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Cystic fibrosis in Brazil: achievements in survival

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Cystic fibrosis (CF) is an autosomal recessive genetic disease that is chronic and progressive, being characterized by multisystem involvement.[1] CF is caused by mutations in a gene that is located on the long arm of chromosome 7 and that encodes the cystic fibrosis transmembrane conductance regulator (CFTR) protein, an epithelial cell chloride channel that allows the cotransport of sodium and chloride along with water across the cell membrane.[2] The estimated incidence of CF in Brazil is 1:7,576 live births; however, the incidence of CF differs across regions in Brazil, being highest in the southern and southeastern regions.[3] According to data from the Brazilian CF Patient Registry, a total of 5,517 patients were followed at referral centers in 2018.[4]

In recent decades, advances in the diagnosis and treatment of CF have significantly increased the life expectancy of CF patients. According to data from the Cystic Fibrosis Foundation Patient Registry, median survival is 46.2 years in the USA,[5] whereas, in Brazil, median survival is 43.8 years.[4] Newborn screening for CF is currently performed in all Brazilian states. Therefore, age at diagnosis has decreased, the median age at diagnosis of CF being 3.7 months in 2018.[4] Early initiation of treatment at a specialized referral center by a multidisciplinary team improves clinical outcomes, having a positive impact on patient prognosis.[6] According to data from the Brazilian CF Study Group, there are over 50 CF referral centers in 22 Brazilian states.[4] Treatment advances include control of respiratory infections, mucolytics, pancreatic enzyme replacement therapy, dietary supplementation, respiratory therapy, and physical exercise, all of which influence the survival of CF patients.[6] New drugs such as CFTR modulators are likely to increase the life expectancy of CF patients, allowing treatment of the molecular cause of CF. To date, four CFTR modulators have been developed for the treatment of patients with specific mutations.[7] However, these drugs remain unavailable for most CF patients in Brazil.

Although CF is a multisystem disease, lung disease is the primary cause of morbidity and mortality in CF patients. A vicious cycle of airway mucus accumulation, chronic inflammation, and recurrent infections leads to epithelial damage, tissue remodeling, and progressive lung function decline.[8] Patients with CF experience episodes of acute worsening of respiratory symptoms (pulmonary exacerbation) requiring oral antibiotics (for mild exacerbations) or hospitalization for intravenous antibiotic therapy in many cases.[9] Frequent exacerbations negatively influence prognosis and accelerate lung function decline, as well as being associated with increased morbidity and mortality in CF patients.[10] As the disease progresses and lung function declines, advanced-stage CF patients are referred for lung transplantation. However, the decision to pursue transplantation involves comparing the likelihood of survival with and without transplantation, as well as assessing the effect of wait-listing and transplantation on patient quality of life. In any case, lung disease is the most common cause of death in CF patients.[4,5,11] According to the Cystic Fibrosis Foundation,[5] there has been a steady decline in the mortality rate for patients with CF.[5] Although the median age at death has increased in recent years in Brazil (to 18.4 years),[4] it remains lower than those in the USA (32.4 years)[5] and Europe (29.0 years).[11]

In the current issue of the *Jornal Brasileiro de Pneumologia*, Santo et al.[12] describe causes of death and mortality data related to CF in Brazil on the basis of data from death certificates. For the 1999-2017 period, the overall CF-related number of deaths was 2,854, with CF being reported as the underlying cause of death in 83.5% of the death certificates. A continuous upward trend in the death rates was observed, with a significant annual percent change of 6.84% among males and 7.50% among females, the median age at death having increased from 7.5 years in 1999 to 56.5 years in 2017. According to the authors, the results are counterintuitive because the advances in CF diagnosis and treatment might result in an increase in the age at death but not in the mortality rates. However, the increasing mortality trend might be related to an increased number of patients being diagnosed with CF as a result of increased newborn screening for CF in Brazil. The most important finding in the study by Santo et al.[12] is the significant increase in the median age at death, probably due to advances in diagnosis and treatment.

In conclusion, advances in diagnosis and treatment, as well as improvements and expansion in multidisciplinary care centers, have changed the situation for CF patients in Brazil, resulting in a significant increase in life expectancy. Expanding the use of new drugs can result in improved mortality rates, life expectancy, and quality of life for CF patients in Brazil.

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