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REVIEW ARTICLE

CAQ Corner

CAQ Corner: Evolution of liver allocation policy

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INTRODUCTION

The US urgency-based liver transplantation (LT) policy has two components: allocation and distribution of donor livers. The Model for End-Stage Liver Disease (MELD) score, the metric of waitlist mortality, was implemented on February 29, 2002. Since then, there have been several evidence-based dynamic changes to the allocation and distribution scheme in attempts to be fair, just, and equitable (Figure 1).

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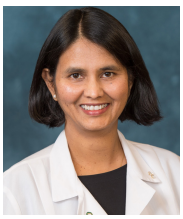

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ALLOCATION

Pre-MELD allocation

The National Organ Transplantation Act (NOTA Sections 371–376 of the Public Health Services Act) was enacted in 1984 to govern and provide regulatory oversight for transplantation through the creation of an Organ Procurement and Transplantation Network (OPTN). Prior to NOTA, there were no formal guidelines for allocation. After the passage of NOTA and until 1996, the allocation of donor livers was stratified as urgent (Status 1: fulminant hepatic failure) and nonurgent. The nonurgent status was further subdivided into hospitalized in intensive care unit (ICU) setting (Status 2), non-ICU setting (Status 3), and ambulatory (Status 4).[1] Later, Status 2, 3, and 4 were reclassified as Status 2A, 2B, and 3, respectively. Candidates were ranked based on their waiting time in these status-based categories with broad ranges of disease severity. The location-based status designation was susceptible to covert and overt manipulation. As a result, the allocation policy was amended and a Child-Turcotte-Pugh (CTP) score of 7 was adopted as the minimal listing

Abbreviations: AFP, alpha-fetoprotein; AST, aspartate aminotransferase; CCA, cholangiocarcinoma; CF, cystic fibrosis; CKD, chronic kidney disease; CrCl, creatinine clearance; CT, computed tomography; CTP, Child-Turcotte-Pugh; CVVH, continuous venovenous hemodialysis; CVVHF, continuous venovenous hemofiltration; DSA, donor-specific area; eGFR, estimated glomerular filtration rate; FAP, familial amyloid polyneuropathy; FEV_1, forced expiratory volume in 1 s; GFR, glomerular filtration rate; HAT, hepatic artery thrombosis; HCC, hepatocellular carcinoma; HPS, hepatopulmonary syndrome; ICU, intensive care unit; INR, international normalized ratio; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; MELD-Na, Model for End-Stage Liver Disease–sodium; MMaT, median Model for End-Stage Liver Disease score; MPAP, mean pulmonary artery pressure; MPaT, median Pediatric End-Stage Liver Disease score at transplant; NLRB, National Liver Review Board; NOTA, National Organ Transplantation Act; OPO, organ procurement organization; OPTN, Organ Procurement and Transplantation Network; PaO_2, partial pressure of arterial oxygen; PELD, Pediatric End-Stage Liver Disease; PVR, pulmonary vascular resistance; SLKT, simultaneous liver–kidney transplantation; *TTR*, transthyretin; WU, wood unit.

