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Kidney Failure and Liver Allocation: Current Practices and Potential Improvements

Varun Saxena and Jennifer C. Lai

In February 2002, the United Network for Organ Sharing implemented a system for prioritizing candidates for liver transplantation that was based on the risk of 90-day mortality as determined by the Model for End-Stage Liver Disease (MELD) score. As the MELD score is driven in part by serum creatinine as a marker of kidney function, the prevalence of kidney dysfunction and failure in patients with end-stage liver disease at the time of listing and at transplantation has steadily risen. In this review, we discuss current practices in liver transplantation in patients with kidney dysfunction focusing briefly on the decision to perform simultaneous liver-kidney transplantation. We then discuss pitfalls to the current practices of liver transplantation in patients with kidney dysfunction. We conclude by discussing potential improvements to current practices including the use of the MELD-Na score, alternatives to creatinine and creatinine-based equation for estimating kidney function, and the use of intraoperative kidney replacement therapy during liver transplantation.

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Key Words: Acute kidney injury, Biomarkers, Creatinine, Liver transplant, Model for end-stage liver disease

INTRODUCTION

The growing deficit in liver donor supply relative to demand has raised the issue of liver allocation to the forefront of debate in the field of liver transplantation. In the late 1990s, the controversy surrounding prioritization of candidates for liver transplantation centered around the use of waiting time, which is not associated with mortality,¹ and subjective factors that could be manipulated to assign priority to liver transplant candidates. These practices prompted an Institute of Medicine report² recommending that liver allocation be based solely on objective predictors of mortality.¹ In response to this recommendation, the United Network for Organ Sharing (UNOS) implemented a new liver allocation system in February 2002 that was based on the Model for End-Stage Liver Disease (MELD) score, a laboratory-based metric that accurately predicts 90-day risk of death.^{3,4}

This system has been highly effective in reducing mortality on the liver transplant wait-list.⁵ The 3 variables comprising MELD—serum creatinine, the international normalized ratio, and total bilirubin—encompass the major manifestations of decompensated end-stage liver disease (ESLD), including kidney dysfunction, coagulopathy, and cholestasis, respectively. Because an estimation of a candidate's kidney function using serum creatinine as a surrogate marker is included, implementation of the MELD scoring system shifted donor liver prioritization to transplant candidates with kidney dysfunction. From 2002 to 2013, the percentage of simultaneous liver-kidney (SLK) transplants among all liver transplantations has nearly doubled, increasing from 4.2% to 8.1% (Fig 1). This is anticipated to further increase in light of the "Share 35" liver distribution system, implemented in 2013, in which liver transplant candidates with MELD scores ≥ 35 receive priority for organs from a broader geographic area (ie, regional rather than local distribution area) than candidates with MELD score less than 35.⁶

In this review, we address the current practices in liver transplantation in patients with kidney dysfunction, the pitfalls of these practices, and potential improvements.

CURRENT PRACTICES IN LIVER TRANSPLANTATION IN PATIENTS WITH KIDNEY DYSFUNCTION

Conceptually, the decision to proceed with liver transplantation alone vs SLK transplantation is simple: patients with acute kidney injury are expected to regain sufficient native kidney function after liver transplant, whereas those with underlying CKD will not. It is this latter group who should undergo SLK transplantation.

In practice, however, identifying exactly who will recover native kidney function after liver transplant alone is less clear-cut. Some candidates with AKI have underlying CKD that will worsen after liver transplant alone, whereas other candidates with subacute/chronic kidney insufficiency from hepatorenal syndrome (HRS) type 2 may recover enough kidney function after transplant to achieve favorable outcomes with liver transplant alone. Given the challenges of accurately assessing kidney function in patients with ESLD using currently and widely available markers, the most commonly used surrogate marker for post-transplant kidney recovery is the length of time that a candidate has been on kidney replacement therapy. But the data are conflicting regarding how long this length of time should be: 4, 8, or 12 weeks.

