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POLICY FORUM

Regulations' Impact on Donor and Recipient Selection for Liver Transplantation: How Should Outcomes be Measured and MELD Exception Scores be Considered?

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Introduction

The allocation of donated livers to patients waiting for transplantation is a classic example of a medical ethical conflict, rooted in the challenge of balancing urgency and utility in a limited resource setting. Current allocation policy, which determines the order in which waitlisted patients are offered an available liver, is based on the Model for End-Stage Liver Disease (MELD) score, a validated measure, based on patients' objectively verifiable lab values, of the likelihood of death without transplant. By prioritizing a patient with the highest MELD score, the system is explicitly designed to reduce the likelihood of patients' dying while waiting for a liver, rather than choosing those patients who are likely to have the best posttransplant survival [1]. It is possible to compare organ allocation to similarly resource-limited clinical challenges, such as triage during a mass trauma, the protocols of which dictate that those patients with the highest chance of long-term survival are given top priority [2]. Transplantation differs from trauma care in key ways, however, notably in the extended time to make allocation decisions among waitlisted patients, our limited ability to predict long-term outcomes after transplant, and the variable quality of donor organs, which are seen as gifts that oblige stewardship. Consequently, the United Network for Organ Sharing (UNOS) has implemented a liver transplant allocation policy that seeks to reduce the risk of dying immediately rather than attempting to predict future survival after transplant [3, 4].

In marked contrast to allocation policy, transplant programs are evaluated principally on posttransplant liver graft and patient survival. Thus, despite a system that prioritizes transplant for the sickest patients on the waiting list, centers are required to maintain posttransplant graft survival rates that are generally greater than 90 percent at one year [5]. We explore here how these well-intentioned but conflicting policy decisions result in unanticipated challenges in transplant care by describing the current system of regulating center performance and its impact on both patient selection and liver graft selection.

The Transplant Environment under the Medicare Conditions of Participation

In the United States, federal law requires that transplant center outcomes are universally tracked and publicly reported, serving as a prime example of transparency in health care delivery. Solid organ transplantation practice has been regulated by the federal government under the National Organ Transplant Act (NOTA) since 1984 [6]; however, the regulatory landscape dramatically changed in 2007 when new Conditions of Participation (CoPs) were issued by the Centers for Medicare and Medicaid Services (CMS) [7, 8]. Under the new rules, minimum risk-adjusted posttransplant graft and patient survival rates are required for Medicare certification and reimbursement. CMS promulgated these rules for transplant center certification in the name of advancing patient safety and improving transplant outcomes [7, 8]. However, since implementation of the CoPs, some experts have questioned whether these rules have improved outcomes or simply resulted in restricted access for higher-risk patients and reduced innovation [9-12].

The current CoP requirements are based on risk-adjusted one-year graft and patient survival outcomes in patients transplanted over a 2.5-year period, as reported by the Scientific Registry of Transplant Recipients (SRTR) [8]. Outcomes are based on data reported by transplant programs and validated through comparison with the National Social Security Death Master File. Data are risk-adjusted using donor and recipient characteristics (e.g., age, race, cause of liver failure, cause of donor death) to account for differences in patients and donors. Unfortunately, risk adjustment methods remain imperfect and many important factors (e.g., cardiovascular disease) are poorly captured in risk-adjusted outcomes. Centers are flagged for poor performance when all three of the following criteria are met for either death or graft failure one year after transplant: (1) the ratio of observed outcomes to risk-adjusted outcomes (standardized mortality ratio) is greater than 1.5; (2) observed outcomes minus expected outcomes ("excess") is greater than 3; and (3) the difference between observed and expected outcomes is statistically significant (one-sided p-value < 0.05). There are appeals processes in place should centers be sanctioned for poor performance (referred to as "mitigating circumstances"); however, many of these appeals have been unsuccessful and the centers still receive significant sanctions that result in costly process improvement agreements [10, 13]. Furthermore, although the CoPs have been established through federal regulation, commercial insurers tend to use similar data to qualify programs for Centers of Excellence status and determine network eligibility [14]. Both directly and indirectly, the regulatory environment heavily influences transplantation practice and outcomes.

