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ORIGINAL ARTICLE

Impact of the acuity circle model for liver allocation on multivisceral transplant candidates

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Liver allocation was updated on February 4, 2020, replacing a Donor Service Area (DSA) with acuity circles (AC). The impact on waitlist outcomes for patients listed for combined liver-intestine transplantation (multivisceral transplantation [MVT]) remains unknown. The Organ Procurement and Transplantation Network/United Network for Organ Sharing database was used to identify all candidates listed for both liver and intestine between January 1, 2018 and March 5, 2021. Two eras were defined: pre-AC (2018–2020) and post-AC (2020–2021). Outcomes included 90-day waitlist mortality and transplant probability. A total of 127 adult and 104 pediatric MVT listings were identified. In adults, the 90-day waitlist mortality was not statistically significantly different, but transplant probability was lower post-AC. After risk-adjustment, post-AC was associated with a higher albeit not statistically significantly different mortality hazard (sub-distribution hazard ratio[sHR]: 8.45, 95% CI: 0.96–74.05; $p = .054$), but a significantly lower transplant probability (sHR: 0.33, 95% CI: 0.15–0.75; $p = .008$). For pediatric patients, waitlist mortality and transplant probability were similar between eras. The proportion of patients who underwent transplant with exception points was lower post-AC both in adult (44% to 9%; $p = .04$) and pediatric recipients (65% to 15%; $p = .002$). A lower transplant probability observed in adults listed for MVT may ultimately result in increased waitlist mortality. Efforts should be taken to ensure equitable organ allocation in this vulnerable patient population.

KEYWORDS
clinical research/practice, health services and outcomes research, intestine/multivisceral transplantation, liver transplantation/hepatology, organ allocation, organ procurement and allocation, organ procurement and transplantation network (OPTN), registry/registry analysis, united network for organ sharing (UNOS)

Abbreviations: AC, acuity circle; BMI, body mass index; DSA, donor service area; IQR, interquartile range; IRB, institutional review board; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; MVT, multivisceral transplantation; PELD, Pediatric End-Stage Liver Disease; sHR, sub-distribution hazard ratio; SRTR, Scientific Registry of Transplant Recipients; STAR, Standard Transplant and Research; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; UNOS, United Network for Organ Sharing.

1 | INTRODUCTION

The allocation of livers was updated on February 4, 2020, replacing the previous donor service area (DSA)-based allocation model, which was characterized by regional boundaries in the liver and intestinal organ distribution, with an acuity circle (AC)-based model.[1] The new model is based on radially oriented zones around potential donors and involves converting each transplant center's median Model for End-Stage Liver Disease (MELD) score at transplant (MMAT) to reflect transplants performed within a 250 nautical mile radius.[1] Although it aims to increase the number of pediatric transplants and reduce waitlist mortality, concerns have been raised regarding the potential of limiting transplant access for disadvantaged patients.[2]

Patients listed for combined liver and intestine transplantation, herein referred to as multivisceral transplantation (MVT), which also includes the pancreas, represent a particularly vulnerable patient population, who often have undergone multiple prior abdominal operations, typically have a loss of abdominal domain that mandates specific donor/recipient size matching and have suffered the physiologic effects of chronic malnutrition.[3,4] As these candidates are also undergoing intestine and, frequently, pancreas transplantation in addition to liver transplantation, they also have specific quality requirements for suitable donors. For this reason, they were previously attributed amongst the highest status levels on the liver match run. In the United States, although MVT candidates are registered both on the liver and intestine waitlists, organ allocation is determined strictly according to their ranking in the liver waitlist. They are typically granted MELD exception points because their laboratory scores are often low. Hence, the MELD-Na score alone is not an accurate reflection of their mortality risk. Short gut syndrome with hepatic fibrosis is an appropriate indication for MVT and carries a high mortality risk without transplantation, despite a low MELD score in these patients. Transplantation represents a life-saving option for such patients and affords an opportunity for improvement in quality of life.[5] In addition to technical and physiologic challenges, donor suitability is critical, as the liver, intestine, and pancreas all have to be transplantable from the same donor. Consequently, the available donor pool is considerably smaller, typically younger and non-obese donors. This further underscores the need for prioritization when a rare suitably matched donor is identified. This is of particular concern because the current allocation model is routinely prioritizing these organs to a liver alone candidate that does not have the same size and quality limitations and a high "competitive" MELD score who will likely be allocated another liver promptly. In contrast, many MVT candidates will need to wait for extended periods for the next suitable donor to become available. The lack of access for MVT candidates has not been fully addressed by either the MELD-Na-based allocation system or the new AC policy and has not been included in the Scientific Registry of Transplant Recipients (SRTR) models to analyze competing policy proposals. The impact that the AC policy has had on patients listed for MVT thus remains to be clarified.

We sought to evaluate the effect of the AC policy on waitlist outcomes, specifically regarding waitlist mortality and transplant probability, for patients listed for MVT.

2 | METHODS

This study used data from the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) registry from the Standard Transplant and Research (STAR) file, containing information from all patients who were listed for transplantation up until March 5, 2021 in the United States. Patients listed for combined liver and intestine transplantation, herein referred to as MVT (waitlist code of WLIN), listed between January 1, 2018 and March 5, 2021, were identified. Separate analyses were performed for pediatric (<18 years at listing) and adult (≥18 years at listing). A Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) compliant figure of full patient inclusion and exclusion is shown in Figure 1A (adults) and Figure 1B (pediatric). This study was approved for an institutional review board (IRB) waiver after review.

As AC was introduced on February 4, 2020, two periods were defined according to the date of listing; pre-AC (January 1, 2018 to February 4, 2020) and post-AC February 4, 2020 [inclusive] to March 5, 2021.