In 1 large study of over 2000 patients, the vast majority (1819 of 1989 [91%]) of liver transplant recipients who received less than 4 weeks of hemodialysis recovered native kidney function after liver transplant alone.⁷ In the same study, even among those who received hemodialysis for more than 4 weeks but less than 6 weeks before

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liver transplant, 84 of 95 (88%) recovered kidney function after transplant.⁷ Recipient factors that independently predicted kidney nonrecovery within 6 months of liver transplant alone were duration of pre-transplant kidney replacement therapy per day (hazard ratio [HR] 1.04, 95% confidence interval [CI] 1.02-1.05), age at liver transplant per 5 years (HR 1.10, 95% CI 1.02-1.18), retransplant (HR 1.60, 95% CI 1.10-2.23), and type 2 diabetes (HR 1.80, 95% CI 1.27-2.56).⁷ Similarly, in a separate study comparing outcomes among liver transplant alone vs SLK transplantation among patients with acute kidney injury who received less than 4 weeks of hemodialysis ($n = 102$), 1-year survival was 64% among liver transplant-alone recipients and 66% among SLK transplant recipients ($P = .88$).⁸ Although SLK transplant recipients experienced a significantly lower need for post-transplant hemodialysis (55% vs 89%; $P < .01$), only 3 of 80 (4%) patients who underwent liver transplant alone remained on long-term hemodialysis after transplant.⁸ For patients who received more than 8 weeks of pre-transplant hemodialysis, SLK transplantation conferred significantly higher 1-year survival over liver transplant alone (88% vs 66%; $P = .04$).⁸ This suggests that the critical duration of pre-transplant hemodialysis after which candidates should receive SLK transplant vs liver transplant alone is 8 weeks, not 4 weeks. However, a separate UNOS-based study comparing long-term outcomes among 19,137 liver transplant alone and 1032 SLK transplant recipients confirmed that length of time on dialysis was a significant predictor of long-term outcomes after liver transplant alone, but only after the duration of dialysis was more than 12 weeks.⁹

It is reasonable to conclude from these data that patients with AKI requiring hemodialysis for more than 12 weeks should be considered for SLK transplantation and those on hemodialysis for less than 4 weeks should receive liver transplant alone. However, for liver transplant candidates receiving hemodialysis between 4 and 12 weeks at the time of transplant, whether to proceed with SLK transplant vs liver transplant alone remains controversial. Given significantly lower survival observed in those who do not experience kidney recovery post-transplant, a conservative cutoff of 4 weeks of kidney failure has been established

as the time after which SLK transplantation should be considered but not necessarily required.^{10,11} An algorithm based on 2 different expert consensus guidelines for considering SLK transplant in liver transplant candidates with kidney dysfunction is shown in Figure 2.^{12,13} Briefly, liver transplant candidates with estimated glomerular filtration rate (eGFR) ≤ 30 mL/min for a duration from 4 to 8 weeks or with eGFR more than 30 mL/min and evidence of CKD should be evaluated for SLK transplantation.

PITFALLS TO CURRENT PRACTICES:

Given that MELD scores at transplant are rising,¹⁴ more patients are undergoing liver transplant with kidney dysfunction. However, at the current time, the only marker of kidney dysfunction that has been incorporated into the current liver transplant candidate allocation system is serum creatinine. Serum creatinine can be an unreliable surrogate marker for kidney function in the setting of ESLD. First, creatinine is predominantly generated in skeletal muscle, so serum creatinine values will overestimate true kidney function in patients with sarcopenia, a common complication of cirrhosis. Second, serum bilirubin, often elevated in patients with decompensated cirrhosis, can interfere with creatinine measurement resulting in inaccurately low creatinine values.¹⁵ Third, the assays for creatinine measurement themselves can lead to significant discrepancies in reported creatinine values, resulting in clinically significant variation in MELD scores.¹⁶