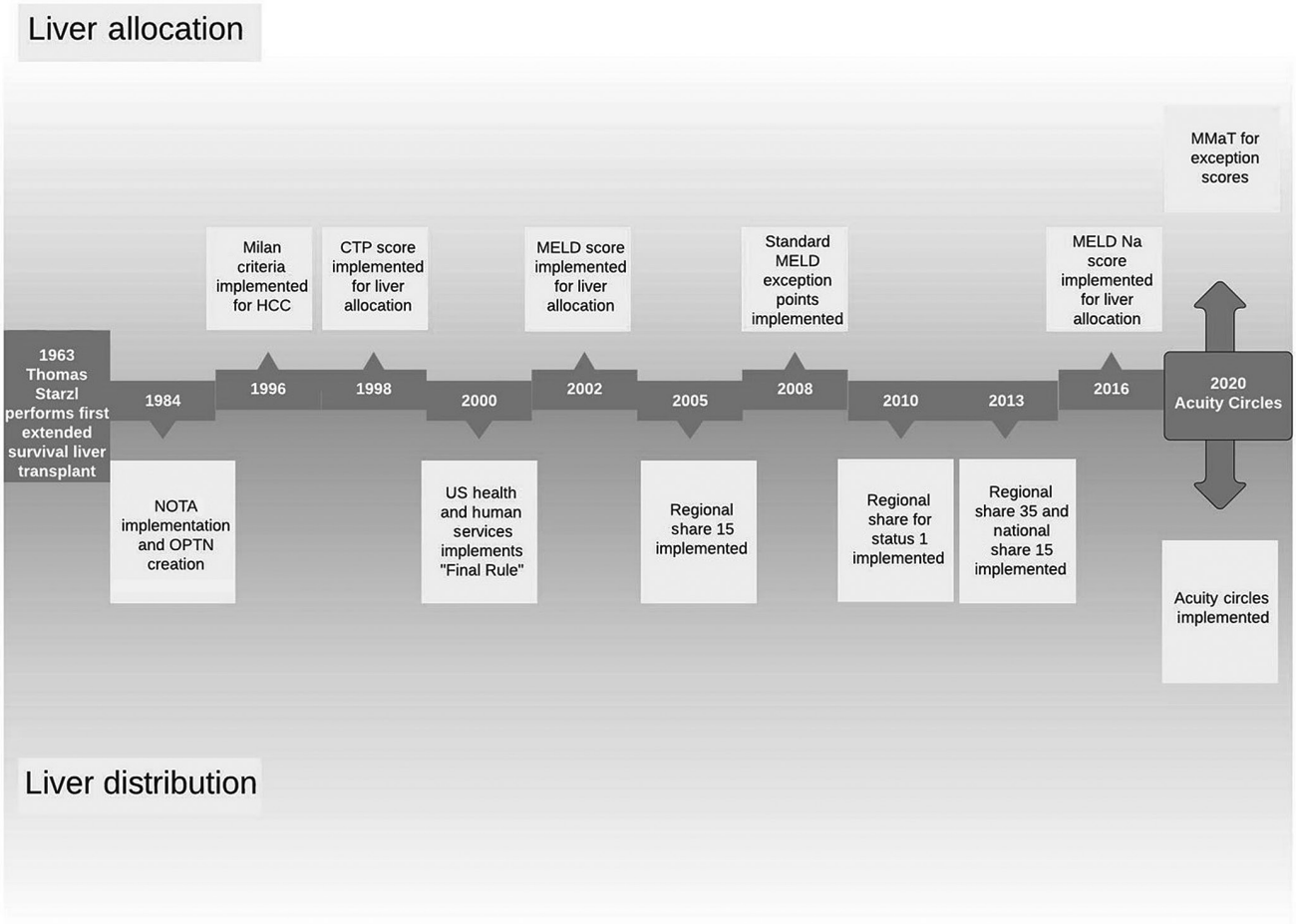

FIGURE 1 Evolution of LT allocation and distribution in the United States.

criteria for LT.[2] However, this did not improve the inequities and inefficiencies in the allocation associated with gaming the system because of the subjectivity of criteria and waiting times. The US Department of Health and Human Services stated in a Final Rule in 1999 that organ allocation rules should be based on objective medical criteria, ideally based on continuous measures of medical urgency.[3] The Final Rule clearly advocated for a system that would promote equity by reducing disparities in waitlist outcomes.

MELD-based allocation

MELD score, originally developed to risk-stratify patients undergoing an elective transjugular intrahepatic portosystemic shunt procedure,[4] was further refined and validated in other data sets, including hospitalized patients and ambulatory patients with cholestatic and noncholestatic liver disease, with excellent performance characteristics. MELD score performed superior to CTP score (concordance statistic, 0.82) in predicting 3-month mortality among 3437 candidates on the waiting list.[5]

MELD score is based on serum creatinine, serum bilirubin, and international normalized ratio (INR) of prothrombin time (Figure 2) and was implemented for allocation with few caveats: (1) the etiology of the liver disease was dropped to avoid subjectivity but the coefficient was kept, (2) the lower bound of serum creatinine and serum bilirubin was set at 1.0 mg/dl to avoid a negative score, (3) the upper bound of creatinine was set at 4.0 mg/dl if the candidate is on dialysis or creatinine >4.0 mg/dl to avoid undue advantage to kidney disease, and (4) the upper bound of the MELD score was set at 40.

Introduction of the MELD score in the United States was associated with a 12% reduction in waitlist registrations (particularly among those with MELD scores <10), a 3.5% reduction in waitlist mortality, and an increase in LT rates distributed across all demographic and epidemiologic strata with unchanged early patient and graft survival rates despite patients who are sicker receiving a higher proportion of donor livers.[6]

Kim et al. and others[7] showed that hyponatremia was an independent predictor of waitlist mortality and the addition of serum sodium to the MELD score could reduce waitlist mortality by as much as 7%.[8] Sharma et al. demonstrated that the survival benefit of LT

MELD score: 0.957 x Log_e (creatinine mg/dL) + 0.378 × Log_e (bilirubin mg/dL) + 1.120 × Log_e (INR) + 0.643

MELD-Na = MELD(i) + 1.32×(137-Na) – [0.033×MELD(i)×(137-Na)]

PELD score: 0.436 (Age (<1 year)) – 0.687 × Log_e (albumin g/dL) + 0.480 × Log_e (total bilirubin mg/dL) + 1.857 × Log_e (INR) + 0.667 (growth failure*)

FIGURE 2 Formula to calculate MELD score, MELD-Na score, and PELD score. *More than 2 standard deviations based on age and sex using the most recent Centers for Disease Control and Prevention's National Center for Health Statistics pediatric clinical growth chart.

increased significantly with decreasing serum sodium at MELD scores ≥12.[9] However, the survival benefit of LT was not affected by serum sodium for patients with MELD scores ≤11. The MELD–sodium (MELD-Na)–based policy (Figure 2) went into effect January 2016.

Despite best efforts and modifications, the MELD score does not account for many other factors (e.g., frailty, albumin) and sex differences, leading to disparities in transplantation. Over time, modifications of the MELD score have been proposed, most recent being the MELD 3.0 incorporating sex and serum albumin to improve waitlist mortality prediction.[10]

Candidates aged <12 years receive a Pediatric End-Stage Liver Disease (PELD) score. The components of the PELD score include age, serum bilirubin, serum albumin, INR, and growth failure.

Waitlist maintenance

Mandatory MELD score reassessment and recertification by the transplant center is required by OPTN, the governing body overseeing organ transplantation. MELD scores must be submitted periodically for recertification, with updates at more frequent intervals for higher MELD scores, for example, every 7 days for those with MELD scores ≥24. Recertification must be based on the most recent laboratory test results and diagnosis, including the dates of the laboratory tests. Failure to do so in accordance with the schedule may result in reassignment to a previous lower MELD score. The candidate may remain at that previous lower score for the period allowed based on the recertification schedule for the previous lower score minus the time spent in the uncertified score. If the candidate remains uncertified past the recertification due date for the previous lower score, the candidate will be assigned a MELD score of 6.

Adult Status 1A

Adult candidates with severe, life-threatening liver dysfunction (life expectancy <7 days without LT) in the absence of prior liver disease are given the highest medical priority for allocation of deceased donor liver ahead of all candidates with MELD scores via 1A status (Table 1). In this category, patients are rank ordered based on waiting time. Although the MELD score is not used to allocate livers in this category, MELD las are updated every 7 days.

