Journal of Transplantation Technologies & Research

Pham and Pham, J Transplant Technol Res 2020, 10:1
DOI: 10.4172/2161-0991.1000E115

Editorial Open Access

Clinical Decision-Making Dilemna: Liver alone or Simultaneous Liver-Kidney Transplantation?

Phuong-Thu T. Pham[1]* and Phuong-Chi T. Pham[2]

[1]*Department of Medicine, Nephrology Division, David Geffen School of Medicine at UCLA, Kidney Transplant Program, Los Angeles, CA 90095, USA*
[2]*Department of Medicine, Nephrology and Hypertension Division, UCLA-Olive View Medical Center, Sylmar, CA 91342, USA*

With the introduction of the MELD score for the allocation of orthotopic liver transplant (OLT) in February 2002, a striking 278% increase in the number of simultaneous liver-kidney transplants (SLKT) was observed during the 9-year period post-MELD when compared with the preceeding 9-year in the pre-MELD era (pre- *vs.* post-MELD era, n= 1049 *vs.* 2914, respectively) [1]. For OLT candidates with simultaneous end-stage kidney failure, SLKT is a well-established effective therapeutic option for virtually all suitable candidates. However, there have been no well-defined guidelines to determine whether a kidney transplant should be offered to OLT candidates who have chronic kidney disease (CKD) or prolonged acute kidney injury (AKI) secondary to hepatorenal syndrome (HRS) or acute tubular necrosis (ATN) while awaiting a liver transplant. Specific challenges in the decision making process include the accurate assessment of the degree of existing renal dysfunction in those with CKD and the prediction of the extent of renal function recovery in those with AKI with or without underlying CKD.

In 2008, a multidisciplinary American consensus conference convened to examine listing criteria for SLKT [2]. It was recommended that automatic approval for SLKT listing should be granted to patients with:

i. End-stage renal disease with cirrhosis and symptomatic portal hypertension or hepatic vein wedge pressure gradient > 10 mmHg

ii. End-stage liver disease (ESLD) and CKD with glomerular filtration rate (GFR) ≤ 30 mL/min

iii. AKI or HRS with creatinine ≥ 2.0 mg/dL and dialysis ≥ 8 weeks

iv. End-stage liver disease (ESLD) and CKD and biopsy demonstrating> 30% glomerulosclerosis or 30% fibrosis.

All other requests should be evaluated to determine appropriateness.

In 2011, a panel of experts consisting of representatives from the OPTN (Organ Procurement Transplantation Network) liver and kidney committees from various OPTN regions as well as experts from the previous consensus conference assembled in Los Angeles to set forth novel guidelines for SLKT in waitlisted OLT candidates [3]. The SLKT Summit attendees recommended that SLKT should be considered in:

i. OLT candidates with persistent AKI ≥ 4 weeks with one of the following:

(a) Stage 3 AKI as defined by modified Risk Injury Failure Loss End-stage criteria (RIFLE) (i.e. a 3-fold increase in serum creatinine (SCr) from baseline, Scr ≥ 4 mg/dL with an acute increase of ≥ 0.5 mg/dL or on renal replacement therapy

(b) eGFR ≤ 35 mL/min (MDRD-6 equation) or GFR ≤ 25 mL/min (iothalamate clearance).

ii. Candidates with CKD, as defined by the National Kidney Foundation, for 3 months with one of the following:

(a) eGFR ≤ 40 mL/min (MDRD-6 equation) or GFR ≤ 30 mL/min (iothalamate clearance)

(b) Proteinuria ≥ 2 g a day

(c) Kidney biopsy showing > 30% global glomerulosclerosis or > 30% interstitial fibrosis

(d) Metabolic disease

While current guidelines provide well-defined criteria for SLKT listing for the majority of OLT candidates with either well-defined acute or chronic kidney disease, many SLKT-indicated candidates fall short of the strict criteria set forth by such guidelines. In the authors' opinion, classifying OLT candidates into those with 1) AKI, 2) CKD, and 3) AKI superimposed on CKD, along with assessing risk factors for poor renal function recovery could potentially more fairly identify the subset of OLT candidates who would benefit from a simultaneous kidney transplant.

Acute Kidney Injury (AKI)

Studies on the potential factors predicting non recovery of renal function or progressive CKD after OLT have yielded variable and conflicting results. Nonetheless, similar to the non-transplant settings, potential risk factors for poor renal recovery may include the presence of pretransplant comorbid conditions such as diabetes mellitus, hypertension, coronary artery disease, and advanced age. Prolonged ischemic or toxic insult to the kidneys prior to transplantation such as hemodynamic instability, bacterial infections and the repeated use of nephrotoxic drugs, and prolonged acute tubular necrosis (ATN) associated with severely reduced renal perfusion may all lead to irreversible renal damage and progressive chronic kidney disease. Additionally, the duration of pretransplant renal dysfunction must play a role in postoperative non-recovery of renal function [4].

The American consensus guidelines suggest AKI or HRS with creatinine ≥ 2.0 mg/dL and dialysis ≥ 8 weeks as a threshold for SLKT in OLT candidates with AKI requiring renal replacement therapy [2]. The 2012 SLK Transplantation Summit guidelines suggest SLKT in OLT candidates with persistent AKI (eGFR ≤ 35 mL/min by MDRD-6 equation or ≤ 25 mL/min by iothalamate studies) of ≥ 4 week duration or Stage 3 AKI as defined by modified RIFLE [3]. Different transplant programs set forth different thresholds for SLKT ranging from 4 to 12 weeks on dialysis. Similarly, serum creatinine cut off values at which OLT candidates are listed for SLKT vary widely among centers.

