

III. Policy Proposals

At-a-Glance

- **Proposed listing requirements for simultaneous liver-kidney transplant candidates**
- **Policy proposed: Policy 3.5.10 (Simultaneous Liver-Kidney Transplantation)**
- **The Kidney Transplantation Committee and the Liver and Intestinal Organ Transplantation Committee**
- This proposal would set minimum criteria for candidates listed for simultaneous liver-kidney (SLK) transplantation. The intent of this proposal is first to identify candidates who are unlikely to regain renal function following liver transplantation. Once identified, these proposed policy changes would provide priority for these candidates to receive a SLK transplant. The goal of this proposal is to improve patient and renal graft survival following SLK transplant.
- **Affected groups:** candidates listed for kidney-liver transplant, transplant surgeons, transplant physicians, transplant coordinators

Proposed listing requirements for simultaneous liver-kidney transplant candidates

Policy proposed: Policy 3.5.10 (Simultaneous Liver-Kidney Transplantation)

Kidney Transplantation Committee and Liver Intestinal Organ Transplantation Committee

Summary and Goals of the Proposal:

This proposal would set minimum criteria for candidates listed for simultaneous liver-kidney (SLK) transplantation. The intent of this proposal is first to identify candidates who are unlikely to regain renal function following liver transplantation. Once identified, these proposed policy changes would provide priority for these candidates to receive a SLK transplant. The goal of this proposal is to improve patient and renal graft survival following SLK transplant.

Background and Significance of Proposal:

Currently OPTN/UNOS Policy does not contain listing requirements for candidates who require a simultaneous liver-kidney transplant (SLK). Reports in the peer-reviewed literature and from national consensus conferences suggest that SLK transplantation rates vary greatly among transplant centers, even among similar patient populations.¹ When the liver allocation system was changed to the current Model for End Stage Liver Disease (MELD) in 2002, a substantial amount of priority was given to liver transplantation candidates with renal insufficiency.² An unintended consequence of the MELD policy change may have been a rapid increase in the number of SLK transplants performed.

The increase in SLK transplants since the introduction of the MELD in 2002 prompted a joint review by the Kidney Transplantation Committee and the Liver Intestinal Organ Transplantation Committee. Findings from this review indicate that the number of SLK transplants has increased four fold from 82 in 1995 to 400 in 2006 (Figure 1).

¹ Davis CL, Feng S, Sung R, Wong F, Goodrich NP, Melton LB, Reddy KR, Guidinger MK, Wilkinson A, Lake J. Simultaneous liver-kidney transplantation: evaluation to decision making. *Am J Transplant*. 2007 Jul;7(7):1702-9.

² Locke JE, Warren DS, Singer AL, Segev DL, Simpkins CE, Maley WR, Montgomery RA, Danovitch G, Cameron AM. Declining outcomes in simultaneous liver-kidney transplantation in the MELD era: ineffective usage of renal allografts. *Transplantation*. 2008 Apr 15;85(7):935-42.