Pediatric Status 1A/1B

Similar to their adult counterparts, pediatric LT candidates are stratified according to medical necessity and, depending on the objective clinical criteria, may achieve priority in listing for lifesaving LT as pediatric Status 1A or 1B candidates, superseding calculated and/or exception MELD/PELD scores (Table 1).

MELD/PELD exceptions

As in the case with any mathematical model or risk score, the MELD score does not reflect the disease severity in certain conditions such as hepatopulmonary syndrome (HPS), portopulmonary hypertension, cholangiocarcinoma (CCA), and hepatocellular carcinoma (HCC). Hence, a system of exception MELD score has been in place to award increased priority to candidates whose disease severity is not captured by the calculated MELD score. These broadly fall into standardized and nonstandardized MELD/PELD exception scores (Table 2).[11] The candidates' transplant team submits a vignette with a request for standard MELD exception or a customized exception score request to the National Liver Review Board (NLRB). The NLRB, implemented in 2019, consists of volunteer independent medical experts (transplant hepatologists and transplant surgeons). The review board decides whether the requested score is reasonable based on the patient's current medical condition and the likelihood that the recipient will do well after transplantation. The board makes its decision based solely on the medical facts supplied by the transplant hospital aided by their own medical judgment and guidance from the OPTN. The review

TABLE 1 LT candidate allocation

Adult candidates (aged ≥18 years at time of registration)	Pediatric candidates (aged <18 years at time of registration)
Adult Status 1A	Pediatric Status 1A
a. Fulminant liver failure (onset of hepatic encephalopathy within 56 days of the first signs or symptoms of liver disease in a candidate without a preexisting diagnosis of liver disease. Candidate must be admitted in the ICU with at least one of the following conditions: • Is ventilator dependent • Requires dialysis, CVVH • Has an INR >2.0 b. Anhepatic candidates c. Primary nonfunction of a transplanted whole liver or liver segment from a deceased or living donor within 7 days of transplant with AST ≥3000 U/L and at least one of the following: • INR ≥2.5 • Arterial pH ≤7.30 • Venous pH ≤7.25 • Lactate ≥4 mmol/L d. HAT within 7 days of transplant, with AST ≥3000 U/L and at least one of the following: • INR ≥2.5 • Arterial pH ≤7.30 • Venous pH ≤7.25 • Lactate ≥4 mmol/L e. Acute decompensated Wilson disease	a. Fulminant liver failure (onset of hepatic encephalopathy within 56 days of the first signs or symptoms of liver disease in a candidate without a preexisting diagnosis of liver disease. Candidate must have one of the following conditions: • Is ventilator dependent • Requires dialysis, CVVHF, or CVVH • Has an INR >2.0 b. Primary nonfunction of a transplanted liver within 7 days of transplant, evidenced with at least two of the following: • AST ≥2000 U/L • INR ≥2.5 • Total bilirubin ≥10 mg/dl • Acidosis, defined as one of the following: ◦. Arterial pH ≤7.30 ◦. Venous pH ≤7.25 ◦. Lactate ≥4 mmol/L c. HAT in a transplanted liver within 14 days of transplant d. Acute decompensated Wilson disease Pediatric Status 1B a. Biopsy-proven hepatoblastoma without evidence of metastatic disease b. Organic acidemia or urea cycle defect and an approved MELD or PELD exception meeting standard criteria for metabolic disease for at least 30 days c. Chronic liver disease with a calculated MELD or PELD score >25 (and/or is a combined liver–intestine candidate) and has at least one of the following criteria: • Is on a mechanical ventilator • Has gastrointestinal bleeding requiring at least 30 ml/kg of red blood cell replacement (10 ml/kg for liver–intestine candidates) within the previous 24 h • Has renal failure or renal insufficiency requiring dialysis, CVVHF, or CVVH • Has a Glasgow coma score <10 within 48 h before the Status 1B assignment or extension

Abbreviations: AST, aspartate aminotransferase; CVVH, continuous venovenous hemodialysis; CVVHF, continuous venovenous hemofiltration; ICU, intensive care unit; INR, international normalized ratio; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; PELD, Pediatric End-Stage Liver Disease.

board may grant or deny the exception score requested. If the initial request is denied, the transplant team listing the candidate can choose to appeal up to three times.

Median MELD score at transplant/median PELD score at transplant

The median Model for End-Stage Liver Disease score at transplant (MMaT)/median Pediatric End-Stage Liver Disease score at transplant (MPaT) are used in assigning standard MELD/PELD disease exception scores. The MMaT/MPaT score is calculated by using the median of the MELD (aged ≥12 years)/PELD (aged <12 years) scores at the time of LT of all recipients who received transplants at hospitals within 250 nautical miles of the candidate's listing hospital in a prior 365-day period. The MMaT/MPaT calculations exclude Status 1A/1B transplants and the recipients of living donor, donation after circulatory death, and donors procured >500 nautical miles from the transplant hospital. The OPTN recalculates the MMaT/MPaT every 6 months based on an updated cohort of LTs within 250 nautical miles of the transplant hospital during a prior 365-day period if there were ≥10 qualifying transplants and during a prior 730-day period if there were <10 qualifying transplants.

Standard MELD/PELD exceptions

The OPTN Liver and Intestinal Organ Transplantation Committee has developed guidance for adult MELD exception candidates. These standardized recommendations were proposed after reviewing the 2006 MELD Exception Study Group Conference.[12] The objective criteria of standardized MELD/PELD exception conditions and criteria to qualify for exception status are shown in Table 2.