2.1 | Covariates evaluated

Covariates evaluated at listing and at transplant included gender (male or female), age in years (continuous variable), body mass index (BMI) (kg/m^2), MELD score (continuous), Pediatric End-Stage Liver Disease (PELD) (continuous), life support requirement (yes/no), dialysis requirement in the week prior to listing and transplant, ascites (yes/no), hepatic encephalopathy (yes/no) (at transplant only), kidney listing (which was coded as either WLKP [candidate listed for simultaneous kidney-pancreas] or WLKI [candidate listed for simultaneous kidney]), pancreas listing (which was coded either WLKP or WLPA [candidate listed for simultaneous pancreas]), and exception points awarded (yes/no). Exception points were defined if MELD_DIFF_REASON_CD included code 1 (Not applicable if Candidate is Status 1), 3 (MELD/PELD Exception approved), 8 (Meets Criteria for HCC), 12 (Not applicable, Candidate is Status 2A), 14 (Lab Score plus 10% risk of 3-month mortality for liver/intestine), 15 (Not applicable, candidate is Status 1A), 16 (Not applicable, Candidate is Status 1B), 17 (Lab Score plus 23 points for pediatric liver/intestine), 18 (MELD/PELD exception override). In addition, exception points were assigned as awarded if the case was listed as an exception case (EXC_CASE).

2.2 | Analysis of waitlist and post-transplant outcomes

The 90-day waitlist outcomes were analyzed using a competing risk analysis with outcomes, including improvement on the waitlist (removal code 12), transplantation (removal codes 2–4, 18, 19, 21, and 22), or death, including removal for being too sick (removal codes 5, 8, and 13). Data were censored if none of the abovementioned events had occurred before the end of the set period. Because differences in follow-up time can result in withdrawal bias, patients

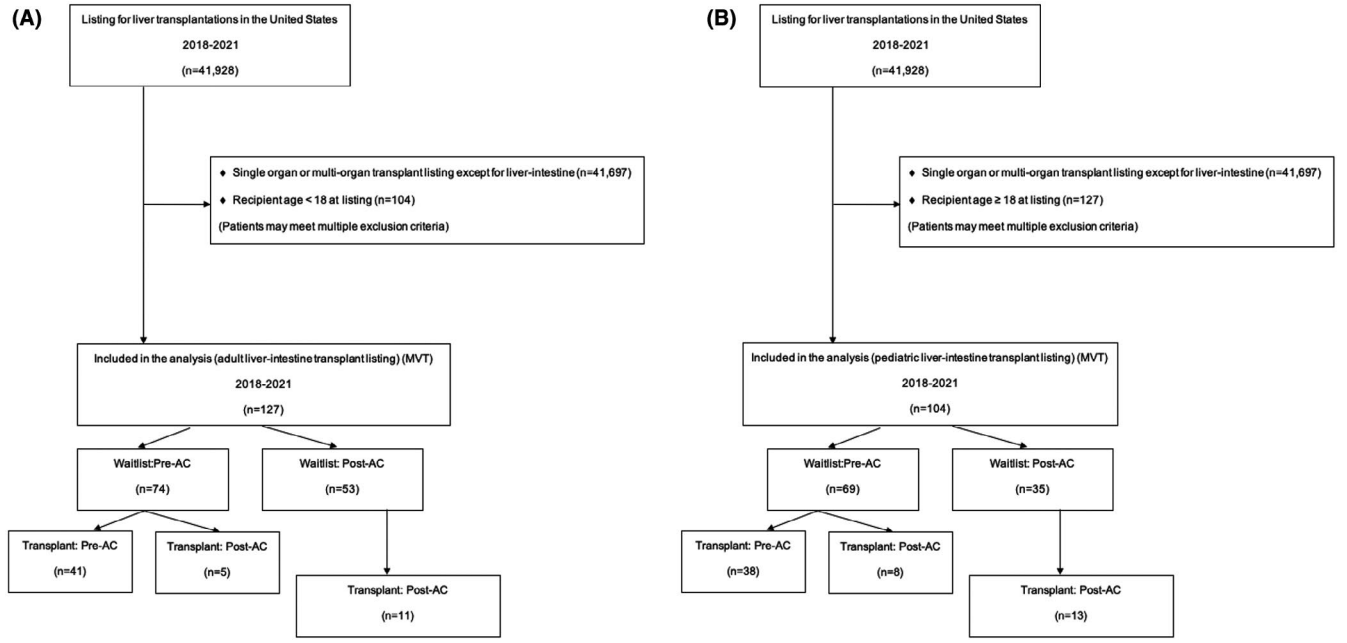

FIGURE 1 (A) Flowchart of patient inclusion and exclusion for adult patients. (B) Flowchart of patient inclusion and exclusion for pediatric patients

registered in each era were censored on the last day of that era (February 4, 2020 and March 5, 2021, respectively).

The 90-day post-transplant patient survival was also compared between eras. In these comparisons, patients who were listed and transplanted in the same era were included.

2.3 | Statistical analysis

Descriptive data for continuous variables were expressed as and medians with interquartile range (IQR). These were compared using the Mann–Whitney U test. Categorical variables were expressed as number and percentage and were compared using chi-square and Fischer exact test. For comparisons of variables in patients who received a transplant, the two groups included patients listed pre-AC and transplanted pre-AC and patients listed post-AC and transplanted post-AC. Patients listed pre-AC but transplanted post-AC were thus excluded from the pre-AC group in the abovementioned bivariate analysis. For the waitlist analysis, instead of a Kaplan–Meier approach, which censors for competing events, a cumulative incidence approach was used to account for the presence of competing risks of transplant and waitlist dropout due to mortality.[6] A Gray's modified log-rank test was used to compare unadjusted estimates on the waitlist. For assessing the relative change in the hazard of waitlist dropout due to mortality, a Fine-Gray proportional hazards model was used to account for transplant as a competing event.[7] The effect of the exposure of interest (AC era) was evaluated by multivariable adjustment of confounding variables. Post-transplant patient survival was compared using the log-rank test. A p-value <.05 was considered statistically significant for all analyses. All statistical analyses were performed using R (R version 4.0.3 [2020–10–10], R foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org/). Competing risk analysis was performed using the package "cmprsk."

