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Naples prognostic score as a novel prognostic prediction indicator in adult asthma patients: A population-based study

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ABSTRACT

Objective: This study was to evaluate the prognostic value of the Naples prognostic score (NPS) in adult patients with asthma.

Methods: Data on 44 601 participants from the 1999–2018 National Health and Nutrition Examination Survey (NHANES) were analyzed. The NPS was calculated based on serum albumin, total cholesterol, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR), and participants were divided into 3 groups. Self-administered questionnaires were used to collect information on asthma, and mortality was identified using the National Death Index through December 31, 2019. Multiple logistic regressions were used to analyze the relationship between NPS and its components and the prevalence of asthma. Kaplan-Meier survival analysis, Cox proportional regressions, and the random survival forest (RSF) were used to assess the significance of NPS and its components in predicting all-cause and cause-specific (cardiovascular, cancer, and respiratory diseases) mortality in asthma patients.

Results: The mean age of the participants was 47.59 ± 0.18 years, and 48.47% were male. The prevalence of asthma was 13.11%. The participants were categorized into 3 groups: 8306 (18.6%) participants were in group 0 (NPS 0), 30 842 (69.2%) were in group 1 (NPS 1 or 2), and 5453 (11.2%) were in group 2 (NPS 3 or 4). Compared to the reference group, participants in group 2 had a higher prevalence of asthma (odds ratio [OR] = 1.40 [1.24–1.56]). Participants with asthma in group 2 had a significantly increased risk of all-cause mortality (hazard ratio [HR] = 2.42 [1.67–3.50]), cardiovascular mortality (HR = 2.68 [1.50–4.79]), cancer mortality (HR = 2.10 [1.00–4.45]), and respiratory disease mortality (HR = 3.00 [1.18–7.65]) compared to those with asthma in group 0. The RSF showed that NPS had the highest value in predicting all-cause mortality in adults with asthma, compared to its components.

Conclusions: The results of this study indicate that the NPS is a powerful prognostic indicator for outcomes in asthma patients.

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INTRODUCTION

Asthma is a heterogeneous disease characterized by the presence of respiratory symptoms that vary over time and in intensity, along with variable expiratory airflow limitation.[1] It poses a significant global health problem, with a growing prevalence in numerous countries and regions.[2] According to the Centers for Disease Control and Prevention (CDC), approximately 49.1% of adults experienced asthma in the past year.[3] In the United States (US) alone, almost 25 million individuals suffer from asthma.[4] The estimated cost of treatment and mortality for asthma amounts to $81 billion.[5] Despite the preventability of a significant proportion of the disease burden through appropriate interventions, asthma has not received as much attention as other prominent diseases, such as cardiovascular disease, cancer, or diabetes.[6]

Asthma is widely recognized as a chronic inflammatory disease of the airways,[7] with inflammation playing a pivotal role in its development.[8] Both local and systemic inflammation can exacerbate asthma.[9,10] Current studies suggest that a range of inflammation-related indicators may be associated with outcomes in patients with asthma,[11,12] including the neutrophil-to-lymphocyte ratio (NLR) and the lymphocyte-to-monocyte ratio (LMR).[13] Furthermore, some nutritional indicators, such as low serum albumin levels and high total cholesterol (TC) levels, have been identified in asthma patients.[14,15] However, the generalizability of these predictors to the overall condition of asthma patients is limited.

The Naples Prognostic Score (NPS) is a novel scoring system designed to assess the prognostic outcomes of colorectal cancer.[16] Comprising serum albumin, TC, NLR, and LMR, the NPS reflects the inflammatory and nutritional status of patients. Notably, the NPS has been identified as an independent prognostic factor in endometrial cancer, pancreatic cancer, and metastatic colorectal cancer.[17,18] However, the association between NPS and survival in patients with asthma has not yet been evaluated. Therefore, using data from the 1999–2018 National Health and Nutrition Examination Survey (NHANES), this study examines the relationship between NPS and asthma prevalence. Additionally, we analyze the correlation between NPS and mortality among participants with asthma. Our study aims to provide a valuable prognostic indicator that can guide the individualized treatment of asthma.