Variability in the assays to measure serum creatinine introduces additional challenges to the use of serum creatinine as a marker of kidney function in ESLD.^{15,17} For example, the Jaffe reaction is a commonly used assay that is susceptible to interference from high bilirubin levels (≥ 10 mg/dL), resulting in falsely low serum creatinine readings.¹⁸ In contrast, enzymatic colorimetric reaction has been shown to remain accurate in the setting of hyperbilirubinemia.¹⁹ This variation can translate into significant differences in a patient's calculated MELD score and, thus, priority for liver transplantation.^{16,20} In a study examining 4 different Cr assays (O'Leary modified Jaffe, compensated kinetic Jaffe, enzymatic, and standard kinetic Jaffe) in 403 consecutive samples from 158

CLINICAL SUMMARY

- The prevalence of kidney dysfunction in patients with end-stage liver disease awaiting liver transplantation and utilization of simultaneous liver-kidney transplantation are increasing.
- Liver transplant candidates with glomerular filtration rate (GFR) of 30 mL/min or less for more than 4 to 8 weeks, proteinuria more than 2 g/d, or kidney biopsy with more than 30% interstitial fibrosis or global glomerulosclerosis should be evaluated for simultaneous liver/kidney transplant.
- Assessing kidney dysfunction in patients with end-stage liver disease using serum creatinine is prone to inaccuracies particularly with sarcopenia, assay interference with hyperbilirubinemia, and interassay variations.
- The impact of implementing Model for End-Stage Liver Disease-Na score for liver allocation on candidates with kidney dysfunction is not clear but likely will increase their prioritization.
- Promising improvements over serum creatinine as a surrogate measure of kidney function in end-stage liver disease and predictor of post-transplant kidney function include cystatin C and urinary biomarkers.
- Use of improved surrogate measures of kidney function in end-stage liver disease in organ allocation should be expedited to help eliminate disparities in both simultaneous liver-kidney and liver transplant alone.

Figure 1. Number and percentage of SLK by year. Based on United Network of Organ Sharing data abstracted February 2014. Abbreviation: SLK, simultaneous liver-kidney transplants.

patients with ESLD, Cholongitas and colleagues¹⁶ show the effect hyperbilirubinemia can have on Cr levels by assay and resultant MELD scores (Table 1).

Two separate studies by Poge and colleagues²¹ and Gonwa and others²² highlighted serum creatinine's low accuracy as a surrogate for kidney function in ESLD patients. Using inulin clearance as the gold standard for estimating kidney function, Poge and colleagues²¹ showed that the creatinine (Cockcroft-Gault and Modification of Diet in Renal Disease [MDRDs])-based equations for eGFR overestimated kidney function by 104% to 154% in

patients with ESLD. Comparing eGFR calculated by Cockcroft-Gault, Nankivell, MDRD-4 variable, MDRD-5 variable, and MDRD-6 variable to iothalamate clearances in patients with cirrhosis awaiting liver transplantation, Gonwa and others²² showed that a "normal" serum creatinine level (1.0-1.3 mg/dL) may be seen in patients with a GFR as low as 20 mL/min. To understand this differences' impact on a candidate's MELD score, let us assume we have an "average," 60-year-old, nonblack, male patient with cirrhosis with BUN = 13 mg/dL, albumin = 2.8 g/dL, bilirubin = 2.5 mg/dL, international normalized

Figure 2. An algorithm to evaluate a liver transplant candidate with renal dysfunction for simultaneous liver-kidney transplant.^{12,13} Abbreviations: ESLD, end-stage liver disease; GFR, glomerular filtration rate.

