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EDITORIAL

Management of chronic obstructive pulmonary disease: are we going anywhere?

S. Rennard[+], M. Carrera*, A.G.N. Agustí*

The gold standard for a clinical intervention is the randomized controlled trial [1]. In contrast, evaluating a clinical outcome based on historical comparisons is fraught with numerous problems due to changes in a variety of factors including: a) diagnostic criteria and techniques; b) management of comorbid conditions; c) disease associated behaviours; and d) research methods, to name a few. As a result, conclusions based on historical comparisons are generally regarded as highly suspect. It is, nevertheless, important to view historical trends carefully as important lessons may be gleaned from such reviews.

In this context, review of the survival of patients with hypoxaemic chronic obstructive pulmonary disease (COPD) in a historical context is instructive. The now classic, Medical Research Council (MRC) oxygen trial conducted in the 1970′s provided clear evidence for the benefit of oxygen therapy in hypoxaemic patients with COPD who showed evidence of right sided heart failure [2]. The Nocturnal Oxygen Therapy Trial conducted at about the same time supported the notion that continuous oxygen was superior to nocturnal oxygen supplementation in hypoxaemic COPD patients who were not selected for evidence of right-sided heart failure [3]. Based on these trials, it would, at the present time, be regarded as unethical to perform a survival study in hypoxaemic COPD patients managed without oxygen support. Several subsequent studies, however, have been conducted which provide evidence for the survival of hypoxaemic COPD patients managed with oxygen support [4–6]. Interestingly, these studies seem to show a progressive improvement in survival with time (fig. 1).

As noted, there are several nonexclusive reasons, which could account for this trend. Patient selection may be an important one. Specifically, provision of oxygen therapy to individuals who were not as ill as those originally studied would result in an apparent improved survival due entirely to subject selection. These changes in subject selection may have been due to an aggressive change in diagnostic practice, for example implementation of percutaneous oximetry and increased case ascertainment. However, the raw comparison of several potential confounding variables determined at entry in the study (table 1) suggests that this was not the case. Alternatively, implementation of other therapies, for example aggressive use of bronchodilator treatment, pulmonary rehabilitation, *etc*. may account for improved survival. Likewise, survival may have changed with altered behaviour in the patient population, for example decreased cigarette smoking. Finally, management of comorbid conditions, *e.g.* cardiac disease may have contributed to improved survival. It is, nevertheless, of interest that COPD mortality appears to have improved over the past few decades (fig. 1) while survival for patients with lung cancer has changed relatively little despite their similar demographics [7].

While there are many questions raised by the trends in COPD mortality as discussed, there are also several lessons to be learnt. First, much of the thinking about COPD, particularly regarding its natural history, is based on historical studies. Probably, the natural history of the disease, at least with regard to survival, now differs from these historical studies. As advances are continued to be made in the understanding and management of COPD, it is essential not to be bound by the out-moded conclusions of older studies. Perhaps more importantly, credit needs to be taken for the advances achieved over the past few decades. The situation certainly appears to look better for the hypoxaemic COPD patient now than it did in the 1970s. As many clinicians will recognize, patients with COPD and overt *cor pulmonale* have almost disappeared from the

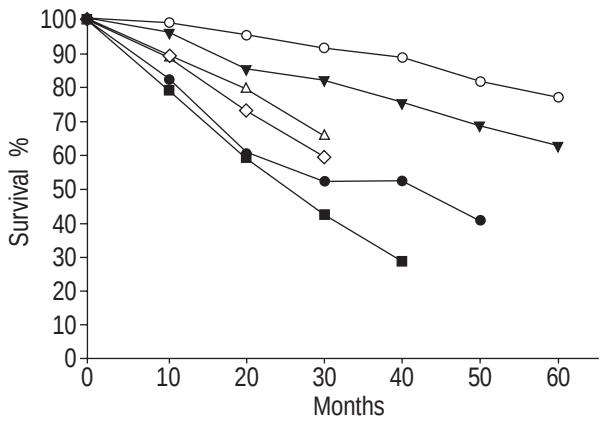

Fig. 1. – Survival of patients with chronic obstructive pulmonary disease and chronic respiratory failure treated with long-term oxygen therapy reported by several studies in the literature [2–6]. Note a trend towards increased survival in more recent studies. ○ : Carrera *et al*. [6] (with O_2) 1999; ▼ : Cooper *et al*. [4] (with O_2) 1987; △ : Nocturnal Oxygen Therapy Trial group [3] (with O_2) 1980; ◇ : Ström [5] (with O_2) 1983; ● : Medical Research Council [2] (with O_2) 1981; ■ : Medical Research Council [2] (without O_2) 1981.

[+]The University of Nebraska Medical Centre, Omaha, NE, USA. *Hospital Universitario Son Dureta, Palma de Mallorca, Spain.

Correspondence: A.G.N. Agustí, Servei Pneumologia, Hospital Universitario Son Dureta, Andrea Doria 55, 07014 Palma de Mallorca, Spain. Fax: 34 971175228

Table 1. – Comparison of potential confounding variables at entry in the studies included in figure 1

Reference	N	Age yrs	Sex % male	Follow-up yrs	FEV1	P_{a,O_2} mmHg	P_{a,CO_2} mmHg
MRC [2]	87	58	76	5	700 mL	50	54
NOTT [3]	203	65	79	3	29% ref	51	43
COOPER [4]	72	60	74	12	780 mL	43	48
STRÖM [5]	403	68	50	2.5	700 mL	50	49
CARRERA [6]	257	70	79	3	840 mL	53	48

FEV1: forced expiratory volume in one second; P_{a,O_2}: oxygen tension in arterial blood; P_{a,CO_2}: carbon dioxide tension in arterial blood. MRC: Medical Research Council; NOTT: Nocturnal Oxygen Therapy Trial.

hospitalization wards now. Whilst it may be hard to explain which portions of the current management contributes to this improved outlook and by what measure credit should be taken for these advances. Too many physicians and patients are complacent about the diagnosis and management of COPD based on the assumption that relatively little is effective. This prejudice may be complicated by the fact that many patients with COPD suffer from a self-inflicted chronic disease. It is particularly paradoxical that the approach to COPD is relatively passive when the historical record suggests that gains have been made in COPD management.

Without doubt, the current management of patients with COPD leaves much to be desired. Currently ongoing investigations hold much promise for improved therapy in the near and not so near future [8, 9]. These therapies, however, are most likely to be developed on a changing natural history of COPD. It is positive that these therapies will continue this historical trend and that, over the next few decades, the management of COPD will continue to improve.

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