only in KTx alone but also in CLKTx.

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Figure 1: Time course from combined liver-delayed kidney transplant to 12-month follow-up

Legend: (A) Description of important events in pre, peri, and post transplant. Liver transplant surgery (POD0) was very difficult due to adhesions, scarring of the cirrhotic liver, and thrombocytopenia, requiring 30 units packed red blood cells, 16 units fresh frozen plasma, and 3 units platelets. His immediate postoperative course was complicated requiring multiple pressor support and reintubations for pulmonary edema and altered mentation. The patient started on CVVH on POD12. A kidney biopsy on POD42 confirmed the ATN. Post biopsy, he developed a perinephric intraperitoneal hematoma requiring transfusion and operative exploration. In April 2018, his right inguinal hernia was repaired – by this time, he had improving urine output and creatinine and was trialed off of hemodialysis after surgery. (B) Renal scan 6-month after the transplant showing activity on the transplanted kidney in the left iliac fossa. (C) Native kidneys (studied exclusively in this figure) showed no uptake of radioactive material indicating no function of native kidneys, and confirming that renal function and creatinine clearance only depend on the transplanted kidney.

(*) Continuous veno-venous hemofiltration (CVVH) dialysis started which eventually converted to intermittent hemodialysis. (#) The patient's renal function recovered and he was completely off hemodialysis. OLTx: orthotopic liver transplant, KTx: kidney transplant, s-Cre: serum creatinine, ATN: acute tubular necrosis, IHR: inguinal hernia repair, HD: hemodialysis, CCC: calculated creatinine clearance according to Cockcroft-Gault formula, POD: post operative day. Nov-17: November 2017. Dec-17: December 2017. Apr-18: April 2018. mo: month post transplant.

Figure 1