MATERIALS AND METHODS

Study population

The NHANES is a comprehensive population-based study aimed at assessing the health and nutritional status of children and adults.[19] The NHANES health examination is conducted by professional medical staff in a Mobile Examination Center (MEC) and focuses on collecting basic physical and biochemical examinations and other medically relevant information. All data are available for download from the official website (https://www.cdc.gov/nchs/nhanes). The research protocols were approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board, and all participants provided informed consent.

In this study, we analyzed data from the 1999–2018 NHANES. We excluded participants under the age of 18 and those with missing asthma assessment data. Participants who were pregnant, lacked data for NPS assessment (serum albumin, TC, and CBC count), had an extreme energy intake (men: >4200 or <800 kcal/day; women: >3500 or <500 kcal/day),[20] or had no follow-up information were also excluded.

The protocols involved were approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB), and informed consent from all participants was documented.

Assessment of NPS

The NPS was defined based on the levels of serum albumin, TC, NLR, and LMR by the method

of Galizia et al (the cutoff values of NLR and LMR were defined by MaxStat analysis).[16] According to the previous reports, serum albumin ≥40 g/L, TC > 180 mg/dL, NLR < 2.96, or LMR > 4.44 was scored as 0, while serum albumin <40 g/L, TC ≤ 180 mg/dL, NLR ≥ 2.96, or LMR ≤ 4.44 was scored as 1; NPS is the sum of the scores of each of the 4 factors. In addition, participants were divided into three groups according to NPS as described in a previous study (Table S1);[21] group 0, patients with a score of 0; group 1, patients with a score of 1 or 2; and group 2, patients with a score of 3 or 4.

Assessment of asthma

The NHANES study collected information on asthma and its associated symptoms through a self-administered questionnaire.[22] Participants who answered "yes" to both of the following questions were defined as having current asthma: "Has a doctor or other health professional ever told you that you have asthma?" and "Do you still have asthma?". Participants who answered "no" to either question were used as the control group.

Assessment of mortality

In this study, participants who had passed away were identified by linking the study data to the National Death Index (NDI). As of December 31, 2019, we obtained records of all-cause mortality as well as cause-specific mortality, including cardiovascular mortality, cancer mortality, and respiratory disease mortality, for participants through the 2019 Linked Mortality File (LMF). This file reports the most recent associations made between selected NCHS surveys and the NDI.

Covariates

Baseline data of study participants were collected using questionnaires and laboratory tests, including age (in years), sex (male or female), educational attainment (below high school, high school, or above high school), race/ethnicity (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, or other race), and body mass index (BMI; <25.0, 25.0–29.9, or >29.9 kg/m2). Poverty was assessed using the poverty income ratio (the ratio of family income divided by a poverty threshold specific for family size using guidelines from the US Department of Health and Human Services) and categorized as ≤1.0, 1.1–3.0, and >3.0.[23,24] Never smokers were defined as those who reported smoking less than 100 cigarettes over their lifetime. Current smokers were those who smoked more than 100 cigarettes over their lifetime, while former smokers were those who had smoked more than 100 cigarettes but had quit.[25] Drinking status was classified as nondrinker, low-to-moderate drinker (<2 drinks/day in men and <1 drink/day in women), or heavy drinker (≥2 drinks/day in men and ≥1 drinks/day in women).[25] Physical activity was classified as inactive (no leisure-time physical activity), insufficiently active (moderate activity 1–5 times per week with metabolic equivalents [MET] 3–6 or vigorous activity 1–3 times per week with MET >6), or active (more moderate or vigorous activity than the previously mentioned).[25,26] Energy intake (kcal/day) was calculated by averaging 2 values obtained from two 24-h recall interviews.

Statistical analysis

Continuous variables were reported as medians and interquartile ranges (IQRs), while categorical variables were presented as numbers and percentages. The normality of continuous variables was examined using the Shapiro-Wilk test. Student's t-test was used for normally distributed continuous variables, and the Mann-Whitney *U* test was used for non-normally distributed continuous variables. The chi-square test was used for comparing categorical variables. Missing data were imputed using the "mice" package in R, based on the Random Forest algorithm.

