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Original Article

Dietary Inflammatory Index and Clinical Outcome Measures in Adults With Moderate-to-Severe Asthma

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What is already known about this topic? Diet is increasingly recognized as an immunomodulatory factor for lung health. The Dietary Inflammatory Index (DII) scores the inflammatory potential of a diet. Whether a pro- or anti-inflammatory diet is associated with asthma outcomes is unclear.

What does this article add to our knowledge? Most patients with moderate-to-severe asthma had a proinflammatory diet associated with lower forced vital capacity values. However, few and inconsistent associations were observed for DII and specific pro- or anti-inflammatory food groups with other functional, clinical, and inflammatory outcomes.

How does this study impact current management guidelines? Although not supportive of pro- or anti-inflammatory diets affecting asthma outcomes, our cross-sectional study does not allow recommendations for asthma management. Well-designed experimental studies should determine whether targeting the inflammatory potential of a diet improves asthma outcomes.

BACKGROUND: Diet is increasingly recognized as a modifiable factor in lung health, predominantly due to the immunomodulatory effects of nutrients. The Dietary Inflammatory Index (DII) is a score developed to express the inflammatory potential of a diet.

OBJECTIVE: We aimed to assess the association of the DII and food groups, with clinical, functional, and inflammatory asthma outcomes in adults with asthma.

METHODS: Patients with moderate-to-severe asthma were included in this cross-sectional study between June 2019 and October 2021, and completed a 3-day food diary, to calculate the DII and intake of food groups (ie, fruits, whole grains, processed meats, and sugar-sweetened beverages). Functional outcomes included pulmonary function tests and the 6-minute walking distance, whereas clinical outcomes were assessed using questionnaires on asthma control, quality of life, and health care utilization. Inflammatory markers were exhaled nitric oxide and blood leukocytes, eosinophils, and IL-6. Multivariable regression analyses were used to examine the association of DII and food groups with asthma outcomes.

RESULTS: A total of 109 patients participated (35% male, mean ± standard deviation age 51.8 ± 14.2 years, body mass index 27.4 ± 5.3 kg/m^2). Overall, 62% had a DII score >0, indicating a proinflammatory diet, which was not related to asthma severity. A more proinflammatory diet was consistently associated with lower forced vital capacity (%pred), but inconsistent results were observed with respect to airway obstruction. Neither the DII nor food groups were associated with clinical outcomes. Except for higher levels of exhaled nitric oxide in relation to an anti-inflammatory diet, we found no associations between inflammatory markers and the DII.

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Conflicts of interest: H. A. M. Kerstjens reports grants and fees for advisory boards; and lectures from AstraZeneca, Boerhinger Ingelheim, Chiesi, and GSK, all paid to his institution and outside of the submitted work. A. ten Brinke reports grants from AstraZeneca, GSK, and TEVA; fees for advisory boards; and lectures from AstraZeneca, GSK, Novartis, TEVA, and SanofiGenzyme, outside the submitted work. The rest of the authors declare that they have no relevant conflicts of interest.

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Abbreviations used
6MWD- 6-minute walking distance
ACQ- Asthma Control Questionnaire
AQLQ- Asthma Quality-of-Life Questionnaire
BMI- Body mass index
DII- Dietary Inflammatory Index
FeNO- Fractional exhaled nitric oxide
FEV_1- Forced expiratory volume in 1 second
FVC- Forced vital capacity
GINA- Global Initiative for Asthma
HCU- Health care utilization
SD- Standard deviation

CONCLUSION: Results from this cross-sectional study among patients with moderate-to-severe asthma do not support the hypothesis that a proinflammatory diet is associated with worse asthma outcomes, although limitations in study design and dietary intake estimation should be considered. Future well-designed experimental studies are needed to assess whether targeting the inflammatory potential of diet could lead to better outcomes in adults with asthma. **(J Allergy Clin Immunol Pract 2023;11:3680-9)**

Key words: *Severe asthma; Dietary Inflammatory Index; Nutrition; Asthma control; Quality of life; Health care utilization; Airway obstruction; Inflammation*

Asthma is a chronic inflammatory disease characterized by airflow limitation and a variability in respiratory symptoms, including recurrent episodes of dyspnea, wheezing, and cough.[1] As such, the disease has a significant impact on patients' lives. Asthma symptoms are driven by inflammation of the airways, which triggers processes such as mucus production, airway wall remodeling, and bronchial hyper-responsiveness.[2] The main goal of asthma treatment is to achieve good control of symptoms and minimize the risk of exacerbations, airflow limitations, and side effects.[1]

Diet and nutrition are increasingly recognized as modifiable factors for lung health, as their metabolites play an important role in regulating immune responses.[3] Dietary antioxidants—such as vitamin A, vitamin E, and selenium—prevent oxidative and cellular damage by scavenging free radicals, and consumption of antioxidant-rich food has been related to decreased sputum neutrophil activity.[4,5] On the other hand, high intake of saturated fatty acids may induce activation of the proinflammatory nuclear factor kappa-B cascade and has been associated with both airway neutrophilia and eosinophilia.[6,7]

Excellent reviews are available in literature describing the immunomodulatory effects of diet in lung disease.[3,8] More specifically for asthma, a recent review summarized the current evidence for interventions with individual nutrients and dietary factors, with few studies showing simultaneous improvements in asthma-related outcomes and immunological parameters.[9] However, people do not consume individual nutrients or foods, but rather meals and diets that may act differently due to the combined effects of different nutrients.[10,11]

Nutrition research has shifted in recent decades from a focus on individual nutrients and foods to the study of food groups and dietary patterns. Indeed, intervention studies of single-nutrient supplementation for asthma management have been inconsistent and often disappointing.[12-14] Therefore, summary scores have been developed to examine the effects of the overall diet rather than the effects of specific nutrients or foods, such as the Dietary Inflammatory Index (DII). The DII is a tool for measuring the inflammatory potential of an individual's total diet that can be applied to any population.[15,16] It is calculated by summing the intake of single nutrients with anti-inflammatory or proinflammatory effects. A higher DII score reflects a more proinflammatory diet and is characterized by a higher intake of saturated fat and refined carbohydrates, whereas a low score indicates an anti-inflammatory diet rich in antioxidants and fibers.

A higher, more proinflammatory DII score has previously been associated with an increased risk of inflammatory diseases such as rheumatoid arthritis[17] and inflammatory bowel disease,[18,19] and higher odds of having asthma.[20,21] Furthermore, an association of the DII with poorer lung function and asthma control has been suggested.[20,22] However, no studies have examined the DII in the context of a complete clinical asthma profile, assessing functional and clinical outcomes, and asthma-specific inflammation.

Therefore, our aim in the present study was to assess the association between the DII and clinical, functional, and inflammatory outcomes in a population of patients with moderate-to-severe asthma. In addition, we assessed 4 specific food groups commonly believed to have beneficial or adverse health effects because of the high concentration of anti-inflammatory or proinflammatory nutrients in these foods, and we expect these to have a similar association with asthma outcomes as for the DII.

METHODS

Study population

In this cross-sectional study, we consecutively recruited patients (aged ≥18 years) with moderate-to-severe asthma from the regular pulmonary outpatient clinic and a severe asthma center of a tertiary teaching hospital in the Netherlands,[23] between June 2019 and October 2021. The long recruitment period was due to COVID-19 restrictions during study enrollment. All patients had a confirmed asthma diagnosis according to a positive bronchodilator reversibility test or a positive methacholine challenge test, and asthma severity was assessed using Global Initiative for Asthma (GINA) 2019 step 3 to 5 treatment.[1] Patients with concurrent respiratory diseases—including chronic obstructive pulmonary disease, acute respiratory tract infection, or asthma exacerbation in the previous month—and pregnancy were excluded. Patients with a recent asthma exacerbation were excluded because we were interested in the association between diet and general asthma outcomes and not in those aggravated by acute exacerbations. In addition, changes in diet during exacerbations could bias the results if included. The study was approved by the local medical ethics committee (RTPO 1067; April 29, 2019), and all patients provided written informed consent.

