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REFERENCES

1. **Holgate S,** Buhl R, Bousquet J, *et al*. The use of omalizumab in the treatment of severe allergic asthma: a clinical experience update. *Respir Med* 2009;**103**:1098–113.
2. **Verbruggen K,** Van Cauwenberge P, Bachert C. Anti-IgE for the treatment of allergic rhinitis – and eventually nasal polyps? *Int Arch Allergy Immunol* 2009;**148**:87–98.
3. **Penn R,** Mikula S. The role of anti-IgE immunoglobulin therapy in nasal polyposis: a pilot study. *Am J Rhinol* 2007;**21**:428–32.
4. **Guglielmo M,** Gulotta C, Mancini F, *et al*. Recalcitrant nasal polyposis: achievement of total remission following treatment with omalizumab. *J Investig Allergol Clin Immunol* 2009;**19**:158–9.
5. **Fokkens W,** Lund V, Mullol J. European Position Paper on Rhinosinusitis and Nasal Polyps group. *Rhinol Suppl*. 2007;(20):1–136. Review.

Outcomes following non-invasive ventilation for hypercapnic exacerbations of chronic obstructive pulmonary disease

Many carefully crafted studies with different end points have shown significant benefits with non-invasive ventilation (NIV) over and above conventional medical treatment alone in the management of hypercapnic exacerbations of chronic obstructive pulmonary disease (COPD).[1] However, most data have evaluated highly selected patients within stringent realms of randomised controlled trials. Since strict criteria need to be fulfilled before clinical trial entry (often excluding elderly patients and those with major co-morbidities, electrolyte disturbance and severe exacerbations), outcomes may not be reflective of everyday practice. We wished to highlight demographics, physiological variables, outcomes and 1-year survival in a large cohort of patients receiving ward-based NIV for hypercapnic exacerbations of COPD.

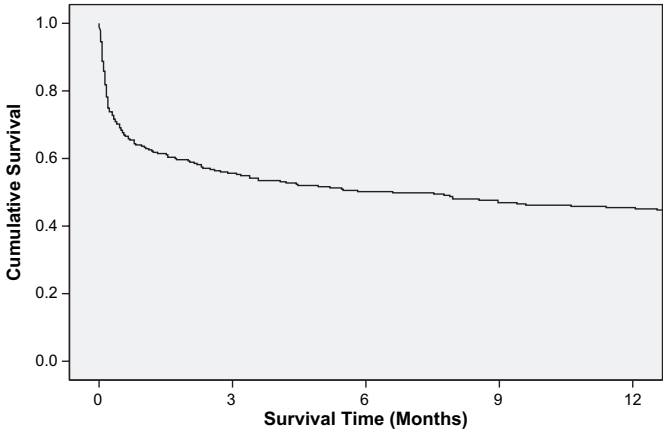

Figure 1 Kaplan–Meier curve showing cumulative survival over 12 months in patients who received non-invasive ventilation for a hypercapnic exacerbation of chronic obstructive pulmonary disease.

Data were gathered retrospectively from a password-protected database for all patients commenced on ward-based NIV for respiratory failure. All individuals had been admitted to the respiratory unit in Aberdeen Royal Infirmary (a large teaching hospital in the north-east of Scotland) between January 2006 and June 2009 inclusive and had been assessed by a middle grade respiratory physician or above regarding suitability for NIV. In all patients, appropriate pharmacological treatment was initiated and NIV pressures were titrated upwards as tolerated.

Over a 3.5-year period, 275 separate patients (158 females (57%) with mean age 71 years) received NIV with a mean baseline pH and Pco_2 of 7.24 and 10.23 kPa, respectively. Of the 275 patients, 89 (32%) died in hospital (5 of these failed to tolerate NIV and were not considered candidates for intensive care), 174 (63 %) were discharged home and 12 (5%) were transferred to intensive care after failing treatment with NIV. No patients received domiciliary NIV following hospital discharge. Of those discharged, cumulative all-cause mortality after 3, 6, 9 and 12 months was 44%, 50%, 52% and 55%, respectively (figure 1).

