Diet in COPD

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Chronic obstructive pulmonary disease is one of the leading causes of morbidity and mortality worldwide and a growing healthcare problem. Several dietary options can be considered in terms of COPD prevention and/or progression. Although definitive data are lacking, the available scientific evidence indicates that some foods and nutrients, especially those nutraceuticals endowed with antioxidant and anti-inflammatory properties and when consumed in combinations in the form of balanced dietary patterns, are associated with better pulmonary function, less lung function decline, and reduced risk of COPD.

antioxidant
chronic obstructive pulmonary disease
dietary pattern
inflammation
lung function
Mediterranean diet
nutrition
oxidative stress
polyphenol
polyunsaturated fatty acid

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality and healthcare burden worldwide, affecting around 10% of the adult populations aged 40 years and older [1]. According to WHO estimates mainly from high-income countries, 65 million people have moderate to severe COPD, but a great proportion of COPD worldwide may be underdiagnosed, mostly in low- and middle-income countries. COPD burden is projected to dramatically increase due to chronic exposure to risk factors and the changing age structure of the world population and is expected to be the third leading cause of death worldwide by 2030 (WHO 2019. Burden of COPD https://www.who.int/respiratory/copd/burden/en). Therefore, prevention and management of COPD is currently considered a major health problem, with important social and economic issues.

COPD encompasses a group of disorders, including small airway obstruction, emphysema, and chronic bronchitis, and is characterized by chronic inflammation of the airways and lung parenchyma with progressive and irreversible airflow limitation [2]. Symptoms of COPD include dyspnea (distress with breathing), cough, and sputum production. The natural history of COPD is punctuated by recurrent episodes of acute exacerbations, which often require hospitalization and negatively affect patients' quality of life, accelerate the rate of decline in lung function, and are associated with mortality.

Diagnosis, assessment, and management of COPD are mostly guided by the degree of airflow limitation as assessed by the forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio, although other physiological measurements such as the inspiratory capacity to total lung capacity (TLC) ratio, arterial blood gases, and exercise capacity provide complementary information on the severity of the disease [3]. To account for the complexity of the disease and aiding in disease severity assessment, multidimensional indices mainly based on clinical and functional parameters have been developed. However, significant heterogeneity in terms of clinical presentation, physiology, imaging, response to therapy, lung function decline, and survival exists in COPD, challenging the oversimplification regarding definition and assessment of COPD and leading to effort in identifying subgroups of patients called phenotypes, resulting from different endotypes (biologic mechanisms) and displaying distinct prognostic and therapeutic value. Accordingly, several COPD phenotypes have been recently described, which exhibit significant differences in age, symptoms, co-morbidities, and predicted mortality [4][5][6][7]. Most studies described COPD heterogeneity using a limited range of variables, and in some cases the clinical relevance of identified phenotypes needs to be determined [8]. Despite these current limitations, the phenotypic characterization of COPD patients with insight into the underlying biological processes and related biomarkers may ultimately allow for a better risk stratification and personalization of therapies [9].

The predominant risk factor for COPD development is former or current tobacco smoking. However, not all smokers develop COPD, suggesting that other environmental factors are also involved, including outdoor and indoor air pollution (e.g., biomass fuel exposure), occupational hazards, infections, and second-hand smoke during pregnancy or early childhood. Furthermore, genetic susceptibility (e.g., deficiency in α1-antitrypsin) and epigenetic influences have also been implicated in the pathogenesis of COPD [10]. Recent new insights suggest that these different factors may impinge on lung function and reciprocally interact starting early in life (i.e., in utero and during early childhood), thus determining many potential trajectories of the natural course of the disease, which ultimately predispose to the development of COPD and its different clinical appearances as well as of other coexisting chronic diseases in later life [10][11].

With regard to COPD management, the most important public health message remains smoking cessation, but the multifactorial nature of COPD requires attention to other modifiable risk factors. Compared with other chronic diseases with similar burdens on quality of life and healthcare costs, such as cancer and cardiovascular disease (CVD), less is known about how lifestyle factors other than—and independent of—smoking influence pulmonary function and the development of COPD. Diet has been recognized as a modifiable risk factor for chronic diseases development and progression [12], and recent evidence has also increasingly pointed to a role in obstructive lung diseases, including COPD [13][14][15]. Importantly, changes in diet over the past few decades, with decreased consumption of fruits, vegetables, wholegrains, and fish, and increased consumption of processed and refined foods, have been invocated to contribute to the increased prevalence of chronic diseases, including COPD, mainly in developing countries.

Dietary factors may modulate the impact of adverse environmental exposures or genetic predisposition on the lung [16] but can also have direct (protective or harmful) effects on the biological processes involved in lung function, disease development, and outcomes [17][18]. The impact exerted by early-life and cumulative dietary choices on later-life health has been increasingly recognized for respiratory diseases, thus offering a greater window of opportunity for disease prevention [19]. Furthermore, the abnormal nutritional status observed in advanced COPD patients, with unintended weight loss, muscle loss, low fat, and fat-free mass associated with the presence of emphysema is a recognized independent determinant of COPD outcomes and provides targets for nutritional interventions [20]. On the other hand, although the phenomenon of the obesity paradox, i.e., the prognostic advantage of increased body mass index (BMI) in COPD (due to the reduction in static volume), has been reported, the role of abdominal visceral adiposity compared with subcutaneous fat in exacerbating the pro-inflammatory state and the CV risk in patients with COPD deserves clinical attention and treatment [21], mostly because a fat redistribution toward more visceral fat and an associated increased systemic inflammatory status have been shown in mild-to-moderate nonobese patients with COPD compared to control subjects [21].