TABLE 2 LT standard and nonstandard exception scoring

Specific standardized MELD/PELD score exceptions	
HCC • Indication that candidate is not eligible for resection and imaging evidence ruling out extrahepatic spread/macrovascular disease/metastatic disease with dynamic contrast enhanced CT or magnetic resonance imaging and CT chest • Candidates with T2 (one lesion ≥2 cm and ≤5 cm in size or up to three lesions each ≥1 cm and ≤3 cm in size) HCC lesions and an AFP level ≤1000 ng/ml • Candidates with T2 HCC but with an AFP >1000 ng/ml may be treated with locoregional therapy. If AFP level falls <500 ng/ml after treatment, the candidate is eligible for a standardized MELD/PELD exception as long as AFP level remains <500 ng/ml. Candidates with an AFP level ≥500 ng/ml following locoregional therapy at any time must be referred to the NLRB for consideration of a MELD/PELD exception • Candidates with HCC beyond T2 but within downstaging inclusion protocol (one lesion >5 cm and ≤8 cm or up to three lesions each >3 cm and ≤5 cm with a total diameter of all lesions ≤8 cm or up to five lesions each <3 cm with a total diameter of all lesions ≤8 cm) and subsequently meet T2 criteria after locoregional therapy • Candidates with lesions that do not initially meet the downstaging protocol inclusion criteria who are later downstaged and then meet eligibility for T2 lesions are not automatically eligible for a standardized MELD/PELD exception and must be referred to the NLRB for consideration of a MELD/PELD exception	HCC exception scores • Candidates aged ≥18 years: ◦ Initial request/first extension: ▪ Higher value between MELD score of 6 or calculated MELD ◦ Subsequent extensions: ▪ MMaT-3 • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MELD score of 40 • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MELD score of 40
CCA • Candidate meets the diagnostic criteria for unresectable (because of technical considerations or underlying liver disease) hilar CCA with a malignant appearing stricture on cholangiography and at least one of the following: • Biopsy or cytology results demonstrating malignancy • Carbohydrate antigen 19-9 >100 U/ml in absence of cholangitis • Aneuploidy • Hilar mass <3 cm in radial (perpendicular to the duct) diameter • No history of transperitoneal aspiration or biopsy of the primary tumor, cross-sectional imaging of the chest and abdomen excluding intrahepatic/extrahepatic metastasis, administration of neoadjuvant therapy before transplantation, and negative regional hepatic lymph node involvement and peritoneal metastases by operative staging after completion of neoadjuvant therapy	CCA exception scores • Candidates aged ≥18 years: ◦ Initial request and any extension: ▪ MMaT 3 • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT
Portopulmonary hypertension Candidate will receive a MELD/PELD score exception if all of the following are met: • Documentation of portal hypertension at the time of initial exception • Document via heart catheterization initial MPAP ≥35 mm Hg and initial PVR ≥240 dynes × s/cm^5 (or ≥3 WU) from the same test date • Other causes of pulmonary hypertension have been assessed and determined to not be a significant contributing factor • Initial transpulmonary gradient to correct for volume overload • Documentation of treatment • Document via heart catheterization within 90 days prior to submission of the initial exception either of the following: • Posttreatment MPAP <35 mm Hg and posttreatment PVR <400 dynes × s/cm^5 (or <5 WU) from the same test date • Posttreatment MPAP ≥35 mm Hg and <45 mm Hg and posttreatment PVR <240 dynes × s/cm^5 (or <3 WU) from the same test date	Portopulmonary hypertension exception scores • Candidates aged ≥18 years: ◦ Initial request and any extension: ▪ MMaT 3 • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT
HPS Candidate will receive a MELD/PELD score exception if all of the following are met: • Ascites, varices, splenomegaly, or thrombocytopenia • A shunt shown by either contrast echocardiogram or lung scan • PaO_2 <60 mm Hg on room air within 30 days prior to submission of the initial exception request • No clinically significant underlying primary pulmonary disease	HPS exception scores • Candidates aged ≥18 years: ◦ Initial request and any extension: ▪ MMaT 3 • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT

(Continues)

TABLE 2 (Continued)

Specific standardized MELD/PELD score exceptions	
CF Candidate will receive a MELD/PELD score exception diagnosis if all of the following are met: • Diagnosis confirmed by genetic analysis • FEV_1 <40% of predicted FEV_1 within 30 days prior to submission of the initial exception request	CF exception scores • Candidates aged ≥18 years: ◦ Initial request and any extension: ▪ MMaT 3 • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT
FAP Candidate will receive a MELD/PELD score exception diagnosis if all of the following are met: • Concurrently listed for heart transplant or echocardiogram performed within 30 days prior to submission of the initial exception request an ejection fraction >40% • Able to walk without assistance • Confirmed *TTR* gene mutation • Biopsy-proven amyloid	FAP exception scores • Candidates aged ≥18 years: ◦ Initial request and any extension: ▪ MMaT 3 • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT
Primary hyperoxaluria Candidate will receive a MELD/PELD score exception diagnosis if all of the following are met: • Concurrently listed for kidney transplantation • Alanine glyoxylate aminotransferase deficiency proven by liver biopsy using sample analysis or genetic analysis • eGFR by the six-variable Modification of Diet in Renal Disease formula or GFR measured by iothalamate or iohexol ≤25 ml/min on two occasions at least 42 days apart	Primary hyperoxaluria exception scores • Candidates aged ≥18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT + 3 • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT + 3
Metabolic disease Candidate will receive a MELD/PELD score exception diagnosis if all of the following are met: • Evidence of urea cycle disorder or organic acidemia	Metabolic disease exception scores • Candidates aged ≥12 and <18 years: ◦ Initial request and any extension: ▪ MMaT • Candidates aged <12 years: ◦ Initial request and any extension: ▪ MPaT
HAT Candidate will receive a MELD score exception for HAT if the candidate is aged ≥18 years at registration and has HAT within 14 days of transplant but does not meet criteria for Status 1A	HAT disease exception score • MELD score of 40
Nonstandardized MELD/PELD score exceptions	
Adult MELD exception review • Budd Chiari syndrome • Hepatic epithelioid hemangioendothelioma • Hepatic hydrothorax • Hereditary hemorrhagic telangiectasia • Multiple hepatic adenomas • Neuroendocrine tumors • Polycystic liver disease • Primary sclerosing cholangitis or secondary sclerosing cholangitis • Diffuse ischemic cholangiopathy	Pediatric PELD exception review • Growth failure or nutritional insufficiency • Infections • Complications of portal hypertension, including ascites and gastrointestinal bleeding • Pruritus • Metabolic liver diseases • Metabolic bone disease