These real-life data indicate that in unselected patients with hypercapnic exacerbations of COPD who require NIV, almost two-thirds survive to hospital discharge. As expected, our inpatient mortality was greater than that reported in randomised controlled trials. For example, in one study (n=236 randomised individuals), the inpatient mortality in NIV-treated individuals (n=118) was 10% versus 20% in those receiving usual medical care (p=0.05).[2] In another study (n=85 randomised individuals), the inpatient mortality was 9% in those receiving NIV versus 29% in the control group (p<0.05).[3] In these studies, the mean pH (7.32 and 7.27, respectively) was greater than the pH in our study (7.24). There is a paucity of published data regarding long-term survival of patients discharged from hospital following treatment with NIV. We have shown that the all-cause mortality rate was as high as 44% within the first 3 months of hospital discharge, although this figure only rose by a further 11% over the subsequent 9 months. This suggests that further studies are required to identify clinical features associated with death within 3 months of hospital discharge. All patients discharged after receiving NIV should be established on optimal pharmacological treatment and considered for interventions such as early pulmonary rehabilitation.[4] The role of domiciliary NIV in this patient group also needs further evaluation.[5]

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REFERENCES

1. **Lightowler JV,** Wedzicha JA, Elliott MW, *et al*. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ* 2003;**326**:177–8.
2. **Plant PK,** Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000;**355**:1931–5.

3. **Brochard L,** Mancebo J, Wysocki M, *et al*. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;**28**:817—22.
4. **Man WD-C,** Polkey MI, Donaldson N, *et al*. Community pulmonary rehabilitation after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study. *BMJ* 2004;**329**:1209.
5. **Schönhofer B.** Non-invasive positive pressure ventilation in patients with stable hypercapnic COPD: light at the end of the tunnel? *Thorax* 2010;**65**:765—7.

CORRESPONDENCE

Comment on: Morbidity and mortality associated with the restrictive spirometric pattern: a longitudinal study

We read with interest the paper by Guerra *et al*[1] profiling the demographic/clinical characteristics and prospectively assessing the prognosis of subjects with a restrictive spirometric pattern enrolled in the TESAOD population-based study. The manuscript has the merit of following up a large number of patients for 14 years and investigating how selected co-morbidities are relevant to survival.[2]

The results of this study deserve comparison with those published in 2008 by our research group on 1265 subjects aged 65—97 years.[3] First, in an older population (mean age 73.4 years) we found a comparable prevalence of restriction at spirometry (12% vs 10.9%), although restriction is an age-related phenomenon and, thus, is expected to be much lower in the younger population (ie, 6.6% in a population aged 42.2 years[4]). Secondly, the study by Guerra and colleagues strongly reproduces the increased mortality risk rates (MRRs) observed in our work: for all (HR 1.89; 95% CI 1.15 to 3.11 (Scarlata *et al*) vs HR 1.7; 95% CI 1.3 to 2.3 (Guerra *et al*)), cardiac (MRR 1.51; 95% CI 0.60 to 3.78 (Scarlata *et al*) vs HR 2.0; 95% CI 1.3 to 3.1 (Guerra *et al*)) and cerebrovascular (MRR 4.79; 95% CI 1.54 to 14.84 (Scarlata *et al*) vs HR 2.4; 95% CI 0.9 to 6.3 (Guerra *et al*)). This finding is consistent with restrictive lung dysfunction affecting survival in a predictable manner.

At variance with our study, that of Guerra and colleagues lacks information about clinical correlates of restrictive pulmonary disease. The Cox proportional hazard models are adjusted only for sex, age and body mass index, but not for concomitant conditions known to be associated with restriction. Indeed, we found that co-morbidities such as kyphosis of the spine (OR 2.40; 95% CI 1.58 to 3.64) and diabetes mellitus (OR 1.66; 95% CI 1.00 to 2.74) as well as the physical (Activities of Daily Living scale, OR 2.17; 95% CI 1.32 to 3.58; 6 minute walking test, OR 1.75; 95% CI 1.15 to 2.67) and cognitive (Mini Mental State Examination, OR 2.05; 95% CI 1.27 to 3.32) status are strong independent correlates of restriction.