We conducted multiple logistic regression analysis to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) to investigate the association between NPS and its components and the prevalence of asthma. We used the Kaplan-Meier method and log-rank test to calculate cumulative survival rates and compare them between three groups based on NPS. Cox regression analysis was used to calculate adjusted hazard ratios (HRs) and 95% CIs for all-cause and cause-specific mortality in participants with asthma.

We performed Spearman's correlation analysis to assess the correlation coefficients among NPS and its components. We utilized the random survival

forest method to compare the predictive value of NPS and its components for all-cause and cause-specific mortality in asthmatic patients. To mitigate the potential bias of reverse causality, we also conducted a sensitivity analysis by excluding cases where death occurred within the first two years of follow-up. Moreover, we further adjusted for medication use, such as oral glucocorticoids (yes, or no), and statins (yes, or no), and major non-communicable diseases, including cardiovascular (yes, or no), emphysema (yes, or no), cancer (yes, or no), and diabetes (yes, or no). All statistical analyses were conducted using R software (version 4.2.0).

RESULTS

Characteristics of study participants

Between 1999 and 2018, a total of 101 316 participants took part in the NHANES. We excluded participants under the age of 18 and those with missing asthma assessment data (n = 46 235). Further exclusions were made for pregnant participants (n = 1305), those without NPS assessment data (n = 6326), and participants with excessive energy consumption (n = 2849). We also excluded eleven asthma participants who were not interviewed, resulting in a total of 5837 asthma participants for survival analysis (Fig. 1).

Table 1 shows the baseline characteristics of the three NPS groups in the 1999–2018 NHANES. The study population had a mean age of 47.59 ± 0.18 years, with 48.47% males, and predominantly non-Hispanic white (44.93%). The prevalence of asthma was 13.11%. The median values for serum albumin, TC, NLR, and LMR were 43.00 [IQR 41.00, 45.00] g/L, 193.00 [IQR 167.00, 221.00] mg/dL, 2.00 [IQR 1.51, 2.61], and 3.80 [IQR 3.00, 4.80], respectively. According to the NPS system, 8306 (18.6%)