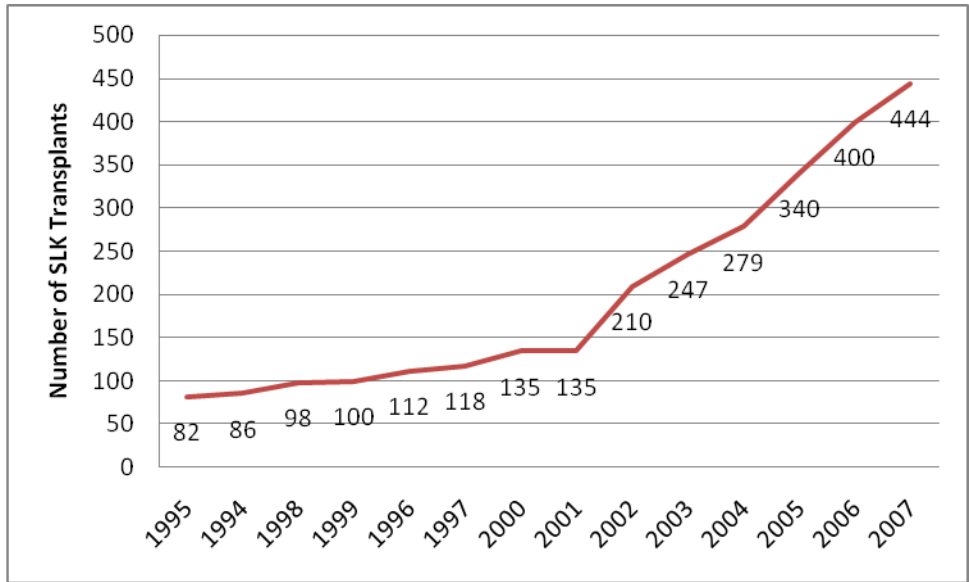


Figure 1: Number of SLK Transplants pre/post MELD implementation in 2002

While the number of SLK transplants has increased steadily since 2002, patient survival, as well as kidney graft survival following SLK transplantation has declined. In a retrospective study of adult recipients of deceased donor liver transplants, kidney transplants, and SLK transplants, Locke, et al, found that patient survival for SLK recipients diminished from 87% in 2002 to 76.1% in 2005.^{3 4}

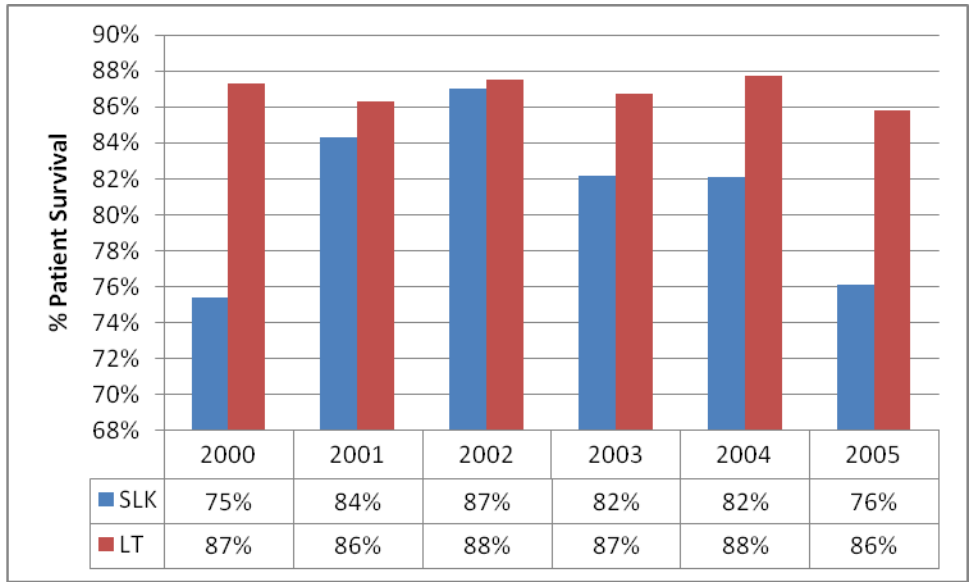


Figure 2: Patient survival following simultaneous liver kidney (SLK) transplant versus liver transplant (LT)

³ *ibid.*

⁴ *ibid.*

Current allocation for SLK or heart-kidney transplantation is based primarily on the life-saving organ. While candidates must be registered on the waiting list for each organ, the allocation is determined by the heart or liver match run. If the candidate is in the same donor service area (DSA) as the donor, then the kidney must be shared with the life-saving organ. If the candidate is in a different DSA than the donor, then sharing of the kidney is recommended but not mandatory (see OPTN/UNOS Policy 3.9.3).