3 | RESULTS

3.1 | Waitlist patient cohort

3.1.1 | Adult patients

A total of 127 adult MVT listings were identified in the study period (Figure 1A). Patient characteristics at listing were similar between the eras except for a statistically significantly higher Model for End-stage liver disease (MELD) score at listing in the post-AC era group (median [IQR] 12 Pre [8–20] vs. 15 Post [11–23]; $p = .04$) (Table 1). The proportions of patients listed with exception points were similar (52% vs. 60%, $p = .41$). For the patients who received exception points and had data available on points requested (waitlist pre-AC 16/36; waitlist post-AC 9/27; transplanted pre-AC 5/17; transplanted post-AC 1/1), the requested points were not statistically significantly different between the two eras (waitlisted patients median [IQR] 34 [30–36] vs. 32 [30–33]; $p = .22$; transplanted patients 35 [32–35] vs. 32 [32–32]; $p = .77$) (Table S1). The proportions of patients listed for a kidney or a pancreas transplant in addition to MVT were not statistically significantly different between the eras (kidney 16% vs. 15%; $p = .86$; pancreas 100% vs. 100%).

3.1.2 | Pediatric patients

A total of 104 pediatric MVT listings were identified in the study period (Figure 1B). Patient characteristics at listing were similar

TABLE 1 Waitlist characteristics of patients listed for liver-intestinal transplantation (MVT) stratified by era (adults)

	Pre-AC (*N* = 74)	Post-AC (*N* = 53)	*p* value
Gender, male, n (%)	27 (37%)	21 (40%)	.72*
Age at listing, years, median (IQR)	45 (32, 55)	42 (35, 50)	.89**
BMI at listing, median (IQR)	23 (21, 27)	22 (20, 27)	.10**
MELD score at listing, median (IQR)	12 (8, 20)	15 (11, 23)	.04**
Life support at listing, n (%)	5 (7%)	4 (8%)	.77*
N-Missing	0	4	
Dialysis requirement in the week prior to listing, n (%)	6 (8%)	7 (13%)	.35*
Ascites at listing, n (%)	27 (37%)	22 (42%)	.57*
Exception points awarded, n (%)	36 (52%)	27 (60%)	.41*
Listing with kidney, n (%)	12 (16%)	8 (15%)	.86*
Listing with pancreas, n (%)	74 (100%)	74 (100%)	—

Abbreviations: AC, acuity circle; BMI, body mass index (kg/m^2); IQR, interquartile range; MELD, Model for End-Stage Liver Disease.

*Kruskal–Wallis rank sum test.; **Pearson's Chi-squared test.

TABLE 2 Waitlist characteristics of patients listed for liver-intestinal transplantation (MVT) stratified by era (pediatric)

	Pre-AC (*N* = 69)	Post-AC (*N* = 35)	*p* value
Gender, male, n (%)	28 (41%)	15 (43%)	.82*
Age at listing, years, median (IQR)	3 (1, 7)	4 (1, 9)	.53**
BMI at listing, median (IQR)	18 (16, 19)	18 (17, 19)	.90**
PELD score at listing, median (IQR)	7 (0, 17)	3 (−3, 16)	.44**
Life support at listing, n (%)	14 (20%)	5 (15%)	.53*
N-Missing	0	2	
Dialysis requirement in the week prior to listing, n (%)	2 (3%)	1 (3%)	.98*
N-Missing	1	0	
Ascites at listing, n (%)	4 (15%)	0 (0%)	.10**
N-Missing	43	19	
Exception points awarded, n (%)	40 (63%)	21 (62%)	.94*
Listing with kidney, n (%)	5 (7%)	3 (9%)	.81*
Listing with pancreas, n (%)	68 (99%)	34 (97%)	.62*

Abbreviations: AC, acuity circle; BMI, body mass index (kg/m^2); IQR, interquartile range; PELD, Pediatric End-Stage Liver Disease.

*Kruskal–Wallis rank sum test.; **Pearson's Chi-squared test.

between the eras, including the proportion of patients with exception points (63% vs. 62%, $p = .94$). For the patients who received exception points and had data available on points requested (waitlist pre-AC 19/40; waitlist post-AC 4/21; transplanted pre-AC 10/24; transplanted post-AC 0/2), the requested points were not statistically significantly different between the two eras (waitlisted patients median [IQR] 40 [35–60] vs. 35 [35–35]; $p = .15$; transplanted patients 38 [35–60] vs. 35 [35–35]; $p = .38$) (Table S2). The proportions of patients listed for a kidney combined transplant in addition to MVT were not statistically significantly different between the eras (kidney 7% vs. 9%; $p = .81$) (Table 2).

3.2 | Waitlist outcomes

3.2.1 | Adult patients

The cumulative incidence of 90-day waitlist mortality was increasing but did not yet reach significance in the post-AC era ($p = .08$) (Figure 2A), and transplant probability was significantly lower in the post-AC era ($p = .02$) (Figure 2B). After multivariable adjustment for Model for End-Stage Liver Disease (MELD) score at listing, receipt of exception points, life support requirement at listing, and dialysis requirement in the week before listing, the post-AC era was associated with increased, albeit not statistically significant, 90-day waitlist mortality hazard compared to the pre-AC era (sub-distribution hazard ratio [sHR] 8.45, 95% CI 0.96–74.05; $p = .054$) but a statistically significantly lower 90-day probability of transplant (sHR 0.33, 95% CI 0.15–0.75; $p = .008$) (Table 3).

3.2.2 | Pediatric patients

The cumulative incidence of 90-day waitlist mortality (Figure 3A) and transplant probability (Figure 3B) was not significantly different between the eras. After multivariable adjustment for PELD score at listing, receipt of exception points, life support requirement at listing, and dialysis requirement in the week prior to listing, the post-AC era was associated with similar 90-day waitlist mortality and transplant probability as the pre-AC era (90-day waitlist mortality sHR 0.47, 95% CI 0.02–9.76; $p = .63$; 90-day transplant probability sHR 1.02, 95% CI 0.47–2.25; $p = .95$) (Table 4).