Design and measurements

Each patient underwent a comprehensive clinical, functional, and laboratory assessment as part of regular care. Data on demographics, medical history, and medication use were gathered from the patient's medical record. Anthropometric measurements were taken, and spirometry before and after inhalation of 400 μg of salbutamol was performed,[24] along with the measurement of fractional exhaled nitric oxide (FeNO). Functional exercise capacity was assessed with the 6-

minute walking distance (6MWD), which was carried out according to European Respiratory Society/American Thoracic Society guidelines and expressed as percentage of predicted.[25,26] Venous blood was taken to measure peripheral blood differential cell counts, and the systemic inflammatory markers C-reactive protein, TNF-α, and IL-6. The latter 2 were analyzed in 2 batches using ELISA kits (R&D Systems, Minneapolis, Minn) and Immunoassay Cobas E601 (Roche, Basel, Switzerland) (see this article's Online Repository at www.jaci-inpractice.org). Last, all patients completed questionnaires on quality of life (AQLQ),[27] asthma control (ACQ-6),[28] health care utilization in the previous year (HCU),[29] and physical activity (Short QUestionnaire to ASsess Health-enhancing physical activity [SQUASH]).[30]

Dietary assessment

After study enrollment, patients received a food diary and written instructions to record their dietary intake at home on 2 weekdays and 1 weekend day. These dates were randomly selected by the researcher to reflect habitual intake and to avoid bias. Patients reported the consumption of foods and beverages using fixed portion sizes (eg, slices of bread and pieces of fruit) and commonly used household measures (eg, cups and spoons). During the physical examination at the hospital, the food diaries were checked with the patient on specific details and portion sizes by a qualified dietitian, who also completed the data entry. Foods were categorized into food groups according to the 2015 Dutch Dietary Guidelines,[31-33] and the nutrient and energy intake was calculated using the 2019 Dutch food composition table.[34] The daily intake of both food groups and nutrients was expressed in grams/day and calculated as the weighted average of the 3 days. We assessed 4 food groups based on their nutrient density and known health effects.[31] These were the groups "fruit" and "wholegrain products" supposed to have favorable health effects, and "processed meat" and "sugar-sweetened beverages," which are considered to have unfavorable health effects.

Next, we calculated the DII to assess the inflammatory potential of an individual's diet. The development and validation of the DII has been described previously.[15,35] Briefly, based on an extensive literature review and dietary data from 11 populations around the world, a database of 45 food parameters has been developed representing the global mean intake and inflammatory effect score for each parameter. For each food parameter, z scores are derived by subtracting the global mean intake from the patients' reported daily intake and dividing it by the global standard deviation (SD). These z scores are then transformed to centered percentiles and multiplied by the corresponding inflammatory effect score. Finally, the food parameter−specific inflammatory scores are summed to calculate the total DII score for each patient, ranging from maximally −8.87 (strongly anti-inflammatory) to +7.98 (strongly proinflammatory), with 0 indicating a neutral inflammatory status of the diet. For this study, 28 food parameters (see Table E1 in this article's Online Repository at www.jaci-inpractice.org) were available from the dietary assessment. For analyses, the DII score and food group intakes were categorized into tertiles. These tertiles were created based on the observed range of DII scores and food group intakes in our population.

Statistical analyses

Patient characteristics are presented for the total study population and for tertiles of the DII. Results are given as mean ± SD (parametric data), median and interquartile range (nonparametric data), and frequencies (categorical data). Between-group differences were tested accordingly with the 1-way analysis of variance, Kruskal-Wallis test, or χ^2 test.

Next, multiple imputation was performed to account for missing data (2.9% of all data points, 6 variables with >5% missing, n = 42 patients) in all patients for whom dietary data were available, using chained equations and predictive mean matching modeling. Twenty sets of imputed data were generated, and the results of the analyses below were pooled to obtain a single final estimate. More information about the model specifications and the number of missing data for each imputed variable can be found in Table E2 in this article's Online Repository at www.jaci-inpractice.org.

To answer the main study objective, multivariable regression analyses were used to assess the association between the DII/food groups (independent variables in tertiles) and asthma outcomes (dependent variables). Linear regression models were used for continuous outcomes (forced expiratory volume in 1 second [FEV_1], forced vital capacity [FVC], FEV_1/FVC, 6MWD, ACQ, AQLQ, and inflammatory markers), and predicted means were reported for each tertile of the DII/food groups. Natural log transformed values were used for the inflammatory markers (ie, FeNO, leukocytes, eosinophils, and IL-6). For the categorical outcome (HCU), a binary logistic regression was performed and predicted probabilities were reported for each tertile of the DII/food groups. All models were adjusted for the confounders sex, age, body mass index (BMI), educational level, and smoking history. These confounders are known to be associated with the DII and asthma outcomes.[20,22]

To assess the robustness of our findings, we performed several sensitivity analyses. The regression analyses for the association between DII and asthma outcomes were repeated with the following alterations: (1) a model excluding patients with unreliable food data, as based on the ratio between energy intake and energy expenditure (<1.0 or ≥2.4);[36] (2) a model without BMI in view of the complex relation between diet, obesity, and asthma;[37] (3) a model with additional adjustment for energy intake; (4) a model with additional adjustment for dietary supplements use to account for health conscious behavior; and (5) a model with DII and food groups as continuous independent variables instead of tertiles.

A P value of <.05 indicated statistical significance. All analyses were performed using IBM SPSS Statistics, version 28.0 (IBM Corp, Armonk, NY).

RESULTS

Population description

We identified 114 patients, of whom 109 participated in this study; 33 (30%) of whom were recruited from the severe asthma center and the remaining patients from the regular pulmonary outpatient clinic. The majority was female (65%), and the mean ± SD age was 51.8 ± 14.2 years (Table I). About half of the study population had a high level of education (47%) and had ever smoked (45%). The mean BMI was 27.4 ± 5.3 kg/m^2 with 70% having overweight or obesity.

Regarding disease characteristics, 17 patients had moderate (GINA 3, 16%), 34 patients moderate-to-severe (GINA 4, 31%), and 58 patients severe asthma (GINA 5, 53%). Atopy was present in 51% of the patients, and 57% had developed asthma in adulthood. As indicated by a mean ACQ of 1.7 ± 1.1, our study population had relatively poor asthma control. Indeed, 52% experienced ≥1 exacerbations in the past year. All patients received ICS medication (n = 49 high dose, n = 46 medium dose, and n = 14 low dose according to GINA 2019[1]), with

TABLE I. Patient characteristics of the total study population and by tertiles of the DII

	No.	Total population (N = 109)	Anti-inflammatory (N = 37)	Neutral inflammatory (N = 36)	Proinflammatory (N = 36)	*P* value
Demographics						
DII	109	0.48 ± 1.58	−1.20 ± 0.86	0.49 ± 0.36	2.19 ± 0.91	<.01
Males	109	38 (35)	19 (51)	9 (25)	10 (28)	.03
Age (y)	109	51.8 ± 14.2	51.0 ± 12.9	54.9 ± 14.8	49.6 ± 14.9	.25
High educational level	109	51 (47)	23 (62)	13 (36)	15 (42)	.06
Ever smoked	109	49 (45)	11 (30)	20 (56)	18 (50)	.07
Pack years	102	0 [0-7]	0 [0-4]	0.5 [0-9]	0 [0-8]	.12
MVPA (h/wk)	104	8 [3-17]	8 [3-17]	9 [4-20]	6 [2-16]	.30
BMI (kg/m^2)	109	27.4 ± 5.3	25.9 ± 4.6	27.1 ± 4.3	29.3 ± 6.4	.02
BMI ≥25 kg/m^2	109	76 (70)	20 (54)	27 (75)	29 (81)	.03
Energy (kcal/d)	109	2110 ± 503	2371 ± 582	2002 ± 422	1948 ± 379	<.01
Dietary supplement use	109	64 (60)	25 (68)	20 (56)	19 (58)	.53
Functional outcomes						
FEV_1 (%pred, pre-bd)	108	91.3 ± 18.8	92.8 ± 18.8	87.1 ± 20.8	93.8 ± 16.6	.27
FVC (%pred, pre-bd)	108	106.6 ± 15.1	108.9 ± 16.2	107.0 ± 14.9	104.0 ± 14.2	.38
FEV_1/FVC (%, pre-bd)	108	70.5 ± 12.7	69.1 ± 12.6	67.4 ± 14.1	75.0 ± 10.3	.03
6MWD (%pred)	99	82.6 ± 15.9	83.6 ± 17.7	84.7 ± 13.9	79.2 ± 15.6	.35
Clinical outcomes						
Adult-onset asthma	108	61 (57)	22 (60)	21 (60)	18 (50)	.63
Severe asthma (GINA 5)	109	58 (53)	20 (54)	18 (50)	20 (56)	.89
Atopic asthma	105	53 (51)	15 (41)	18 (56)	18 (56)	.32
ACQ-6 (0-6)	105	1.7 ± 1.1	1.7 ± 1.1	1.6 ± 1.0	1.7 ± 1.1	.90
AQLQ (1-7)	107	5.3 ± 1.0	5.6 ± 0.98	5.3 ± 1.0	5.3 ± 0.9	.64
≥1 exacerbations	104	54 (52)	18 (49)	17 (49)	19 (59)	.60
≥1 emergency visits	103	47 (46)	15 (43)	14 (41)	18 (53)	.57
Inflammatory outcomes						
FeNO (ppb)	102	20 [12-36]	26 [17-46]	15 [11-27]	22 [10-36]	.02
Leukocytes (×10^9/L)	104	7.0 ± 1.9	6.5 ± 1.6	6.9 ± 1.89	7.5 ± 1.9	.06
Eosinophils (×10^9/L)	102	0.10 [0.05-0.20]	0.10 [0.05-0.30]	0.20 [0.05-0.20]	0.10 [0.05-0.20]	.75
Eosinophils ≥0.3 × 10^9/L	102	23 (23)	10 (29)	7 (21)	6 (18)	.17
C-reactive protein (mg/L)	102	2.0 [0.5-4.0]	1.0 [0.5-2.0]	2.5 [1.0-5.3]	3.0 [1.0-8.3]	<.01
IL-6 (pg/mL)	106	1.5 [1.0-2.2]	1.1 [0.9-1.9]	1.5 [1.0-2.5]	1.6 [1.0-3.2]	.05
TNF-α (pg/mL)	107	0.69 [0.59-0.87]	0.71 [0.59-0.87]	0.68 [0.59-0.83]	0.69 [0.57-0.95]	.70