Supporting Evidence and/or Modeling:

The transplant community discussed trends in SLK transplantation data in March 2006 and September 2007 during consensus conferences to review data related to SLK transplantation including incidence and outcomes. Based on the recommendations from these conferences, the Liver and Kidney Transplantation Committees evaluated the thresholds for dialysis time and glomerular filtration rate (GFR) to determine how many candidates would meet the following criteria for a liver-kidney transplant:

- a. If a patient is on chronic maintenance dialysis, documentation of initiation of dialysis with the chronic dialysis provider's name included. If available, a copy of the CMS Form 2728 should be provided; OR
- b. Documentation of $GFR \leq 25$ ml/min for 6 weeks or more by MDRD6 or direct measurement (iothalamate or iohexol); OR
- c. Dialysis for 6 weeks or more (defined as dialysis at least twice per week for 6 consecutive weeks); OR
- d. Metabolic disease requiring liver-kidney transplantation (such as hyperoxaluria, etc) with documentation from a nephrologist stating that the patient requires a combined liver-kidney transplant and the specific reason for the kidney graft listing (hyperoxaluria, dialysis for >6weeks, etc); OR
- e. Documentation of $GFR \leq 30$ ml/min by MDRD6 or direct measurement (iothalamate or iohexol), with proteinuria (>3 grams protein per day with 24 hour protein measurement or urine protein/creatinine ration >3.0)

A snapshot of the liver waiting list on January 31, 2008 was analyzed to determine the number of candidates who would meet at least one of the above criteria. Pediatric (0-11 years) candidates were excluded. In addition, a cohort of liver transplants (> 11 years) from March 1, 2002- through September 30, 2007 was analyzed to determine the number of recipients who would have met at least one of the proposed criteria for a combined liver-kidney transplant at the time of the transplant. GFR was estimated using the abbreviated MDRD formula:

Abbreviated MDRD (aMDRD) = $186 \times [\text{serum creatinine}(\text{mg/dL})]^{-1.154} \times [\text{age}]^{-0.203} \times [0.742 \text{ if patient is female}] \times [1.21 \text{ if patient is African-American}]$

Serum creatinine values were available from the laboratory values required for determining the MELD score of the liver candidate. Dialysis status (defined as dialyzed twice within the prior week) is another required component of MELD, and for candidates listed for both organs, current dialysis status is also collected on the kidney waiting list, along with date of first dialysis. However, unless the MELD labs are updated on a weekly basis, it is not possible to determine precisely if the candidate has had dialysis twice per week for six consecutive weeks or if the candidate's GFR was less than 25 ml/min for six consecutive weeks. As such, we can provide only a very crude estimate of the number of candidates or recipients who met these criteria. Primary oxalosis was the only metabolic disease that was considered as a criterion for a kidney transplant.

Based on data collected on the OPTN Liver waiting list, it is feasible to determine if the candidate or recipient qualified according to criteria b), c), and d). Because protein concentration data are not collected on the waiting list, it was not possible to evaluate criterion e). Additionally, at this time, the OPTN can not ascertain if a candidate is on chronic maintenance dialysis via CMS form 2728.

In order to be considered for the dialysis/GFR criteria in this analysis, the candidate must have had at least one MELD update no greater than eight weeks prior to the snapshot date (for the waiting list analysis) or the transplant date (for the transplant analysis). For example, a candidate with an estimated GFR < 25 ml/min or who was on dialysis based on one MELD update eight weeks prior to the date of interest (but no later updates) was assumed to have met the criteria. It is of course possible that the candidate later had a higher GFR and/or did not require further dialysis and therefore would not have satisfied the criteria. On the other hand, a candidate with one MELD update nine weeks prior to the date of interest would not meet the criteria, even if the candidate was reported to be on dialysis or to have an estimated GFR < 25 ml/min.

In addition, a candidate with any combination of dialysis or GFR < 25 ml/min for at least six consecutive weeks was considered to have met the dialysis/GFR requirement. For example, if a candidate was on dialysis for three weeks followed by three weeks of GFR < 25 ml/min prior to the date of interest, then that candidate met the criteria.