3.3 | Post-transplant outcomes

3.3.1 | Adult patients

A total of 41 and 11 adult patients were listed and transplanted in the pre- and post-AC eras, respectively. Patient characteristics at

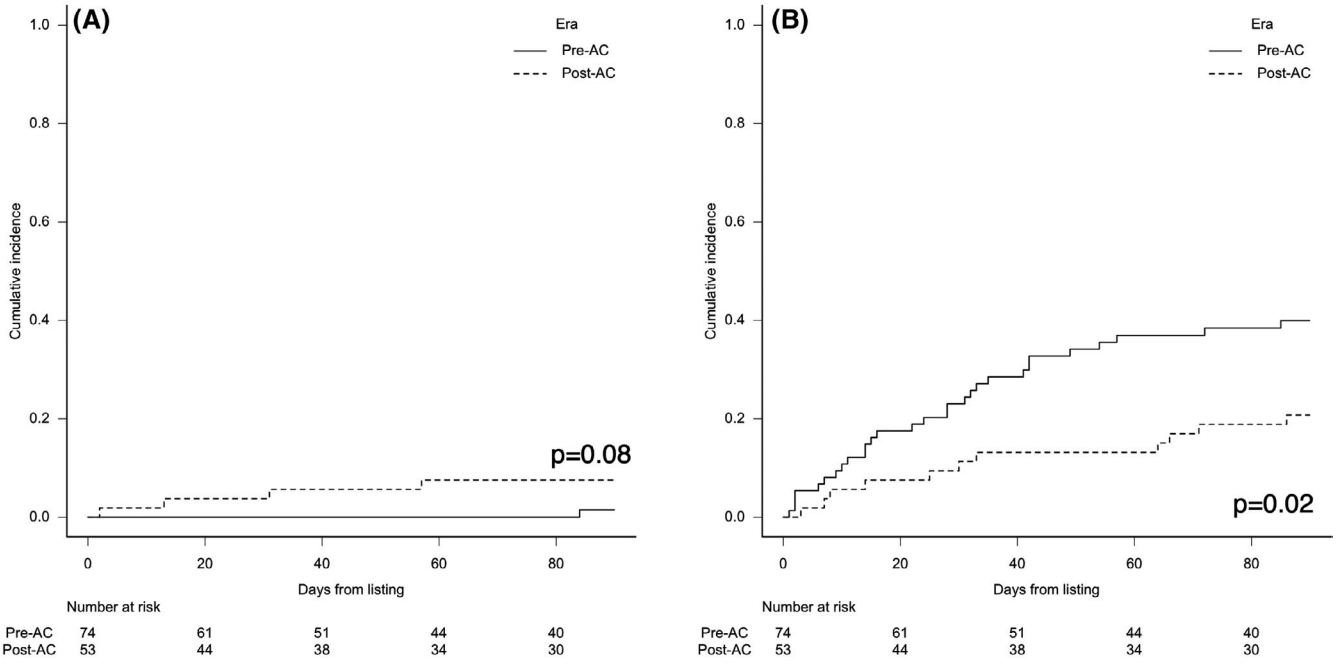

FIGURE 2 (A) 90-day waitlist mortality stratified by era (adults); (B) 90-day waitlist transplant probability stratified by era (adults)

TABLE 3 Impact of era (post-AC vs. pre-AC) 90-day waitlist outcomes (adults)

	Reference: Pre-AC	
Outcome[a]	**sHR (95% CI)**	***p*-value**
Mortality	8.45 (0.96–74.05)	.054
Transplant	0.33 (0.15–0.75)	.008

Abbreviations: AC, acuity circle; CI, confidence interval; MELD, Model for End-Stage Liver Disease; sHR, subdistribution hazard ratio.

[a]Adjusted for MELD score at listing, life support at listing, exception points awarded, and dialysis requirement week prior to listing.

transplant were similar between the eras, except for a significantly lower proportion of patients having been awarded exception points in the post-AC era (44% vs. 9%; $p = .04$). The distance to donor hospital (377 miles vs. 335 miles, $p = .74$) or share type of organs (national share 49% vs. 36%, $p = .59$) was not changed in the post-AC era (Table 5). There was no significant difference in laboratory MELD-Na score at the time of transplant in patients with or without exception points when stratified by era (patients with exception points patients median [IQR] 21 [15–28] vs. 6 [6–6]; $p = .12$; patients without exception points 17 [9–28] vs. 25 [17–27]; $p = .29$) (Table 5). There was no significant difference in 90-day post-transplant patient survival between the pre- and post-AC eras ($p = .59$) (Figure 4A).

3.3.2 | Pediatric patients

There were 38 and 13 pediatric patients who were listed and transplanted in the pre- and post-AC eras. At transplant, a significantly lower proportion of patients were awarded exception points in the post-AC era (65% vs. 15%; $p = .002$) (Table 6). The distance to donor hospital (548 miles vs. 334 miles, $p = .13$) or share type of organs (national share; 79% vs. 69%, $p = .70$) was unchanged in the post-AC era. There was no significant difference in laboratory MELD-Na score at the time of transplant in patients with or without exception points when stratified by era (patients with exception points median [IQR] 5 [2–18] vs. 2 [–2–6]; $p = .34$; patients without exception points 9 [3–12] vs. 20 [10–26]; $p = .07$) (Table 6). There was no significant difference in the 90-day patient survival rate between the eras ($p = .09$) (Figure 4B).

4 | DISCUSSION

Organ allocation in MVT is dictated by the liver transplant waitlist. Similar to liver transplant alone candidates, MVT candidates are listed and ranked according to their MELD-Na score, which might be quite low even in extremely ill patients because they often have an absence of advanced liver cirrhosis as the isolated indication for transplant. The current allocation system assigns adult MVT candidates additional points equivalent to an additional 10% three-month mortality,[8] but that is inadequate to put these patients into the more competitive MELD-Na score categories. This rule of exception points for MVT candidates has remained unchanged in the AC-based allocation policy, but liver allografts are now shared broadly and utilized as isolated transplants for patients with higher laboratory MELD-Na scores. This study evaluated the effects of the AC-based allocation on waitlist outcomes in MVT candidates. It demonstrated that the transplant probability is significantly lower for adult patients listed for MVT after implementing the new AC allocation, and 90-day waitlist mortality is climbing but has not yet reached significance.