Table 1. Mean Values of MELD Scores From Different Creatinine Assays by Different Concentrations of Serum Bilirubin and Severity of Liver Disease¹⁶

Bilirubin, mg/dL (μ mol/L)	Method of Creatinine and Resultant MELD Measurement			
	MELD mJCr*	MELD cJCr	MELD ECr	MELD JCr
<5.85 mg/dL (<100 μ mol/L)	13.3 $\pm$ 4.7	13 $\pm$ 4.5	13 $\pm$ 4.4	13.2 $\pm$ 4.5
$\geq$ 5.86 and <11.6 mg/dL ($\geq$ 100 and <200 μ mol/L)	23 $\pm$ 4.6	22 $\pm$ 4.8	21.9 $\pm$ 4.8	22.2 $\pm$ 4.7
$\geq$ 11.6 and <23.4 mg/dL ($\geq$ 200 and <400 μ mol/L)	26.7 $\pm$ 5.4	24.8 $\pm$ 5.2	24.5 $\pm$ 5.4	25 $\pm$ 5.4
$\geq$ 23.4 mg/dL ($\geq$ 400 μ mol/L)	31.3 $\pm$ 5.3	27.7 $\pm$ 6	27.1 $\pm$ 6	28.3 $\pm$ 6
MELD score (using mJCr)				
0-15	10.2 $\pm$ 1.2	10.2 $\pm$ 1.2	10.2 $\pm$ 1.2	10.2 $\pm$ 1.2
15-19	17 $\pm$ 3.1	16.5 $\pm$ 2.8	16.5 $\pm$ 2.7	16.7 $\pm$ 2.7
20-24	22.2 $\pm$ 2	21.2 $\pm$ 1.4	21 $\pm$ 1.5	21.5 $\pm$ 1.3
$\geq$ 25	30.5 $\pm$ 4.5	28 $\pm$ 4.9	27.5 $\pm$ 5	28.4 $\pm$ 4.9

Abbreviations: cJCr, creatinine measured using the compensated (rate blanked) kinetic Jaffe method; ECr, creatinine measured using enzymatic creatinine method; JCr, creatinine measured using the standard kinetic Jaffe method; mJCr, creatinine measured using the O'Leary modified Jaffe method.

*MELD mJCr is the reference creatinine. The differences among MELD mJCr, MELD cJCr, and MELD JCr scores were all significant for all comparisons when bilirubin $\geq$ 3.6 mg/dL (62 μ mol/L).

ratio = 1.5, and Cr in the normal range at 1.2 mg/dL. The MDRD-6 equation, which performed the best in patients with cirrhosis,²² calculates an eGFR of 62 mL/min and an MELD score of 16. If the patient's true GFR is at 20 mL/min, then his back-calculated corresponding serum creatinine would be 3.7 mg/dL yielding an MELD score of 27 representing an 11-point MELD score change.

The 24-hour urine creatinine clearance (CrCl) provides increased accuracy in estimating GFR over creatinine-based eGFR equations²³ but is limited in its clinical applicability because of challenges with obtaining an accurate urine collection,²⁴ overestimation of GFR when tubular secretion is increased,²⁵⁻²⁷ and influence by muscle metabolism and meat-rich diets increasing 24-hour CrCl by up to 37%.²⁶ When studied specifically in patients with ESLD, 24-hour CrCl overestimated GFR particularly in patients with lower GFR.²³ Conversely, because the total amount of creatinine excreted in patients with ESLD is lower than the minimum expected creatinine excretion in the urine, 24-hour CrCl may further underestimate true GFR in this population.²⁸ For these reasons, CrCl, based on 24-h CrCl, leads to inappropriate classification and/or therapeutic adjustment in patients with ESLD about half the time.²³

Lastly, gender-based differences in the estimation of kidney function by serum creatinine also results in overestimation of kidney function in women relative to men. Multiple studies have demonstrated that, compared with men, women have worse kidney function and, therefore, higher wait-list mortality at any given level of serum creatinine.²⁹⁻³² Although the median serum creatinine at listing was .9 mg/dL for women vs 1.0 mg/dL ($P < .01$) for men, estimated GFR by MDRD-4 was 70 vs 83 mL/min ($P < .01$), respectively. As such, use of the MELD-based liver allocation system systematically disadvantages women with respect to prioritization for liver transplantation. Several studies have demonstrated that women were more likely than men to die or become too sick for liver transplantation in the post-MELD era. In 3 separate studies

analyzing data from the national UNOS registry, the proportion of liver transplant candidates who died or were delisted for being too sick for liver transplantation was 24% to 28% for women and 20% to 22% for men.³³⁻³⁵ Furthermore, women were less likely than men to receive a liver transplant (35% to 40% for women vs 45% to 49% in men).³³⁻³⁵ Further study is needed to quantify the degree to which this gender disparity can be "directly" attributed to gender differences in assessment of kidney function by serum creatinine.