All analyses were based on OPTN data as of March 8, 2008. The results appear in Table 1 and Table 2.

Table 1. Number of Candidates on the OPTN Liver Waiting List on 1/31/08. Pediatric (0-11) candidates excluded. Dialysis and GFR estimates obtained from MELD components.

| Active on Liver WL? | On Kidney WL? | Oxalosis? | 6+ Weeks of GFR < 25 or Dialysis? | Frequency | Percent |
|---------------------|---------------|-----------|-----------------------------------|-----------|---------|
| N | N | N | N | 3463 | 22.19 |
| N | N | N | Y | 7 | 0.04 |
| N | N | Y | N | 2 | 0.01 |
| N | Y | N | N | 63 | 0.40 |
| N | Y | N | Y | 15 | 0.10 |
| N | Y | Y | N | 1 | 0.01 |
| Y | N | N | N | 11776 | 75.45 |
| Y | N | N | Y | 13 | 0.08 |
| Y | N | Y | N | 1 | 0.01 |
| Y | Y | N | N | 185 | 1.19 |
| Y | Y | N | Y | 76 | 0.49 |
| Y | Y | Y | N | 4 | 0.03 |
| Y | Y | Y | Y | 1 | 0.01 |
| TOTAL | | | | 15607 | 100.0 |

Table 2. Deceased donor liver transplants, 3/1/02 – 9/30/07. Pediatric (0-11) recipients excluded. Dialysis and GFR estimates obtained from MELD components.

| Liver-Kidney Transplant? | Oxalosis? | 6+ Weeks of GFR <25 or Dialysis? | Frequency | Percent |
|--------------------------|-----------|----------------------------------|-----------|---------|
| N | N | N | 28407 | 93.67 |
| N | N | Y | 120 | 0.40 |
| N | Y | N | 6 | 0.02 |
| N | Y | Y | 3 | 0.01 |
| Y | N | N | 1364 | 4.50 |
| Y | N | Y | 394 | 1.30 |
| Y | Y | N | 20 | 0.07 |
| Y | Y | Y | 12 | 0.04 |
| TOTAL | | | 30326 | 100.0 |

Table 1 provides data based on a snapshot of the liver waiting list. Pediatric (0-11 years) candidates were excluded. Dialysis data and GFR estimates were obtained from the available MELD information prior to the snapshot date. Of 15,607 candidates on the 1/31/08 snapshot, 345 (2.2%) candidates were simultaneously listed for a kidney transplant. Of these candidates, 97 (28.1%) met at least one of the proposed criteria for a combined liver-kidney transplant at the time of the snapshot. Of the remaining liver candidates who were not simultaneously listed for a kidney transplant, 23 (0.15%) met at least one of the proposed criteria for a combined liver-kidney transplant at the time of the snapshot.

Table 2 provides data on deceased donor liver transplants from 3/1/02 – 9/30/07. Pediatric (0-11 years) recipients were excluded. Dialysis data and GFR estimates were obtained from the available MELD information prior to transplant. There were 30,326 liver transplants during the period, 1790 of which (5.9%) were combined liver-kidney transplants. Of the liver-kidney transplants, 426 (23.8%) recipients met at least one of the proposed criteria for a combined liver-kidney transplant. Of the other liver transplants, 129 (0.45%) met at least one of the proposed criteria for a combined liver-kidney transplant at the time of the transplant.