Therefore, improved understanding of dietary impact on prevention and/or outcomes of COPD may increase scientific and clinical awareness about the importance of nutritional approaches as well as provide directions for future research and strategies to promote lung health and prevent disease onset and progression.

There is an expanding literature on the topic regarding diet–COPD relation. A literature search performed with the PubMed database to identify papers with the following terms “diet” and “chronic obstructive pulmonary disease risk” retrieved 233 manuscripts (from 1989 to 2019). The resulted manuscripts were analyzed using the bio-informatic data analysis tool VOSviewer [22], which extracts and analyzes the words in the titles and abstracts of the publications, relates them to citation counts, and visualizes the results as a bubble or term map, based on the strength of the co-occurrence links within the terms. The terms with greatest total link strength were selected and highlighted as bubbles. The analysis returned 750 words, of which 127 met the threshold levels (minimum number of occurrence of a term = 5). As shown in **Figure 1**, diet has been the focus of relevant scientific attention, and several of the words retrieved from the analysis were connected to diet, feeding behaviors, and specific foods and nutrients (fruits and vegetables, antioxidants, unsaturated fatty acids, meat products), suggesting some of the main key research categories that have been the attention focus in the topic diet and COPD risk.

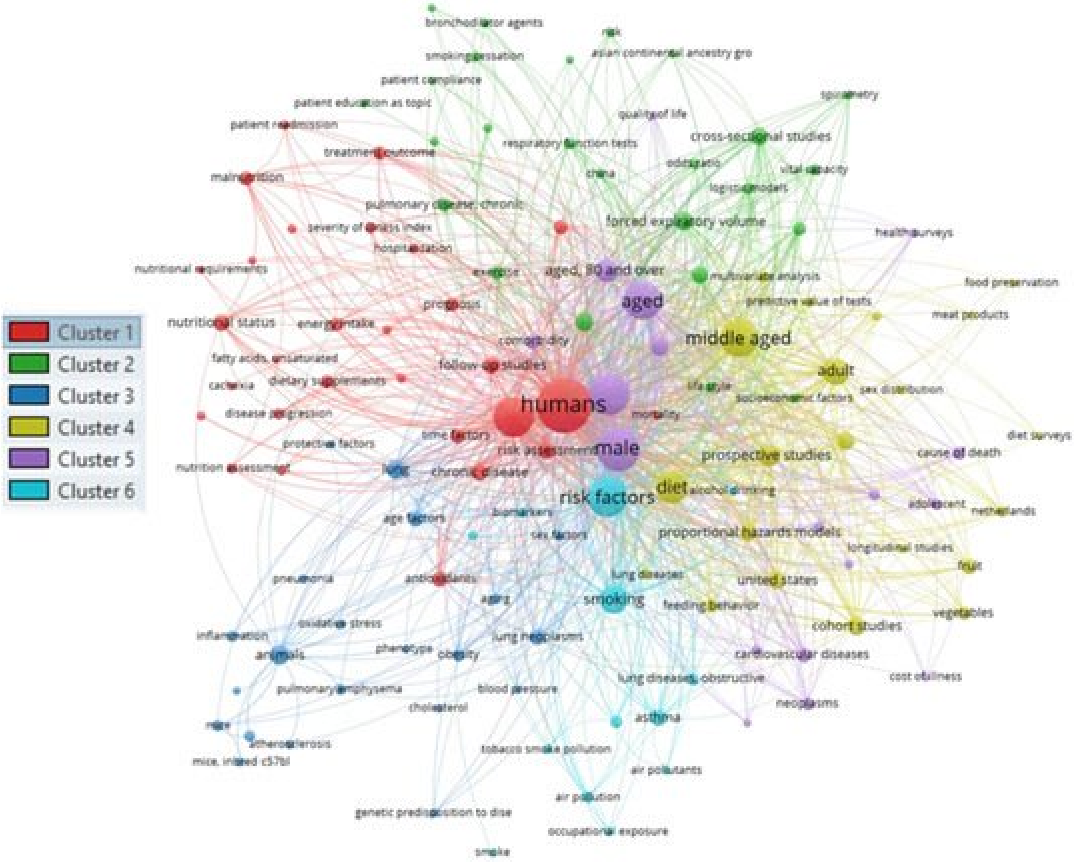

Figure 1. The bubble map visualizes 127 keywords extracted from published papers retrieved in PubMed under the search terms “diet” and “chronic obstructive pulmonary disease risk” between 1989 and 2019. Bubble size indicates the frequency of occurrence of the words, while bubble color represents the cluster of belonging. Words are clustered based on direct citation relations; thus, each cluster corresponds to a set of closely related words. Two bubbles are in closer proximity if the two words had more frequent co-occurrence.