Anti-inflammatory: DII < −0.23; neutral inflammatory: DII ≥ −0.23 and <1.08; and proinflammatory: DII ≥1.08.
Data are presented as mean ± standard deviation, median [interquartile range], or n (%) before multiple imputation.
6MWD, 6-minute walking distance; *ACQ*, Asthma Control Questionnaire; *AQLQ*, Asthma Quality-of-Life Questionnaire; *BMI*, body mass index; *DII*, dietary inflammatory index; *FeNO*, fractional exhaled nitric oxide; *FEV_1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *GINA*, Global Initiative for Asthma 2019; *MVPA*, moderate-to-vigorous physical activity; *pre-bd*, prebronchodilator.

adjunctive therapy including long-acting β-agonist (n = 102), long-acting muscarinic antagonist (n = 39), leukotriene-receptor antagonist (n = 25), biologics (n = 20), and maintenance oral corticosteroids (n = 3).

Dietary Inflammatory Index

The mean DII was 0.48 ± 1.58 and ranged from −3.73 to 4.17. As shown in Figure 1, 62% of patients had a DII ≥0, indicating a proinflammatory diet. The proportion of patients with this higher DII score was not different according to GINA severity grading. We then divided the DII into tertiles, resulting in cutoff values of DII < −0.23 to define an anti-inflammatory group, and DII ≥ 1.08 to define a proinflammatory group, and a neutral inflammatory group with values in between. Again, the distribution of GINA classes did not vary within these tertiles. However, patients with an anti-inflammatory dietary profile were more often male, had a higher educational level, were less likely to have smoked, and had a lower BMI and a higher daily energy intake compared with patients with a more neutral or proinflammatory diet (Table I).

Association of a pro- or anti-inflammatory diet and food groups with asthma outcomes

The association of tertiles of the DII and food groups with asthma outcomes—adjusted for aforementioned confounders—is shown in Figure 2 for functional outcomes, Figure 3 for clinical outcomes, and Figure 4 for inflammatory markers. Data are also described in Tables E3-E5 in this article's Online Repository at www.jaci-inpractice.org.

When first considering the functional outcomes, we found that a more proinflammatory diet was associated with lower FVC

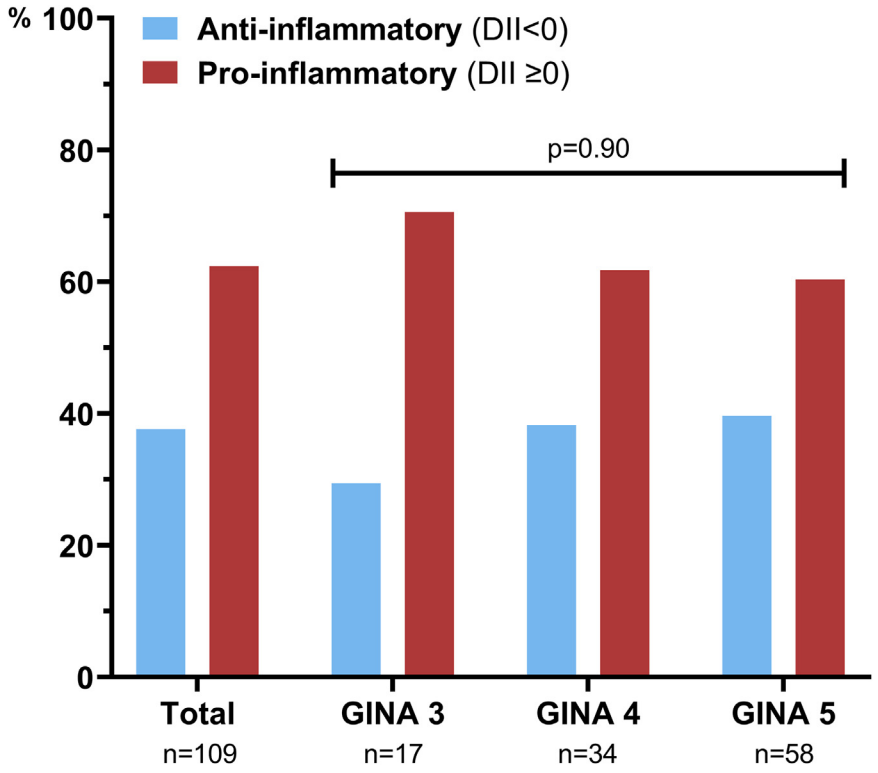

FIGURE 1. Distribution of the Dietary Inflammatory Index (DII) within categories of asthma severity. *GINA*, Global Initiative for Asthma 2019.

(Figure 2, *B*). Consistent with this, lower intakes of fruits and whole grains and higher intakes of processed meats and sugar-sweetened beverages were also associated with lower FVC, albeit not statistically significantly so. A less consistent picture was observed for FEV_1 and FEV_1/FVC (Figure 2, *A* and *C*). Although patients with a low intake of processed meat and a high intake of fruit had higher values of FEV_1 and FEV_1/FVC, no such—and even an opposite—effect was shown for whole grains and the DII. In fact, the proinflammatory subgroup showed less airway obstruction. The 6MWD was not related to any of the dietary factors.

Regarding the clinical outcomes (Figure 3), we found no association between a pro- or anti-inflammatory diet or food groups and the ACQ, AQLQ, exacerbation rate, or emergency visits.

Finally, for the inflammatory markers, higher FeNO levels (Figure 4, *A*) were observed in patients with an anti-inflammatory DII score and correspondingly—but not statistically significantly different from the other tertiles—also in patients with a higher intake of fruit and whole grains and lower meat intake. Furthermore, a higher intake of whole grains was associated with lower IL-6 levels (Figure 4, *D*), and accordingly, a nonsignificant trend was observed between an anti-inflammatory diet and lower IL-6 levels. However, the opposite effect was true for meat, as higher IL-6 levels were observed in patients with a low intake of processed meat. We found no consistent associations between a pro- or anti-inflammatory diet or food groups and levels of blood eosinophil and leukocyte levels.

Sensitivity analyses

Results of the sensitivity analyses are shown in Table E6 in this article's Online Repository at www.jaci-inpractice.org. Eleven patients had unreliable food data, but exclusion of these patients did not affect effect estimates or conclusions regarding the association between the DII and asthma outcomes (n = 98). The same applies for excluding BMI as covariate (n = 109), additional adjustment for energy intake (n = 109), or additional adjustment for use of dietary supplements (n = 106). Last, assessing DII and food groups as continuous variables, rather than as tertiles, also did not affect the main conclusion of this study (n = 109, data not shown).

DISCUSSION

In this study, we examined the relationship between the DII and a wide range of functional, clinical, and inflammatory outcomes in patients with moderate-to-severe asthma. The majority of patients had a proinflammatory diet, which was not related to disease severity. In addition, our results show that the intake of a proinflammatory diet or foods with a proinflammatory nature were related to lower FVC, but inconsistent results were observed in relation to airway obstruction. Neither the DII nor the food groups were associated with clinical outcomes, whereas the association with inflammatory markers was not evident. The results of this study do not support the hypothesis that a proinflammatory diet is associated with worse outcomes in adults with moderate-to-severe asthma, although there are some important limitations, which will be discussed below.

