Background: With no previous research evaluating whether disparities influence outcomes in children with cystic fibrosis (CwCF) on the waitlist for lung transplantation (LTx) or who undergo LTx in the United States, we explored this important question using a national registry. We examined whether survival differences exist between white non-Hispanic (WNH) and non-white (NW) black, Hispanic, Asian, or other CwCF on the waitlist for LTx or who underwent LTx. Methods: The United Network for Organ Sharing Registry was queried for CwCF (aged <18) who had been waitlisted for or underwent LTx between January 1, 2000, and December 31, 2021. Chi-square and nonparametric median tests were used to compare categorical and continuous variables, respectively. Data are presented as medians with interquartile ranges (IQRs). Statistical significance was defined as p < 0.05. Results: Eight hundred twenty-eight CwCF were placed on the waitlist for LTx (660 WNH, 198 NW). WNH CwCF were older (age 15 [12–16] vs 14 [10.25–15], p < 0.001), taller (150 cm [138–157.5 cm] vs 146.6 cm [128.8–154.9 cm], p = 0.02), and on the waitlist longer (180 [41–540.25] days vs 109 [31–349] days, p = 0.001). There were no differences in sex, body mass index (BMI), weight, lung allocation score, or mean pulmonary artery pressure between the two cohorts. NW CwCF (n = 47, 27.9%) were significantly more likely to die on the waitlist or be removed from it because their condition was deteriorating than WNH CwCF (n = 123, 18.6%) (p = 0.007). There was no difference between the two cohorts for removal for undergoing LTx or improved condition (WNH: n = 455, 68.9%; NW: n = 104, 61.9%; p = 0.4). There were no differences in sex, body mass index (BMI), weight, lung allocation score, or mean pulmonary artery pressure between the two cohorts. NW CwCF (n = 47, 27.9%) were significantly more likely to die on the waitlist or be removed from it because their condition was deteriorating than WNH CwCF (n = 123, 18.6%) (p = 0.007). There was no difference between the two cohorts for removal for undergoing LTx or improved condition (WNH: n = 455, 68.9%; NW: n = 104, 61.9%; p = 0.08) or other/unknown (WNH: n = 82, 12.4%; NW: n = 17, 10.1%; p = 0.4). Figure 1 shows Kaplan-Meier survival curves for WNH and NW CwCF on the waitlist for LTx (Figure 1a) and after LTx (Figure 1b). Cox proportional model multivariate analysis for the key clinical variables (age, height, weight, BMI, lung allocation score, mean pulmonary artery pressure) for NW and WNH CwCF did not identify significant confounders contributing to waitlist survival. There was no difference in post-LTx survival between NW (mean survival: 3099 days, 95% CI, 2304–3876 days) and WNH (mean survival: 3055 days, 95% CI, 2727–3393 days) children (p = 0.8) (Figure 1b). During this same period, there were no disparities found in waitlist outcomes between WNH and NW CwCF on the waitlist for LTx or who underwent LTx.

Conclusions: A significant LTx waitlist disparity for NW CwCF was identified. Despite the fact that advances in CF transmembrane conductance regulator (CFTR) modulator therapy have greatly affected the pediatric CF population and reduced the need for LTx in WNH CwCF, we anticipate the need for LTx to continue in NW CwCF until specific discoveries can address the more common CFTR mutations in the NW CF population. There is a pressing need to address the waitlist disparity in NW CwCF, given the impact of this issue.

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predicted forced expired volume in 1 second (FEV,pp) of less than 50%, and no prior LTx, with attention to enrollment of participants from communities of concern, defined as Medicaid insurance, non-white race, Hispanic ethnicity, or high school education or less. Participants were recruited from CF centers in the United States and randomized to ToT or UNOS within FEV,pp strata (30–50%, <30%). The co-primary outcomes were feasibility of completion of the 2-week study visit and participant rating of preparedness for LTx discussion via the PrepDM at 2 weeks. The primary analysis compares mean PrepDM score between the ToT and UNOS arms using linear mixed models. Secondary outcomes included change in Decisional Conflict Scale [2], Likert rating of preparedness for LTx discussions, LTx knowledge assessment (14 questions, investigator designed), and mental health (Patient Health Questionnaire-9 [3], Generalized Anxiety Disorder-7 [4]) and quality-of-life (Cystic Fibrosis Questionnaire Revised) endpoints [5]. We will also explore dose-response relationships by estimating the association between change in outcomes from baseline to 2 weeks and 2 weeks to 4 weeks and time spent using ToT.