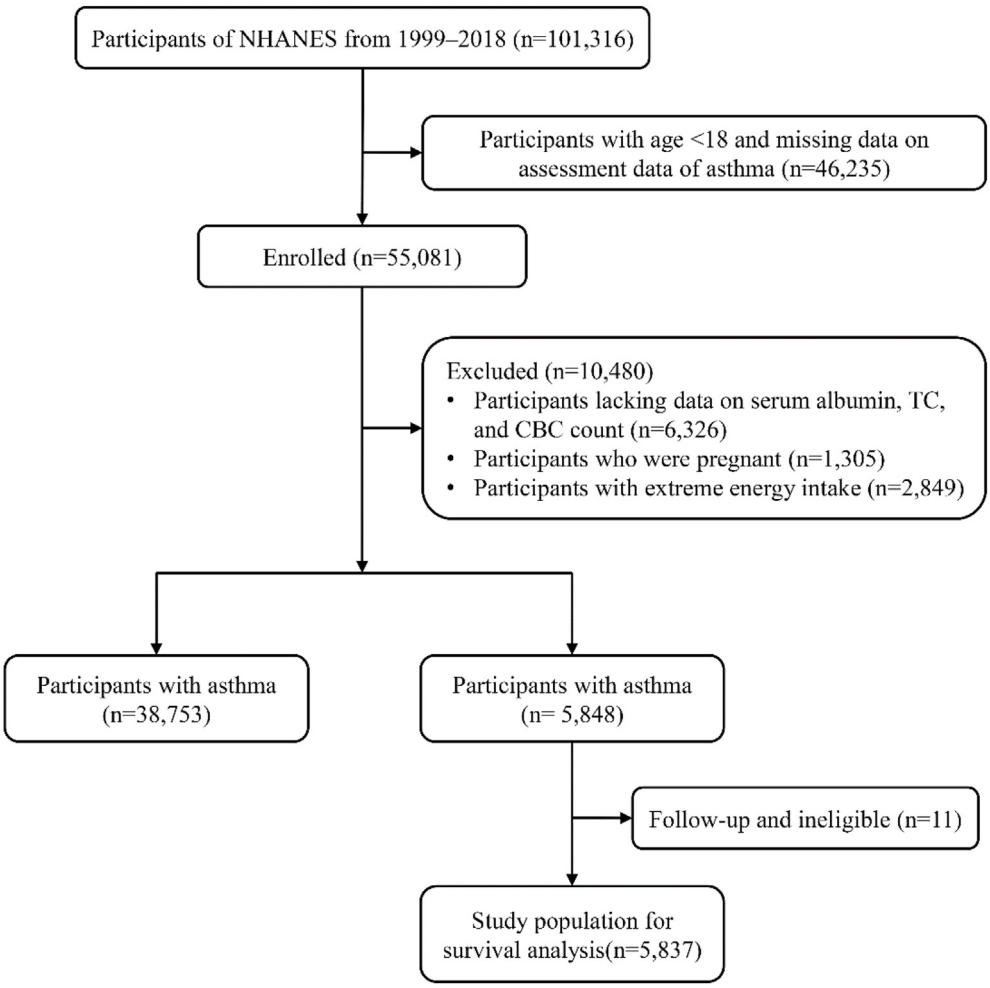

Fig. 1 Flowchart of the study participants

Characteristics	Total	NPS, points			*P* value
		0	1–2	3–4	
Participants, N	44,601	8306	30,842	5453	
Age, years	47.59 (0.18)	45.86 (0.22)	47.14 (0.20)	53.20 (0.37)	<0.001
Male, %	21 618 (48.47)	3300 (37.98)	15 524 (49.96)	2794 (48.28)	<0.001
Race/ethnicity, %					<0.001
Mexican American	7814 (17.52)	1813 (10.43)	5225 (7.62)	776 (6.74)	
Other Hispanic	3720 (8.34)	779 (6.63)	2541 (5.49)	400 (4.96)	
Non-Hispanic White	20 039 (44.93)	2877 (61.17)	14 393 (70.66)	2769 (71.58)	
Non-Hispanic Black	8849 (19.84)	1816 (12.11)	5934 (9.83)	1099 (10.79)	
Other race	4179 (9.37)	1021 (9.66)	2749 (6.40)	409 (5.94)	
Education level, %					<0.001
Below high school	11 967 (26.83)	2283 (17.93)	8144 (16.51)	1540 (18.62)	
High school	10 246 (22.97)	1870 (23.47)	7071 (23.70)	1305 (25.15)	
Above high school	22 388 (50.20)	4153 (58.61)	15 627 (59.79)	2608 (56.23)	
Family PIR, %					<0.001
≤1.0	9115 (20.44)	1682 (13.95)	6266 (13.85)	1167 (16.00)	
1.1–3.0	18820 (42.2)	3406 (35.42)	12884 (35.54)	2530 (40.03)	
>3.0	16 666 (37.37)	3218 (50.62)	11 692 (50.61)	1756 (43.97)	
Smoking status, %					<0.001
Never smoker	24 243 (54.36)	4795 (55.77)	16 790 (54.13)	2658 (51.00)	
Former smoker	11 266 (25.26)	1726 (21.44)	7793 (25.24)	1747 (29.25)	
Current smoker	9092 (20.39)	1785 (22.79)	6259 (20.63)	1048 (19.75)	
Drinking status, %					<0.001
Nondrinker	10 396 (23.31)	1973 (19.01)	6935 (18.12)	1488 (23.92)	
Low-to-moderate drinker	30 749 (68.94)	5792 (72.80)	21 368 (72.23)	3589 (68.11)	
Heavy drinker	3456 (7.75)	541 (8.19)	2539 (9.66)	376 (7.98)	

(continued)