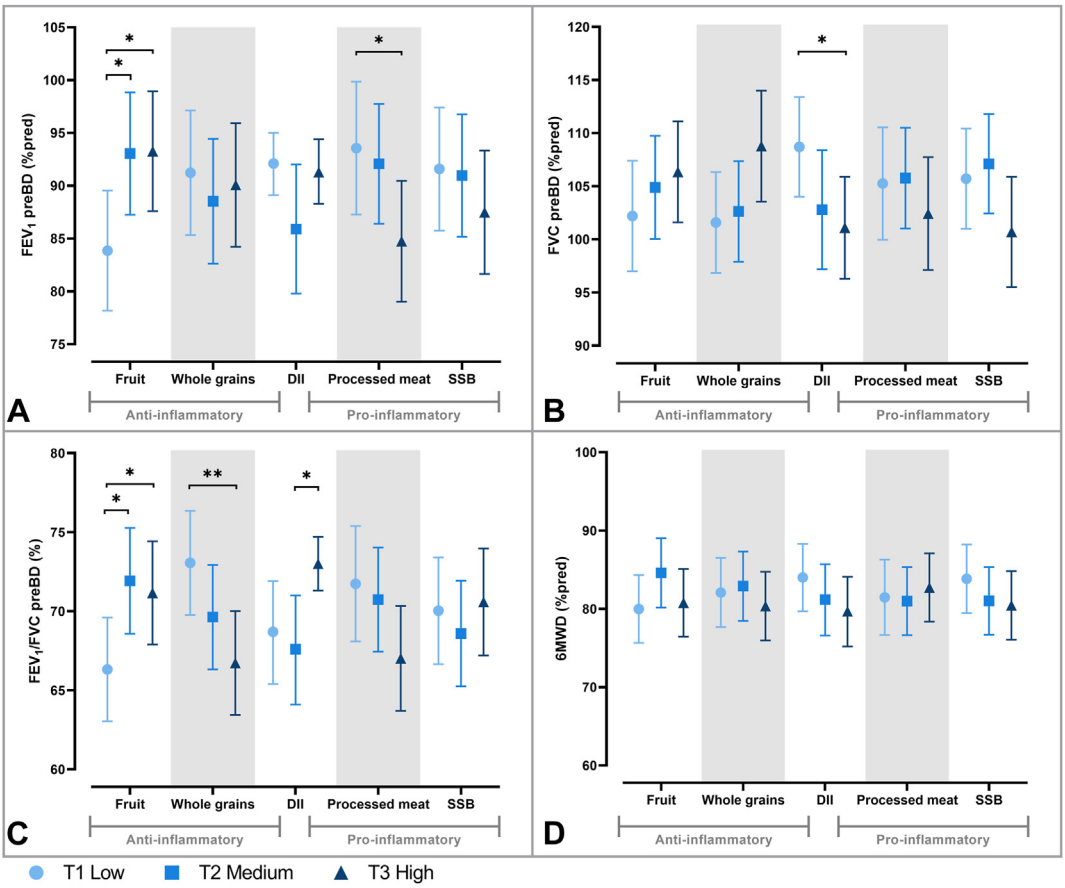

FIGURE 2. Functional asthma outcomes related to the Dietary Inflammatory Index (DII) and food groups. (**A**) FEV_1 (%pred) pre-bronchodilator (preBD), (**B**) FVC (%pred) preBD, (**C**) FEV_1/FVC (%) preBD, and (**D**) 6-minute walking distance (%pred). Covariates: sex, age, BMI, educational level, and smoking history. Values are presented as predicted means for tertiles of the DII and food groups. $*P < .05$, $**P < .01$. *6MWD*, 6-minute walking distance; *BMI*, body mass index; *FEV_1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *SSB*, sugar-sweetened beverages; *T1-T3*, tertiles.

We found a mean DII score of 0.48 ± 1.58 in our study population, indicating a proinflammatory diet. This is in line with previous findings by Özbey et al[22] among patients with asthma from Turkey, but higher than the mean DII of −1.40 ± 0.23 reported by Wood et al,[20] suggesting a more anti-inflammatory diet among this sample of patients with asthma from Australia. This difference could be explained by using other dietary assessment methods or by differences in dietary habits between the Netherlands and Australia. A comparable mean DII score as in the current study has been shown in Dutch patients with inflammatory bowel disease,[38] but no data are available on the DII score of Dutch healthy individuals.

In the current study, we showed that a higher DII was related to lower FVC values, which is consistent with previous studies.[20-22,39] However, in contrast to our findings, these studies also reported associations between a proinflammatory diet and worse FEV_1 in a population of both asthma patients and healthy controls,[20] as well as in adults without asthma,[21,39] suggesting that this is not asthma specific but rather reflective of the general population. Furthermore, the evidence for an association of the DII or food groups with airway obstruction was inconsistent in the current study, whereas others also found no relation with FEV_1/FVC.[20-22,39] Therefore, the question arises whether a proinflammatory diet is related to airway obstruction or rather to the lung volume due to a third factor that is strongly correlated with both a proinflammatory diet and lung development, such as body composition or socioeconomic status.

Data on the relationship between the DII and clinical outcomes in asthma are limited. In a Turkish study of patients with mild asthma, a proinflammatory diet was associated with poorer asthma control.[22] However, no such association was found when food groups were assessed in Portuguese adults with controlled and uncontrolled asthma.[40] Our study confirms and extends these latter findings by demonstrating the absence of a significant relationship not only with ACQ but with a whole range of clinical outcomes.

Furthermore, in asthma, there is limited data on the relationship between DII and inflammatory markers, with the exception of IL-6. In line with Wood et al[20] and what is generally observed in other diseases, we also found a trend between a proinflammatory diet and higher IL-6 levels, although not significant. Our study adds to previous studies by

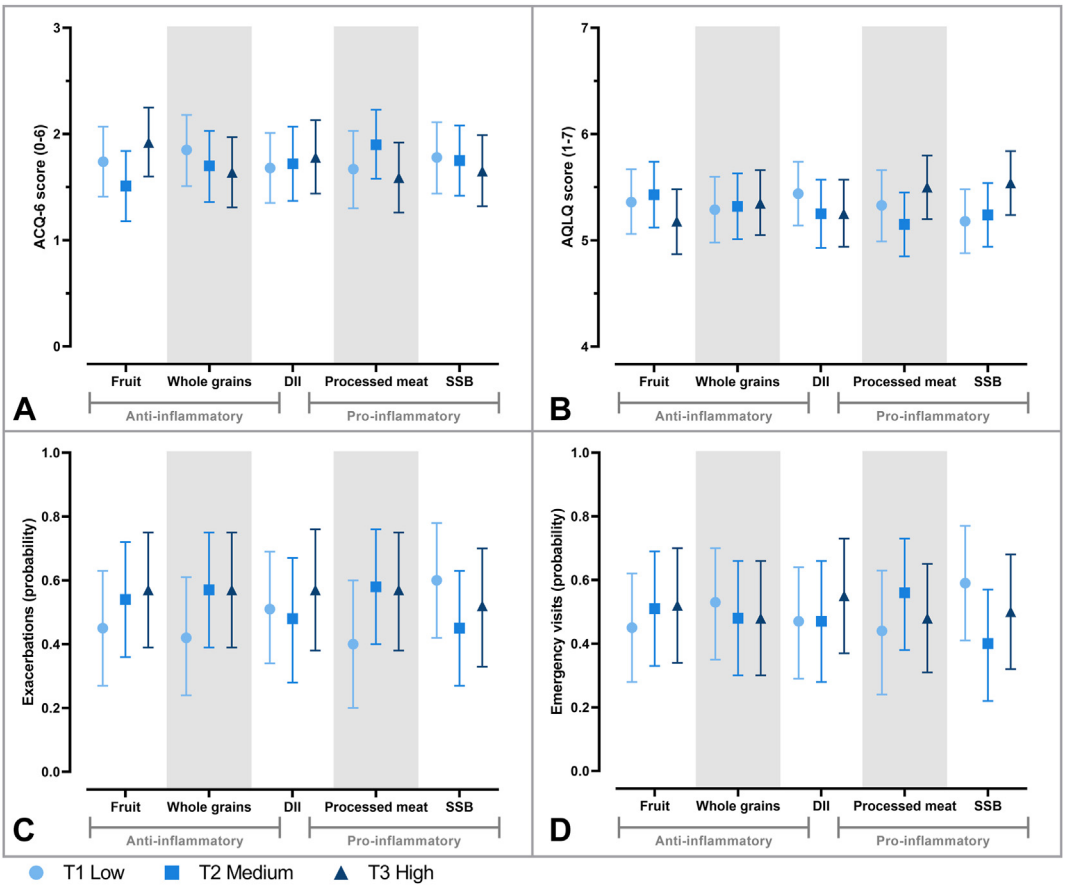

FIGURE 3. Clinical asthma outcomes related to the Dietary Inflammatory Index (DII) and food groups. (**A**) Asthma control score, (**B**) asthma quality of life score, (**C**) ≥1 exacerbations in preceding year, and (**D**) ≥1 emergency visits in preceding year. Covariates: sex, age, BMI, educational level, and smoking history. Values are presented as predicted means and predicted probabilities for tertiles of the DII and food groups. *ACQ*, Asthma Control Questionnaire; *AQLQ*, Asthma Quality-of-Life Questionnaire; *BMI*, body mass index; *SSB*, sugar-sweetened beverages; *T1-T3*, tertiles.