POTENTIAL IMPROVEMENTS TO CURRENT PRACTICES

The decision to perform liver transplant alone vs SLK transplantation highlights the tension between optimizing outcomes in the individual patient with maximizing organ utilization for the organ transplant population as a whole. On the one hand, liver transplant recipients with post-transplant CKD experience lower post-transplant survival.¹⁰ On the other hand, allocating a kidney to a liver transplant recipient who would have recovered native kidney function after liver transplant removes an organ from the kidney transplant pool. Given the pitfalls of the current practices of SLK transplant allocation, several methods have been proposed to improve the identification of candidates with AKI who will and will not do well with liver transplant alone.

MELD-Na Score

Patients with ESLD are vulnerable to developing hyponatremia because of impairments in the kidney diluting system as a result of persistent splanchnic vasodilation secondary to portal hypertension, diuretic use, or kidney injury from other common causes of volume depletion such as diarrhea or gastrointestinal bleeding. Low serum sodium has increasingly been recognized as a key determinant of outcomes in patients with ESLD, particularly those with HRS and ascites.³⁶⁻⁴⁵ It has been shown to add to the

Table 2. Alternatives to Creatinine and Creatinine-Based Equations for Estimating Kidney Function and Acute Kidney Injury

Technique for Estimating Kidney Function	Advantages	Disadvantages
Cystatin C and cystatin C-based equations for estimating GFR	<ul style="list-style-type: none"> • Routinely available • Not influenced by gender, age, muscle mass, serum bilirubin, inflammation, or malignancy • Promising initial results in ESLD patients 	<ul style="list-style-type: none"> • Expensive • May need more standardization • Influenced by infection and medications • May be a marker of liver fibrosis progression
Urinary biomarkers	<ul style="list-style-type: none"> • Theoretic advantage of focusing on structural kidney injury • Helpful in differentiating causes of AKI in ESLD patients 	<ul style="list-style-type: none"> • Not validated • Not widely available • Likely difficult to use in settings outside of differentiation causes of AKI
Resistive index	<ul style="list-style-type: none"> • Early marker of renal dysfunction • Value in predicting renal dysfunction post-liver transplantation • Noninvasive • Widely available 	<ul style="list-style-type: none"> • Not correlated to GFR • Expensive

prognostic value of the MELD score using the MELD-Na equation:⁴⁶

$$\text{MELD} - \text{Na} = \text{MELD} + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD} \times (137 - \text{Na})],$$

where serum sodium is corrected for serum glucose, with a lower limit of 125 mEq/L and an upper limit of 137 mEq/L.

MELD-Na better discriminates between those who did and did not experience wait-list mortality compared with MELD (C-statistic 0.868 vs 0.883, $P < .001$).⁴⁷ In a validation cohort of liver transplant candidates from 2006, use of MELD-Na for liver allocation was predicted to result in 52 fewer total (wait-list and post-transplant) deaths per year compared with the current MELD-based liver allocation system.⁴⁶ It is, therefore, anticipated that the UNOS will incorporate MELD-Na, replacing MELD, into the liver allocation system by 2016.⁴⁸ Although the exact impact is not clear, MELD-Na-based liver allocation will likely further prioritize candidates with earlier kidney dysfunction and potentially reduce the number of candidates with kidney dysfunction who would meet current criteria for SLK transplant evaluation.