This proposal does not adopt the recommendations from the 2007 consensus conference wholesale. Due to practical limitations of organ allocation, two recommendations are not being included in this proposal. The first, that patients with end stage liver disease who also have evidence of chronic kidney disease undergo kidney biopsy at the time of OLT, was excluded for several reasons. For one, estimated GFR is an acceptable measure of kidney function and is less invasive than biopsy which may pose a risk

to patients due to their coagulopathy. Some centers may not be equipped to perform biopsies in this patient population. Finally, due to the timing of organ allocation, it is impractical to perform the biopsy at the time of OLT to determine the need for a kidney as recommended.⁵ The second recommendation, that patients with Child's A cirrhosis must have a hepatic vein wedge pressure gradient of less than 10 mm Hg, was intended to ensure that candidates listed for a CLK qualify for a liver transplant. Because listing criteria for liver allocation belongs in Policy 3.6 (Allocation of Livers), separate language can be developed for this purpose for inclusion in the liver policy. The Liver Committee may also consider a more inclusive statement mentioning other legitimate reasons for liver transplantation (e.g., a candidate with HCC who is a Child's A cirrhotic). This proposal may result in unintended consequences such as candidates who do not regain renal function following OLT returning to the kidney waiting list. For this reason, a safety-net provision has been established so that these candidates receive additional priority (**Error! Reference source not found.**).

⁵ Eason 2008.

Donors <35

Kidney-Pancreas (according to pancreas allocation rules)

| | |
|-----------|--|
| Pediatric | 0-MM local OMM pediatric, ABO identical |
| Pediatric | 0-MM Regional with CPRA $\geq 80\%$, ABO identical |
| Pediatric | 0-MM National with CPRA $\geq 80\%$, ABO identical |
| Pediatric | 0-MM Regional with CPRA $< 80\%$, ABO identical |
| Pediatric | 0-MM National with CPRA $< 80\%$, ABO identical |
| Pediatric | 0-MM local OMM pediatric, ABO compatible ⁶ |
| Pediatric | 0-MM Regional with CPRA $\geq 80\%$, ABO compatible |
| Pediatric | 0-MM National with CPRA $\geq 80\%$, ABO compatible |
| Pediatric | 0-MM Regional with CPRA $< 80\%$, ABO compatible |
| Pediatric | 0-MM National with CPRA $< 80\%$, ABO compatible |
| Pediatric | Prior Living Organ Donors |
| Adult | Prior Living Organ Donors |
| Pediatric | Local, non 0-MM, ABO identical or A2→B ⁷ |
| Adult | Local, Liver-Recipients with Continued Kidney Nonfunction |
| Adult | Local or (CPRA $\geq 80\%$ and OMM), ABO identical or A2→B |
| Pediatric | Regional, non 0-MM, ABO identical or A2→B |
| Adult | Regional, ABO identical or A2→B |
| Pediatric | National, non 0-MM, ABO identical or A2→B |
| Adult | National, ABO identical or A2→B |

Donors ≥ 35

Kidney-Pancreas (according to pancreas allocation rules)

| | |
|-------|--|
| Adult | Prior Living Organ Donors |
| Adult | Local, Liver-Recipients with Continued Kidney Nonfunction |
| Adult | Local or (CPRA $\geq 80\%$ and OMM), ABO identical or A2→B |
| Adult | Regional, ABO identical or A2→B |
| Adult | National, ABO identical or A2→B |

Figure 3: Allocation sequence for liver-recipients with continued renal dysfunction

Expected Impact on Program Goals, Strategic Plan, and Adherence to OPTN Final Rule:

This policy proposal addresses the program goal to increase the average number of life-years gained following kidney transplant.

Plan for Evaluating the Proposal:

Overall, this proposal should reduce the number of SLK transplants for candidates who could regain renal function following OLT. The following metrics will be used to evaluate this policy proposal:

- The number/characteristics of candidates listed for simultaneous liver-kidney transplant pre and post policy change
- The number/characteristics of candidates who require a kidney transplant following a liver transplant
- Patient and graft survival following SLK and OLT followed by kidney transplant
- The overall number of SLK transplants and number by transplant center

This evaluation would begin at six months following policy implementation and continue at six month intervals. If the number of candidates requiring a kidney transplant following a liver transplant increases, then the Committees will evaluate the characteristics of these candidates to determine if the requirements should be loosened.