2. Pathophysiological Aspects in COPD

Several pathogenic processes are thought to be involved in COPD development and progression, including local and systemic oxidative stress (i.e., oxidants in excess compared with antioxidant capacity) and inflammation (neutrophils, macrophages, eosinophils, cytokines, chemokines, eicosanoids, Toll-like receptors, acute phase proteins), procatabolic status, protease/antiprotease imbalance, alteration of immune responses and cell proliferation, apoptosis, and cellular senescence, and remodeling of the small-airway compartment and loss of elastic recoil by emphysematous destruction of parenchyma [2]. Oxidative stress may directly cause lung damage through modification of DNA, lipids or proteins, as well as initiate cellular responses that can drive the inflammatory response within the lung, leading to lung tissue degradation (emphysema). Molecular switches triggering inflammatory responses in COPD involve the activation of redox-sensitive transcription factors (e.g., nuclear factor (NF)-κB), induction of autophagy, and unfolded protein response [23]. In particular, NF-κB plays a crucial role in the chronic inflammatory responses found in COPD, regulating the expression of genes for pro-inflammatory mediators (e.g., IL-1, IL-6, IL-8, MCP-1, TNF-α) and chemotactic factors (e.g., IL-17A and MIP-1a) involved in triggering lung infiltration by inflammatory cells, thus amplifying oxidative stress and inflammation, as well as causing emphysema, fibrosis of small airways and remodeling of airway walls, ultimately impairing lung function. Indeed, the number of NF-κB-positive epithelial cells and macrophages increased in smokers and COPD patients and correlated with the degree of airflow limitation [24].

Although primarily affecting the lungs, COPD is associated with extra-pulmonary (systemic) manifestations such as weight loss, malnutrition, and skeletal muscle dysfunction, which contribute to the morbidity, reduced quality of life, and, possibly, mortality of this disease. Furthermore, other chronic diseases (also called co-morbidities), including CVD and especially coronary artery disease (CAD), osteoporosis, metabolic syndrome, depression, and lung cancer, among others, are highly prevalent in patients with COPD, can be considered part of the nonpulmonary sequelae of the disease, with the low-grade systemic inflammation playing a decisive role in their pathogenesis, and importantly contribute to worsening health status and vital prognosis of COPD patients. In particular, CV-related co-morbidities are the leading cause of morbidity and mortality in patients with COPD, sharing various risk factors and pathophysiological aspects (inflammation-associated oxidative stress) [25]. Reduced lung function is a marker for all-cause, respiratory- and CV-related mortality [26], thus representing a clinically relevant therapeutic target for preventing the development of COPD and its life-threatening complications.

3. Epidemiological Studies on Diet and Pulmonary Function: Some Methodological Issues

The methodological approaches used and the specific challenges of nutrition research should be taken into consideration when evaluating single study findings and, most importantly, their potential contribution to evidence-based recommendations. Apart from a few randomized intervention trials, most of the available evidence on the impact of diet on outcomes, such as lung function (FEV1, FVC, FEV1/FVC), symptoms, incidence, prevalence or severity of COPD, and its progression over time, largely comes from observational studies, either cross-sectional or, to a lesser extent, longitudinally in both the general population and at-risk or diseased subjects. The strength of some studies is the use of objective measures of lung function that limit the bias arising from self-reported or physician-diagnosed disease: Post-bronchodilator spirometry is the gold standard for the diagnosis of COPD, minimizing misclassification.

Assessment of dietary intake usually included a 24 h recall and food-frequency questionnaire, both with inherent limitations, including the poor measurement of usual intake due to daily variation in food intake (mostly for 24 h recall), the semiquantitative nature of the assessment, the measurement error, the variation in diet definitions, and the lack of generalizability of study findings among different populations [12]. To estimate the independent association of diet with lung function and COPD, in most studies, the confounding bias is tackled by performing the adjustment for multiple confounding factors known to influence pulmonary function or dietary behavior, including age, gender, BMI, physical activity, intake of other foods or nutrients, energy intake, educational level, and most importantly, tobacco exposure. Sex differences in susceptibility to COPD have been increasingly recognized, with evidence that women are at a greater risk of smoking-induced lung function impairment [27] and poorer health status for the same level of tobacco exposure compared to men [28], and that gender differences may also extend to different food choices [29]. Furthermore, the increased tobacco use recently registered in women likely contributes to the epidemic of COPD in women and influences interpretation of study results. Notably, smokers tend to follow an unhealthy diet compared to ex-smokers [30] and have a higher level of oxidative stress, which is targetable by diet. Moreover, a healthy diet may be associated with other beneficial lifestyles (e.g., higher level of physical activity, higher education, lower BMI, less smoking). Even after adjustment, residual confounding of dietary associations still remains possible and contributes to some inconsistencies across studies.