Characteristics	Total	NPS, points			*P* value
		0	1–2	3–4	
Body mass index, kg/m^2					<0.001
<25.0	13 204 (29.6)	2329 (30.05)	9307 (31.55)	1568 (30.16)	
25.0–29.9	15 144 (33.95)	2959 (35.03)	10 598 (33.82)	1587 (28.29)	
>29.9	16 253 (36.44)	3018 (34.92)	10 937 (34.63)	2298 (41.56)	
Physical activity, %					<0.001
Inactive	12 393 (27.79)	2198 (21.55)	8203 (21.29)	1992 (30.45)	
Insufficiently active	16 492 (36.98)	3179 (41.62)	11 513 (40.36)	1800 (35.79)	
Active	15 716 (35.24)	2929 (36.82)	11 126 (38.35)	1661 (33.77)	
Energy intake, kcal/day	1978.00 [1489.00, 2581.00]	1915.00 [1445.00, 2489.00]	2001.00 [1511.00, 2608.00]	1934.00 [1453.00, 2513.00]	<0.001
Serum albumin, 40 g/L	43.00 [41.00,45.00]	43.00 [42.00, 45.00]	43.00 [41.00, 45.00]	39.00 [38.00, 43.00]	<0.001
Total cholesterol, mg/dL	193.00 [167.00, 221.00]	214.00 [197.00, 239.00]	192.00 [167.00, 219.00]	161.00 [144.00,174.00]	<0.001
NLR	2.00 [1.51,2.61]	1.53 [1.21,1.91]	2.00 [1.56, 2.53]	3.32 [2.71, 4.00]	<0.001
LMR	3.80 [3.00, 4.80]	5.33 [4.80, 6.25]	3.67 [3.00, 4.33]	2.75 [2.17, 3.40]	<0.001
Asthma, %	5848 (13.11)	988 (12.77)	4021 (13.64)	839 (15.88)	<0.001

Table 1. (Continued) Characteristics of adult participants in NHANES 1999–2018. *Normally distributed continuous variables are described as means ± SEs, and continuous variables without a normal distribution are presented as medians [interquartile ranges]. Categorical variables are presented as numbers (percentages). N reflect the study sample while percentages reflect the survey-weighted. PIR, poverty income ratio; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio*

participants were in group 0 (NPS 0), 30,842 (69.2%) in group 1 (NPS 1 or 2), and 5453 (11.2%) in group 2 (NPS 3 or 4). Compared to group 0, participants in group 2 were more likely to be older non-Hispanic white males with lower education and income levels, non-drinkers, non-smokers, physically inactive, higher BMI, and higher prevalence of asthma. Table S2 summarizes the baseline characteristics of participants with and without asthma.

Over a median follow-up of 8.25 years, there were 849 (14.5%) all-cause deaths among 5837 adults with asthma (Table 2). Compared to survivors among adults with asthma, those who died of all causes were more likely to be older non-Hispanic white males with lower education and income levels, current smokers, heavy drinkers, physically inactive, higher energy intake, and higher NPS. In addition, all-cause deaths were more likely to have lower levels of serum albumin ($P < 0.001$) and LMR ($P < 0.001$), while higher levels of TC ($P = 0.020$) and NLR ($P < 0.001$).

Associations between NPS and the prevalence of asthma

NPS was classified into 3 groups, with group 0 as the reference category, and assessed for their association with asthma prevalence (Fig. 2). The crude model revealed a positive correlation between NPS and the prevalence of asthma (OR = 1.29 [1.14–1.45]). After adjusting for age, sex, and race, this relationship remained statistically significant (OR = 1.40 [1.24–1.56]). Participants in group 2 were significantly associated with a higher prevalence of asthma compared to the reference group in Model 2 (OR = 1.40 [1.24–1.56]). We also analyzed the association between serum albumin, TC, NLR, and LMR and the prevalence of asthma (Table S3). After adjusting for all confounding factors, we found that albumin <40 g/L (OR = 1.26 [1.15–1.38]), TC ≤ 180 mg/dL (OR = 1.18 [1.09–1.27]), and NLR > 2.96 (OR = 1.15 [1.04–1.26]) were significantly associated with a higher prevalence of asthma. Furthermore, the relationship between NPS and asthma prevalence remained stable when NPS was divided into 5 groups (Table S4).