In conclusion, the paper by Guerra and colleagues has the merit of confirming that the restrictive spirometric pattern is highly prevalent and is associated with a clinical profile and risk factors differing from those of obstructive lung disease. However, research is needed to expand our knowledge of the mechanisms underlying restriction as well as to explain the link between restriction and frailty. Clarifying these issues will allow the implementation of both guided screening and preventive interventions.

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REFERENCES

1. **Guerra S,** Sherrill DL, Venker C, *et al*. Morbidity and mortality associated with the restrictive spirometric pattern: a longitudinal study. *Thorax* 2010;**65**:499—504.
2. **Mannino DM,** Buist AS, Petty TL, *et al*. Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. *Thorax* 2003;**58**:388—93.
3. **Scarlata S,** Pedone C, Fimognari FL, *et al*. Restrictive pulmonary dysfunction at spirometry and mortality in the elderly. *Respir Med* 2008;**102**:1349—54.
4. **Mannino DM,** Ford ES, Redd SC. Obstructive and restrictive lung disease and functional limitation: data from the Third National Health and Nutrition Examination. *J Intern Med* 2003;**254**:540—7.

Authors' response

We appreciate the interest shown in our study by Scarlata and colleagues.[1] We agree with them that, in line with several previous reports,[2 3] the prevalence of the restrictive spirometric pattern was strikingly similar in the TESAOD[4] and SARA[5] studies, despite the substantial difference in age distribution between the two populations (the TESAOD report included subjects ≥21 years and the SARA study subjects ≥65 years of age).

However, a direct comparison of cause-specific mortality between the two studies should be interpreted with caution because of the different assessment of the restrictive spirometric pattern, which was evaluated at a single point in time in the SARA study and prospectively in the TESAOD study. Not all subjects with the restrictive spirometric pattern at baseline will have a consistent restrictive spirometric pattern (the one that was used for comparison in the letter by Scarlata *et al*) over time. Actually, in TESAOD only one out of three such subjects did. The remaining two-thirds either had an inconsistent restrictive longitudinal pattern or developed airflow limitation at some point during the follow-up. Profiles of cause-specific mortality risk differed notably across these three longitudinal groups. For example, hazard ratios for mortality by cardiac disease were 2.0, 2.7 and 1.6, respectively.

We believe that the most novel contribution of our study does not lie in confirming the mortality risk associated with the cross-sectional restrictive spirometric pattern, but rather in assessing spirometric patterns prospectively, for two main reasons. First, our data indicate that up to 38% of subjects with a restrictive spirometric pattern at enrolment developed airflow limitation during the study follow-up. These subjects were more likely to be smokers, to have a physician-confirmed diagnosis of asthma at enrolment, and—unlike those with recurrent or inconsistent restrictive patterns—to die of COPD during follow-up. These results suggest that an underlying airway obstruction may be present in a significant proportion of cases with spirometric restriction assessed at a single time point, and this may explain the finding (apparently conflicting with ours) of an increased pulmonary mortality risk associated with spirometric restriction in the SARA study. Second, the prospective analyses of our study demonstrate that, among subjects who do not develop an obstructive pattern over time, both the recurrent and the inconsistent spirometric restriction increase all-cause mortality risk by a substantial magnitude.

Although what causes increased mortality in these groups remains to be determined, our findings do suggest that this pulmonary condition predisposes to (or at least is linked to) other extrapulmonary conditions such as cardiovascular disease and diabetes. Thus, these comorbidities may be in the causal pathway from spirometric restriction to mortality and we therefore elected not to include them among covariates in our Cox proportional hazards models. We definitely agree with Scarlata and colleagues that further research is required to understand the factors that are related aetiologically to spirometric restriction, the molecular mechanisms that drive its effects on all-cause and cause-specific mortality, and the possible implications of these findings for early identification of subjects at risk.

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