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Xingxing Cheng

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Is prioritization of kidney allografts to combined liver-kidney recipients appropriate? CON

Xingxing S. Cheng

Division of Nephrology, Department of Medicine, Stanford University School of Medicine,
Palo Alto, CA

Corresponding author:
Xingxing S. Cheng
Stanford University School of Medicine
750 Welch Road
Suite 200
Palo Alto, California
United States
xscheng@stanford.edu
The debate over simultaneous liver-kidney (SLK) transplantation centers on two interrelated but distinct questions: 1) at what degree of kidney dysfunction would the liver transplant candidate benefit from a SLK? 2) to what extent should SLK candidates be prioritized over kidney-alone transplant (KAT) candidates? Much of recent discourse and policy efforts have been directed toward the first question. The United Network for Organ Sharing (UNOS) SLK policy that took effect in the summer of 2017, for instance, set minimal medical eligibility criteria for SLK\(^1\), implying that liver transplant candidates who do not meet those criteria are unlikely to benefit from SLK over liver transplant alone, while leaving open which patients do benefit from SLK\(^2\). Meanwhile, the second question regarding the prioritization of SLK candidates has received much less attention and shall be my focus for this article.

Current SLK and all other kidney-utilizing multi-organ transplants [MOTs] supersede the Kidney Allocation System (KAS): whenever the liver or other non-kidney organ is allocated to a patient based on the non-kidney allocation system, the kidney automatically follows, bypassing the entire KAT waitlist. The traditional justification for this system, in the case of SLK, is that SLK candidates are sicker, i.e. have a greater medical urgency, and therefore can less afford to “wait” compared to KAT candidates. Two objections to this justification exist: 1) the waitlist mortality of SLK candidates is driven by end-stage liver, rather than kidney, disease, and therefore should not be used to justify kidney allocation; 2) as Westphal et al. have recently demonstrated, KAT candidates bypassed due to kidney-utilizing MOTs suffer a striking 55% increase in mortality on the waitlist, compared to their counterparts one position ahead who
received the mate kidney of the kidney-utilizing MOT\(^3\). Therefore, contrary to traditional belief, KAT candidates cannot truly afford to “wait” either.

The sad state of organ shortage has turned allocation into a zero-sum game: benefit to one patient group necessarily comes at the expense of another. Any incremental improvement to the system should therefore focus on 1) growing the proverbial pie, by increasing organ availability or decreasing transplant demand; or 2) where growing the pie is not possibility, preserving equitability that underlies solid organ transplantation. On these fronts, the current prioritization of SLK and kidney-utilizing MOTs over KAT is indefensible for three reasons.

*Reducing overall supply of kidneys:* Increasing kidney supply relies on promotion of living donation or expanding use of non-standard deceased donors, e.g. donation after cardiac death donors [DCD]. The ever-lengthening KAT waitlist\(^4\) creates a powerful incentive for living donation for KAT candidates—those remaining on the list generally do not have viable living donors. Candidates of SLK and kidney-utilizing MOT are utterly shielded from the incentive to find living donors. Indeed, the Safety Net provision of the 2017 SLK policy, which prioritizes not only SLK recipients, but all liver transplant recipients who develop end-stage kidney disease within 1 year of transplant, likely exacerbated this problem—even if a liver transplant recipient, freshly dialysis-dependent, had potentially living donors, he/she is not incentivized to pursue donation. Regarding expanding deceased donor utilization, outcomes of DCD SLK transplants are poor\(^5\), and most SLK and kidney-utilizing MOTs utilize only the best deceased donor kidneys\(^6\). The
current allocation system, by virtue of its incentives, therefore contribute to the perpetuation of the zero-sum game and shrinking pie size.

*Increasing demand for KAT:* 12% of the KAT waitlist in 2018 consists of patients who outlived a prior kidney transplant and are seeking re-transplantation. Prolonging kidney allograft lifespan therefore reduces the system-wide demand for KAT. This argument underlies the current KAS, which seeks to match the best kidneys with candidates with the best projected posttransplant survival. Here, SLK and kidney-utilizing MOT work in opposite directions. Kidneys utilized by SLK and kidney-utilizing MOT typically are high-quality, thereby reducing the average quality of kidneys that KATs utilize. As their overall organ quality is reduced by SLK and kidney-utilizing MOTs, KAT end up returning to the KAT waitlist sooner, thereby worsening the kidney allograft shortage from the demand side.

*Lack of equitability:* Equitability refers to the ethical principle that people ought to be treated equitably—patients in need of organ transplants ought to be prioritized based on medical needs and not systemic biases. To justify the prioritization of all SLK and kidney-utilizing MOT candidates ahead of all KAT candidates, one needs to establish that the benefit all SLK and kidney-utilizing MOT recipients derive from the incremental kidney is greater than that of all KAT candidates. This has never been shown and is unlikely to be true, given that, even in the best scenario, SLK appears to offer an incremental benefit in survival over liver-alone transplantation on the order of a few months. While some KAT candidates certainly may be doing well on dialysis, and derive benefit from transplant mostly in health-related quality of life, kidney transplant is life-saving in the long-run to many KAT candidates. While prioritizing some SLK and
kidney-utilizing MOT ahead of some KAT candidates may be equitable, prioritization of
all ahead of all is not.