Results: Of 38 participants enrolled in the pilot RCT, 24 (63%) are from communities of concern, and 100% completed 2-week study visits. We expect the last participant to finish the study protocol in September 2022. No interim efficacy results are available.

Conclusions: Final data will be available for presentation at the 2022 North American Cystic Fibrosis Conference.

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References

Survival outcomes after liver transplantation for individuals with cystic fibrosis in North America

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Background: Liver disease affects approximately 10% of people with cystic fibrosis (CF), with about 5% experiencing severe cirrhosis and portal hypertension. Timing for liver transplantation in CF is controversial, and similar parameters are often used to prioritize people on the waiting list regardless of underlying disease, but the course of CF liver disease is unique, and individuals with cirrhosis and portal hypertension can remain stable for years without transplantation, making it challenging to select the optimal time for listing. There is little literature on outcomes after liver transplantation in the CF population. The objectives of this study were to describe the characteristics and health outcomes of individuals who undergo liver transplantation in North America.

Methods: Data from the Canadian Cystic Fibrosis Registry and the U.S. Cystic Fibrosis Foundation Patient Registry (CFFPR), supplemented with data from the United Network for Organ Sharing (UNOS), were used. The CFFPR was probabilistically linked to UNOS liver data using LinkPlus software, matching on name, birth date, sex, and ZI code. A cohort of individuals who underwent liver transplantation between 1987 and 2019 were included. Liver-lung transplantation was excluded. Type of organ donor (cadaveric vs living), time on waitlist, and deaths on waitlist were calculated according to donor type. Linear regression analyses were used to investigate trends over time using a Davies test to find change points in trends. Time to death after liver transplantation was calculated from transplantation to date of death. Individuals were censored on December 31 of their last year of follow-up. Median survival time after liver transplantation and 1-, 3-, and 5-year survival probabilities were calculated using the Kaplan-Meier method.

Results: Between 1987 and 2019, there were 431 liver transplant recipients (8.4% in Canada, 91.6% in the United States; 61.7% male). Median age at transplantation was 15.2 (range 0.5–63.1), and 66% of transplants were done in people younger than 18: 68.4% of donors were cadaveric, 13.2% were living, and the status of 18.3% was unknown. Median time on the waitlist was 0.4 years (interquartile range [IQR] 0.1–1.0) years. Median lung function before liver transplant was 69.8% predicted (IQR 53.9–83.1%; n = 385), 20% of recipients were underweight (body mass index (BMI) < 18.5 kg/m² for adults, BMI percentile ≤ 25% for children), 42.5% had CF-related diabetes, 97% were pancreatic insufficient, and 51% were homozygous F508del. The median age of liver transplantation has been increasing significantly from a median age of 12.7 in 1987 to 16.8 in 2019 (β = 0.13, p = 0.02). Since the estimated change point of 1996, the percentage of liver transplants over time has been steadily and significantly decreasing—from 0.066% in 1996 to 0.036% in 2019 (β = 0.001, p < 0.001). Median survival after transplant was 13.7 years (95% CI, 11.4–15.9 years). Overall probability of survival was 88.1% (95% CI, 85.9–91.2%) at 1 year, 82.4% (95% CI, 78.8–86.2%) at 3 years, and 76.5% (95% CI, 72.4–80.8%) at 5 years. There was no statistical evidence of a difference in survival between male and female subjects (log-rank p = 0.10).

Conclusions: Liver transplantation is less common than lung transplantation in CF and occurs more frequently in children. There is a high chance of survival even 5 years after liver transplantation. Further analysis will be conducted to compare the impact of cadaveric with living donors on outcomes for the North American Cystic Fibrosis Conference.

CLINICAL GENETICS

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Initiation of standardized care pathway for individuals with cystic fibrosis transmembrane conductance regulator–related metabolic syndrome at a large cystic fibrosis center

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Background: With initiation of newborn screening (NBS) for cystic fibrosis (CF), there has been an increase in inconclusive diagnoses and infants with suspected CF transmembrane conductance regulator (CFTR)-related metabolic syndrome (CRMS). Children’s Healthcare of Atlanta and the Emory University Pediatric CF Program identified a need for consistency in care of individuals diagnosed with CRMS. At our institution, individuals