predicted forced expiratory volume in 1 second (FEV1,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 FEV1,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.

Acknowledgements: This work was supported by National Institutes of Health R01HL158728 and K23HL138154 and Cystic Fibrosis Foundation RAMOS20AA-KB and RAMOS17A0. We acknowledge the life and contributions of Dr. Mara Hobler and thank the following groups for their contributions to this work: people with CF across the United States, the ToT Study Group, the University of Washington Clinical Informatics Research Group, and the Cystic Fibrosis Foundation Community Voice (Bethesda, MD).

References

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

A. Stephenson1,2, K. Ramos1, J. Sykes1, S. Stanojevic1, X. Ma1, B. Quon7, E. Cromwell1, B. Marshall1, J. Ostrenga4, A. Faro5, A. Elbert8, C. Goss4,9.

1Toronto Adult Cystic Fibrosis Centre, St. Michael’s Hospital, Unity Health Toronto, Toronto, Ontario, Canada; 2Hearne Research Centre, Li Ka Shing Knowledge Institute, St. Michael’s Hospital, Unity Health Toronto, Toronto, Ontario, Canada; 3Institute of Health Policy, Management and Evaluation, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; 4Department of Medicine, University of Washington, Seattle, WA; 5Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; 6Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada; 7Medicine, University of British Columbia, Vancouver, British Columbia, Canada; 8Cystic Fibrosis Foundation, Bethesda, MD; 9Division of Pulmonary Medicine, Department of Pediatrics, University of Washington, Seattle, WA

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 0.1–10) 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 percentiles ≤12% 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 = 0.03, 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 85–91.2%) 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.

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

E. Barr1,2, S. Pendley3, B. Baxter1, M. McKinnon3, E. Kallam1,4, R. Timmemann1,4,1 Human Genetics, Emory University, Atlanta, GA; 2Pediatrics, Division of Pulmonology, Asthma, Cystic Fibrosis and Sleep, Children’s Healthcare of Atlanta, Atlanta, GA; 3Children’s Healthcare of Atlanta, Atlanta, GA; 4Emory University School of Medicine, Atlanta, GA

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

CLINICAL GENETICS

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

E. Barr1,2, S. Pendley3, B. Baxter1, M. McKinnon3, E. Kallam1,4, R. Timmemann1,4,1 Human Genetics, Emory University, Atlanta, GA; 2Pediatrics, Division of Pulmonology, Asthma, Cystic Fibrosis and Sleep, Children’s Healthcare of Atlanta, Atlanta, GA; 3Children’s Healthcare of Atlanta, Atlanta, GA; 4Emory University School of Medicine, Atlanta, GA

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
diagnosed with CRMS may be followed by CF providers or general pulmonologists. European guidelines published in 2021 [1] precipitated an effort to standardize care across providers at our large CF center, as well as in general pulmonology groups. This quality initiative developed a standard CRMS care pathway based on guidelines and provider preference and established a CRMS clinic.

**Methods:** A survey about CRMS management was distributed to all pediatric CF providers. The survey consisted of seven multiple choice and one open-response question. Questions focused on provider preference for management such as follow-up timeline, throat and sputum cultures, and age of transition.

**Results:** Surveys were completed by 123 of 290 NYS infants referred between December 1, 2017, and November 30, 2021. CRMS was indicated for 34 (27.6%) infants, 110 infants were referred to an annual CRMS clinic, and 46 infants were not referred to CRMS or as CF unlikely or CF carrier. Parental phasing studies confirmed that all CFTR variants were in cis for 32 infants, or the second variant was reclassified as non-CF-causing (n = 16). SCCs reported that 97 of 273 (35.5%) families saw a trained genetic counselor. CF physicians provided genetic counseling to 51 families (18.7%). Genetic counseling was not provided to 79 families (28.9%); data were not reported for 46 families (16.8%). Reasons provided for lack of genetic counseling included that a genetic counselor was not available (n = 15), the family already had knowledge because of prior child or prenatal testing (n = 3), the infant was adopted or in foster care (n = 2), and the family declined (n = 9). Genetic counseling rates at NYS CF centers for this population ranged from 0% to 100%.

**Conclusions:** Genetic counseling is provided inconsistently to parents of infants with a positive CFNBS result in NYS; in nearly one-third of cases in which genetic counseling was noted, the CF physician provided it. Inaccessibility of a genetic counselor was the primary reason given when genetic counseling was not performed. Additional efforts are needed to address access barriers to implement CF recommendations regarding genetic counseling for parents of infants with a positive CFNBS result.