***Corresponding author:** Phuong-Thu T. Pham, MD, Clinical Associate Professor of Medicine, Director Outpatient Services, Department of Medicine, Nephrology Division, David Geffen School of Medicine at UCLA, Kidney Transplant Program, Los Angeles, CA 90095, USA, Tel. (310) 794-1757; E-mail: PPham@mednet.ucla.edu

Received July 01, 2020; **Accepted** July 03, 2020; **Published** July 05, 2020

Citation: Pham PTT, Pham PCT (2020) Clinical Decision-Making Dilemna: Liver alone or Simultaneous Liver-Kidney Transplantation? J Transplant Technol Res 2:e115. doi:10.4172/2161-0991.1000e115

In the authors opinion, SLKT should be considered at slightly higher GFR (e.g. eGFR 36-40 mL/min by MDRD-6) than those suggested by current guidelines in the subset of patients with AKI and concurrent comorbid conditions such as long-standing history of diabetes (particularly those with evidence of proliferative diabetic retinopathy) or poorly controlled hypertension, and older age due to worse renal recovery potential [5]. The SLKT Summit expert panels acknowledge that current guidelines provide enough guidance to those who should receive a concurrent kidney graft but yet retain enough flexibility to allow clinical decision making until we have adequate data to support policy development.

Chronic Kidney Disease(CKD)

The 2008 American consensus guidelines suggest SLKT in OLT candidates with an estimated GFR of ≤ 30 mL/min and criteria for CKD as defined by the National Kidney Foundation (i.e. duration >90 days) [2]. The 2012 SLKT Summit guidelines propose SLKT in OLT candidates with an eGFR ≤ 40 mL/min (MDRD-6) or GFR ≤ 30 mL/min (iothalamate clearance) [3].

In clinical practice, assessing for SLKT in OLT candidates with CKD and an estimated baseline GFR (MDRD-6) between 41-44 mL/min/1.73 m^2 (a GFR level not quite meeting current guidelines for SLKT listing) can be particularly challenging. Proper risk stratification may assist clinicians predict the rate of progression of the patients' underlying CKD and the need for dual organ transplantation at the time of liver transplantation. In the authors' opinion, SLKT should be considered in OLT candidates with CKD–with baseline eGFR in the aforementioned range, and concomitant risk factors including long-standing history of diabetes with evidence of proliferative diabetic retinopathy, microalbuminuria, or overt proteinuria, long-standing history of poorly controlled hypertension or history of hypertension with evidence of other end-organ damage such as left ventricular hypertrophy or hypertensive retinopathy, known cardiovascular disease, superimposed AKI from exposure to nephrotoxins, ATN from repeated episodes of sepsis/septic shock or hemodynamic instability, persistent microhematuria after excluding urological causes, structural renal disease (e.g. reflux nephropathy, obstructive uropathy or recurrent pyelonephritis or infected stones, massively enlarged and/or symptomatic polycystic kidney disease that may necessitate native nephrectomies), or family history of stage 5 CKD [6]. Other risk factors that may be considered include dyslipidemia and older age. Renal ultrasound to assess kidney sizes and echogenicity can be an invaluable adjunctive prognostic tool. In OLT candidates with significant muscle wasting, isotopic GFR should be performed to better classify CKD stage.

AKI superimposed on CKD

Identification of patients who are best suited for double-organ transplantation necessitates careful evaluation of the risk of progression to advanced CKD early after liver transplantation. Although no guidelines exist, predicting renal prognosis could be improved by assessing risk factors for renal function recovery in the setting of underlying CKD including baseline eGFR, severity and duration of AKI, preexisting microalbuminuria or overt proteinuria, presence of comorbid conditions, and cause of underlying CKD (if known). The presence of risk factors for suboptimal AKI recovery warrants SLKT in patients with AKI superimposed on advanced stage 3 CKD who do not meet the strict SLKT criteria by either AKI or CKD criteria (e.g. eGFR of 36-40 mL/min/1.73 m^2 and AKI duration greater than 4 weeks in contrast to guideline criteria for SLKT where GFR should be ≤ 35 mL/min/1.73 m^2).

In conclusion, when a kidney biopsy cannot be performed due to underlying coagulopathy and the associated increased risk of bleeding, proper risk stratification of patients with AKI and/or CKD is critical to distinguish patients with good renal prognosis from those with poor prognosis in whom SLKT is warranted. Until large prospective, multicenter, observational studies evaluating patient and graft outcomes of OLT candidates with AKI and/or CKD undergoing solitary liver *vs.* SLK transplants are conducted, evidenced-based clinical practice guidelines remain undefined. With the ever-increasing donor organ shortage, SLKT must be used judiciously.

References

1. United Network for Organ Sharing and Organ Procurement Transplantation Network (UNOS/OPTN) database as of September 2012.
2. Eason JD, Gonwa TA, Davis CL, Sung RS, Gerber D, et al. (2008) Proceedings of consensus conference on simultaneous liver-kidney transplantation (SLK). Am J Transplant 8: 2243-2251.
3. Nadim MK, Sung RS, Davis CL,Andreoni KA, Biggins SW, et al. (2012) Simultaneous Liver-Kidney transplantation Summit: Current state and future directions. Am J Transplant [Epub ahead of print].
4. Pham PT, Pham PC, Wilkinson AH (2007)Renal function outcomes following liver transplantation and combined liver-kidney transplantation. Nat Clin Pract Nephrol 3: 507-514.
5. Bagshaw SM (2006) Epidemiology of renal recovery after acute renal failure. Curr Opin Crit Care 12:544-550.
6. Pham PT, Pham PC (2012) Liver alone or simultaneous liver-kidney transplantation. www.curbsideconsultant.com