Alternatives to Creatinine and Creatinine-Based Equations for Estimating Kidney Function

Several methods have emerged to more accurately assess kidney function in patients with ESLD (Table 2). These methods may improve our ability to identify which liver transplant candidates with AKI have reversible kidney dysfunction and those whose AKI is a reflection of underlying worsening CKD.

Cystatin C. The most promising marker of kidney dysfunction is serum cystatin C. Cystatin C, a cysteine proteinase inhibitor, is an ideal GFR marker as it has a constant secretion rate by all nucleated cells and, because of its low molecular weight, passes freely through the glomeruli.^{49,50} In contrast to serum creatinine, cystatin C is present in the serum in equal proportions regardless of

gender, age, or muscle mass and is not influenced by serum bilirubin, inflammation, or malignancy.^{51,52} In a meta-analysis of non-ESLD patients, cystatin C was better correlated with GFR, as measured directly by inulin clearance, than creatinine.⁵³

In recent publications, Mindikoglu and colleagues⁵⁴ and De Souza and others⁵⁵ examined cystatin C-based equations in patients with ESLD. Using clearance of exogenous markers as the gold standard to calculate GFR, both studies found that equations including either cystatin C alone (CKD-EPI cystatin C [2012] equation⁵⁶) or cystatin C combined with serum creatinine (CKD-EPI creatinine-cystatin C [2012] equation⁵⁶) were superior to equations estimating GFR using serum creatinine alone or the 24-hour CrCl. This was particularly apparent among those with GFR less than 60 mL/min/1.73 m².

Although serum cystatin C is easy to obtain routinely, it has several limitations. The assay is significantly more costly than serum creatinine assays.⁵⁷ Serum cystatin C is influenced by infection and some drugs including corticosteroids, angiotensin-converting enzyme inhibitors, or calcineurin inhibitors.^{58,59} In addition, cystatin C could be a marker of progression of liver fibrosis^{60,61} potentially creating bias in the assessment of kidney function in ESLD patients. With these limitations in mind, additional studies are needed to determine whether cystatin C can improve on predictions of wait-list mortality compared with the creatinine-based MELD score and feasibly be implemented as part of a national liver allocation scheme.

Urinary Biomarkers. Urinary biomarkers of structural kidney injury, such as neutrophil gelatinase-associated lipocalin, interleukin-18, and kidney injury molecule-1,⁶²⁻⁶⁴ may prove valuable in differentiating between prerenal azotemia, acute tubular necrosis (ATN), and HRS as causes of AKI in cirrhotics.⁶⁵ In a prospective cohort study of 188 patients with ESLD and AKI, median values for urinary neutrophil gelatinase-associated lipocalin, interleukin-18, kidney injury molecule-1, and liver-type fatty acid-binding protein helped to differentiate between ATN and other etiologies of AKI.⁶⁶ The likelihood of being

diagnosed with ATN increased stepwise with the number of urinary biomarkers above optimal diagnostic cutoffs. Use of urinary biomarkers, however, did not distinguish HRS from other causes of AKI.⁶⁶ In a separate study, Levitsky and colleagues⁶⁷ showed that multianalyte plasma/urine kidney injury protein panels might improve the prediction of pre-liver transplant kidney injury recovery after liver transplantation, providing evidence for the role of urinary biomarkers in establishing appropriate SLK transplant candidates. Nonetheless, need for validation of these results, establishment of diagnostic cutoffs that are both sensitive and specific for causes of AKI, and more availability of these urinary biomarker assays are required before these markers can be widely adopted in clinical practice.