4. Oxidant–Antioxidant Imbalance and Diet Quality in COPD

Oxidative stress and associated inflammation in the lung and in the circulation in response to exposure to air pollution, tobacco smoke, infection, or potentially obesity are leading pathogenic processes in COPD. Compared to healthy controls, patients with COPD tend to have increased systemic and airway oxidative damage markers (relative to DNA, lipid, and proteins) [31], coupled to altered antioxidant defense, as evidenced by marked reduction in both plasma antioxidant capacity and soluble and enzymatic antioxidants levels [31][32][33]. Moreover, oxidative stress persists long after smoking cessation as a result of continuous production of pro-oxidants [34]. Low serum antioxidant vitamin levels appeared to increase the risk of obstructive airways diseases associated to smoking exposure [35]. In accordance, higher levels of oxidative markers in COPD were correlated with decreased lung function [36][37][38], while higher serum levels of antioxidant enzymes (catalase, superoxide dismutase, glutathione peroxidase) [37][38], as well as of soluble antioxidants (vitamins, carotenoids, etc.) [32][39][40], were positively associated with lung function. Therefore, it can be hypothesized that targeting oxidative stress with antioxidants or boosting endogenous levels of antioxidants might be beneficial in COPD.

Diet may contribute to antioxidant/oxidant and inflammatory status in COPD. Compared to healthy controls, COPD subjects have diets with lower fruit and vegetable intake [41] and with poorer antioxidant content, which was correlated with impaired lung function and risk of having COPD [32][33]. Moreover, lower energy intake (accompanied by elevated resting energy expenditure), unbalanced intake of macronutrients (e.g., low proteins), and defective intake of several micronutrients (minerals and vitamins, e.g., iron, calcium, potassium, zinc, folate, vitamin B6, retinol, niacin) have been documented in COPD patients compared to healthy controls [42], mostly in the presence of obesity [43], suggesting an increased risk of malnutrition and related adverse consequences in COPD.

The poor diet quality and the nutrient deficiencies in COPD, which are related to disease-specific factors such as symptoms (e.g., dyspnea, fatigue, anxiety, depression, anorexia, periodontal disease, loss of taste, poor dentition, dysphagia, poor chewing and swallowing ability) or social problems (e.g., living or eating alone, or poverty) [44], require improvement through dietary intervention to satisfy nutritional requirements and even to supplement further protective factors able to counteract disease pathogenesis. The inflammatory/oxidative status in COPD and the associated procatabolic state contributing to weight loss and muscle wasting in severe COPD represent further possible targets for nutritional intervention.

5. Individual Foods and Nutrients, Lung Function, and COPD

5.1. Role of Antioxidant and Anti-Inflammatory Foods: Fruits and Vegetables

The dietary quality and the nutritional status of COPD patients as well as the oxidative–inflammatory pathogenic basis of COPD provided the rationale to verify the respiratory effects of antioxidant and anti-inflammatory dietary components. Consistent epidemiologic evidence from cross-sectional [33][35][45][46][47][48] and longitudinal studies [39][49][50][51][52] reported potential beneficial effects of a high intake of antioxidant nutrients (vitamins and nonvitamins) and of foods rich in antioxidants, mostly fresh, hard fruits and, to a lesser extent, vegetables, on lung function and COPD symptoms [32][33][46][47][48], decline in lung function [39][46][53], incidence of COPD [49][51][52], and mortality [50].

5.2. Vitamin and Nonvitamin Antioxidants

Plausible mechanisms underlying fruit and vegetable protective effects include their antioxidant and anti-inflammatory activities, as suggested by the epidemiologic association observed between fruit and vegetable consumption and lower markers of oxidative stress and inflammation, and higher levels of antioxidant markers [54][55]. Fruits' and vegetables' beneficial effects on respiratory function may be partially contributed by their high content in vitamin and nonvitamin antioxidants. Accordingly, higher dietary intakes of vitamin C, a hydrophilic antioxidant, were associated with higher levels of FEV1 [32][56] and with a lower rate of decline in FEV1 after a 9-year follow-up period [56]. Other studies did not confirm a significant effect of vitamin C dietary intake on lung function (FEV1), its longitudinal decline [46], COPD incidence [49] or mortality [50]. Although not consistently [56], a protective role has also been credited to other vitamins such as vitamin E or tocopherol, a lipid soluble antioxidant acting in synergy with vitamin C and able of breaking lipid peroxidation chain reaction and protecting the lung against oxidative damage [33][50]. Lower serum vitamin E levels have been observed in COPD during exacerbation compared to stable condition [57]. Randomized trials of vitamin E supplementation in clinical populations have, however, reported mixed results, including both protective [58] and no effects [59] on the risk of developing COPD.