Abbreviations: AFP, alpha-fetoprotein; CCA, cholangiocarcinoma; CF, cystic fibrosis; CT, computed tomography; eGFR, estimated glomerular filtration rate; FAP, familial amyloid polyneuropathy; FEV_1, forced expiratory volume in 1 s; GFR, glomerular filtration rate; HAT, hepatic artery thrombosis; HCC, hepatocellular carcinoma; HPS, hepatopulmonary syndrome; MELD, Model for End-Stage Liver Disease; MPAP, mean pulmonary artery pressure; NLRB, National Liver Review Board; PaO_2, partial pressure of arterial oxygen; PELD, Pediatric End-Stage Liver Disease; PVR, pulmonary vascular resistance; *TTR*, transthyretin; WU, Wood unit.

Nonstandard MELD/PELD exceptions

Certain decompensation events such as ascites, hepatic encephalopathy, and gastrointestinal bleeding lack adequate evidence to support granting specific MELD exception scores. However, there are additional complications of disease severity that are not reflected in the MELD score and are not covered under standard

MELD/PELD exceptions. These nonstandard MELD/PELD exceptions are shown in Table 2.

Distribution

Distribution can be defined as the order in which organs are offered to waitlist candidates.[13]

Donor specific area–OPTN region–national

Historically, deceased donor liver distribution was based on a local–regional–national gradient to the most degree. The donor-specific area (DSA) is the distinct, nonoverlapping geographic area served by each of the 58 federally certified organ procurement organizations (OPOs). DSAs may include one or more transplant programs of a given organ and one or more donor hospitals.[14] These DSAs were grouped into 11 (OPTN) regions before viewing the nation.

Geographic variability in access to LT, measured by median MELD score at transplant, is a major contributor to inequitable access across the OPTN regions. Based on a Scientific Registry of Transplant Recipients report in 2019, the median MELD score varied from 19 to 36 by recipient DSA.[15] The "Regional Share 15," "Regional Share Status 1," and "Regional Share 35" were the major changes in the distribution scheme to mitigate this variability.

Merion et al. demonstrated significant overall survival benefit from LT for patients with MELD scores ≥18.[16] Based on 1 year post-LT mortality risk, the survival benefit of LT diminished for patients with MELD scores <15. Hence, the Regional Share 15 policy was implemented. Under this change in policy, after initial offer within the local DSA to patients with MELD scores >15, organs were offered regionally before being offered locally again to patients with MELD scores <15.

In line with the tenants of the "Final Rule" prioritizing access to organ transplantation for the patients who are sickest, Regional Share Status 1 was implemented in 2010 in which patients listed as Status 1 would receive priority for transplant ahead of all other patients listed within that OPTN region. This policy change improved the access to LT by increasing the probability of LT and reduced the waitlist mortality for adult Status 1 candidates without negatively affecting waitlist mortality for non–Status 1 patients in the same region.[17]

The Regional Share 35 rule was implemented to prioritize access to the patients who are sickest in the OPTN region. Sharma et al. demonstrated that candidates listed for LT with a MELD score range of 36–40 had similar waitlist mortality risk and post-LT survival compared with Status 1A and yet were not prioritized for LT within the region as their Status 1A/1B counterparts.[18] These results were validated by the OPTN Liver and Intestinal Committee; thus Regional Share 35 was implemented in 2013 to improve access to LT for patients with high MELD scores within the OPTN regions. These policy changes increased transplant rates for patients with MELD scores ≥35, with a corresponding decrease in waitlist mortality by 30% for the patients who were sickest and by 8% overall.[19]

Acuity circle distribution system

Despite the earlier changes in the distribution scheme and the creation of the NLRB, significant geographical variability persisted in the median MELD scores across different regions.[20] Coupled with legal challenges toward a broad geographical rational of organ distribution, a donor liver distribution system based on concentric geographical circles (similar to donor lung distribution) around a donor site hospital was examined. Simulation modeling of concentric circles demonstrated improved access to LT and increased travel time as a tradeoff. This change in distribution system was accepted by the OPTN after public comments and was implemented in 2020[21] (Figure 3).

Under acuity circles, all livers from adult deceased donors are first offered to compatible Status 1A and 1B candidates listed at transplant hospitals within a radius of 500 nautical miles of the donor hospital. Subsequently, livers from deceased adult donors (aged ≥18 years) are distributed based on the deceased donor's age and mechanism of death to patients stratified by MELD score ranges through concentric zones of distribution at 150 nautical miles, 250 nautical miles, and 500 nautical miles of the donor hospital in a tiered approach. To increase priority for pediatric candidates over their adult counterparts at similar levels of medical urgency, livers from pediatric donors (aged <18 years) are initially offered to compatible pediatric candidates listed at any transplant hospital within a 500 nautical mile radius of the donor hospital (Figure 4).