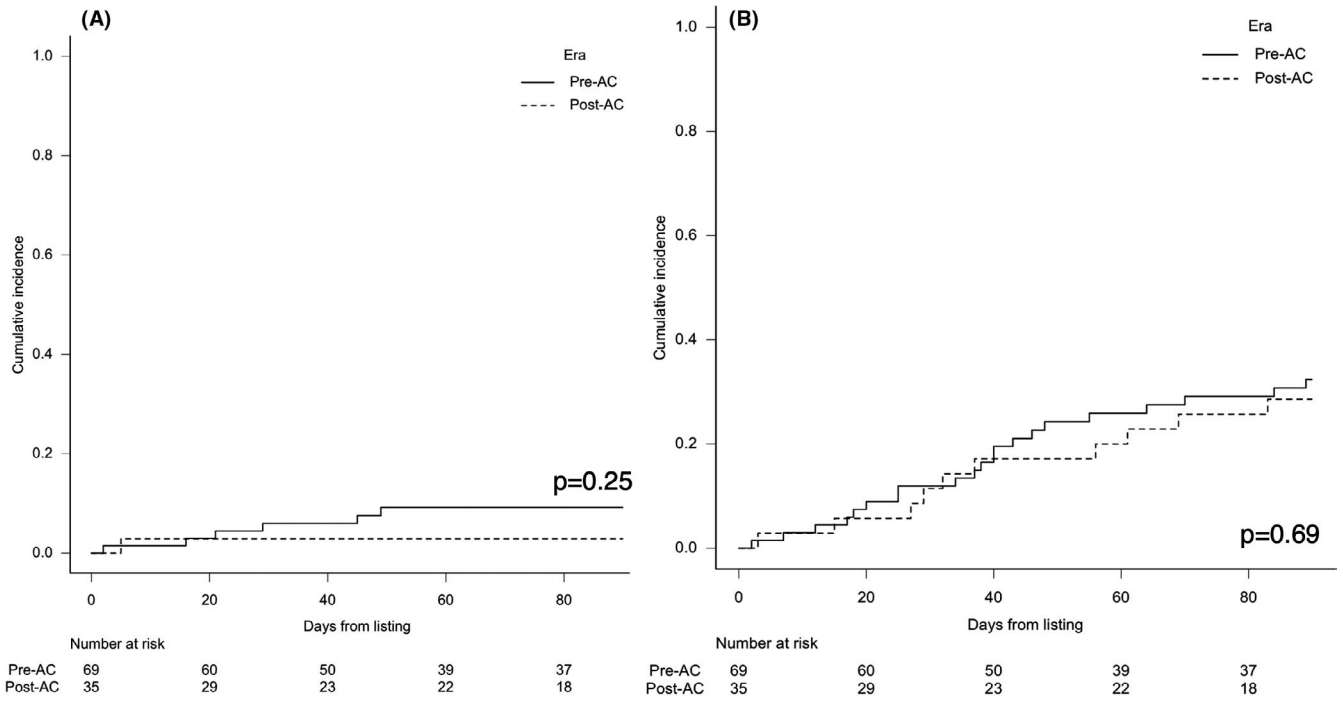

FIGURE 3 (A) 90-day waitlist mortality stratified by era (pediatric); (B) 90-day waitlist transplant probability stratified by era (pediatric)

TABLE 4 Impact of era (post-AC vs. pre-AC) 90-day waitlist outcomes (pediatric)

	Reference: Pre-AC	
Outcome[a]	**sHR (95% CI)**	***p*-value**
Mortality	0.47 (0.02–9.76)	.63
Transplant	1.02 (0.47–2.25)	.95

Abbreviations: AC, acuity circle; CI, confidence interval; PELD, Pediatric End-Stage Liver Disease; sHR, subdistribution hazard ratio.

[a]Adjusted for PELD score at listing, life support at listing, exception points awarded, and dialysis requirement week prior to listing.

According to the findings of this study, over 60% of MVT candidates were granted MELD exception points. However, this adjustment may be insufficient to offer these patients access to organs commensurate with their increased risk. More importantly, although the proportions of patients listed with exception points were unchanged, those who received MVT with exception points were significantly lower in the post-AC era in adult (44% to 9%) and pediatric (65% to 15%) patients. These results indicate that the exception points given to those populations would not provide adequate opportunities for transplantation. Adult candidates waiting for a liver and intestine experience waitlist mortality twice as high as adult candidates waiting for a liver only.[9,10] Given that MVT patients comprise less than 1% of all liver transplants performed in the last decade (632 of 69,694), the impact of ensuring adequate prioritization for transplantation is likely to have a negligible effect on liver alone candidates.[11]

The AC-based allocation was implemented to alleviate the regional disparity of liver transplant access. According to the recent report, the AC-based allocation significantly increased transplant probability in liver alone and liver-kidney transplant candidates, and the positive impact was more clearly observed in the areas where transplant MELD scores were higher (higher MELD regions). While there were concerns about the possible negative effects of the AC-based allocation on liver transplant candidates in the lower MELD score regions, a significant impact on waitlist mortality or transplant probability has not yet been demonstrated.[12] However, this study indicates that we should be concerned that AC-based allocation has had an adverse effect on waitlist outcomes of MVT candidates. This population is particularly vulnerable and with extremely high mortality without transplantation. They often have unique medical and surgical issues, including multiple prior surgical procedures frequently with enterocutaneous fistulae, short gut syndrome with resulting nutritional challenges, total parenteral nutrition dependence, and line access issues. Other patients may be listed with a need for liver transplantation but with diffuse portomesenteric thrombosis,[13] or patients with otherwise unresectable neuroendocrine tumors.[14] These conditions are associated with life-threatening complications, which may not be well reflected by the MELD-Na score. According to the Final Rule, the organs shall be allocated based on medical urgency. However, this may not be a suitable yardstick for patients who are waiting for MVT. A sole reliance on MELD in MVT patients is not ideal, as once these patients reach a high physiologic MELD score, they may be too sick to transplant and would not tolerate the procedure and recovery. The rules for MVT allocation and exception points may require urgent revision to provide meaningful transplant opportunities to this vulnerable and disadvantaged patient population.