investigating a possible relationship with markers of type 2 inflammation and shows no, or inconsistent, associations with eosinophils in peripheral blood and FeNO.

Strengths of our study include a well-characterized study population, the assessment of a whole range of clinical, functional, and inflammatory parameters, and the detailed data on food intake. We used a prospective dietary assessment method, which was discussed afterward with a qualified dietitian, thereby reducing the risk of recall bias. However, socially desirable responding remains a potential source of bias that is difficult to control in nutrition research. Indeed, a lower energy intake was reported in patients with a more proinflammatory diet and a higher BMI compared with those with an anti-inflammatory diet, suggestive of under-reporting. Therefore, a sensitivity analysis excluding participants with unreliable dietary data was performed, which yielded similar results. Furthermore, the study population was consecutively recruited without the application of strict selection criteria, which increases the generalizability of our findings to other clinical asthma populations. Although we had some missing data (2.9%), we used multiple imputation to obtain unbiased estimates.

Some limitations should also be noted. First, this was a cross-sectional study with a relatively small sample size and the (lack of) findings could be due to limited statistical power or reverse causality. Patients with more asthma-related symptoms may have changed their diet to relieve symptoms. In addition, we observed a negative relationship between energy intake and the DII score, with a higher energy intake in patients with a more anti-inflammatory diet. This may be partly explained by the higher proportion of men in this tertile. However, associations remained similar when models were additionally adjusted for energy intake. Furthermore, the DII score was not calculated using the full range of food parameters. Data for herbs, spices, and flavonoids were missing, resulting in less variation in the DII score.[16] However, most studies using the DII have scores derived from 25 to 30 parameters, and these show a similar range of the DII as ours.[16,20,38,39,41] Furthermore, 60% of our study population used dietary supplements, such as multivitamins, minerals, and fish oil. These components are considered anti-inflammatory but are not included in the DII. However, additional correction for supplement use did not affect the results. Nevertheless, the presence of uncontrolled confounding remains a challenge in any observational study.

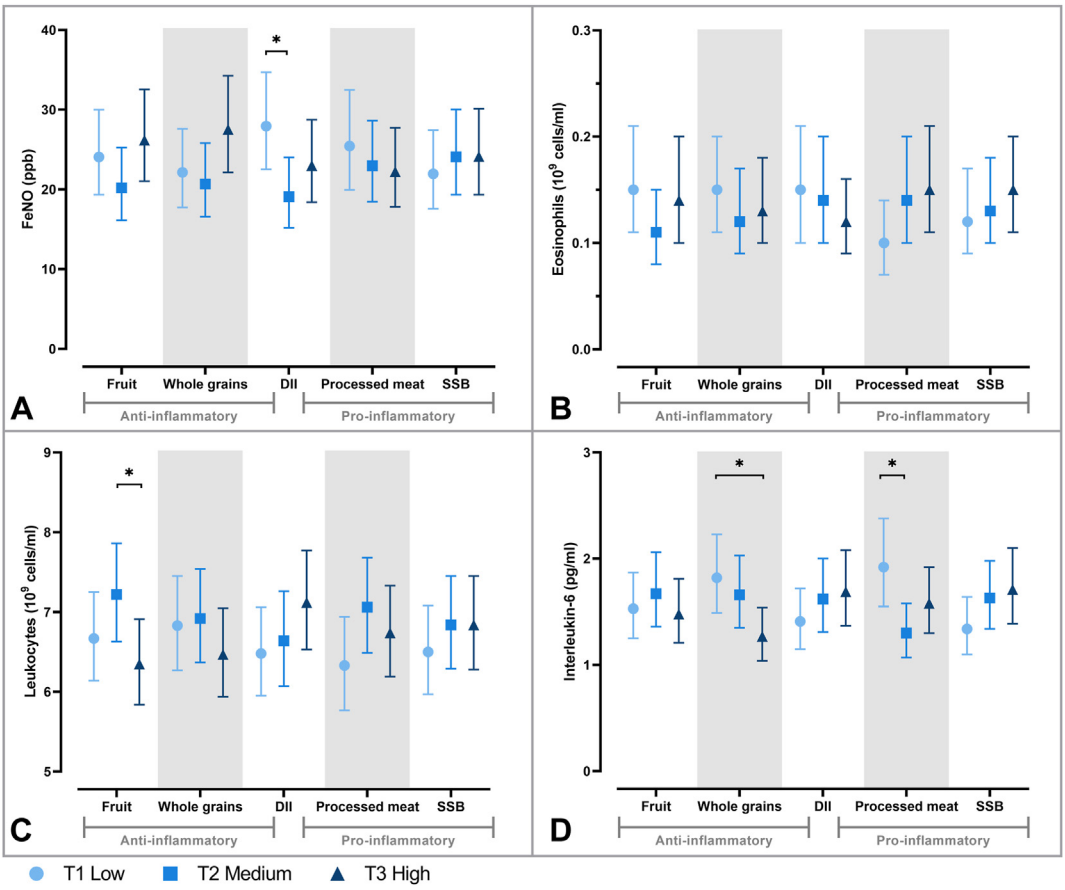

FIGURE 4. Inflammatory markers related to the Dietary Inflammatory Index (DII) and food groups. (**A**) Fractional exhaled nitric oxide (FeNO), (**B**) eosinophils in blood, (**C**) leukocytes in blood, and (**D**) IL-6 in blood. Covariates: sex, age, BMI, educational level, and smoking history. Values are presented as predicted means for tertiles of the DII and food groups. *$P < .05$. *BMI*, Body mass index; *SSB*, sugar-sweetened beverages; *T1-T3*, tertiles.

We deliberately chose to also assess food groups with known beneficial or adverse health effects, as we would expect to see the same directional relationship for these as for the DII subgroups. Fruit is indeed a rich source of antioxidants and flavonoids, whereas whole grain products contain dietary fiber and B vitamins, all nutrients used to calculate the DII. However, as useful as the DII may be for assessing the inflammatory potential of diets, the inconsistent associations of the DII and food groups with asthma outcomes in this study make us question the applicability of the DII in its current form in asthma populations. Summary measures are appealing due to their ability to simplify complex dietary intake concepts, but may be inadequate because the different contributions of the diet cannot be captured by a single measure. Dietary intake and combinations of foods are also subject to variation over time, and interactions with host characteristics are not accounted for in such measures. In addition, foods that are generally considered healthy and beneficial may still cause inflammatory responses in asthma, such as foods containing histamine, gluten, and certain food additives. For example, processed meats contain high levels of saturated fat, sodium, and nitrite-based food additives, the latter 2 of which are not included in the DII but are potentially harmful to people with asthma.[42-44] Because these substances are not available in food composition tables, they are often not included in nutritional research. More research on this topic is needed to fully elucidate the role of diet in asthma and could be considered in the further development of the DII as a tool to measure the inflammatory potential of a diet. In addition, the lack of reference values for the DII in the general population, as well as minimal clinically important differences, complicates the interpretation of the DII. Last, the literature suggests that the method of dietary assessment may affect the determination of the DII.[45,46] Further research is needed to establish a gold standard of dietary assessment for calculating the DII.