Recent data reports from the OPTN demonstrated increased LT rates for Status 1A/1B candidates and those with MELD/PELD scores of ≥29, increased rates of deceased donor liver-alone transplants, and decreased geographic variability in median urgency scores at transplant.[22] Going forward, all organ allocation systems will transition to a continuous distribution model where all candidates are considered collectively versus specific groups, with candidates receiving priority on a sliding scale formula based on a composite allocation score of medical urgency, posttransplant survival, candidate biology, patient access, and placement efficacy.[23]

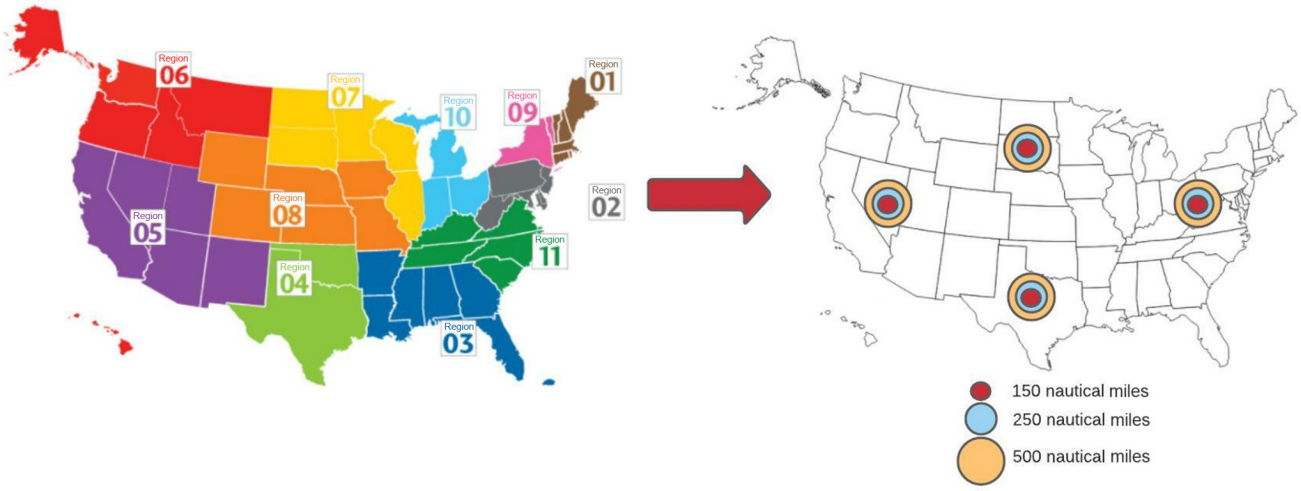

FIGURE 3 Shift toward acuity circle distribution

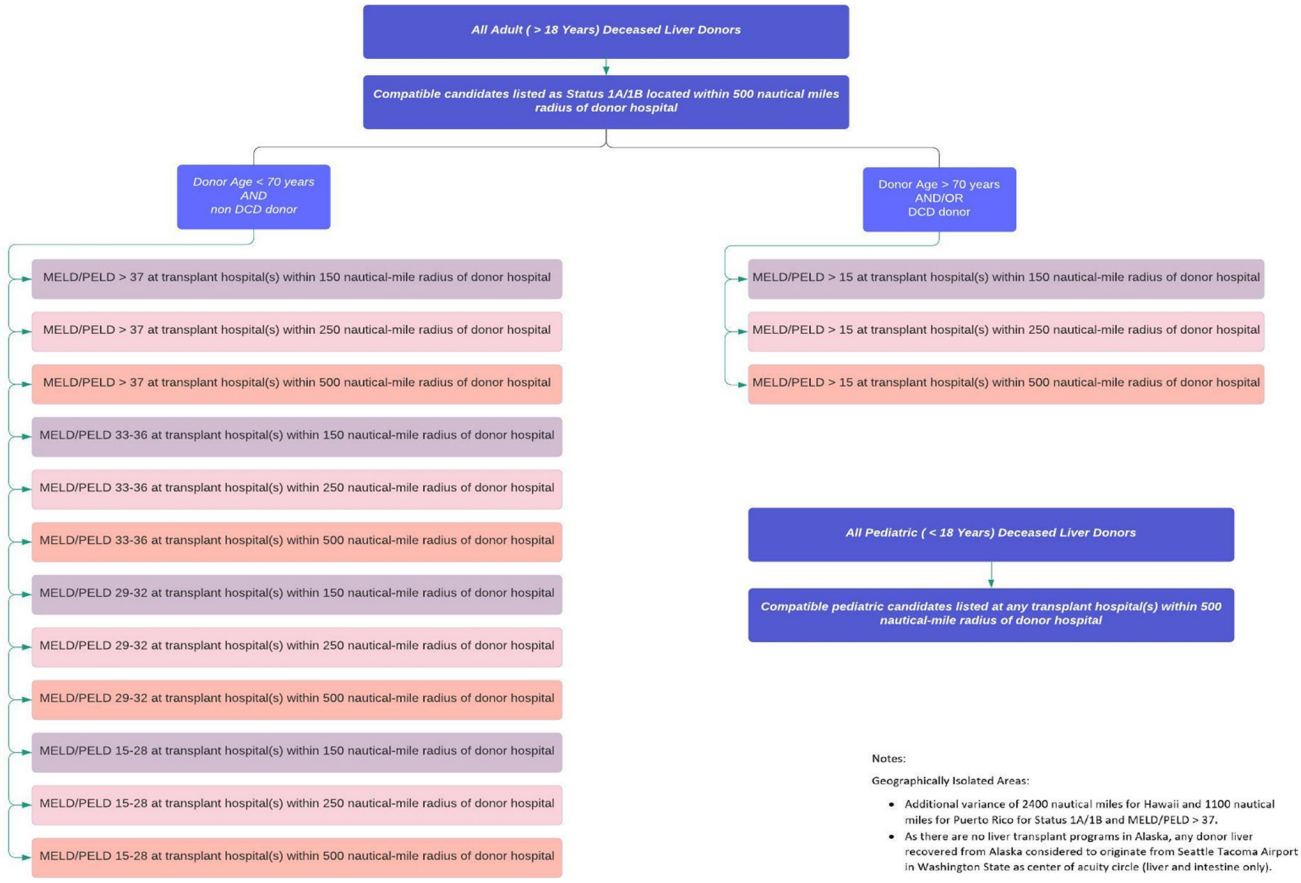

FIGURE 4 Current acuity circle distribution of deceased donor livers

Simultaneous liver–kidney transplantation

Simultaneous liver–kidney transplantation (SLKT) is a therapeutic option for LT candidates with advanced chronic kidney disease (CKD), sustained irreversible acute kidney injury, and inherited metabolic diseases such as primary hyperoxaluria and comprises 8%–10% of all LTs. Since the implementation of MELD in 2002, the incidence of SLKT has increased significantly.[24]