5.3. Minerals

Among micronutrients, cross-sectional studies have found deficient intake of some minerals in COPD patients. Indeed, dietary intakes and serum levels of calcium, magnesium, and selenium were found to be below the recommended values in older, underweight patients with severe COPD [60]. Lower intakes of calcium and zinc were observed in elderly COPD patients compared with non-COPD subjects [42]. Some minerals have been studied in relation to lung function and COPD risk and symptoms. A case-control study in Japanese adults found a positive association between intake of calcium, phosphorus, iron, potassium, and selenium and lung function measures (e.g., FEV1), and an inverse association between dietary calcium intake and COPD risk (35% reduction) [61]. FEV1 was independently and positively associated with serum levels of selenium, normalized calcium, chloride, and iron, and was inversely related to potassium and sodium in the general population [40]. Other cross-sectional studies confirmed the association between serum levels of selenium as well as copper and higher lung function [62]. A randomized placebo-controlled trial reported that selenium supplementation (200 µg/d L-selenomethionine), either alone or in combination with vitamin E (400 IU/d all rac-α-tocopheryl acetate), did not affect decline in FEV1 or

FEF25–75, a marker of airflow, but attenuated decline in FEF25–75 (by 59 mL/second/year) in current smokers, who may benefit most from selenium supplementation due to its potent antioxidant properties linked to the glutathione peroxidase activity [63].

5.4. Wholegrains and Fibers

Among dietary factors largely investigated, mostly in relation to CVD and cancer, research has also focused on wholegrains. Observational studies reported an independent beneficial effect of a high wholegrain intake on lung function [48][64], and against mortality from chronic respiratory disease [65]. Wholegrains are rich in phenolic acids, flavonoids, phytic acid, vitamin E, selenium, and essential fatty acids, which may additively or synergistically contribute to wholegrain documented beneficial effect on respiratory as well as nonrespiratory diseases.

Part of the protective action of wholegrains as well as of fruits and vegetables is attributable to the antioxidant and anti-inflammatory properties of their fiber content [66]. Indeed, epidemiological data indicated that fiber intake is associated with lower serum levels of C-reactive protein and cytokines (IL-6, TNF-α) and higher level of adiponectin, an insulin-sensitizing adipocytokine with anti-inflammatory properties [67]. In line with these beneficial properties, cross-sectional and longitudinal studies found a negative and independent association between total fiber intake and lung function decline, and COPD incidence and prevalence [68][69][70]. Indeed, higher dietary intake of total fiber reduced by about 40% the risk of COPD in large prospective studies [69][70]. Considering fiber types (cereal, fruit, vegetable), the beneficial association was observed mostly for cereal fiber intake mainly in current smokers and ex-smokers, but evidence exists also for fruit and vegetable fiber intake [69][70].

5.5. Alcohol and Wine

Other significant associations with respiratory health have been documented in the general population for intake of alcohol and wine. Previous epidemiologic studies found that subjects with low alcohol consumption (1–30 g/day) had higher levels of FEV1, lower prevalence of COPD symptoms [48], and a decreased risk of COPD compared to nonconsumers [49]. By contrast, heavy alcohol intake, as assessed by both dietary and serum biomarker measurements, was shown to have negative effects on lung function, additive to that of smoking [71]. Among the different alcohol sources, only wine intake (>7.4 g/day) was found to be positively associated with FEV1 in the general population [72], as well as with a lower risk of airway obstruction, defined as an abnormally low FEV1/FVC ratio, predominantly in smokers [73]. Beyond direct protective effects of alcohol as previously reported [74], putative candidates accounting for the observed beneficial effect of wine are flavonoids [47], as well as the stilbene resveratrol [73], both associated with improved measures of lung function. Congruently, resveratrol has been reported to exert anti-inflammatory properties in airway epithelial cells [75], alveolar macrophages derived from COPD patients [76], and airways smooth muscle cells [77], and the flavonol quercetin has been shown to attenuate rhinovirus-induced lung inflammation and emphysema progression in a mice model of COPD [78].

Interestingly, the independent beneficial effects of a favorable intake of fruits (>180 g/day), wholegrains (>45 g/day), and alcohol (1–30 g/day) on FEV1 and COPD symptoms were additive (favorable vs. unfavorable intake, 139 mL higher FEV1 and COPD symptoms prevalence OR = 0.44, $p < 0.001$) [48], suggesting important interaction among nutrients and food groups. Moreover, findings from the ECLIPSE study in COPD subjects demonstrated that recent consumption of “healthy” foods, such as fruits (grapefruit and bananas), fish, tea, dairy products, and alcohol, was associated with higher lung function and less decline over time, less emphysema and emphysema progression, greater 6-minute walk and St. George’s Respiratory Questionnaire (SGRQ) scores, and lower levels of inflammatory markers (C-reactive protein, white blood cells, surfactant protein D, total neutrophils) [79]. These data extend the role for dietary intakes to phenotypic features of COPD patients.

5.6. Vitamin D

Limited evidence also supports a direct correlation between vitamin D levels, which mainly depend on sun exposure in addition to diet, and lung function, COPD incidence, symptoms, severity and progression [80][81][82]. Genetic variants in the vitamin D-binding protein associated with lower plasma vitamin D levels have also been linked to COPD risk [83]. Mechanistic studies support a role for vitamin D other than calcemic effects and in particular in normal growth and development of the lung as well as in immune responses and COPD progression. Vitamin D supplementation trials to prevent COPD exacerbation reported conflicting results but, collectively, pointed to a benefit only in patients with low baseline vitamin D levels (i.e., levels of active metabolite 25-hydroxyvitamin D <25 nmol/L) [84]. Although further studies are needed, taking into account the highly prevalent osteoporosis and risk of falls in COPD patients and also the supposed beneficial effects of vitamin D beyond bone health, screening for vitamin D deficiency (25-hydroxyvitamin D <50 nmol/L) may be important in COPD patients.