By design, the CoP outcomes standards are designed to identify centers in which graft loss or patient death significantly exceeds risk-adjusted expected values. CMS officials point to empirical evidence that the CoP standards have improved posttransplant outcomes [7]. Although there is no published data on the effect of the CoP standards on

liver transplantation, the data on kidney transplantation is illustrative: in an initial review of 15 kidney transplant centers that entered systems improvement agreements as a result of CoP citations, the standard mortality ratio for one-year post-transplant survival decreased from 2.05 to 1.17 over a two-year period [10]. CMS argues that these data demonstrate that CoPs have led to improved post-transplant survival for patients undergoing kidney transplantation at those centers [10]. As another added benefit, hospitals were required to increase the amount of resources available to transplant centers as a requirement to remain in the Medicare program [8]. However, there is also clear evidence that failure to meet the publicly reported outcome standards can have a devastating impact on transplant programs [9, 15]. Not surprisingly, when centers receive low performance evaluations, they perform fewer transplants and reduce the size of their waitlists for both kidney [12] and liver [16] transplantation. Centers cited for poor outcomes often see dramatic reductions in referrals [17], resulting in fewer new listings for transplant and substantial losses of clinical volume and hospital revenue.

Impact of CMS Regulations on Donor and Recipient Selection

It is important to recognize that the CoP criteria are contingent on only two metrics: one-year post-transplant patient survival and one-year graft survival [18, 19]. These metrics do not capture outcomes over patients' entire episodes of care, which extend from the onset of advanced organ failure to death with or without a transplant. The CoPs do not evaluate the center rates of transplantation, impose no penalties for higher-than-expected waitlist mortality, or consider low acceptance rates of riskier donors or recipients. Because the CoPs do not incorporate measures of pretransplant outcomes (e.g., waitlist mortality), they have created a dilemma for transplant centers: *Should a transplant center become risk-averse and perform fewer, lower-risk transplants with likely better early posttransplant outcomes or should the center be more aggressive and perform potentially riskier transplants by using marginal organs to provide a greater population-level benefit but face a higher risk of sanctions under the CoPs?*

The CoPs have also directly undermined the efforts of UNOS to increase utilization of all deceased organ donors. To improve posttransplant outcomes, many centers choose to decline offers for marginal donor organs [17, 20], including livers with moderate-to-severe steatosis ("fatty liver"), which have a higher rate of early dysfunction, or livers donated following cardiac death (DCD), which have increased rates of biliary complications. Aggressive centers that seek opportunities to expand the organ supply by using these marginal, lower-quality organs are potentially at greater regulatory risk. These programs can be cited for minimal decreases in posttransplant survival, despite the benefit resulting from substantial increases in the overall rate of transplant. Some of these more aggressive centers have been able to successfully convince CMS that they qualify for "mitigating circumstances" and should not be subject to regulatory penalties. However, doing so requires substantial and costly investments and is not always

successful [15]. Accordingly, the rate at which these "marginal" organs are declined appears to be increasing since the CoPs were announced [21].

Because the impact of poor performance evaluations is so drastic, potentially affecting not only certification and reimbursement but also referrals, many transplant centers are altering their patient selection criteria to reduce risk of a negative evaluation [20]. Because race, ethnicity, and socioeconomic status are known risk factors for poorer liver transplant outcomes, but are inadequately accounted for in the risk-adjusted outcome models [22], already-disadvantaged groups are disproportionately affected by transplant centers that are less willing to engage in "riskier" transplants. Despite inclusion of risk adjustment in the CoP assessment of transplant outcomes, centers are *de facto* incentivized to avoid listing patients perceived as having a high risk of early graft failure or mortality. These incentives are relevant from an ethics perspective because they can disproportionately affect patients who are also commonly disadvantaged: patients who are older or have advanced comorbid conditions, have a higher body mass index, or are of low socioeconomic status.