There was a continued controversy in the transplant community that multiorgan transplants were drawing deceased donor kidneys away from the kidney transplant

TABLE 3 Current SLKT policy

Candidate's transplant nephrologist confirms a diagnosis of	Transplant program must document at least one of the following
CKD with a measured or calculated GFR ≤60 ml/min for >3 months	At least one of the following: • The candidate has begun regularly administered dialysis as a patient with end-stage renal disease in a hospital-based, independent non–hospital-based, or home setting • At the time of registration on the kidney waiting list, the candidate's most recent measured or calculated CrCl or GFR is ≤30 ml/min • On a date after registration on the kidney waiting list, the candidate's measured or calculated CrCl or GFR is ≤30 ml/min
Sustained acute kidney injury	At least one of the following, or a combination of both of the following, for the past 6 weeks: • The candidate has been on dialysis at least once every 7 days • The candidate has a measured or calculated CrCl or GFR ≤25 ml/min at least once every 7 days If the candidate's eligibility is not confirmed at least once every 7 days for the past 6 weeks, the candidate is not eligible to receive a liver and a kidney from the same donor
Metabolic disease	A diagnosis of at least one of the following: • Hyperoxaluria • Atypical hemolytic uremic syndrome from mutations in factor H or factor I • Familial nonneuropathic systemic amyloidosis • Methylmalonic aciduria

Abbreviations: CKD, chronic kidney disease; CrCl, creatinine clearance; GFR, glomerular filtration rate; LT, liver transplantation; SLKT, simultaneous liver–kidney transplantation.

candidate pool. Moreover, mostly donor kidneys with low kidney donor profile index are used in multiorgan transplantation, including SLKT. Therefore, the OPTN convened a working group that consisted of members of OPTN kidney, liver, and intestinal committee, OPO ethics, minority affairs, and operations & safety committees to develop SLKT policy through data review, discussion, deliberation, and compromise. This policy was ratified by the OPTN Board of Directors in June 2016 and was implemented on August 10, 2017.[25]

The current policy is based on medical eligibility criteria[26] (Table 3) and has a "safety net" option. The medical eligibility criteria are stratified by the presence of CKD, acute kidney injury, or select metabolic diseases (Table 1). The safety net is for those LT recipients who remained dialysis dependent or subsequently develop advanced, persistent renal dysfunction within 60–365 days of LT alone. Safety net candidates are assigned significant allocation priority in the kidney allocation system to receive an expedited kidney after LT, appearing ahead of other local adult candidates.

Data suggest that the 2017 policy change was successful in establishing more directed use of deceased donor kidneys for SLKT without affecting posttransplant outcomes. There was no significant change in the overall rate of SLKT over time, but a reduction in SLKT use in patients with estimated glomerular filtration rates (eGFRs) >30 ml/min was seen.[27]

CONCLUSION

MELD and PELD have proved to be useful tools in the development of liver allocation in the United States, contributing to transparency of the allocation system and use of objective elements. Evidence-based incremental changes are the best path forward to further refine and inform future policy recommendations.

KEY POINTS

1. MELD score is the mortality risk score used to allocate diseased donor liver for decompensated cirrhosis.
2. MELD score performed better than CTP score in predicting waitlist mortality.
3. Addition of serum sodium to MELD score improved the waitlist mortality by 7%.
4. Creation of NLRB and implementation of acuity circles have improved the variability in MELD scores across the OPTN region.
5. SLKT policy has medical eligibility criteria and a "safety net" option.

QUESTIONS

1. Under the principles of the Organ Procurement and Transplantation Act (OPTN) policy and the National Organ Transplantation Act (NOTA), which one of the following characteristics would most likely make a patient ineligible for liver transplantation?
   a. Advanced age
   b. Citizenship status
   c. Incarcerated status
   d. Lack of insurance
   e. Repeat transplantation

2. A 30-year-old man presents with a 4-month history of itching, unintentional weight loss of 30 lbs, and a 3-week history of jaundice. He denies any history of diarrhea. He has no history of alcohol use or use of herbal and dietary supplements. Serological testing for viral hepatitis is negative. Laboratory tests show bilirubin 5 mg/dl, platelets 250,000 per ml, INR 1.1, albumin 3.5 g/dl, CA 19-9 levels of 200 U/ml, and normal quantitative immunoglobulins. Magnetic resonance cholangiopancreatography (MRCP) showed multiple intrahepatic and extrahepatic biliary strictures, with a common hepatic duct dominant stricture measuring 2.5 cm. There is no imaging evidence of ascites. An endoscopic retrograde cholangiopancreatography (ERCP) was done with stent placement, and brushings showed atypical cells with fluorescence in situ hybridization (FISH) showing polysomy. What is the recommended next step?
   a. Endoscopic ultrasound (EUS) for confirmation of cholangiocarcinoma (CCA)
   b. Referral for liver transplantation
   c. Referral for surgical resection
   d. Referral for neoadjuvant therapy prior to possible liver transplantation
   e. Referral to palliative care
3. Which of the following clinical scenarios is acceptable for a standard MELD exception?
   a. Hepatic encephalopathy refractory to medical management
   b. Diagnosis of cystic fibrosis confirmed by genetic analysis and forced expiratory volume at 1 s (FEV_1) <40% of predicted normal value
   c. Cirrhosis secondary to primary biliary cholangitis (PBC) complicated with medically refractory pruritis
   d. Recurrent bleeding from esophageal varices despite secondary prophylaxis
   e. Grade 3 ascites requiring repeated large-volume paracentesis
4. In general, a criterion for the diagnosis of acute liver failure (ALF) and listing for priority (Status 1A/1B) includes the exclusion of a prior history of liver disease and/or cirrhosis except for which of the following etiologies?
   a. Wilson disease
   b. Primary biliary cholangitis
   c. Alcohol associated liver disease
   d. Hepatitis B virus
   e. Hepatitis C virus
5. Under the newly adopted acuity circle distribution system, all livers from adult deceased donors are first offered to compatible Status 1A and 1B candidates listed at transplant hospitals within a radius of 500 nautical miles of the donor hospital. Subsequently, livers are further distributed based on
   a. Donor age alone
   b. Donor mode of death alone
   c. Donor sex
   d. Donor steatosis
   e. Donor age and mode of death

CONFLICT OF INTEREST

Nothing to report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the authors upon reasonable request.