5.7. Coffee and Its Components

Given its widespread consumption, interest has been growing around the potential role of coffee in respiratory health. Findings from literature reviews point to an association between regular (not decaffeinated) coffee intake and improved lung function and reduced mortality from respiratory disease, but not COPD [85], with contributory roles for its constituents, caffeine (bronchodilator, anti-inflammatory) and polyphenols (antioxidant, anti-inflammatory). Smoking is a major confounder in these studies because it may accelerate the hepatic metabolism and clearance of caffeine or may dilute or dampen the beneficial effects of coffee through its potent pro-oxidant and pro-inflammatory action [85].

5.8. Role of Fish and n-3 Polyunsaturated Fatty Acids

α-Linolenic acid (ALA, C18:3) and its long-chain derivatives eicosapentaenoic acid (EPA, C20:5) and docosahexaenoic acid (DHA, C22:6) are polyunsaturated fatty acids (PUFA) of the *n-3* (omega-3) family. Due to the low efficiency of endogenous synthesis from precursors, they are considered nutritionally essential and depend on exogenous source, mainly seafood (fatty fish). *n*-3 PUFAs and fish display potent anti-inflammatory properties with beneficial effects and, in most cases, clinical applications in several chronic inflammatory diseases, including CVD, cancer, rheumatoid arthritis, and diabetes [86]. Opposite effects have been described for *n*-6 PUFAs, including linoleic acid (LA, C18:2) and its long-chain derivative arachidonic acid (AA, C20:4), mainly found in vegetable oils (soybean, corn, and sunflower oils), grain-fed animals, dairy, and eggs. Indeed, metabolism of long-chain *n-6* PUFA produces eicosanoids (such as thromboxane(TX) A2, prostaglandin(PG) E2 and leukotriene(LT) B4) which are more potent mediators of inflammation, thrombosis, and vaso- and bronco-constriction than similar products derived from *n*-3 PUFAs (PGs of the 3-series and LTs of the 5-series) [87]. Some EPA and DHA metabolites via cytochrome P450 enzymes, which are highly expressed in the lungs, are potent vasodilators and bronchodilators and show anti-inflammatory properties. Other metabolites of long-chain *n*-3 PUFAs include the inflammation-resolving eicosanoids resolvins and protectins, which act to remove inflammatory mediators and promote healing.

5.9. Foods with Potential Deleterious Effects on Lung Function and COPD

Among potential deleterious foods, a statistically significant inverse association between frequent consumption of cured (bacon, hot dogs, and processed meats) and red meats and pulmonary function has been reported, in agreement with evidence of detrimental effects in other nonrespiratory diseases, including CAD, diabetes, and cancer [88][89], and all-cause mortality [90]. Increased intake of cured meats was independently associated with an obstructive pattern of spirometry in a cross-sectional analysis in the third National Health and Nutrition Examination Survey [91] and with an increased risk of newly diagnosed COPD in both men and women in US prospective cohorts, independent of Western dietary pattern (highly loaded with red meat) or other associated dietary intakes (refined grains, desserts, etc.) [92][93]. Importantly, more recent large Swedish population-based prospective studies confirmed this detrimental effect for both baseline and long-term consumption of processed (not unprocessed) red meat [94][95]. Another study found that cured meat intake increased the risk of COPD readmission [96]. Collectively, as summarized in a recent meta-analysis, available evidence indicated a 40% increased risk of COPD with higher consumption of processed red meat (>75–785.5 g/week) [97].

These data suggest that health-promoting activities should include specific advice on lowering red/processed meat consumption. It would be important to confirm these results in those populations experiencing nutrition transition with an increased consumption of Westernized foods, including processed meats.

In addition to the high content in cholesterol and saturated fatty acids, drawbacks of processed red meat include the presence of nitrites, which are added to processed meat during the manufacturing process as a preservative, antimicrobial, and color fixative. Nitrites generate reactive nitrogen species, such as peroxynitrite, with the subsequent nitrosative stress that can contribute to, and amplify, inflammatory processes in the airways and lung parenchyma, causing DNA damage, inhibition of mitochondrial respiration, and cell dysfunction. Moreover, tyrosine nitration in connective tissue proteins, including collagen and elastin, can alter their function. Higher levels of nitrotyrosine have been observed in subjects with COPD and were correlated to disease severity [98]. Accordingly, in animal models, chronic exposure to nitrite caused emphysema-like pathological changes in the lungs [99]. Nitrites are also byproducts of tobacco smoke; thus, nitrite generation may be one of the mechanisms by which tobacco smoke causes COPD. Congruently, the combination of smoking and higher cured meat consumption is indeed associated with the highest risk of newly diagnosed COPD [93]. Cured meats also contain a high amount of sodium that may increase bronchial hyper-reactivity and may elicit inflammation [100]. Sodium dietary intake has been reported to be higher in COPD patients compared to healthy controls and to be associated with lower lung function [61].