Although this cross-sectional study does not suggest a role for the inflammatory potential of diet in asthma outcomes, this does not rule out the possibility that a pro- or anti-inflammatory diet may influence long-term outcomes. Indeed, previous experimental studies have shown effects of a low-antioxidant diet on reduced lung function, a high-fat meal and increased neutrophilic airway inflammation, and better asthma control following diet exercise and behavioral interventions to improve diet quality.[47-50] In addition, better lung function and quality of life were suggested after intervention with a Mediterranean diet, whereas increased eosinophilic airway inflammation was shown after consuming a proinflammatory meal after exercise.[51,52] Unfortunately, because

of COVID-19 restrictions, we were only able to obtain a limited number of sputum samples (n = 18) and were therefore unable to examine such associations between diet and airway inflammation.

CONCLUSION

We found no clear evidence of an association between a proinflammatory or anti-inflammatory diet and a wide range of asthma outcomes in a well-characterized moderate-to-severe asthma population. However, given the limitations of this study design and in estimating dietary intake, future well-designed experimental studies are needed to assess whether targeting the inflammatory potential of diet could lead to better outcomes in adults with asthma.

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ONLINE REPOSITORY

Information on the analysis methods of TNF-α and IL-6

Both TNF-α and IL-6 were analyzed in 2 batches using ELISA (R&D Systems, Minneapolis, Minn) and Immunoassay Cobas E601 (Roche, Basel, Switzerland). The mean TNF-α values for batch 1 (n = 63, mean ± standard deviation [SD] = 0.76 ± 0.27) and batch 2 (n = 45, mean ± SD = 0.74 ± 20.25) were comparable. The mean IL-6 values for batch 1 (n = 63, mean ± SD = 2.13 ± 1.74) and batch 2 (n = 45, mean ± SD = 2.03 ± 2.28) were also comparable, although the variation in batch 2 was a bit larger.

Model specifications multiple imputation

Overall, 42 (39%) patients had missing data, with 2.9% of all data points missing. The highest number of missing data was imputed for the 6-minute walking distance (Table E2). The percentage of missing data was higher in patients from the regular pulmonary outpatient clinic (3.1% of all data points missing) than those recruited of the severe asthma center (2.5% of all data points missing). Patients of the severe asthma center were systematically evaluated during a 1-day visit at the center as part of regular care, and therefore had less missing data. In patients of the regular pulmonary outpatient clinic, some study assessments were not always embedded in regular care and were therefore more often missing. So missing data may depend on clinical setting and not on any of the variables itself. Therefore we assume that the missing data are missing at random.

Multiple imputation was performed by fully conditional specification and predictive mean matching. The number of imputations was 20, and the maximum number of iterations was also 20.

TABLE E1. Food parameters available to calculate the DII

	Anti-inflammatory	Proinflammatory
Available	Alcohol, vitamin B6, β-carotene, fiber, folic acid, magnesium, MUFA, niacin, n-3 fatty acids, n-6 fatty acids, PUFA, riboflavin, selenium, thiamin, vitamin A, vitamin C, vitamin D, vitamin E, zinc	Vitamin B12, carbohydrate, cholesterol, energy, total fat, iron, protein, saturated fat, *trans*-fat
Not available	Anthocyanidins, caffeine, eugenol, flavan-3-ol, flavones, flavonols, flavonones, garlic, ginger, green/black tea, isoflavones, onion, pepper, rosemary, saffron, thyme/orgeno, turmeric	

DII, Dietary Inflammatory Index; *MUFA*, monounsaturated fatty acids; *PUFA*, polyunsaturated fatty acids.

TABLE E2. Missing data before multiple imputation

Variable	N (%) missing (out of 109)
Sex	–
Age	–
Educational level	–
Medication use	–
Smoking history	–
Weight	–
FEV_1, prebronchodilator	1 (0.9)
FVC, prebronchodilator	1 (0.9)
FEV_1/FVC, prebronchodilator	1 (0.9)
AQLQ	2 (1.8)
Tumor necrosis factor α	2 (1.8)
IL-6	3 (2.8)
ACQ-6	4 (3.7)
Leukocytes	5 (4.9)
Exacerbations	5 (4.9)
Physical activity	5 (4.9)
Emergency visits	6 (5.5)
Pack years	7 (6.4)
FeNO	7 (6.4)
Blood eosinophils	7 (6.4)
C-reactive protein	9 (8.3)
6-minute walking distance	10 (9.2)

ACQ, Asthma Control Questionnaire; *AQLQ*, Asthma Quality-of-Life Questionnaire; *FeNO*, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; *FVC*, forced vital capacity.

TABLE E3. Functional asthma outcomes related to the Dietary Inflammatory Index (DII) and food groups

				FEV_1 (%pred)			FVC (%pred)			FEV_1/FVC (%)			6MWD (%pred)		
		No.	Cutoff value	PM	SE	*P**	PM	SE	*P**	PM	SE	*P**	PM	SE	*P**
DII	T1 | Anti-infl.	37	< -0.23	92.1	2.94	.15[a]	108.7	2.38	.12[a]	68.7	1.67	.65[a]	84.0	2.21	.38[a]
	T2 | Neutral	36	$-0.23 < 1.08$	85.9	3.12	.19[b]	102.8	2.86	.64[b]	67.6	1.77	.02[b]	81.2	2.34	.63[b]
	T3 | Pro-infl.	36	≥ 1.08	91.3	3.04	.87[c]	101.1	2.46	.03[c]	73.0	1.73	.08[c]	79.7	2.29	.18[c]
Fruit (g/d)	T1 | Low	36	<92.6	83.9	2.90	.03[a]	102.2	2.65	.46[a]	66.3	1.67	.02[a]	80.0	2.21	.14[a]
	T2 | Medium	37	$92.6 < 198.0$	93.1	2.96	.96[b]	104.9	2.47	.67[b]	71.9	1.71	.74[b]	84.6	2.26	.22[b]
	T3 | High	36	≥ 198.0	93.3	2.89	.02[c]	106.4	2.42	.25[c]	71.2	1.67	.04[c]	80.8	2.21	.80[c]
Whole grains (g/d)	T1 | Low	36	<64.9	91.2	3.01	.51[a]	101.6	2.41	.75[a]	73.1	1.68	.14[a]	82.1	2.25	.79[a]
	T2 | Medium	37	$64.9 < 116.4$	88.5	3.01	.72[b]	102.6	2.41	.09[b]	69.6	1.69	.22[b]	82.9	2.26	.42[b]
	T3 | High	36	≥ 116.4	90.1	2.99	.79[c]	108.8	2.66	.05[c]	66.7	1.67	.01[c]	80.4	2.23	.59[c]
Processed meat (g/d)	T1 | Low	36	<39.0	93.6	3.21	.73[a]	105.3	2.70	.89[a]	71.7	1.86	.69[a]	81.5	2.46	.89[a]
	T2 | Medium	37	$39.0 < 80.2$	92.1	2.90	.08[b]	105.8	2.41	.36[b]	70.7	1.68	.12[b]	81.0	2.22	.58[b]
	T3 | High	36	≥ 80.2	84.8	2.92	.04[c]	102.4	2.70	.47[c]	67.0	1.69	.06[c]	82.7	2.23	.70[c]
SSB (g/d)	T1 | Low	38	0.0	91.6	2.98	.88[a]	105.7	2.41	.67[a]	70.0	1.72	.54[a]	83.9	2.23	.35[a]
	T2 | Medium	36	$0.1 < 246.4$	91.0	2.95	.41[b]	107.1	2.38	.07[b]	68.6	1.70	.41[b]	81.0	2.21	.86[b]
	T3 | High	35	≥ 246.4	87.5	2.98	.33[c]	100.7	2.65	.16[c]	70.6	1.72	.82[c]	80.5	2.23	.28[c]

Covariates: sex, age, BMI, educational level, and smoking history.

6MWD, 6-minute walking distance; *Anti-infl.*, anti-inflammatory; *BMI*, body mass index; *FEV_1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *PM*, predicted mean; *Pro-infl.*, pro-inflammatory; *SE*, standard error; *SSB*, sugar-sweetened beverages; *T1-T3*, tertiles.

*Pairwise comparison between tertiles: [a]T1 vs T2, [b]T2 vs T3, [c]T3 vs T1.

