Mortality: a neglected outcome in OCS-treated severe asthma

To the Editor:

Severe asthma, especially if associated with a T2 phenotype, often responds well to new emerging therapies, which have led to a reduction in the use of systemic oral corticosteroids (OCS) [1]. However, OCS-dependent patients still exist and are affected by the well-known (and potentially severe) side effects of such dependency. Longitudinal data that document the outcomes, including death, for these patients are lacking [2]. Here, we present our findings from a long-term severe asthma cohort, which indicate that mortality is a critical issue for these patients.

In this prospective study of real-life asthma management in an expert centre devoted to severe asthma, 52 patients were enrolled in a 20-year observational study (starting in 1994) (IRB 2017_CLER-MTP_07-028).

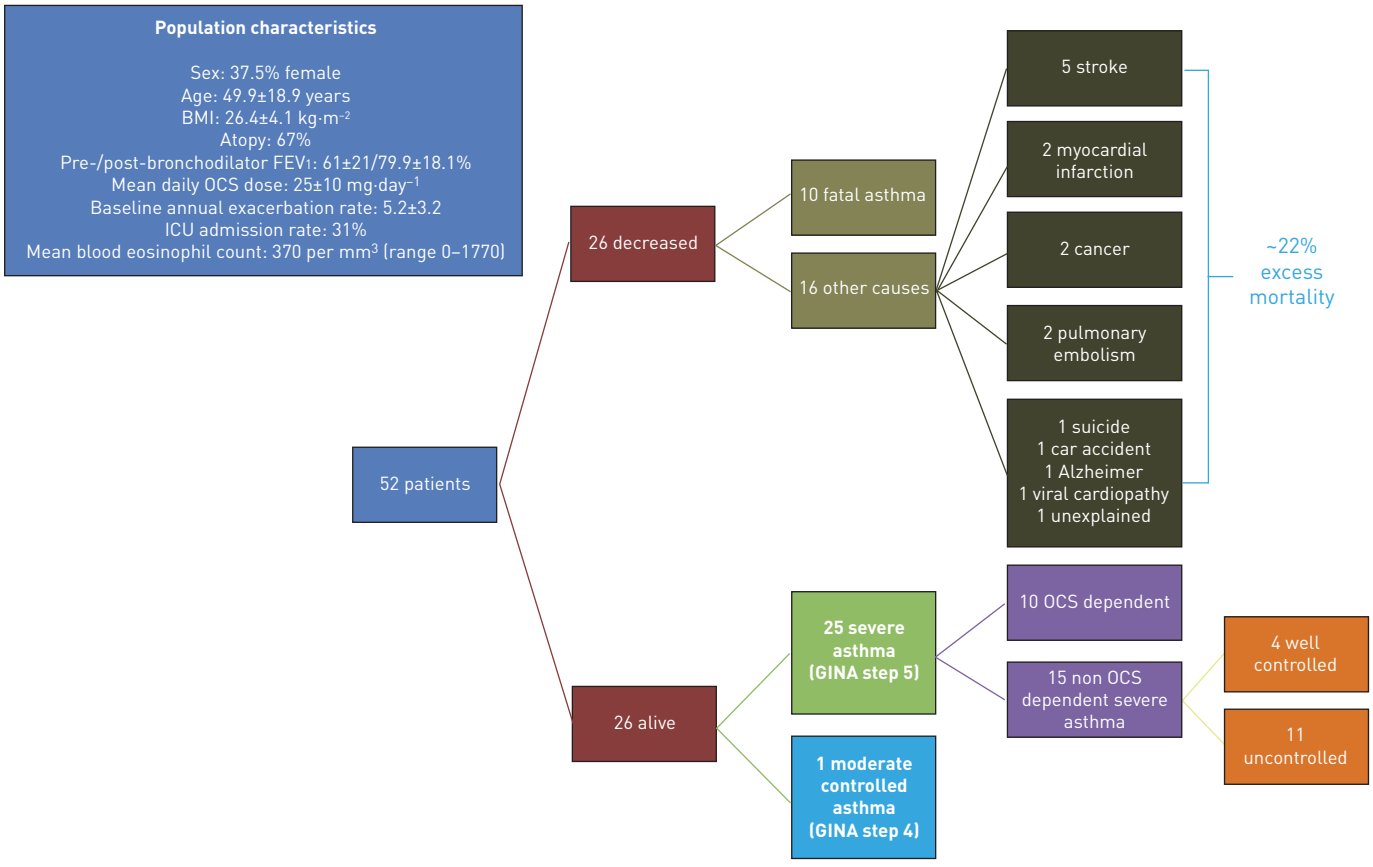

FIGURE 1 Patient characteristics and outcome flowchart during the 20-year study period. Bold font denotes the best prognosis. BMI: body mass index; FEV1: % predicted forced expiratory volume in 1 s; OCS: oral corticosteroid; ICU: intensive care unit; GINA: Global Initiative for Asthma.

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Findings from a long-term severe asthma cohort indicate mortality is a critical issue for OCS-dependent patients http://ow.ly/rO8e30fZrPo

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Exclusion criteria eliminated patients who had successful OCS-weaning trials in Year 1 (with no exacerbations during the year) and for whom environmental/adherence factors might have influenced OCS use.

Figure 1 shows patient characteristics and outcomes. Over 20 years, 26 patients died (50%), with mortality attributable to a fatal asthma episode (death in a medical unit confirmed as a fatal asthma episode, or the health care provider overseeing a fatal event attributed the cause of death to asthma) in 10 patients. The median number of years until death was nine (interquartile range (IQR) 25–75: 3–13, range 1–19), and this was similar between fatal asthma cases and others. Overall mortality predictors were baseline poor asthma control and the number of exacerbations during Year 1. The 50% death rate represented a significant increase in mortality compared to the expected survival rate adjusted for location (French department), age, and gender. The relative survival rate (RSR) was 0.778 with a 95% CI of 0.567–0.990, which corresponds to an absolute adjusted excess risk of death of ~22%. For comparison, the 15-year RSR after aortic valve replacement has been estimated to be 0.749 [3]; the 10-year RSR for diabetes, 0.695 [4]; and the 20-year RSRs for melanoma or cancers of the uterus, testes or thyroid range from 0.73–0.963 [5, 6].

Regarding the 26 patients who were alive at Year 20, asthma was considered to be moderate in one (Global Initiative for Asthma (GINA) treatment step 4) and severe in 25 (GINA treatment step 5). Ten (38.5%) had severe comorbidities, among which, six were directly attributable to OCS. At Year 20, 10 patients were still OCS-dependent (8.8±12.8 mg·day^{-1}). The OCS-dependent patients had two or more exacerbations per year, with two patients requiring repeated hospitalisation. Omalizumab was maintained in two patients, and three patients were treated with an investigational drug. Among the 15 non-OCS-dependent patients, 11 remained uncontrolled (including eight patients with two or more exacerbations per year). Four patients had asthma that remained well controlled, three of whom nevertheless had severe comorbidities.

In this 20-year study, we provide evidence for excess mortality among OCS-treated severe asthma patients that rivals that of other chronic diseases and certain cancers. Furthermore, only a small fraction of survivors achieved control of the condition. In contrast, the majority of 20-year survivors presented a mix of severe comorbidities associated with high exacerbation rates. These observations underline the continuing need for research and treatment discovery in severe asthma [7–9].

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