Meat is also an important source of saturated fatty acids (SFAs), which can trigger inflammation, also in the airways [101], and have been associated with both impaired lung function [102] and an elevated risk of coronary heart disease and metabolic diseases [103]. This risk seems to be mainly attributable to medium and long chain SFAs (C14:0–C18:0) highly present in meat compared to other animal sources such as dairy products. By contrast, increased intake of low-fat dairy products [104] as well as of short and medium chain SFAs, as assessed by 24 h recall [105], may exert protective effects on lung function, possibly through their anti-inflammatory action.

An important feature of the Western lifestyle and diet is the consumption of foods with high glycemic index, such as refined grains, desserts, sweets, and sweetened beverages. In addition to increasing the risk of obesity, hyperglycemia may trigger oxidative stress-related inflammatory responses [106], is associated with impaired lung function [107] and poor COPD outcomes [108], and may promote pulmonary infection, at least in part, by an effect on airway glucose concentrations [109]. Part of the detrimental effects of hyperglycemia is mediated by the formation of advanced glycation end-products (AGEs), which are elevated in lung tissues of COPD patients and are known to be associated with lung inflammation and pathophysiology [110]. Compared to no consumption, high levels of soft drink consumption (>0.5 L/day, sweetened or not), an important component of the Western lifestyle and diet, were associated with a higher prevalence of COPD (OR = 1.79, 95% CI: 1.32, 2.43, $p < 0.001$) and asthma (OR = 1.26, 95% CI: 1.01, 1.58, $p = 0.014$), in an additive manner with smoking [111]. Moreover, consumption of excess fructose-sweetened soft drink (>5 times/week) was significantly correlated to chronic bronchitis in US adults (OR = 1.80, 95% CI: 1.01, 3.20, $p = 0.047$) [112], as well as to pediatric asthma [113], possibly due to the formation of AGEs from the interaction between unabsorbed free fructose and dietary proteins in the gastrointestinal tract. These results clearly emphasize the public health implication of interventions targeting modern unhealthy lifestyle habits.

6. Dietary Patterns, Lung Function, and COPD

Dietary patterns have been widely investigated in relation to cancer, CVD or diabetes [12], but limited data are available on their association with respiratory outcomes with relevance to COPD. As shown in a recent meta-analysis [14], most studies were performed in Europe and North America, limiting the generalizability of study findings, and were observational in design. Overall, the evidence concordantly indicated that the pattern of dietary intake is an important factor in the pathogenesis and prevention of COPD and provided support for specific dietary modifications as a clinically relevant tool to promote lung health. Moreover, examination of dietary patterns complements the evaluation of the effects of individual food and nutrient intake on COPD. **Table 1** summarizes findings from main epidemiological studies addressing the relation between diet and lung function, COPD risk, symptoms, and progression.

Table 1. Main findings from epidemiological studies linking dietary patterns to adult lung function and chronic obstructive pulmonary disease (COPD) (incidence, prevalence, and severity).

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
Data-driven dietary patterns									
Meat–dim sum pattern and vegetable–fruit–soy pattern	China (SCHS)	P (5.3 year)	General population *n* = 52,325	F, M (45–74 year)	FFQ and PCA	New onset of cough with phlegm	Self-reported	The meat-dim sum pattern was associated with increased incidence of cough with phlegm (fourth vs. first quartile, OR = 1.43, 95% CI: 1.08, 1.89, *p* for trend = 0.02))	[114]
Prudent pattern and Western pattern	USA (HPFS)	P (12 year)	Health professionals *n* = 42,917	M (40–75 year)	FFQ and PCA	COPD incidence	Self-reported	The prudent pattern was negatively (highest vs. lowest quintile, RR = 0.50, 95% CI: 0.25, 0.98), while the Western pattern was positively (highest vs. lowest quintile, RR =	[115]

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
								4.56, 95% CI: 1.95, 10.69) associated with COPD risk	
Prudent pattern and Western pattern	USA (NHS)	P (6 year)	Nurses *n* = 72,043	F (30–55 year)	FFQ and PCA	COPD incidence	Self-reported	The prudent pattern was negatively (highest vs. lowest quintile, RR = 0.75, 95% CI: 0.58, 0.98), while the Western pattern was positively (highest vs. lowest quintile, RR = 1.31, 95% CI: 0.94, 1.82) associated with COPD risk	[116]
Prudent pattern and traditional pattern	United Kingdom (HCS)	C	General population *n* = 1391 (F), *n* = 1551 (M)	F, M (mean 66 year)	FFQ and PCA	Primary outcome: FEV1; Secondary outcomes: FVC,	Spirometry	The prudent pattern was positively associated with FEV1 in M and F	[117]

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
						FEV1/FVC, COPD prevalence		(changes in FEV1 between highest vs. lowest quintiles, 180 mL in M, 95% CI: 0.00, 0.16, p for trend<0.001, and 80 mL in F, 95% CI: 0.26, 0.81, p for trend = 0.008), and negatively with COPD in M (top versus bottom quintile, OR = 0.46, 95% CI: 0.26, 0.81, *p* = 0.012)	
Prudent pattern, high-CHO diet, Western pattern	Swiss (SAPALDIA)	C	General population *n* = 2178	F, M (mean 58.6 year)	FFQ and PCA	FEV1, FEV1/FVC, FEF25-75, COPD prevalence	Spirometry	The prudent pattern was positively associated with lung function and negatively with COPD prevalence (NS)	[118]

