Thorax

Editorials

Modelling survival in cystic fibrosis

M Corey

The mantra of improving survival permeates virtually every paper related to prognosis or treatment for cystic fibrosis (CF) in the past two decades. However, the upward trend in the expected duration of life for patients with CF may have lost its momentum. The US and Canadian national CF registries show estimated median survival age increasing to around 32 years in 1989 and 1996, respectively, but in subsequent years no further improvement is seen.[1 2] Although the timing of a plateau in median survival age may differ, consistent patterns are seen in several other population based studies.[3–5] An impressive reduction in infant and childhood CF mortality is almost universal, but projections for these rescued children as they move through adolescence and adulthood cannot be simply extrapolated from the experience of older survivors of less fortunate cohorts. The current life table method, based on age specific mortality in a recent period, can only predict the experience of a cohort if age specific survival rates are stable over time. This is clearly not the case in CF. Cohort survival curves of patients with CF in the UK[5] show declining mortality rates in all age groups over almost three decades, as well as an apparent stabilisation of mortality rates in the youngest children in recent years. If long term prognosis in these young survivors is definitively altered, median survival age from current life tables will eventually increase. Current survival curves continue to be useful to describe the shape and evolution of CF mortality in different populations.

More complex analytical methods are needed to explain why some patients still succumb in childhood while others survive into middle age. Proportional hazards regression analysis provides estimates of the relative importance of variables thought to be associated with increased or decreased risk of dying. Not surprisingly, forced expiratory volume in 1 second (FEV_1) has been shown to be the most significant and consistent predictor of mortality risk in CF.[6 7] Sex, age at diagnosis, and measures of nutritional status and airway microbiology were also related to mortality risk, although all but sex were confounded to some degree by their association with FEV_1. In this issue of *Thorax*, Sharma and colleagues[8] focus on the importance of nutritional status, measured as percentage of ideal weight, as an independent predictor of mortality. The authors surmise that the significance of percentage ideal weight in their models, compared with the models of Kerem *et al*,[9] may relate to better overall nutritional status in their patient population so that poor weight better reflects disease progression. However, the patient population studied by Kerem *et al* was well documented as the earliest group of patients with CF to display near normal growth parameters with the modern aggressive approach to nutrition.[10] The more likely explanation for the unique findings in this paper relate to the specific patient group, which is older and displays more advanced disease parameters than those in the previous studies. This clinic based study population may overrepresent patients with CF at later stages in the disease process. Follow up studies at highly specialised clinics like this can define risk variables more precisely and isolate factors and subsets for further study in population based studies. The insidious and lengthy progression of lung disease in CF, and the changing background of diagnosis and treatment practices, make the modelling of CF survival a major challenge. In addition, the proportional hazards estimates do not always translate easily to prospective predictions. It is likely that CF prognosis is affected by different CFTR mutation combinations, the effects of modifier genes, and the interaction of these multiple genetic factors with environmental factors. Diet and dietary interventions may well be the most significant alterable environmental factors in the prognosis of CF.

M COREY

Population Health Sciences,
The Hospital for Sick Children,
555 University Avenue,
Toronto,
Ontario M5G 1XB,
Canada
mary.corey@sickkids.ca

1 Canadian Cystic Fibrosis Foundation. *Canadian patient data registry national report 1998*. Toronto: Canadian Cystic Fibrosis Foundation, 2001.
2 Cystic Fibrosis Foundation. *Patient registry annual data report 2000*. Bethesda: Cystic Fibrosis Foundation, 2001.
3 Rault G, Guilloud-Bataille M, Feingold J. Mucoviscidosis: comparative analysis of epidemiological data of french and north american registries. *Rev Pneumol Clin* 1995;**51**:115–21.
4 Wiiedemann B, Steinkamp G, Sens B, *et al* for the German Cystic Fibrosis Quality Assurance Group. The German Cystic Fibrosis Quality Assurance Project: clinical features in children and adults. *Eur Respir J* 2001 (in press).
5 Dodge JA, Morison S, Lewis PA, *et al* (the UK Cystic Fibrosis Survey Management Committee). Incidence, population, and survival of cystic fibrosis in the UK, 1968–95. *Arch Dis Child* 1997;**77**:493–6.
6 Corey M, Farewell V. Determinants of mortality from cystic fibrosis in Canada, 1970–1989. *Am J Epidemiol* 1996;**143**:1007–17.
7 Rosenfeld M, Davis R, Fitzsimmons S, *et al*. Gender gap in cystic fibrosis mortality. *Am J Epidemiol* 1997;**145**:794–803.
8 Sharma R, Florea VG, Bolger AP, *et al*. Wasting as an independent predictor of mortality in patients with cystic fibrosis. *Thorax* 2001;**56**:746–50.
9 Kerem E, Reisman J, Corey M, *et al*. Prediction of mortality in patients with cystic fibrosis. *N Engl J Med* 1992;**326**:1187–91.
10 Gurwitz D, Corey M, Francis P, *et al*. Perspectives in cystic fibrosis. *Pediatr Clin North Am* 1979;**26**:603–15.