The impact of the CoPs on donor and recipient selection appears to be mitigated, in part, by the competitiveness of the local transplant environment. The first geographic unit for liver allocation is the donor service area (DSA). It has been useful to conceptualize DSAs as 58 individual markets or transplant "micromarkets." These DSA "micromarkets" vary considerably in a number of factors such as the size of the waiting list, the number of transplant centers, and the "market share" controlled by each [23]. "Market share" within a DSA matters, as DSAs with one dominant center and three smaller centers are less competitive than those with four centers each possessing a relatively equal market share [23]. Listing practices vary widely among DSAs as a consequence of different practice environments [24]. More competitive DSAs, in which a greater number of transplant centers compete for the care of transplant patients, tend to transplant patients who are sicker. These centers also tend to accept riskier (lower-quality) organs [23]. In other words, in competitive environments, the need for patients drives centers to aggressively pursue available organs to retain volume despite concerns about posttransplant outcomes.

Currently, there are efforts to promote broader sharing of liver allografts among micromarkets, which may have the effect of increasing *de facto* competition and encouraging more aggressive listing and organ utilization practices [23, 25]. By combining DSAs of differing levels of competition into larger organ allocation regions, these policies effectively make every allocation region in the country "more competitive." In turn, this may encourage more aggressive listing and organ utilization practices, reducing the cherry-picking of donors and recipients that can lead to systemic disadvantages for certain patients [25-27].

Measuring Outcomes: Limitations and Innovations

Despite nearly two decades of public reporting, metrics used to assess transplant center outcomes are significantly limited by several key factors, including sample sizes and the lack of detailed clinical data. An individual transplant center's annual volume of procedures performed can range from 1 to 200, providing insufficient statistical power to detect statistically significant differences between observed and expected outcomes in many centers [5]. The SRTR addresses this issue by basing observed and expected one-year survival rates on center data aggregated over 2.5-year cohorts. Despite frequent data collection, the prolonged analytic period results in substantial delay in recognizing changes in center performance, with reported outcomes that may appear worse than expected outcomes despite meaningful process improvement during the 2.5-year period. Finally, key factors including the patient's cardiac status and the degree of steatosis in the liver allograft are not captured in national data.

Several potential solutions to these limitations have been proposed. For example, cumulative sum (CUSUM) charts intended for real-time assessment of program-specific clinical outcomes are available on a confidential basis to transplant centers but have not been used for regulatory review [27]. CUSUM charts provide more responsive, real-time data. However, these methods are designed for process improvement, not regulation; they have high sensitivity and relatively low specificity when identifying poorly performing centers, and this limits enthusiasm for broadening their use.

In an effort to respond to concern about the reliability of the older metrics used to assess performance, the SRTR recently introduced new performance assessment tools using Bayesian methods [11, 28]. These methods adjust the precision of the outcomes assessment according to the size of the program and national data, to provide a more reliable estimate of performance. Of concern, it appears that more centers will be identified as poor performers under the Bayesian system [11, 28]. This methodology has yet to be adopted by CMS under the CoPs; however, the data are publically reported and are available for patients and other payers. In theory, the Bayesian methods provide a more robust assessment of performance; unfortunately, in practice, the results are more difficult to interpret and the current choice of signaling thresholds is likely to exacerbate the issues of risk aversion and organ discard. Furthermore, the new or proposed models remain limited by the same lack of key clinical variables data for risk adjustment as the current models.