Another critical finding of this study is organ share type and distance of donor hospital from the transplant center. The AC-based

TABLE 5 Transplant characteristics of patients listed for liver-intestinal transplantation (MVT) stratified by era (adults)

	Pre-AC ($N = 41$)	Post-AC ($N = 11$)	p value
Distance donor hospital to transplant center, nautical miles, median (IQR)	377 (147, 646)	335 (187, 714)	.74*
Organ sharing, n (%)			.59**
Local	9 (22%)	2 (18%)	
Regional	12 (29%)	5 (46%)	
National	20 (49%)	4 (36%)	
Gender, male, n (%)	15 (37%)	3 (27%)	.56**
Age at transplant, years, median (IQR)	45 (34, 57)	49 (34, 52)	.81*
BMI at transplant, median (IQR)	25 (22, 31)	26 (24, 29)	.65*
MELD score at transplant, median (IQR)	17 (10, 29)	24 (16, 26)	.76*
MELD score at transplant for patients with exception points, median (IQR)	21 (15, 28)	6 (6, 6)	.12*
MELD score at transplant for patients without exception points, median (IQR)	17 (9, 28)	25 (17, 27)	.29*
Life support at transplant, n (%)	5 (12%)	1 (9%)	.15**
N-Missing	0	1	
Dialysis requirement in the week prior to listing, n (%)	10 (24%)	3 (27%)	.85**
Ascites at transplant, n (%)	21 (51%)	6 (55%)	.85**
Hepatic encephalopathy at transplant, n (%)	2 (5%)	1 (9%)	.60**
Exception points awarded, n (%)	17 (44%)	1 (9%)	.04**
Listing with kidney, n (%)	9 (22%)	0 (0%)	.09**
Listing with pancreas, n (%)	41 (100%)	11 (100%)	—
Total cold ischemic time, hours, median (IQR)	7.0 (6.1, 8.4)	8.0 (6.7–8.7)	.32*
Donor age, years, median (IQR)	25 (21, 30)	29 (22, 33)	.52*
Donor BMI, median (IQR)	22.1 (20.5, 25.1)	20.2 (19.5, 22.4)	.06*

Abbreviations: AC, acuity circle; BMI, body mass index (kg/m^2); IQR, interquartile range; MELD, Model for End-Stage Liver Disease.

*Kruskal–Wallis rank sum test.; **Pearson's Chi-squared test.

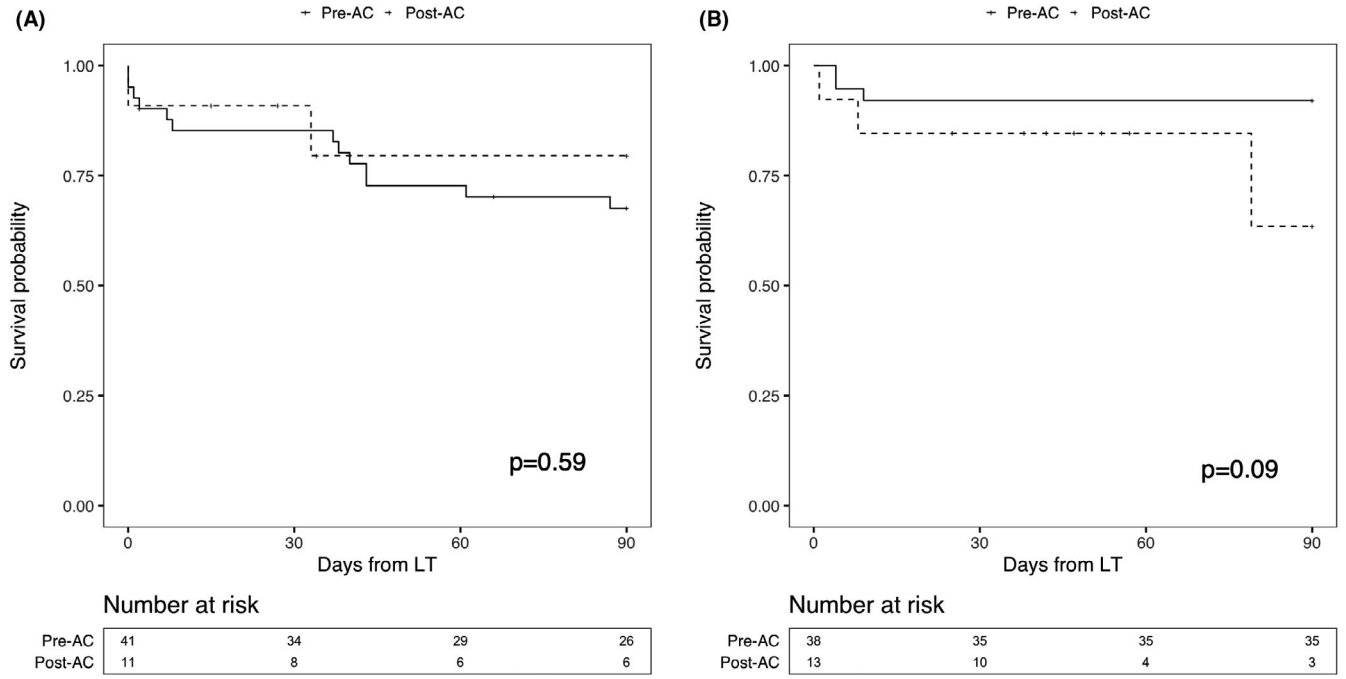

FIGURE 4 (A) 90-day post-transplant patient survival (adults); (B) 90-day post-transplant patient survival (pediatric)