**Reference**

151

**Variable genetic counseling access and services for parents of infants who screen positive for cystic fibrosis in New York State**


New York State Cystic Fibrosis Newborn Screening Consortium.

M. Caggana, H. Sadeghi, C. Kier.

Cystic Fibrosis Center at Mount Sinai Beth Israel, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; Newborn Screening Program, Wadsworth Center, New York State Department of Health, Albany, NY; Cohen Children’s Medical Center, New Hyde Park, NY; State University of New York, Upstate Medical University, Syracuse, NY; Westchester Medical Center, Westchester, NY; Pediatrics, State University of New York, Upstate Medical University, Syracuse, NY; Pediatric Pulmonology, Hassenfeld Children’s Hospital NYU Langone Health, New York, NY; University of Buffalo Medical Center, Buffalo, NY; Albany Medical College, Albany, NY; Pediatrics, University of Rochester Medical Center, Rochester, NY; Cystic Fibrosis Specialty Care Centers, New York, NY; Pediatric Pulmonology, Columbia University Irving Medical Center, New York, NY; Stony Brook Children’s Hospital, Stony Brook Medicine, Stony Brook, NY

**Background:** The Cystic Fibrosis Foundation (CF) has endorsed guidelines recommending genetic counseling by a provider trained in genetics with expertise in CF for all families of infants with a positive cystic fibrosis (CF) newborn screening (CNFBNS) result [1]. The New York State (NYS) CNFBNS Consortium has spearheaded an ongoing quality improvement effort to characterize the processes of the NYS CNFBNS program and CF specialty care centers (SCCs), with a goal of improving outcomes and increasing access to care for referred infants with abnormal CNFBNS results. NYS uses a three-tier immunoreactive trypsinogen (IRT)–deoxyribonucleic acid (DNA)–sequencing (SEQ) algorithm for CNFBNS; infants with two or more CFTR variants of potential clinical relevance are referred for follow-up to an SCC. Infants with one CFTR variant are not referred to an SCC. Because the NYS Department of Health reports complex genetic information that requires interpretation and counseling about its implications, we sought to establish baseline rates of genetic counseling provided to parents of infants with CF screen-positive, inconclusive diagnosis/CF transmembrane conductance regulator (CFTR)-related metabolic syndrome (CFSPID/CRMS) or CF carrier status.

**Methods:** As part of a longer-term follow-up effort by the NYS NBS program and SCCs, a clinical and demographic dataset was compiled for infants referred between December 1, 2017, and November 30, 2021. Genotypes and CFTR phasing data were abstracted from NBS records. Demographic and clinical data, including information about provision of genetic counseling services, were requested from each SCC and tabulated to assess genetic counseling rates. Infants with a positive CNFBNS (high IRT and more than one CFTR variant, with one or more variants of uncertain significance or varying clinical consequence), were included in this analysis. Infants classified as having CF were excluded. The NYS Department of Health Institutional Review Board determined this project to be exempt.

**Results:** Of 290 infants meeting study criteria, 273 (94.1%) were evaluated at least once. Of those, 225 were subsequently classified as having CFSPID/CRMS or as CF unlikely or CF carrier. Parental phasing studies confirmed that all CFTR variants were in cis for 32 infants, or the second variant was reclassified as non-CF-causing (n = 16). SCCs reported that 97 of 273 (35.5%) families saw a trained genetic counselor. CF physicians provided genetic counseling to 51 families (18.7%). Genetic counseling was not provided to 79 families (28.9%); data were not reported for 46 families (16.8%). Reasons provided for lack of genetic counseling included that a genetic counselor was not available (n = 15), the family already had knowledge because of prior child or prenatal testing (n = 3), the infant was adopted or in foster care (n = 2), and the family declined (n = 9). Genetic counseling rates at NYS CF centers for this population ranged from 0% to 100%.

**Conclusions:** Genetic counseling is provided inconsistently to parents of infants with a positive CNFBNS result in NYS; in nearly one-third of cases in which genetic counseling was noted, the CF physician provided it. Inaccessibility of a genetic counselor was the primary reason given when genetic counseling was not performed. Additional efforts are needed to address access barriers to implement CF recommendations regarding genetic counseling for parents of infants with a positive CNFBNS result.

**Reference**