To improve the existing system, I recommend the following incremental changes.

_Innovate on sequential organ transplantation:_ The liver, not the kidney, is the
lifesaving organ in an SLK. A reasonable approach may thus be to transplant the liver
first, followed by a kidney transplant a few months later if the patient remains in kidney
failure. This strategy has recently been made possible by the Safety Net provision of the
SLK policy. Identifying good candidates for this approach should be a priority for liver-
 kidney transplant programs. A successful sequential strategy approach may help on in
four ways: 1) it allows for living kidney donation from donors of liver transplant
candidates, thereby increasing the kidney supply; 2) a sequential kidney transplantation
will be spared from the early complications after liver transplantation and likely have a
longer lifespan, thereby reducing the likelihood that the recipient needs to return to the
KAT waitlist at a later date; 3) some patients who are currently receiving SLK may
recover native kidney function after liver transplant alone, thereby obviating the need for
a kidney transplant and reducing overall kidney demand; 4) liver transplant recipients
would demonstrate that they really have irrecoverable kidney disease, which improves
equitability. Although concern remains regarding the medical and surgical challenges of
supporting patients with kidney failure through liver transplantation and the
postoperative phase, early data on the outcomes of Safety Net show seemingly non-
inferior outcomes to SLK and the community is beginning to embrace Safety Net as a
serious alternative to SLK^{12–14}. 
Incorporate of kidney-utilizing MOT into KAS: Incorporating SLK and kidney-utilizing MOT into the KAS would improve equitability. Rather than blanket prioritizing of a whole group, the decision can be made based on the actual medical urgency and indication of the kidney transplant. For instance, urgency for a kidney transplant candidate with rapidly failing dialysis access is higher than urgency for a SLK candidate with no preexisting kidney disease and acute kidney injury, who can be supported through the liver transplant with renal replacement therapy and has a reasonable chance of recovering off dialysis. This urgency ought to be properly reflected in the KAS. Incorporating kidney-utilizing MOT into the KAS would better reflect the heterogeneity of both SLK and KAT candidates and reduce tragic instances of death by waiting (Table 1).

Adding a “supply”-related approach to kidney-related MOT allocation: To an extent, supply, not demand, of kidneys ought to dictate kidney-related MOT. The demand for kidneys, both from KAT and from kidney-utilizing MOT candidates, clearly exceed the supply. Given that KAT is better established and likely yields more benefit than the incremental kidney in kidney-utilizing MOT, an approach may be to place an upper bound on the proportion of kidneys we are willing to allocate to kidney-utilizing MOT. In a potential iteration, the transplant community can arrive at a number by consensus (say, 5% of deceased donor kidney transplants each year), and tweak the MOT eligibility criteria such that roughly the same number of kidney-MOT candidates qualify each year. Alternatively, we have previously proposed a willingness-to-transplant threshold. The idea of the willingness-to-transplant threshold is: the transplant community can decide what the minimum number of life-years gained from a kidney
transplant is acceptable, and then use that number to decide if the kidney in certain kidney-utilizing MOTs generate enough life-years justify that use.

In future iterations of allocation change for non-kidney solid organs, the impact on kidney-utilizing MOT needs to be examined ahead of time: The adoption of the Model for End-stage Liver Disease (MELD) in 2002 was instrumental in developing an urgency-based liver allocation system. However, as kidney function is a component of the MELD score, more liver transplant recipients had kidney dysfunction at the time of transplant, and the incidence of SLK skyrocketed\(^\text{17}\). Currently, UNOS evaluates solid organ allocation policies within each organ committee and does not solicit comments from other organ groups. A unified MOT policymaking progress should evaluate the potential impacts of each allocation policy on all organ groups\(^\text{18}\).

From their advent to now, SLK and kidney-utilizing MOT have existed outside the purviews of the kidney allocation process and taken automatic precedence over KAT without adequate medical or ethical justification. We need to remedy this systemic bias within the solid organ transplant system. None of the currently proposed changes to the KAT allocation system, continuous distribution or otherwise, will address kidney-utilizing MOTs, and the current practice is undermining the objectives of the KAS. It is time to close this loophole in the system as a concerted nephrology, transplant, and medical community.
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Table 1. Example of incorporating MOT into the allocation sequence for a Kidney Donor Profile Index <20% kidney. Reproduced from Cheng and Reese15 with permission.

| Current Allocation | Potential New Allocation |
|--------------------|-------------------------|
| All MOT            | Tier 1 MOT (high priority) |
| cPRA = 100%        | cPRA = 100%              |
| Prior living donor | Prior living donor       |
| Pediatric candidate| Pediatric candidate      |
| Medically urgent   | Medically urgent         |
| cPRA = 99%         | cPRA = 99%               |
| cPRA = 98%         | cPRA = 98%               |
| Zero mismatch      | Zero mismatch            |
| EPTS 0-20%         | EPTS 0-20%               |
| EPTS > 20%         | Tier 2 MOT (low priority) |
|                    | EPTS > 20%               |
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