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Outcomes of patients with hepatitis C undergoing simultaneous liver–kidney transplantation☆

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***Background/Aims*: The number of simultaneous liver–kidney transplants (SLK) has increased since the MELD era. Data on short- and long-term outcomes of hepatitis C virus positive (HCV+) SLK compared to HCV+ liver transplant alone (LTA) recipients are limited.**

***Methods*: A case-control study comparing outcomes of HCV+ SLK versus transplant year-matched HCV+ LTA (1:1) was performed.**

***Results*: 38/142 (26.7%) SLK recipients were HCV+. LTA controls had lower MELD (17.4 ± 8.6) at transplant than SLK (34.5 ± 6.6) ($p = 0.001$). There were increased early post-transplant infection episodes in SLK (56.3%) versus LTA (21.6%) ($p = 0.001$) and a trend towards increased early mortality in the SLK group ($p = 0.08$). However, there was no difference in long-term patient and graft survival, time to HCV recurrence, % ⩾ stage 2 fibrosis, renal function, and graft function between the groups. Ten SLK recipients were treated for HCV recurrence with pegylated interferon + ribavirin: two had sustained virologic response, five stopped due to side effects, and three had no response. None had liver or kidney rejection on treatment.**

***Conclusion*: Our data represent the largest analysis of HCV+ SLK outcomes to date. We demonstrate increased early complications in SLK versus LTA recipients, likely due to being more critically ill at transplant (higher MELD) and complications unrelated to HCV within the first year. However, long-term outcomes, i.e. HCV recurrence, graft/renal dysfunction, are similar to LTA. In addition, while data are limited, treatment of HCV recurrence with interferon appeared safe in our SLK recipients.**

***Keywords*: Hepatitis C virus; Liver transplantation; Kidney transplantation; Simultaneous liver–kidney transplantation; Interferon; Recurrent disease**

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Abbreviations: SLK, simultaneous liver–kidney transplant; MELD, model for end-stage liver disease; HCV+, hepatitis C virus positive; LTA, liver transplant alone; IFN, interferon; RBV, ribavirin; RRT, renal replacement therapy; SVR, sustained viral response; ICU, intensive care unit; ECD, expanded criteria donor; ALT, alanine aminotransferase.

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1. Introduction

When the United Network for Organ Sharing changed its algorithm for liver allocation to the model for end-stage liver disease (MELD) system in 2002, highest priority shifted to patients with renal insufficiency as a major component of their end-stage liver disease [1]. Critics of the MELD system have suggested that because creatinine is given considerable weight in the MELD formula, liver grafts are being preferentially allocated to patients with renal insufficiency [2,3]. As such, the introduction of the MELD has coincided with a significant increase in the number of simultaneous liver–kidney transplants (SLK) performed annually [2]. However, data are conflicting within studies aimed at predicting which candidates will fail to recover renal function and need SLK, thus creating controversy over the role of SLK transplantation and a clear need for ongoing re-examination of outcomes [1,4–8].

With the impetus towards increased SLK transplants, data on outcomes are needed surrounding the current leading indication for liver transplantation in the United States – Hepatitis C Virus (HCV) [9]. Hepatitis C infection has been associated with the development of chronic kidney disease before and after transplantation, either due to immune complex injury, co-existing diabetes, or other factors [10–14]. What has not been clearly delineated is whether HCV+ SLK recipients have more rapid progression of HCV recurrence or have worse outcomes (rejection, infection, patient/graft survival) compared to liver transplant alone (LTA) recipients. In addition, the management of HCV recurrence in the SLK population is not well-defined or reported. Of concern are studies within the renal transplant literature that have shown an unacceptably high risk of precipitating renal allograft rejection with interferon (IFN) therapy [15–21]. More recent reports have demonstrated successful HCV treatment with pegylated IFN and ribavirin (RBV) in SLK recipients without development of renal rejection on therapy, although data are limited to small numbers of patients [22–24].

Therefore, the purpose of this study was to analyze outcomes of a cohort of patients with hepatitis C undergoing SLK compared to LTA in terms of patient and graft survival, rejection episodes, infectious complications and most importantly hepatitis C recurrence.

2. Patients and methods

2.1. Patients

We performed a retrospective review of data in all HCV+ patients who underwent SLK (cases) at Northwestern Memorial Hospital from June 1, 1999 to January 1, 2007. Cases were matched 1:1 to LTA controls who were transplanted within the same year (randomly selected within the year), primarily to compare the occurrence and progression of HCV recurrence in both groups. Patient data were obtained by reviewing inpatient and outpatient medical records and our electronic transplantation database. Collected and analyzed data included age, sex, cause of liver and kidney diseases, dialysis requirements, MELD score, preoperative and postoperative laboratory results, donor age, infectious complications, post-transplant immunosuppressive regimens, liver and kidney rejections, need for retransplantation, documentation of hepatitis C recurrence (including treatment, outcomes and complications) and patient and graft survival.

Patients received methylprednisolone 500 mg intravenously immediately post-operatively, followed by a prednisone taper over 3 months. Maintenance immunosuppression regimens varied to some degree within this period and are reported in the results. All documented episodes of rejection were based on biopsy. Hepatitis C recurrence was defined by standard histological criteria [25]. Liver biopsies were performed for either liver enzyme elevations or, in the majority, by protocol on a yearly basis. Allograft kidney biopsies were performed when clinically indicated.

In the time period of the study, the allocation system allowed for the use of SLK transplantation based on the best clinical judgment of the transplant program. Therefore, with no reliable algorithms available to predict the reversibility of renal disease/injury in this patient population, we used a standard set of decision-making criteria in each patient regarding the need for combined transplant. These included a serum creatinine >1.5 mg/dl for >1 month (or 0.8 greater than baseline), risk factors for intrinsic renal disease (diabetes, hypertension), and the presence of significant proteinuria and/or the need for renal replacement therapy >3 weeks.

2.2. Definitions and statistical analysis

Differences in patient characteristics and postoperative outcomes between SLK and LTA groups were compared using Student's t-test for continuous variables and Fisher exact test or χ^2 analysis for categorical variables. Sustained virological response (SVR) was defined as an undetectable HCV RNA 24 weeks after cessation of therapy. Patient survival was defined as time from transplantation to death or last follow-up. Liver graft survival was defined as time from transplantation to death, last follow-up, or retransplantation. Kidney graft survival was defined as time from transplantation to death, last follow-up, or return to renal replacement therapy (RRT). Duration of RRT was defined as total inclusive days during which RRT (conventional or continuous) was required. Kaplan–Meier survival analysis and Cox proportional hazard model were conducted to compare patient and graft survival (uncorrected and corrected for age, gender, MELD) and HCV recurrence between SLK and LTA patients using SAS 9.2 (SAS Inc., Cary, NC). Significance was established at an alpha level of 0.05.

3. Results

3.1. Demographics and preoperative characteristics

During the study time period, 142 patients underwent SLK. Thirty-eight (26.7%) of these patients were HCV-positive and 38 LTA patients served as controls. Compared to the LTA group (Table 1), the SLK group had a significantly higher percentage receiving preoperative RRT and previous liver transplantation, higher baseline creatinine and bilirubin, and higher MELD at transplantation. Other baseline characteristics did not differ significantly.

3.2. Patient and graft survival

At the completion of the analysis, 15 (39%) SLK patients and 8 (21.5%) LTA patients had died. The