TABLE E4. Clinical asthma outcomes related to the Dietary Inflammatory Index (DII) and food groups

				ACQ-6 score (0-6)			AQLQ score (1-7)			≥1 exacerbations in preceding year			≥1 emergency visits in preceding year		
		No.	Cutoff value	PM	SE	*P**	PM	SE	*P**	PP	SE	*P**	PP	SE	*P**
DII	T1 | Anti-infl.	37	< −0.23	1.68	0.17	.86[a]	5.44	0.15	.40[a]	0.51	0.09	.80[a]	0.47	0.09	.98[a]
	T2 | Neutral	36	−0.23 < 1.08	1.72	0.18	.80[b]	5.25	0.16	.99[b]	0.48	0.10	.52[b]	0.47	0.10	.55[b]
	T3 | Pro-infl.	36	≥1.08	1.78	0.18	.67[c]	5.25	0.16	.41[c]	0.57	0.10	.70[c]	0.55	0.09	.54[c]
Fruit (g/d)	T1 | Low	36	<92.6	1.74	0.17	.33[a]	5.36	0.16	.77[a]	0.45	0.09	.49[a]	0.45	0.09	.64[a]
	T2 | Medium	37	92.6 < 198.0	1.51	0.17	.08[b]	5.43	0.16	.24[b]	0.54	0.09	.80[b]	0.51	0.09	.92[b]
	T3 | High	36	≥198.0	1.92	0.17	.44[c]	5.18	0.15	.39[c]	0.57	0.09	.35	0.52	0.09	.57[c]
Whole grains (g/d)	T1 | Low	36	<64.9	1.85	0.17	.51[a]	5.29	0.16	.89[a]	0.42	0.09	.26	0.53	0.09	.71[a]
	T2 | Medium	37	64.9 < 116.4	1.70	0.17	.82[b]	5.32	0.16	.88[b]	0.57	0.09	.98[b]	0.48	0.09	.97[b]
	T3 | High	36	≥116.4	1.64	0.17	.39[c]	5.35	0.16	.78[c]	0.57	0.09	.29	0.48	0.09	.70[c]
Processed meat (g/d)	T1 | Low	36	<39.0	1.67	0.19	.34[a]	5.33	0.17	.44[a]	0.40	0.10	.20[a]	0.44	0.10	.38[a]
	T2 | Medium	37	39.0 < 80.2	1.90	0.17	.19[b]	5.15	0.15	.10[b]	0.58	0.09	.92[b]	0.56	0.09	.55[b]
	T3 | High	36	≥80.2	1.59	0.17	.76[c]	5.50	0.15	.44	0.57	0.09	.23	0.48	0.09	.74[c]
SSB (g/d)	T1 | Low	38	0.0	1.78	0.17	.92[a]	5.18	0.15	.79[a]	0.60	0.09	.22[a]	0.59	0.09	.14[a]
	T2 | Medium	36	0.1 < 246.4	1.75	0.17	.68[b]	5.24	0.15	.16[b]	0.45	0.09	.59[b]	0.40	0.09	.43[b]
	T3 | High	35	≥246.4	1.65	0.17	.61[c]	5.54	0.15	.10[c]	0.52	0.09	.51	0.50	0.09	.49[c]

Covariates: sex, age, BMI, educational level, and smoking history.

ACQ, Asthma Control Questionnaire; *Anti-infl.*, anti-inflammatory; *AQLQ*, Asthma Quality-of-Life Questionnaire; *BMI*, body mass index; *PM*, predicted mean; *PP*, predicted probability; *Pro-infl.*, proinflammatory; *SE*, standard error; *SSB*, sugar-sweetened beverages; *T1-T3*, tertiles.

*Pairwise comparison between tertiles, [a]T1 vs T2, [b]T2 vs T3, [c]T3 vs T1.

TABLE E5. Inflammatory markers related to the Dietary Inflammatory Index (DII) and food groups

				FeNO (ppb)				Eosinophils (×10^9/L)				Leukocytes (×10^9/L)				IL-6 (pg/mL)			
		No.	Cutoff value	PM	LL	UL	*P**	PM	LL	UL	*P**	PM	LL	UL	*P**	PM	LL	UL	*P**
DII	T1 | Anti-infl.	37	< −0.23	27.94	22.51	34.71	.02[a]	0.15	0.10	0.21	.46[a]	6.48	5.95	7.06	.71[a]	1.41	1.15	1.72	.36[a]
	T2 | Neutral	36	−0.23 < 1.08	19.09	15.20	24.00	.24[b]	0.14	0.10	0.20	.92[b]	6.64	6.07	7.26	.25[b]	1.62	1.31	2.00	.77[b]
	T3 | Pro-infl.	36	≥1.08	22.99	18.39	28.73	.23[c]	0.12	0.09	0.16	.40[c]	7.12	6.53	7.77	.14[c]	1.69	1.37	2.08	.23[c]
Fruit (g/d)	T1 | Low	36	<92.6	24.07	19.34	29.99	.27[a]	0.15	0.11	0.21	.13[a]	6.67	6.14	7.25	.19[a]	1.53	1.25	1.87	.55[a]
	T2 | Medium	37	92.6 < 198.0	20.19	16.14	25.25	.10[b]	0.11	0.08	0.15	.26[b]	7.22	6.63	7.86	.03[b]	1.67	1.36	2.06	.39[b]
	T3 | High	36	≥198.0	26.18	21.03	32.56	.60[c]	0.14	0.10	0.20	.71[c]	6.35	5.84	6.91	.40[c]	1.48	1.21	1.81	.82[c]
Whole grains (g/d)	T1 | Low	36	<64.9	22.13	17.74	27.58	.66[a]	0.15	0.11	0.20	.34[a]	6.83	6.27	7.45	.83[a]	1.82	1.49	2.23	.50[a]
	T2 | Medium	37	64.9 < 116.4	20.68	16.58	25.82	.07[b]	0.12	0.09	0.17	.69[b]	6.92	6.37	7.54	.26[b]	1.66	1.35	2.03	.06[b]
	T3 | High	36	≥116.4	27.52	22.13	34.26	.17[c]	0.13	0.10	0.18	.61[c]	6.47	5.94	7.05	.38[c]	1.27	1.04	1.54	.01[c]
Processed meat (g/d)	T1 | Low	36	<39.0	25.43	19.93	32.49	.55[a]	0.10	0.07	0.14	.14[a]	6.33	5.77	6.94	.09[a]	1.92	1.55	2.38	.01[a]
	T2 | Medium	37	39.0 < 80.2	22.97	18.45	28.62	.84[b]	0.14	0.10	0.20	.74[b]	7.06	6.49	7.68	.44[b]	1.30	1.07	1.58	.17[b]
	T3 | High	36	≥80.2	22.24	17.83	27.74	.42[c]	0.15	0.11	0.21	.06[c]	6.74	6.19	7.33	.31[c]	1.58	1.30	1.92	.18[c]
SSB (g/d)	T1 | Low	38	0.0	21.96	17.58	27.44	.55[a]	0.12	0.09	0.17	.79[a]	6.50	5.97	7.08	.38[a]	1.34	1.10	1.64	.16[a]
	T2 | Medium	36	0.1 < 246.4	24.09	19.34	30.02	.99[b]	0.13	0.10	0.18	.65[b]	6.84	6.29	7.45	.99[b]	1.63	1.34	1.98	.74[b]
	T3 | High	35	≥246.4	24.14	19.34	30.14	.55[c]	0.15	0.11	0.20	.48[c]	6.84	6.28	7.45	.40[c]	1.71	1.39	2.10	.09[c]

Data are back transformed after natural log transformation. Covariates: sex, age, BMI, educational level, and smoking history.

Anti-infl., Anti-inflammatory; *BMI*, body mass index; *FeNO*, fractional exhaled nitric oxide; *LL*, 95% confidence interval lower limit; *PM*, predicted mean; *Pro-infl.*, proinflammatory; *SSB*, sugar-sweetened beverages; *T1-T3*, tertiles; *UL*, 95% confidence interval upper limit.

*Pairwise comparison between tertiles: [a]T1 vs T2, [b]T2 vs T3, [c]T3 vs T1.

