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Title:

ADVANCED BUT NOT MILD LIVER DISEASE IS A PREDICTOR OF DECREASED SURVIVAL IN CHILDREN WITH CYSTIC FIBROSIS, WITH FAR GREATER IMPACT IN FEMALES: A 27-YEAR REAL-LIFE COHORT STUDY

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What was your research question?

Advances in cystic fibrosis (CF) treatment have contributed to increased longevity. As a consequence, non pulmonary complications such as development of cystic fibrosis-associated liver disease (CFLD) have become increasingly important factors impacting length and quality of life. Many children with CF have mild manifestations of liver disease without functional compromise, some develop advanced disease such as portal hypertension and cirrhosis. Few studies have assessed variables related to the mortality of patients diagnosed with CFLD. This study was designed to determine the impact of liver disease severity on survival of children with cystic fibrosis in a large well-characterised cohort derived from a single center with almost three decades of follow-up.

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Why is this important?

Liver inflammation and damage is likely, to some degree, in most individuals with CF as demonstrated by the frequent finding of abnormal blood and ultrasound tests during life and in autopsy studies. Progression of CFLD in some to advanced liver disease with portal hypertension and or cirrhosis is a serious complication affecting survival and quality of life. Understanding the factors behind development of liver disease and the impact of liver disease severity on future health outcomes is vital for individualization of patient management.

What did you do?

A real life, single center cohort study with 27 years follow up was conducted. Children with CF were followed until the occurrence of liver transplantation, death, or end of follow-up. Mild CFLD was diagnosed as children with abnormal serum liver function tests and abnormal ultrasound. Advanced CFLD was established by the presence of cirrhosis or portal hypertension.

What did you find?

Over a period of 27 years, 290 children were enrolled and followed for a minimum of one year. Forty-eight children (16.5%) developed mild CFLD and 55 (19%) advanced CFLD. Ten children with advanced CFLD and one with mild CFLD died. Based on statistical analysis, mean overall survival age of all CF children to the study end-point was 29.1 years. The mean survival among females with advanced CFLD was 24.7 years compared to 30.4 years for females without advanced CFLD, and this difference was statistically significant. Female gender and development of diabetes were the main factors predicting reduced survival in those with advanced CLFD. Mild CFLD was not associated with decreased survival. The effect of advanced CFLD on survival was mainly borne by females compared to males.

What does this mean and reasons for caution?

Our observations are striking in the relevance of advanced CFLD in female children and the significant impact on mortality. The risk of early death for females with advanced CFLD is 6 times greater than the risk of death for females without advanced CFLD. This data reflects our unit's experience at the Queensland Children's Hospital (Brisbane, Australia), with an apparent female preponderance for poor outcomes in those with advanced CFLD.

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What's next?

These observations require confirmation in larger studies of children with CF. We propose that the early diagnosis of CFLD is essential to monitor the progression of the disease and to provide personalised clinical follow-up strategies, especially for females with advanced CFLD.

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