Kidney Artery Resistive Indices. Because HRS is characterized by kidney vasoconstriction, several studies have explored the prognostic utility of kidney artery resistive indices (RI) as measured by Doppler ultrasound in the setting of ESLD.⁶⁸⁻⁷⁰ In 180 patients with ESLD and "normal" serum creatinine, defined as less than 1.2 mg/dL, RI was noted to be elevated in 76 (42%) patients.⁷⁰ Doubling of initial creatinine to 1.5 mg/dL was noted in 55% (42 of 76) patients with an elevated RI compared with only 6% (6 of 104) of those with normal RI ($P < .01$).⁷⁰ HRS developed in 26% (20 of 76) of subjects with an elevated RI vs 1% (1 of 104) of those with a normal RI ($P < .01$).⁷⁰ Among 42 patients undergoing liver transplantation, patients with an elevated RI ($n = 19$) had a greater risk of subsequent doubling of initial creatinine ($P < .01$), need for hemodialysis ($P < .01$), longer intensive care unit stays ($P < .01$), and longer hospital stays after liver transplant ($P < .05$) compared with patients with a normal RI ($n = 17$).⁷¹ Although promising as a tool to identify ESLD patients at increased risk for kidney dysfunction, kidney artery RI is not correlated with GFR and, therefore, has limited utility for incorporation into predictive models of wait-list mortality for liver allocation schemes.⁷²

Intraoperative Kidney Replacement Therapy:

Patients undergoing liver transplantation often have multiorgan dysfunction including acute kidney injury, severe water/electrolyte and acid/base imbalances, systemic inflammatory responses, thrombocytopenia, and abnormalities of coagulation and fibrinolysis. The challenges of managing this multiorgan dysfunction are exacerbated during liver transplant surgery, an often lengthy, technically complex procedure requiring massive blood products, and other fluid infusions with a high risk of developing severe lactic acidosis, hyperkalemia, and/or cerebral edema.⁷³ The intraoperative course can be further complicated by major hemodynamic changes, cardiac arrhythmias, and post-reperfusion syndrome.^{74,75} The use of intraoperative kidney replacement therapy (ioRRT) during liver transplantation to reduce perioperative morbidity and mortality—and potentially reduce the risk of post-transplant kidney dysfunction of a patients' native kidneys (and, therefore, need for SLK transplantation)—has biologic plausibility.⁷³

Studies evaluating the risks and benefits of ioRRT in the liver transplant setting are limited. In a retrospective study designed to investigate the utility of ioRRT, Agopian and others⁷⁶ compared outcomes from 500 liver transplant recipients: 401 who did not receive ioRRT, 70 who received planned ioRRT, and 29 who received emergent RRT only after surgery. The 29 recipients who received emergent, unplanned RRT experienced significantly more intraoperative complications including arrhythmias and post-reperfusion syndrome and higher 30-day graft loss (28% vs 10%, $P = .004$) than both other groups combined.⁷⁶ Guidelines identifying patients undergoing liver transplantation who would benefit from ioRRT are needed as routine use significantly increases health care costs and resource utilization in an economically burdened health care system.^{77,78} Furthermore, whether ioRRT in patients receiving liver transplantation alone who were borderline candidates for SLK transplantation (ie, preoperative hemodialysis for 4-8 weeks) preserves native kidney function needs further exploration.

CONCLUSIONS

The prevalence of kidney failure in liver transplant candidates is rising, and a greater proportion of liver transplant candidates requires evaluation for SLK transplantation. Serum creatinine, although readily available and inexpensive, often overestimates kidney function in ESLD patients, particularly in those with sarcopenia, hyperbilirubinemia, and in women. Serum cystatin C is a surrogate for kidney function that is emerging as a promising alternative to serum creatinine, although more studies are needed to determine its prognostic value with respect to 90-day mortality relative to the MELD score (which uses serum creatinine as the marker of kidney function). Although the decision to proceed with SLK transplantation in a liver transplant candidate with CKD is relatively straightforward, predicting recovery of native kidney function after liver transplantation in a cirrhotic with acute or subacute kidney injury remains an art rather than a well-defined science. For these patients, current consensus guidelines recommend consideration of SLK transplantation when the duration of kidney failure exceeds 4 weeks. Future research into additional factors to predict native kidney recovery after liver transplantation is greatly needed to help determine which liver transplant candidates will do well with liver transplant alone rather than require SLK transplantation.

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