More evidence for the importance of nutritional factors in chronic obstructive pulmonary disease\textsuperscript{1,2}

Raphaëlle Varraso and Carlos A Camargo Jr

Chronic obstructive pulmonary disease (COPD) is increasingly recognized as a major public health issue (1). Population studies that used spirometry showed an overall COPD prevalence of \(\sim 1\%\), increasing steeply to 8–10\% (or higher) among those aged \(\geq 40\) y (2). Already, COPD is the fourth most common cause of death worldwide and is likely to become the third most common by 2030 (3).

The predominant risk factor for COPD in the developed world is cigarette smoking, but up to one-third of COPD patients have never smoked (4), suggesting that other factors also are important. Diet probably is one of these factors, but data on the diet-COPD association remain scarce, particularly when compared with the enormous literature on the role of diet in other chronic diseases. Over the last decade, there has been growing interest in dietary factors with antioxidant or anti-inflammatory properties that might affect lung function or COPD symptoms (5). Most of these epidemiologic studies were cross-sectional, but a few longitudinal studies have reported favorable associations between specific dietary factors and a slower decline of lung function (5). We previously reported that a high intake of the Prudent dietary pattern decreased the risk of newly diagnosed COPD, whereas a high intake of the Western pattern increased risk (6, 7). We also reported that a high intake of cured meats was a risk factor for newly diagnosed COPD (8, 9), and that fiber intake appeared to reduce this risk (10).

With regard to the clinical course of COPD, particularly mortality, nutritional factors are important. For example, several reports have shown that low BMI is a major predictor of mortality among COPD patients from diverse clinical settings (11). Moreover, the poor prognosis for COPD patients with low BMI was confirmed from a study in the general population (12); mortality was higher among COPD patients with recent BMI loss, likely due to decreases in fat-free mass.

In view of these multiple links between nutritional factors and COPD, it should not surprise us that nutritional support may play an important role in COPD management. Although the benefits would seem intuitive, the literature actually is not supportive. A meta-analysis published in 2000 concluded that nutritional support was not linked to improvements in anthropometric measures or functional exercise capacity among patients with stable COPD (13). The latest Cochrane review, published in 2005, reported similar conclusions (14). Perhaps as a result of these highly visible negative reports, there have been relatively few recent trials on the impact of nutritional support on COPD.

In the systematic review in this issue of the Journal by Collins et al (15), the authors reanalyzed randomized trials of nutritional support in COPD patients to take into account their concerns about these earlier systematic reviews. Most important, the authors wanted to examine not only the differences between intervention and control groups at the end of intervention—as done previously—but also the changes induced by either intervention or control, and the impact of any baseline imbalances. The authors identified 13 trials of nutritional support in stable COPD patients with \(\geq 2\) wk of intervention and a control group that received placebo or no dietary intervention. From this subset of trials, they concluded that nutritional support, mainly in the form of oral nutritional supplements, had important beneficial effects on the quality of nutritional intake (energy and protein), body weight, muscle mass (midarm muscle circumference), and fat mass (skinfold thickness) of COPD patients. They also found that nutritional support caused significant improvement in peripheral muscle strength (handgrip strength) of COPD patients. These results contrast with earlier publications (13, 14) that were based on cross-sectional measures at the end of intervention trials. The authors believe that this methodologic difference explains the different conclusions of their review compared with the earlier ones. Although we are tempted to agree that nutritional support is valuable for COPD, one has to wonder about meta-analyses that differ so much in the studies found worthy of inclusion. We suspect that resolution of this controversy will require additional trials that specifically test the authors’ hypothesis by performing the main analyses using both approaches. Given the many links between nutritional factors and COPD, we believe that nutritional support will be shown to benefit at least some COPD patients. If we can draw any firm conclusions from the current debate, it is that there is no one perfect trial—nor one perfect meta-analysis.

Looking forward, we anticipate that future studies will focus on the inflammatory state that frequently accompanies COPD (16).

\textsuperscript{1}From INSERM, CESP Centre for Research in Epidemiology and Population Health, U1018, Respiratory and Environmental Epidemiology Team, and Université Paris Sud 11, UMRS 1018, Villejuif, France (RV), and the Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA (CAC).

\textsuperscript{2}Address correspondence to CA Camargo, Massachusetts General Hospital, 326 Cambridge Street, Suite 410, Boston, MA 02114. E-mail: ccamargo@partners.org.

First published online May 2, 2012; doi: 10.3945/ajcn.112.039834.
Will the impact of any nutritional interventions differ according to inflammatory status? This possibility is largely unknown, but if there is effect modification, that also should encourage us to reconsider the meaning of null trials of yesteryear. We also support efforts to move beyond total energy intake by further exploring the impact of supplementation with specific nutrients of particular interest for COPD. For example, an 8-wk randomized, double-blind, placebo-controlled trial of PUFA supplementation increased the functional capacity of COPD patients, as shown by improvements in peak exercise capacity and submaximal endurance (17). More recently, there has been strong interest in whether vitamin D deficiency may be a risk factor for the development and clinical course of COPD (18, 19). Although etiologic data remain limited, there is one published study that found that vitamin D supplementation of 100,000 IU/mo for 1 y did not significantly reduce the number of acute exacerbations of COPD, nor improve lung function, compared with placebo (20). However, a post hoc analysis suggested that supplementation may have reduced the risk of COPD exacerbations in the most deficient patients (ie, those with serum 25-hydroxyvitamin D concentrations <10 ng/mL). Because these concentrations are relatively common in COPD patients without regular sun exposure, the impact of vitamin D supplementation merits further study.

In sum, nutritional support in COPD is a surprisingly controversial area of research. Besides the methodologic challenges related to the meta-analysis of these trials, there is a clear need for additional studies of how nutritional factors modify the clinical course of COPD. These studies need to better account for the interrelations of diet, body composition, physical activity, and low-grade systemic inflammation. Future research might also focus on diet as a modifiable risk factor for the development of COPD. Although smoking cessation should remain the focus of primary prevention efforts, dietary interventions may offer a helpful adjunct to the prevention of this major public health problem.

Neither of the authors had a conflict of interest to disclose.

REFERENCES