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REFERENCES

1. Freeman RB Jr, Wiesner RH, Roberts JP, McDiarmid S, Dykstra DM, Merion RM. Improving liver allocation: MELD and PELD. Am J Transplant. 2004;4(Suppl 9):114–31.
2. Schilsky ML, Moini M. Advances in liver transplantation allocation systems. World J Gastroenterol. 2016;22:2922–30.
3. Institute of Medicine (US). Committee on Organ Procurement and Transplantation Policy. Organ procurement and transplantation: assessing current policies and the potential impact of the DHHS final rule. Washington, DC: National Academies Press (US); 1999.
4. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31:864–71.
5. Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology. 2003;124:91–6.
6. Freeman RB, Wiesner RH, Edwards E, Harper A, Merion R, Wolfe R, et al. Results of the first year of the new liver allocation plan. Liver Transpl. 2004;10:7–15.
7. Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. Liver Transpl. 2005;11:336–43.
8. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med. 2008;359:1018–26.
9. Sharma P, Schaubel DE, Goodrich NP, Merion RM. Serum sodium and survival benefit of liver transplantation. Liver Transpl. 2015;21:308–13.
10. Kim WR, Mannalithara A, Heimbach JK, Kamath PS, Asrani SK, Biggins SW, et al. MELD 3.0: the model for end-stage liver disease updated for the modern era. Gastroenterology. 2021;161:1887–95.e4.
11. Liver allocation policy. [cited 2022 Feb 14]. Available from: https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf
12. Freeman RB Jr, Gish RG, Harper A, Davis GL, Vierling J, Lieblein L, et al. Model for end-stage liver disease (MELD) exception guidelines: results and recommendations from the MELD Exception Study Group and Conference (MESSAGE) for the approval of patients who need liver transplantation with diseases not considered by the standard MELD formula. Liver Transpl. 2006;12(Suppl 3):S128–36.
13. Aby ES, Lake JR. Basic principles of liver allocation and development over the years. Curr Opin Organ Transplant. 2020;25:99–103.
14. Wedd JP, Harper AM, Biggins SW. MELD score, allocation, and distribution in the United States. Clin Liver Dis. 2013;2:148–51.
15. Kim WR, Lake JR, Smith JM, Schladt DP, Skeans MA, Noreen SM, et al. OPTN/SRTR 2017 annual data report: liver. Am J Transplant. 2019;19(Suppl 2):184–283.
16. Merion RM, Schaubel DE, Dykstra DM, Freeman RB, Port FK, Wolfe RA. The survival benefit of liver transplantation. Am J Transplant. 2005;5:307–13.

17. Humar A, Khwaja K, Glessing B, Larson E, Asolati M, Durand B, et al. Regionwide sharing for status 1 liver patients—beneficial impact on waiting time and pre- and posttransplant survival. Liver Transpl. 2004;10:661–5.
18. Sharma P, Schaubel DE, Gong Q, Guidinger M, Merion RM. End-stage liver disease candidates at the highest model for end-stage liver disease scores have higher wait-list mortality than status-1A candidates. Hepatology. 2012;55:192–8.
19. Massie AB, Chow EK, Wickliffe CE, Luo X, Gentry SE, Mulligan DC, et al. Early changes in liver distribution following implementation of share 35. Am J Transplant. 2015;15:659–67.
20. Bertsimas D, Papalexopoulos T, Trichakis N, Wang Y, Hirose R, Vagefi PA. Balancing efficiency and fairness in liver transplant access: tradeoff curves for the assessment of organ distribution policies. Transplantation. 2020;104:981–7.
21. Sakamoto S, Uchida H, Takeuchi I, Irie R, Shimizu S, Yanagi Y, et al. Sequential deceased donor intestine transplantation followed by living donor liver transplantation, also known as hybrid intestine-liver transplantation. Transplantation. 2020;104:e42–3.
22. Available from: https://optn.transplant.hrsa.gov/media/53wj54zi/data_report_liver_full_18moallocation_20211203_508_compliant.pdf
23. Available from: https://unos.org/news/innovation/building-more-flexible-system-for-organallocation/
24. Cullaro G, Sharma P, Jo J, Rassiwala J, LB VW, Wong R, et al. Temporal trends and evolving outcomes after simultaneous liver-kidney transplantation: results from the US SLKT Consortium. Liver Transpl. 2021;27:1613–22.
25. Formica RN, Aeder M, Boyle G, Kucheryavaya A, Stewart D, Hirose R, et al. Simultaneous liver-kidney allocation policy: a proposal to optimize appropriate utilization of scarce resources. Am J Transplant. 2016;16:758–66.
26. Bari K, Sharma P. Optimizing the selection of patients for simultaneous liver-kidney transplant. Clin Liver Dis. 2021;25:89–102.
27. Samoylova ML, Wegermann K, Shaw BI, Kesseli SJ, Au S, Park C, et al. The impact of the 2017 kidney allocation policy change on simultaneous liver-kidney utilization and outcomes. Liver Transpl. 2021;27:1106–15.

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