TABLE E6. Sensitivity analyses for the association between the Dietary Inflammatory Index (DII) and asthma outcomes

		T1 | Anti-inflammatory				T2 | Neutral inflammatory				T3 | Proinflammatory			
		PM	LL	UL	P^a	PM	LL	UL	P^b	PM	LL	UL	P^c
FEV_1 (%pred)	MM	92.1	89.1	95.0	.15	85.9	79.8	92.0	.19	85.9	79.8	92.0	.87
	S1	91.5	85.3	97.7	.18	85.2	78.5	91.9	.15	91.9	85.2	98.5	.94
	S2	92.1	86.3	97.8	.15	85.9	79.8	92.0	.18	91.3	85.5	97.2	.87
	S3	91.8	85.7	97.9	.18	85.9	79.7	92.0	.19	91.4	85.4	97.4	.92
	S4	91.6	85.7	97.5	.20	86.0	79.8	92.2	.16	92.0	85.7	98.3	.93
FVC (%pred)	MM	108.7	104.0	113.4	.12	102.8	97.2	108.4	.64	101.1	96.3	105.9	.03
	S1	108.7	103.8	113.7	.15	102.9	96.8	109.0	.78	101.8	96.4	107.1	.07
	S2	108.6	104.0	113.3	.12	102.8	97.2	108.3	.66	101.2	96.4	105.9	.03
	S3	108.5	103.6	113.5	.15	102.8	97.2	108.4	.64	101.1	96.3	105.9	.04
	S4	108.7	103.9	113.5	.12	102.6	96.9	108.3	.87	102.0	97.0	107.0	.06
FEV_1/FVC (%)	MM	68.7	65.4	71.9	.65	67.6	64.1	71.0	.02	73.0	71.3	74.7	.08
	S1	68.1	64.6	71.6	.65	66.9	63.2	70.7	.02	73.0	69.2	76.7	.07
	S2	68.7	65.5	72.0	.65	67.6	64.1	71.1	.02	72.9	69.6	76.3	.08
	S3	68.6	65.2	72.1	.67	67.6	64.1	71.0	.02	73.0	69.6	76.4	.09
	S4	68.2	64.9	71.6	.86	67.8	64.3	71.3	.04	72.9	69.3	76.4	.07
6MWD (%pred)	MM	84.0	79.7	88.3	.38	81.2	76.6	85.7	.63	79.7	75.2	84.1	.18
	S1	84.3	79.9	88.7	.39	81.4	76.7	86.2	.56	79.5	74.8	84.3	.16
	S2	83.6	79.3	88.0	.40	80.9	76.3	85.5	.83	80.2	75.8	84.7	.29
	S3	84.6	80.0	89.2	.31	81.2	76.6	85.8	.60	79.5	75.0	84.0	.13
	S4	83.4	79.0	87.9	.50	81.2	76.6	85.8	.46	78.8	74.1	83.5	.16
ACQ-6 score (0-6)	MM	1.68	1.35	2.01	.86	1.72	1.37	2.07	.80	1.78	1.44	2.13	.67
	S1	1.56	1.22	1.90	.47	1.74	1.38	2.11	.87	1.79	1.42	2.15	.38
	S2	1.69	1.36	2.02	.87	1.73	1.38	2.08	.89	1.77	1.43	2.10	.76
	S3	1.75	1.40	2.10	.92	1.73	1.38	2.08	.87	1.77	1.43	2.11	.95
	S4	1.62	1.29	1.96	.61	1.75	1.40	2.10	.96	1.77	1.41	2.12	.58
AQLQ score (1-7)	MM	5.44	5.14	5.74	.40	5.25	4.93	5.57	.99	5.25	4.94	5.57	.41
	S1	5.55	5.25	5.85	.17	5.24	4.91	5.57	.82	5.29	4.97	5.62	.26
	S2	5.44	5.13	5.74	.40	5.25	4.93	5.57	.95	5.26	4.95	5.57	.43
	S3	5.35	5.03	5.67	.64	5.24	4.93	5.56	.89	5.27	4.96	5.58	.74
	S4	5.52	5.22	5.83	.17	5.21	4.90	5.53	.84	5.26	4.94	5.58	.25
≥1 exacerbations in previous year (predicted probability)	MM	0.51	0.34	0.69	.80	0.48	0.28	0.67	.52	0.57	0.38	0.76	.70
	S1	0.51	0.33	0.69	.79	0.47	0.27	0.67	.66	0.55	0.35	0.76	.74
	S2	0.51	0.34	0.69	.80	0.48	0.28	0.67	.49	0.57	0.38	0.76	.67
	S3	0.55	0.36	0.73	.65	0.48	0.29	0.68	.57	0.56	0.37	0.75	.93
	S4	0.53	0.35	0.71	.66	0.47	0.27	0.67	.62	0.54	0.34	0.74	.96
≥1 emergency visits in previous year (predicted probability)	MM	0.47	0.29	0.64	.98	0.47	0.28	0.66	.55	0.55	0.37	0.73	.54

(continued)

TABLE E6. *(Continued)*

		T1 | Anti-inflammatory				T2 | Neutral inflammatory				T3 | Proinflammatory			
		PM	LL	UL	P^a	PM	LL	UL	P^b	PM	LL	UL	P^c
	S1	0.42	0.24	0.60	.90	0.44	0.24	0.63	.29	0.58	0.39	0.77	.24
	S2	0.47	0.29	0.64	.98	0.47	0.28	0.66	.56	0.55	0.37	0.72	.54
	S3	0.52	0.33	0.71	.71	0.47	0.28	0.67	.63	0.54	0.35	0.72	.93
	S4	0.46	0.28	0.64	.88	0.48	0.29	0.67	.82	0.51	0.32	0.70	.71
FeNO (ppb)	MM	27.9	22.5	34.7	.02	19.1	15.2	24.0	.24	23.0	18.4	28.7	.23
	S1	29.2	23.6	36.1	.03	20.5	16.3	25.8	.66	22.0	17.5	27.6	.08
	S2	27.9	22.5	34.6	.02	19.1	15.2	24.0	.22	23.0	18.5	28.7	.23
	S3	27.1	21.6	34.1	.03	19.0	15.2	23.9	.22	23.1	18.5	28.9	.35
	S4	27.9	22.6	34.3	.03	19.5	15.5	24.4	.21	23.7	18.9	29.7	.31
Eosinophils ($\times 10^9$/L)	MM	0.15	0.10	0.21	.46	0.14	0.10	0.20	.92	0.12	0.09	0.16	.40
	S1	0.13	0.09	0.17	.64	0.14	0.10	0.20	.90	0.15	0.10	0.21	.56
	S2	0.12	0.09	0.17	.47	0.14	0.10	0.20	.93	0.14	0.10	0.20	.52
	S3	0.11	0.08	0.15	.26	0.14	0.10	0.20	.86	0.15	0.11	0.21	.20
	S4	0.12	0.09	0.17	.70	0.13	0.09	0.19	.80	0.14	0.10	0.20	.53
Leukocytes ($\times 10^9$/L)	MM	6.48	5.95	7.06	.71	6.64	6.07	7.26	.25	7.12	6.53	7.77	.14
	S1	6.49	5.95	7.09	.98	6.48	5.90	7.12	.26	6.97	6.35	7.65	.29
	S2	6.43	5.91	7.00	.69	6.60	6.03	7.22	.15	7.21	6.61	7.85	.07
	S3	6.51	5.96	7.13	.77	6.64	6.07	7.26	.26	7.11	6.52	7.76	.18
	S4	6.48	5.95	7.05	.72	6.63	6.04	7.26	.21	7.18	6.55	7.87	.12
IL-6 (pg/mL)	MM	1.41	1.15	1.72	.36	1.62	1.31	2.00	.77	1.69	1.37	2.08	.23
	S1	1.38	1.11	1.70	.65	1.48	1.18	1.85	.48	1.65	1.32	2.07	.26
	S2	1.36	1.10	1.67	.35	1.57	1.26	1.95	.38	1.79	1.44	2.22	.07
	S3	1.45	1.17	1.79	.47	1.62	1.31	2.00	.81	1.68	1.36	2.07	.35
	S4	1.41	1.15	1.73	.42	1.59	1.28	1.98	.57	1.74	1.39	2.17	.18

MM: Covariates: sex, age, BMI, educational level, and smoking history (main model, n = 109).
S1: Same as main model, excluding patients with unreliable food data (n = 98).
S2: Covariates: sex, age, educational level, and smoking history (no BMI) (n = 109).
S3: Covariates: sex, age, BMI, educational level, smoking history, and energy intake (n = 109).
S4: Covariates: sex, age, BMI, educational level, smoking history, and supplement use (n = 106).
Pairwise comparison between tertiles: [a]T1 vs T2, [b]T2 vs T3, [c]T3 vs T1.
6MWD, 6-minute walking distance; *ACQ*, Asthma Control Questionnaire; *AQLQ*, Asthma Quality-of-Life Questionnaire; *BMI*, body mass index; *FeNO*, fractional exhaled nitric oxide; *FEV_1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *LL*, 95% confidence interval lower limit; *PM*, predicted mean; *SE*, standard error; *T1-T3*, tertiles; *UL*, 95% confidence interval upper limit.