Additional data collection:

Recommendations resulting from consensus conferences included the collection of additional data, specifically dialysis duration, to better identify reversible renal insufficiency.⁸ The Committees agreed with this recommendation; as part of this proposal, additional documentation to ascertain duration of dialysis, as well as GFR and proteinuria would be required.

Communication/Education Plan:

The following table proposes how and to whom these policy changes would be communicated if they are approved.

⁸ Davis 2007

| Type of Communication | Audience(s) | Delivery Method(s) | Timeframe |
|----------------------------------|---|--------------------|--|
| Policy Notice | Transplant Administrators, Coordinators, Program Directors, Surgeons, Physicians, Social Workers, Data Coordinators | Email | Distributed 30 days after Board approval |
| UNet SM System Notice | Transplant Coordinators, Administrators, Directors, and Data Coordinators | Email | 4 weeks before implementation |
| UNet SM System Notice | Transplant Coordinators, Administrators, Directors, and Data Coordinators | Email | Date of implementation |

Monitoring and Evaluation:

The UNOS Department of Evaluation and Quality (DEQ) staff conducts routine site surveys of transplant centers to evaluate member compliance with OPTN/UNOS Policies and Bylaws. More specific details about OPTN/UNOS monitoring efforts will be available in the OPTN Evaluation Plan⁹ following approval and implementation of these policy changes.

If this change is approved, UNetSM would be modified to collect the information described in the proposal. UNOS staff would modify monitoring efforts to incorporate a review of this data into the routine site survey process for liver transplant programs.

Policy Proposal:

3.5.10 Simultaneous Liver-Kidney Transplantation

This policy details the minimum criteria that candidates must meet for mandatory sharing of a donor kidney with the donor liver at the local level of allocation. At the regional and national levels of allocation, sharing is recommended but is not mandatory (see policy 3.9.3 Organ Allocation to Multiple Organ Transplant Candidates). This policy includes a description of the criteria and the documentation required to be maintained by the candidate transplant center.

⁹ To read the OPTN Evaluation Plans, please visit the following website: http://www.optn.org/content/policiesAndBylaws/evaluation_plan.asp

3.5.10.1 Documentation Required for Simultaneous Liver-Kidney (SLK) Allocation

Candidates with chronic renal failure, sustained acute renal failure, and metabolic disease meet the requirements for SLK allocation with the following documentation:

- a. Chronic Renal Failure Requiring Dialysis:** For patients on chronic maintenance dialysis for End-Stage Renal Disease (ESRD), transplant centers must document the date of initiation of dialysis and the cause of ESRD.
- b. Chronic Renal Failure Not requiring Dialysis:** Documentation of both GFR ≤ 30 ml/min (by MDRD6 or direct measurement (iothalamate or iohexol)) and proteinuria (> 3 gms protein per day with 24 hr protein measurement or Urine Protein/Creatinine ratio > 3.0) is required.
- c. Sustained Acute Renal Failure Requiring Dialysis:** Documentation of dialysis for 6 weeks or more (defined as dialysis at least twice per week for 6 consecutive weeks) is required.
- d. Sustained Acute Renal Failure (ARF) not Requiring Dialysis:** Documentation of a GFR ≤ 25 ml/min for 6 weeks or more by MDRD6 or direct measurement (iothalamate or iohexol) is required. An acceptable test must be reported at least once a week (every 7 days).¹⁰
- e. Sustained Acute Renal Failure:** Patients may also qualify for SLK listing with a combination of time in categories (c) and (d) above for a total of six weeks.
- f. Metabolic Disease:** Metabolic disease requiring liver-kidney transplantation qualifies with documentation from a nephrologist specifying a diagnosis of hyperoxaluria, atypical HUS from mutations in factor H (and possibly factor I), familial non neuropathic systemic amyloid (arising from amyloidogenic autosomal dominant mutations in APO-A1 - OMIM#107680)

