Mastering breathlessness in patients with advanced respiratory disease

In The Lancet Respiratory Medicine, Irene Higginson and colleagues report the results of a randomised controlled trial of an early integrated breathlessness support service for patients with refractory breathlessness. They assessed mastery of breathlessness as the primary outcome, a composite score from four questions on feeling of control over the disease and its effects on quality of life and function. Mastery of breathlessness was improved in the intervention group at 6 weeks compared with the control group. By contrast, the authors reported no significant differences between intervention and control for all secondary outcomes including intensity of average breathlessness and breathlessness on exertion. The study reported improved outcomes for patients with chronic obstructive pulmonary disease and interstitial lung disease, but not for patients with cancer.

The study shows the benefits of early integration of palliative care in patients with advanced pulmonary diseases. Similar results have been published for patients with cancer and in a smaller trial from the same research group for patients with multiple sclerosis. All these studies have used straightforward interventions, with few palliative care consultations. Therefore, treatment costs were not increased with the palliative-care intervention, because staff costs for the intervention were probably balanced by a reduced number of expensive treatments after the palliative-care consultation.

The most astonishing outcome of the study was the improved survival in the intervention group. This is the first study reporting such a survival advantage with palliative care outside of studies of patients with cancer. This finding is similar to the study of Temel and colleagues, who noted a survival advantage of 3 months (11 months in the intervention group vs 8 months in the control group) with early palliative care for patients with lung cancer. However, in both studies survival was only a secondary endpoint, and the studies had not been designed to test for survival. In Higginson and colleagues’ study, the Kaplan-Meier estimates show an increased advantage in the intervention group even after the first 200 days, but at this time the control group had also received the breathlessness intervention, so the difference between groups should diminish rather than increase. This finding supports the idea that palliative care does not shorten life in comparison with more aggressive treatment options, and indeed that these aggressive treatment options might shorten the lifespan of patients with very advanced disease rather than extend it.

A second important part of this publication is related to the methodology in palliative-care research. The selection of breathlessness mastery instead of breathlessness intensity as the primary endpoint points at the ongoing discussion on outcome assessment in palliative-care research. In a systematic review we identified 528 different outcome assessment techniques, with most used only in one publication and few that were validated. Patient-reported outcome measurements are usually preferred as endpoints, but no consensus has been reached on which measurements should be used. The authors present good arguments why they selected mastery of breathlessness, but nevertheless, if the intensity of breathlessness is not improved, what does this mastery mean? Is the effect of the intervention more related to reduction of anxiety than to alleviation of breathlessness? Improved mastery might not be enough, if it does not lead to reduced levels of breathlessness.
Assessment of single symptoms can be difficult in patients undergoing palliative care, with pain, breathlessness, anxiety, fatigue, and depression influencing each other. Thus, comprehensive care assessments for research will need to use multi-dimensional techniques. However, these longer assessments can tax the cognitive and physical abilities of patients in palliative care. In the advanced stage of disease, patients might not be able to rate even straightforward assessments such as numerical single-item scales, and palliative care trials in these settings often have to resort to proxy ratings from caregivers or medical staff. Insistence on patient-reported measurements would mean that patients with reduced cognitive capacities such as patients in the final stage of life could not participate in trials, excluding this group of patients that need palliative care most from research into optimal symptom control. Even in Higginson and colleagues’ trial, selection bias cannot be excluded. In 2 years, 216 patients were identified as eligible according to a broad range of recruitment pathways. Many more patients with refractory breathlessness were probably treated in that period. Of the 216 patients, only 105 patients participated in the trial. This discrepancy might mean that the intervention is suitable for only a small subgroup of patients.

Despite these methodological considerations, the authors are to be praised for this controlled trial, providing evidence of the benefits of early integration of palliative care for patients with progressive non-cancerous lung disease. Other clinical trials on the early integration of palliative care are urgently needed that investigate survival rates as the primary endpoint.

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Microbial dysbiosis in bronchiectasis

Not so long ago we believed that the lower airway was sterile in health and, in a proportion of patients with chronic lung diseases, became colonised with potentially pathogenic microorganisms. This belief was clearly nonsense—the airways are open from the nose and mouth to the alveoli—yet it took the disruptive technology of 16S rRNA sequencing to confirm the presence of a healthy human lung microbiome.1 We now conceptualise a model in which alterations to this healthy microbiome, or microbial dysbiosis, are associated with disease, or with exacerbation of stable disease, across various respiratory disorders, including bronchiectasis.

This is the age of bronchiectasis. Long neglected, research is flourishing in this challenging and unpleasant condition, exemplified by the recent publication of landmark randomised controlled trials. One of these trials, BLESS,2 was one of three3–4 to report the benefit of long-term macrolides in the prevention of exacerbations of bronchiectasis. Although the mechanism might well not be antibacterial, at least in the traditional sense, long-term use of macrolides nevertheless represents a selection pressure on the lung microbiome.5 Thus far we have not seen substantive data about such effects, but a subsidiary analysis6 from BLESS reported by Geraint Rogers and colleagues in The Lancet Respiratory Medicine changes that, and makes for worrying reading.

The language of the microbiologist can be tricky, with data typically reported through changes in the Bray-Curtis dissimilarity index.7 Developed to assess...