

An international cohort study spanning five decades assessed outcomes of nephropathic cystinosis

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Abstract

Nephropathic cystinosis is a rare disease secondary to recessive mutations of the CTNS gene encoding the lysosomal cystine transporter cystinosin, causing accumulation of cystine in multiple organs. Over the years, the disease has evolved from being a fatal condition during early childhood into a treatable condition, with patients surviving into adulthood. Data on cystinosis are limited by the rarity of the disease. Here, we have investigated factors associated with kidney and growth outcome in a very large cohort of 453 patients born between 1964 and 2016 and followed in Belgium, Germany, Austria, France, Italy, Spain, The Netherlands, Turkey and United Kingdom. From the 1970s to the 1990s, the median increase in kidney survival was 9.1 years. During these years, cysteamine, a cystine-depleting agent, was introduced for the treatment of cystinosis. Significant risk factors associated with early progression to end-stage kidney disease assessed by Cox proportional multivariable analysis included delayed initiation of cysteamine therapy and higher mean leucocyte cystine levels. No significant effect on kidney function was observed for gender, pathogenic variant of the CTNS gene, and the prescription of indomethacin or renin angiotensin system blockers. Significantly improved linear growth was associated with early use of cysteamine and lower leukocyte cystine levels. Thus, our study provides strong evidence in favor of early diagnosis and optimization of cystine depletion therapy in nephropathic cystinosis.