TABLE 6 Transplant characteristics of patients listed for liver-intestinal transplantation (MVT) stratified by era (pediatric)

	Pre-AC (*N* = 38)	Post-AC (*N* = 13)	*p* value
Distance donor hospital to transplant center, nautical miles, median (IQR)	548 (327, 978)	334 (101, 755)	.13*
Organ sharing, n (%)			.70**
Local	3 (8%)	2 (15%)	
Regional	5 (13%)	2 (15%)	
National	30 (79%)	9 (69%)	
Gender, male, n (%)	15 (40%)	5 (39%)	.95**
Age at transplant, years, median (IQR)	3 (1, 7)	4 (2, 10)	.51*
BMI at transplant, median (IQR)	18 (17, 20)	19 (18, 19)	.23*
MELD score at transplant, median (IQR)	8 (2, 14)	15 (9, 25)	.23*
MELD score at transplant for patients with exception points, median (IQR)	5 (2, 18)	2 (−2, 6)	.34*
MELD score at transplant for patients without exception points, median (IQR)	9 (3, 12)	20 (10, 26)	.07*
Life support at transplant, n (%)	10 (26%)	1 (8%)	.72**
Dialysis requirement in the week prior to transplant, n (%)	1 (3%)	1 (8%)	.82**
Ascites at transplant, n (%)	4 (18%)	2 (18%)	1.00**
N-Missing	16	2	
Exception points awarded, n (%)	24 (65%)	2 (15%)	.002**
Listing with kidney, n (%)	3 (8%)	2 (15%)	.43**
Listing with pancreas, n (%)	37 (97%)	13 (100%)	.56**
Total cold ischemic time, hours, median (IQR)	7.1 (5.9, 8.9)	5.9 (5.0–7.1)	.10*
Donor age, years, median (IQR)	1 (0–3)	1 (0, 3)	.69*
Donor BMI, median (IQR)	18.8 (16.0, 21.2)	16.6 (15.6, 18.6)	.10**

Abbreviations: AC, acuity circle; BMI, body mass index (kg/m^2); IQR, interquartile range; MELD, Model for End-Stage Liver Disease; PELD, Pediatric End-Stage Liver Disease.

*Kruskal-Wallis rank sum test.; **Pearson's Chi-squared test.

allocation has increased broad sharing and increased the distance between donor hospitals and transplant centers in the liver transplant alone waitlist.[12] MVT grafts have historically been shared broadly, and transplant teams have been willing to travel nationally even before implementing AC-based allocation. This study revealed that the distance and national share of MVT grafts (sharing organs outside of 250 miles radius) were unchanged in adult and pediatric MVT. The AC-based allocation accelerated the broad sharing of the liver grafts, which might lead to more utilization of non-marginal liver grafts for liver transplant candidates who have higher MELD-Na scores. While this also proved that the AC-based allocation has been functioning as expected, the broad sharing of the liver graft among liver transplant alone patients significantly diminished the opportunities for MVT.

Donor suitability is more critical in MVT, which means that marginal donors, such as donors with advanced age, donation after circulatory death (DCD), steatotic liver grafts, and donors with a high body mass index are often unsuitable for MVT. This has not been well discussed or recognized in the field. Given the complexity of donor selection in MVT, their priority in liver allocation may need to be modified. In addition, according to the results of this study, 100% of adult patients who had the listing code of WLIN (combined with intestine) were listed for a pancreas graft. Consequently, they are registered in the liver, pancreas, and intestine waitlists. The current OPTN/UNOS policy does not address which waitlist match run is used for the second (or third) required organ, resulting in an inconsistent application of organ allocation policies. Multi-organ allocation is often at the discretion of each Organ Procurement Organization (OPO), which sometimes results in the unavailability of pancreas graft, despite liver and intestine grafts being allocated to MVT candidates. While the OPTN/UNOS has started discussions, liver-intestine or liver-intestine-pancreas transplant allocation is not included in this process.[15] Because we have already observed that the AC-based liver allocation adversely impacts MVT waitlist outcomes, multi-organ allocation for this particular population should be discussed and clarified without delay.

Global differences exist in policies regarding organ allocation for MVT patients. In Europe, patients needing a multi-organ liver transplant (not including liver-kidney) can be requested to receive an Approved Combined Organ status (ACO).[16] This status results in prioritization above transplantable patients on the liver match but below patients with a high urgency. Pediatric patients with an ACO

status are prioritized over adult patients with an ACO status.[16] In the United Kingdom, MVT candidates are prioritized ahead of all non-super-urgent liver transplant alone and all kidney and pancreas candidates.[17] In Brazil, MVT candidates receive a MELD score of 50, placing them immediately behind Status 1 candidates. (Information is based on the author's [RV] personal communication.) In Argentina, MVT candidates receive an additional 25 MELD points above their laboratory MELD.[18] The allocation system in the United States has not implemented similar strategies to afford MVT candidates the appropriate prioritization. Moreover, this disadvantage may be further aggravated by the AC policy.

Limitations of this study should be acknowledged. First, the median MELD at transplant (MMaT) was introduced on May 24th, 2019, before introducing AC-based allocation. The MMaT for liver candidates with exception scores is based on recent LTs performed at liver transplant hospitals within the DSA where the candidates are listed.[19] Due to the deidentified nature of the data registry, identification of which center a patient was listed and transplanted in is not possible, which precludes an evaluation of differences in exception points awarded based on MMaT. Instead, we evaluated requested exception points before and after the introduction of MMaT rule, and there was no difference in exception points. Second, the impact that the COVID-19 pandemic has had on allocation practices may represent a source of confounding with potential effects on availability of suitable donors and reduced availability of blood products for major MVT surgery. A recent report of the early effects of AC-based allocation using the same study period showed that for liver transplant candidates, the post-AC era has been associated with overall improved waitlist outcomes with lower 90-day waitlist mortality and a higher transplant probability.[12] Though the COVID-19 pandemic may represent a source of potential confounding, the absence of negative effects for liver transplant alone candidates lends further credence to the effects on MVT candidates observed in our study to be more likely related to the effects of AC-based allocation. Although it is impossible to attribute a causal effect of the AC policy on outcomes in MVT candidates, given the non-randomized, retrospective design with the potential for unmeasured and residual confounding even despite the multivariable analyses performed, this study offers insight into the outcomes in a limited temporal period before and after a significant allocation policy change on a population-level transplant scale.