3.5.10.2 Documentations Requirements for Listing of Liver Recipients in Continued Renal Failure

¹⁰ A measured GFR can be correlated to a serum Cr for that individual patient and will be acceptable as sustained ARF. For example, if an iothalamate scan is performed which results in a GFR of 20 ml/min, and the patient's serum Cr is measured at 3.0 mg/dl that same day, then that patient will be considered to have sustained ARF as long as the serum Cr is not below 3.0 mg/dl. If the serum Cr drops below 3.0 mg/dl, then another direct measurement test (such as a repeat iothalamate clearance) must be performed to consider that patient still in ARF. Once a patient's GFR rises above 25 ml/min, their time in ARF is restarted at time 0.

Liver transplant recipients who had renal dysfunction pre-liver transplant, but did *not* receive a kidney graft and remain on hemodialysis (HD) or peritoneal dialysis (at least twice per week) for at least 90 days after liver transplantation, fall into two categories: those who met the listing criteria prior to liver transplant and those who did not meet the listing criteria prior to liver transplant. For these candidates, additional considerations apply as described below:

- i. **Candidates who met listing criteria for SLK, but did not receive a SLK.** Those who met the listing criteria for SLK and were listed for SLK pre-liver transplant as in 3.5.10.1 above, but were not transplanted with the renal allograft at the time of orthotopic liver transplantation (OLT) should remain on the kidney transplant list until transplanted or inactivated on the kidney list. Candidates must receive chronic maintenance dialysis for at least 90 days following liver transplantation. The transplant center must list the candidate for “kidney after liver transplant” in UNetsm between 90 days and 180 days after liver transplant. The transplant center must document that the candidate has unrecoverable native renal function and requires a kidney transplant.
- ii. **Candidates who did not qualify initially for SLK.** Liver recipients who did not qualify for SLK under policy 3.5.10.1 prior to receiving a liver transplant (3.5.10.1), but who fulfill a less stringent set of criteria (Table 1) and who fail to regain native renal function by 90 days after liver transplant can be listed for kidney transplant.
 1. Liver recipients who *did not qualify* for SLK initially include those on dialysis pre-liver transplant for at least two weeks, and those with intrinsic kidney disease pre-liver transplant, but who had a GFR between 30 and 40 ml/min for at least 4 weeks pre-liver transplant. Also, a patient who has a combination of GFR measured below 40 ml/min and/or dialysis totaling 4 or more weeks is also acceptable (Table 1).

| | | Dialysis Required pre-Liver Transplant | Time Duration | Documentation Requirement |
|---|---|--|---------------|--|
| D. Liver Recipients who did not qualify for SLK initially | 1 | Yes | ≥2 weeks | Documentation of dialysis pre-liver transplant |
| | 2 | No | ≥4 weeks | Documentation of intrinsic kidney disease pre-liver transplant and GFR between 30 and 40 ml/min for at least 4 weeks pre-liver transplant |
| | 3 | Yes | ≥4 weeks | Combination of D1 and D2 documentation for at least 4 weeks |

Table 1: Requirements for Liver Recipients who did not qualify for SLK initially who remain in renal failure post liver-transplant

3.5.10.3 Deceased Donor Waiting List Priority for Liver Recipients in Continued Renal Failure

Liver Recipients in continued renal failure who fulfill the requirements in Table 1 as well as the requirements below (all requirements must be met) will be prioritized locally after prior living organ donors and before payback obligations.

1. Chronic Maintenance Dialysis for at least 90 days after liver transplantation.
 - a. In order to receive additional consideration, the liver recipient must be identified as a candidate for “Kidney after Liver Transplant” in UNetsm between 90 days and 180 days of last liver transplant.
 - b. The transplant program must document that a nephrologist believes the candidate has unrecoverable native renal function and requires a kidney transplant. This documentation must be maintained and provided upon request.