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
Western pattern and prudent pattern	USA (ARIC)	C	General population $n = 15{,}256$	F, M (mean 54.2 year)	FFQ and PCA	Respiratory symptoms (cough, phlegm, wheeze), FEV1, FEV1/FVC, COPD prevalence	Spirometry	The Western pattern was associated with higher prevalence of COPD (fifth vs. first quintile: OR = 1.62, 95% CI: 1.33, 1.97, $p < 0.001$), respiratory symptoms (wheeze OR = 1.37, 95% CI: 1.11, 1.69, $p = 0.002$; cough OR = 1.32, 95% CI: 1.10, 1.59, $p = 0.001$, phlegm OR = 1.27, 95% CI: 1.05, 1.54, $p = 0.031$), and worse lung function (e.g., percent predicted FEV1: fifth quintile 91.8 vs. first	[119]

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
								quintile 95.1, $p < 0.001$). The prudent pattern was associated with lower prevalence of COPD (OR = 0.82, 95% CI: 0.70, 0.95, $p = 0.007$), cough (OR = 0.77, 95% CI: 0.67, 0.89, $p < 0.001$), and higher lung function (e.g., percent predicted FEV1: fifth quintile 94.3 vs. first quintile 92.7, $p < 0.001$)	
Cosmopolitan pattern, traditional pattern, and refined food dietary pattern	Netherlands (MORGEN-EPIC)	C	General population $n = 12{,}648$	F, M (mean 41 year)	FFQ and PCA	FEV1, wheeze, asthma, COPD prevalence	Spirometry and self-reported symptoms	The traditional pattern was associated with lower FEV1 (fifth vs. first quintile, −94.4 mL,	[120]

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
								95% CI: −123.4, −65.5, *p* < 0.001) and increased prevalence of COPD (fifth vs. first quintile, OR = 1.60, 95% CI: 1.1, 2.3, p for trend = 0.001); the cosmopolitan pattern was associated with increased prevalence of asthma (fifth vs. first quintile, OR = 1.4; 95% CI: 1.0, 2.0; *p* for trend = 0.047) and wheeze (fifth vs. first quintile, OR = 1.3, 95% CI: 1.0, 1.5; *p* for trend = 0.001)	

Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
		P (5 y)	General population *n* = 2911	F, M (mean 45 year)	FFQ and PCA	FEV1	Spirometry	The refined food pattern was associated with a nonsignificant greater decline in lung function (−48.5 mL, 95% CI: −80.7, −16.3; *p* for trend = 0.11)	[120]
Alcohol-consumption pattern, Westernized pattern, and MED-like pattern	Spain	C	Smokers with no respiratory diseases *n* = 207	F, M (35–70 year)	FFQ and PCA	Impaired lung function	Spirometry	Alcohol-consumption pattern (OR = 4.56, 95% CI: 1.58, 13.18, *p* = 0.005) and Westernized pattern (in F) (OR = 5.62, 95% CI: 1.17, 27.02, *p* = 0.031) were associated with impaired lung function; a nonsignificant trend for preserved	[121]

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Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
								lung function was found for MED-like pattern (OR = 0.71, 95% CI: 0.28, 1.79, $p > 0.05$)	
Diet quality scores									
Alternate Health Eating Index (AHEI)	USA (NHS and HPFS)	P (16 y NHS; 12 y HPFS)	Nurses n = 73,228 (NHS) Health professionals n = 47,026 (HPFS)	F (30–55 year), M (40–75)	FFQ and diet quality index (AHEI-2010)	COPD incidence	Self-reported	A higher AHEI-2010 diet score was associated with lower COPD risk (for the fourth fifth of the score, HR = 0.67, 95% CI: 0.53, 0.85, p for trend <0.001)	[122]
Health Eating Index (HEI) and MED diet score	Iran	C	Stable COPD n = 121	F, M (mean 66.1 year)	FFQ and diet quality index (HEI, and MED score)	COPD severity	Spirometry	Higher MED score was associated with lower FEV1 and FCV. MED score and AHEI	[123]

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Dietary Patterns	Country (Cohort)	Design (Follow-Up)	Population	Sex (Age)	Diet Assessment Method	Outcome	Outcome Assessment	Main Results	Ref
								decreased as COPD severity increased (NS)	
MED diet score	Spain (ILERVAS)	C	General population *n* = 3020	F (50–70 year), M (45–65 year)	FFQ and MED score	FEV1, FVC, FEV1/FVC	Spirometry	A lower MED diet score was associated with impaired lung function in F (low vs. high adherence, OR = 2.07, 95% CI: 1.06, 4.06, p = 0.033) and the presence of obstructive ventilator defects in M (low vs. high adherence, OR = 4.14, 95% CI: 1.42, 12.1, p = 0.009)	[124]

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