Finally, there also is little agreement on methods to measure outcomes starting from initial diagnosis, because not all potential organ transplant recipients are referred, evaluated, or listed. End-stage organ disease is a population-based problem with a long continuum of care, from the onset of early organ disease, through progression of disease while on the waiting list, and, finally, to posttransplant care for those fortunate enough to receive a transplant. There is clear evidence that many patients who are reasonable

candidates for transplant are never evaluated or listed [29-31]. Currently, transplant centers are not rewarded for increasing access to transplant services or for effectively managing the health of patients on their waiting lists. This clearly fails to incentivize centers to promote the health of their waitlisted patients, let alone the population of patients with end-stage organ failure in their regions. Not only would measuring the quality of care for end-stage organ disease along the entire continuum be a worthwhile endeavor, it could refocus attention from survival of transplanted patients to reducing mortality from liver disease overall.

Impact of MELD Exception Scores on Recipient Selection under the CoPs

Under the current allocation system, a substantial number of liver transplant candidates move up the waitlist after their MELD scores are recalculated incorporating "exception points" designed to address the MELD score's weaknesses in measuring effects on mortality risk of diseases such as hepatocellular carcinoma (HCC). Exception points are awarded independently of the patient's actual MELD score, and the use of these mechanisms varies widely across the country [32]. The current systems have been shown to overestimate the risk of death from HCC, leading to relative overtransplantation of these patients at the expense of patients without malignancies [33]. The population of patients with HCC also tends to be better insured and of higher socioeconomic status [34], which exacerbates the existing economic disparities in access. HCC patients may, in fact, be transplanted too quickly, and posttransplant survival appears to be improved by waiting longer for a liver and selecting patients with less aggressive disease and lower chance of recurrence [35]. Thus, strategies like "ablate and wait" (i.e., radiofrequency ablation as a bridge to transplant to remain within acceptable listing criteria) may prove prudent prior to subjecting patients with aggressive cancers to a major procedure and the need for immunosuppression.

Unfortunately, current quality measures do not reward centers for making such appropriate clinical decisions. The CoPs compound these issues, as centers are strongly incentivized to identify and transplant patients with HCC who, in general, are healthier at the time of transplant and have excellent early patient and graft survival despite the potential for disease recurrence.

Conclusions

Transplantation is a heavily regulated and scrutinized field that has witnessed remarkable improvements in outcomes over the past 20 years. Although much of this improvement is the result of innovation in surgical techniques and immunosuppression, a significant component of continued improvement can justly be attributed to transplant centers' public reporting of outcomes and their desire to achieve excellent outcomes. Transplantation thus has been a leader in transparency by publishing center-specific outcomes and providing national data that centers can use to identify opportunities for self-improvement.

However, using measured outcomes for punitive purposes may have resulted in significant unintended consequences. Transplant professionals will, by necessity, adapt practice to minimize the risk of regulatory citation and loss of transplant volume [36]. This self-protective strategy will contribute to lower transplant rates (typically among higher-risk candidates) and greater organ discard (of low-quality organs) unless transplanting higher-risk patients and acceptance of marginal organs are properly accounted for in CoP criteria that incorporate robust risk-adjustment methodology.

The goal is not to eliminate measurements, but rather to incentivize improvement of meaningful outcomes. One solution to encourage innovation could be to exempt recipients participating in funded IRB-approved trials from a center's reported outcomes. To prevent abuse of this system, a limit on the number of exempt transplants would need to be defined and outcomes would require extra review and regular reporting. To date, the CoPs have not been adapted to support innovation though this type of proposal. Without such a system, programs face strong disincentives for generating novel approaches to the most difficult problem facing transplant clinicians: the need to expand the supply of available organs. Similarly, by choosing appropriate measures to define the CoPs in the future, including a focus on pretransplant outcomes, transplant regulations may actually encourage acceptance of marginal organs and transplantation of higher-risk patients. With the right metrics and appropriate risk adjustment, transplantation will continue to lead in public reporting and transparency, which honors the gift of life given by thousands of donors annually. Without changes, however, we will exacerbate risk aversion in donor and recipient selection and lose an opportunity to provide access to lifesaving procedures.

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Disclosure

Dr. Axelrod is an owner of XynManagement, a private corporation that provides quality monitoring and improvement software to transplant programs.

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