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Exercise and cardiovascular benefit in subjects with COPD: the need for randomised trials

To the Editor:

We read with interest the work on arterial stiffness in patients with chronic obstructive pulmonary disease (COPD) and the potential role of pulmonary rehabilitation by VANFLETEREN *et al.* [1] in the *European Respiratory Journal*. Arterial stiffness, as assessed by aortic pulse wave velocity (PWV), is an independent predictor of cardiovascular outcome and may improve risk stratification in selected patient groups [2]. Furthermore, there is now firm evidence that aortic stiffness is increased in patients with COPD [3, 4], even in those without coexistent diabetes mellitus or overt cardiovascular disease. Increases in arterial stiffness have a number of deleterious nonatherosclerotic consequences including renal, cardiac and further vascular damage.

In addition to age, aortic PWV is affected by structural and functional components as well as the distending pressure: mean arterial blood pressure (MAP). There is accumulating evidence of a role for chronic inflammation [5] in both the functional and structural elements, and interventional anti-inflammatory trials have suggested improved aortic stiffness in other inflammatory conditions. In patients with COPD, several studies have shown associations of aortic stiffness with systemic inflammatory mediators [3, 6] and one determined increased vascular wall inflammation using positron emission tomography/computed tomography fluorodeoxyglucose imaging [7]. Anti-inflammatories may be one way to reduce aortic stiffness in COPD but others also need to be explored.

Numerous therapeutic strategies have been employed to attenuate the increased aortic PWV across many conditions, including pharmacological, nutritional and lifestyle modification, such as optimising exercise. Indeed, interpretation of many trials has proved problematical as many of the interventions, including exercise, have produced significant reductions in MAP [8].

It is against this background that two studies in subjects with COPD have shown significant reductions in aortic PWV with exercise and/or pulmonary rehabilitation [9, 10]. As expected, there were significant reductions in MAP that would largely account for the more modest reduction in aortic stiffness that, in its own right, would confer beneficial cardiological status to subjects. It is therefore very unexpected that the recent study by VANFLETEREN *et al.* [1] failed to produce any decrease in MAP despite a major aerobic component to the training. This may be attributed to the ability of the participants to maintain sufficient exercise intensity or confounders such as medications or timing of assessments. Furthermore, failure to

measure aortic PWV occurred in a large proportion of patients at baseline (n=51, 24%), which is not our or other groups' usual experience and may therefore have inadvertently generated bias.

There is a great deal of heterogeneity between the studies published to date in terms of type and duration of exercise intervention, the magnitude of improvements in the functional outcome measures, inclusion of those with or without established cardiovascular disease, and the arterial bed assessed (carotid–femoral *versus* carotid–brachial), all of which undoubtedly will have contributed to the conflicting results. In the past, a similar controversy regarding the benefits of exercise intervention after myocardial infarction was resolved by the use of well-designed randomised controlled trials, which should be considered before discarding the likely cardioprotective role of pulmonary rehabilitation and the strong public health message of exercise improving cardiorespiratory health.

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RCTs of #pulmrehab or #exercise in patients with #COPD are required to establish potential cardioprotective role http://ow.ly/tROVc

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From the authors:

We thank C.E. Bolton and colleagues for their interest in our report about arterial stiffness in patients with chronic obstructive pulmonary disease (COPD) [1]. Our paper has two major findings: 1) aortic pulse wave velocity (PWV) in COPD is not related to systemic inflammation; and 2) aortic PWV does not respond to pulmonary rehabilitation [1]. According to C.E. Bolton and colleagues, these findings are unexpected as two previous papers did report small, but significant reductions in aortic PWV with exercise and/or pulmonary rehabilitation [2, 3]. However, VIVODTZEV *et al.* [2] used carotid-brachial pulse wave velocity as an outcome of arterial stiffness, which is known to be more susceptible to modification by exercise training than central (aortic) elastic arteries [4]. GALE *et al.* [3] did use aortic PWV as an outcome of arterial stiffness and used similar methodology to our study. While GALE *et al.* [3] suggested that a reduction in mean arterial pressure accounted for the reduction in aortic PWV following rehabilitation in their sample of 22 patients with