

The First Case Series of Combined Liver-Kidney Transplantation (CLKT) from Thailand

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Abstract

From the hospital database, four patients underwent CLKT. Three patients had ESRD and cirrhosis. Causes of cirrhosis were chronic hepatitis B and chronic hepatitis C in two and one patient. The fourth patient underwent CLKT due to subfulminant liver failure and prolonged acute renal failure with severely damaged kidney and required hemodialysis for 5 weeks. The waiting time ranged from 6 to 1988 days. After CLKT, one patient required hemodialysis for 45 days because of prolonged acute tubular necrosis. Mild early liver graft dysfunction occurred in one patient. Induction regimens were IL2-receptor blockers, steroids and tacrolimus in three patients, and steroids combining with tacrolimus in one patient. Maintenance regimens included tacrolimus, mycophenolate mofetil (with or without low-dose prednisolone). One-year graft and patient survival rate was 100%. Median follow-up time was 2.2 years. None developed liver or renal graft rejection. At 6 and 12 months, median creatinine levels were 1.30 and 1.13 mg/dl. At the last visits, median creatinine level was 1.05 mg/dl with median eGFR of 76.45 ml/min. CLKT may be done in the patients with ESRD and viral hepatitis-related cirrhosis even without portal hypertension. Other indication is for patients with acute liver failure with severely damaged ARF.

Keywords: Combined Liver-Kidney Transplantation (CLKT); End-stage renal disease (ESRD); Hepatitis B; Hepatitis C; Cirrhosis

received deceased-donor KT annually. Furthermore, about 6 patients were on the waiting list of CLKT each year.

Introduction

For kidney transplantation (KT) with hepatitis B viral (HBV) or hepatitis C viral (HCV) infection, candidates with decompensate cirrhosis and cirrhotic patients with symptomatic portal hypertension are contraindicated to KT alone [1]. For KT candidates with HBV- or HCV-related compensate cirrhosis without symptomatic portal hypertension, KT alone is a relative contraindication [2]. Since the implementation of the model for end-stage liver disease (MELD) score, more cirrhotic patients underwent liver transplantation with renal failure, and the number of CLKT has risen enormously [3]. The most common causes of acute renal failure complicating the clinical course of decompensate cirrhosis and fulminant liver failure are acute tubular necrosis and hepatorenal syndrome. The role of combined liver kidney transplantation (CLKT) in cirrhosis with renal failure is quite controversial. A recent study revealed the benefit of liver graft and patient survival in cirrhotic patients with renal failure who underwent CLKT over LT alone [4]. Prolong acute renal failure requiring hemodialysis for more than 6-8 week in decompensated cirrhosis and fulminant liver failure is accepted to be an indication of CLKT [3]. Reports from the Thai Red Cross Organ Donation Center (<http://www.organdonate.in.th>), reveals that there were nearly 3000 patients with ESRD waiting for KT but only around 200 patients

Case Presentation

From the database of Ramathibodi hospital, the transplant teams have performed 1784 kidney transplantation and 116 liver transplantation in adult recipients since 1987. Four patients underwent CLKT. All patients were male with mean age of 57.0 years. ESRD on chronic hemodialysis was the primary reason for listing of CLKT in three out of four patients. The decision of CLKT, not KT alone, was made in these three patients because the presence of liver cirrhosis was confirmed by biochemical and radiological studies including transient elastography. Cirrhotic status of two patients were found to be Child's class A and one patient was Child's class B. HBV was the cause of cirrhosis in two patients and HCV in one patient. One case developed small hepatocellular carcinoma while on the waiting list and received chemoembolization for a few sessions before organs became available. The fourth patient underwent CLKT owing to subfulminant liver failure (from Non-A, Non-B or cryptogenic hepatitis) as the primary reason. Prolonged acute renal failure (ARF) requiring hemodialysis for 5 weeks, which suggested severely damaged kidney, was the indication of combining kidney with liver transplantation in the fourth case. Post-transplant renal scan showed evidences of non-reversible kidney injury.

Two patients had blood group A and the rest had blood group O. Mean MELD score (range) was 26 (21-38). Waiting time ranged from 6 to 1988 days. Mean cold and warm ischemic times of the liver grafts were 6.3 hours and 61.8 minutes. After CLKT, one patient in the ESRD group required hemodialysis further for 45 days because of prolonged acute tubular necrosis after CLKT. Post-transplant complications included mild degree of early liver graft dysfunction (in one case), urinary tract infection (in two cases), cytomegalovirus infection (in two cases), pulmonary cryptococcosis (in one case) and pneumonia (in one case). Induction regimens of immunosuppressive therapy included IL2-receptor blockers, steroids and tacrolimus in three patients and steroids combining with tacrolimus in one patient. Maintenance regimens included low-dose tacrolimus, mycophenolate mofetil (with or without low dose prednisolone). One-year graft and patient survival rate was 100%. Median follow-up time was 2.2 years. None of four patients developed liver or renal graft rejection. Liver biopsy was done in one case due to elevation of liver enzymes, and it was found to be a de novo non-alcoholic steatohepatitis (NASH). At 6 and 12 months, median creatinine levels were 1.30 and 1.13 mg/dl. At the last visits, median creatinine level was 1.05 mg/dl with median eGFR (by CKD-EPI) of 76.45 ml/min. For patients with subfulminant liver failure who required hemodialysis for 5 weeks before CLKT, post-transplant renal scan confirmed severe and irreversible impairment of native kidneys.

Discussion

In Thailand, liver transplantation (LT) and CLKT are performed according to blood group identical policy. Our report suggests that CLKT should be a preferable management of two conditions: ESRD with viral hepatitis-related cirrhosis and acute liver failure with prolonged ARF. Recent consensus on CLKT states that ESRD patients with cirrhosis and symptomatic portal hypertension, patients with liver failure and ESRD with glomerular filtration \leq 30 ml/min, patients with acute kidney injury or hepatorenal syndrome with creatinine \geq 2.0 mg/dl and on dialysis \geq 8 weeks, and patients with liver failure and ESRD with biopsy demonstrating $>$ 30% glomerulosclerosis or $>$ 30% fibrosis should be selected for CLKT [1]. Although three cirrhotic recipients in this study had not yet developed symptomatic portal hypertension (but the status of the cirrhotic liver became decompensation in one case), undergoing KT alone put some risks on them in the long term. The chance of developing acute on chronic liver failure which ends up with morbidity and mortality are high if antiviral resistant infection emerges after KT alone is done. For the

recipient with subfulminant liver failure, although he was on hemodialysis for only 5 weeks before CLKT, irreversible damage of the native kidneys already occurred. For the criteria of CLKT in acute fulminant liver with prolong acute renal failure, the duration of required hemodialysis should be reduced from more than 8 to 4 weeks [3]. At post-transplant period, progressive kidney dysfunction of the native kidneys can occur from calcineurin inhibitors if LT alone is performed. Moreover, graft and patient survival of CLKT was reported to be better than LT alone [4,5]. Low levels of immunosuppression can be implemented in CLKT recipients because of the immune privilege of the liver that protects the kidney from allograft rejection [6]. Survival benefit of CLKT is showed in patients with renal failure who are on hemodialysis only [7]. To balance fair and justice, CLKT should be done with well-defined indications to avoid CLKT in reversible liver or kidney failure [8]. The short-term and long-term outcomes of CLKT in our small case series are excellent. CLKT is an idealistic approach for patients with liver and kidney failure. Clear and proper indications of CLKT are needed to be established.

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