In conclusion, the transplant probability became significantly lower in patients listed for MVT after implementing the new AC allocation policy. This, in turn, may lead to an increased waitlist mortality for these patients in the long term. These findings highlight that efforts should be taken to ensure equitable organ allocation in adult MVT patients and prevent future adverse outcomes.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Organ Procurement and Transplantation Network (OPTN). Restrictions apply to the availability of these data, which were used under license for this study. Data are available OPTN at https://optn.transplant.hrsa.gov/data/request-data/ with the permission of OPTN and United Network of Organ Sharing (UNOS).

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REFERENCES

1. United Network for Organ Sharing. System notice: liver and intestinal organ distribution based on acuity circles implemented Feb. 4. 2020. https://unos.org/news/system-implementation-notice-liver-and-intestinal-organ-distribution-based-on-acuity-circles-implemented-feb-4/. Accessed May 10, 2021.
2. Sheetz KH, Waits SA. Outcome of a change in allocation of livers for transplant in the United States. *JAMA Surg*. 2021;156(5):496. doi:10.1001/jamasurg.2021.0137
3. Diamond IR, de Silva N, Pencharz PB, Kim JH, Wales PW. Neonatal short bowel syndrome outcomes after the establishment of the first Canadian multidisciplinary intestinal rehabilitation program: preliminary experience. *J Pediatr Surg*. 2007;42(5):806-811. 10.1016/j.jpedsurg.2006.12.033
4. Stanger JD, Oliveira C, Blackmore C, Avitzur Y, Wales PW. The impact of multi-disciplinary intestinal rehabilitation programs on the outcome of pediatric patients with intestinal failure: a systematic review and meta-analysis. *J Pediatr Surg*. 2013;48(5):983-992. doi:10.1016/j.jpedsurg.2013.02.070
5. Horslen SP, Smith JM, Ahn Y, et al. OPTN/SRTR 2019 Annual Data Report: Intestine. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. 2021;21(Suppl 2):316-355. doi:10.1111/ajt.16498
6. Varadhan R, Weiss CO, Segal JB, Wu AW, Scharfstein D, Boyd C. Evaluating health outcomes in the presence of competing risks: a review of statistical methods and clinical applications. *Med Care*. 2010;48(6 Suppl):S96-105. doi:10.1097/MLR.0b013e3181d99107
7. Zhang X, Zhang M-J, Fine J. A proportional hazards regression model for the subdistribution with right-censored and left-truncated competing risks data. *Stat Med*. 2011;30(16):1933-1951. doi:10.1002/sim.4264
8. OPTN OPTN Policies: the National Liver Review Board (NLRB) policy. 2019. https://optn.transplant.hrsa.gov/media/2795/20190131_nlrb_policy.pdf. Published 2019. Accessed May 12, 2021.
9. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2017 annual data report: liver. *Am J Transplant*. 2019;19:184-283. doi:10.1111/ajt.15276

10. Smith JM, Weaver T, Skeans MA, et al. OPTN/SRTR 2016 annual data report: intestine. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. 2018;18(Suppl 1):254-290. doi:10.1111/ajt.14560
11. OPTN: Build Advanced Report, 2009-2018 Organ Procurement and Transplantation Network. 2021. https://optn.transplant.hrsa.gov/data/view-data-reports/build-advanced/. Published 2021. Accessed May 10, 2021.
12. Nagai S, Ivanics T, Kitajima T, et al. Early effects of acuity circle-based liver allocation during Covid-19 pandemic in the United States. *Am J Transplant*. 2021;21(suppl 3). https://atcmeetingabstracts.com/abstract/early-effects-of-acuity-circle-based-liver-allocation-during-covid-19-pandemic-in-the-united-states
13. Vianna RM, Mangus RS, Kubal C, Fridell JA, Beduschi T, Tector AJ. Multivisceral transplantation for diffuse portomesenteric thrombosis. *Ann Surg*. 2012;255(6):1144-1150. doi:10.1097/SLA.0b013e31825429c0
14. Mazzaferro V, Pulvirenti A, Coppa J. Neuroendocrine tumors metastatic to the liver: how to select patients for liver transplantation? *J Hepatol*. 2007;47(4):460-466. doi:10.1016/j.jhep.2007.07.004
15. OPTN Clarify Multi-Organ Allocation Policy Clarify Multi-Organ Allocation Policy. 2021. https://optn.transplant.hrsa.gov/media/4354/2021_pc_opo_clarify_multi_organ_allocation_policy.pdf. Published 2021. Accessed May 12, 2021.
16. Eurotransplant Chapter 5 ET Liver Allocation System (ELAS). 2019. https://www.eurotransplant.org/wp-content/uploads/2020/01/H5-ELAS-MELD.pdf. Published 2019. Accessed May 12, 2021.
17. Policy T. POLICY POL193/9 Intestinal Transplantation: Organ Allocation Copy Number Effective Summary of Significant Changes POLICY POL193/9 Intestinal Transplantation: Organ Allocation. 1-9.
18. Visto el expediente No. 1-2002-4638000887/16-2 del registro del Instituto Nacional Central Unico Coordinador de Ablacion e Implante. 2017. https://www.argentina.gob.ar/sites/default/files/norm-intest-reso-incucai_065_17.pdf. Published 2017. Accessed May 10, 2021.
19. UNOS NLRB update: MMaT calculation now based on DSA of transplant hospital. 2019. https://unos.org/policy/liver-policy-updates/. Published 2019. Accessed July 11, 2021.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

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