Associations between NPS and mortality among adults with asthma

In this study, we utilized the Kaplan-Meier curve to assess the prognostic significance of NPS in patients with asthma, as depicted in Fig. 3. The results revealed that participants with asthma in group 2 had the highest risk of all-cause and cause-specific mortality when compared to the other two groups stratified based on NPS (log-rank test $P < 0.001$). Upon multivariate adjustment, participants with asthma in group 2 exhibited a significantly increased risk of all-cause mortality (HR = 2.42 [1.67–3.50]), cardiovascular mortality (HR = 2.68 [1.50–4.79]), cancer mortality (HR = 2.10 [1.00–4.45]), and respiratory disease mortality (HR = 3.00 [1.18–7.65]), relative to those in group 0 (Table 3). We also investigated the relationship between serum albumin, TC, NLR, LMR, and the risk of all-cause and cause-specific mortality in patients with asthma (Table S5). Following correction for all potential confounders, our findings indicated that albumin levels <40 g/L were significantly associated with an increased risk of all-cause mortality (HR = 1.60 [1.35–1.90]) and cardiovascular mortality (HR = 2.01 [1.41–2.87]). Additionally, an NLR >2.96 was significantly associated with an elevated risk of all-cause mortality (HR = 1.44 [1.16–1.79]) and respiratory disease mortality (HR = 2.70 [1.65–4.40]). Furthermore, we divided NPS into 5 groups, and the aforementioned associations remained stable (Table S6).

Prognostic value of NPS

We investigated the correlation between NPS and its components, and observed a significant positive correlation between NLR and NPS ($r = 0.49$) (Fig. 4A). In terms of prognostic value, we compared NPS with its components (serum albumin, TC, NLR, and LMR), and found that NPS was the most effective predictor of all-cause mortality in adults with asthma (Fig. 4B). Furthermore, we assessed the value of NPS and its components in predicting cause-specific mortality in asthma patients and determined that NPS

Characteristics	Total (N = 5837)	All-cause mortality		*P* value
		No (N = 4988)	No (N = 849)	
Age, years	45.76 (0.31)	43.57 (0.30)	64.35 (0.60)	<0.001
Male, %	2403 (41.17)	2007 (39.96)	396 (41.80)	0.460
Race/ethnicity, %				0.010
Mexican American	603 (10.33)	533 (5.06)	70 (2.46)	
Other Hispanic	539 (9.23)	492 (6.02)	47 (4.80)	
Non-Hispanic White	2839 (48.64)	2326 (70.23)	513 (77.25)	
Non-Hispanic Black	1343 (23.01)	1163 (11.71)	180 (11.06)	
Other race	513 (8.79)	474 (6.97)	39 (4.43)	
Education level, %				<0.001
Below high school	1341 (22.97)	1021 (13.75)	320 (29.38)	
High school	1288 (22.07)	1092 (21.97)	196 (24.78)	
Above high school	3208 (54.96)	2875 (64.29)	333 (45.84)	
Family PIR, %				<0.001
≤1.0	1395 (23.9)	1172 (16.52)	223 (24.07)	
1.1–3.0	2380 (40.77)	1959 (34.65)	421 (45.13)	
>3.0	2062 (35.33)	1857 (48.83)	205 (30.80)	
Smoking status, %				<0.001
Never smoker	2882 (49.37)	2607 (52.03)	275 (31.38)	
Former smoker	1575 (26.98)	1224 (25.11)	351 (39.05)	
Current smoker	1380 (23.64)	1157 (22.86)	223 (29.57)	
Drinking status, %				<0.001
Nondrinker	1269 (21.74)	1027 (16.51)	242 (27.47)	
Low-to-moderate drinker	4135 (70.84)	3591 (75.03)	544 (63.22)	
Heavy drinker	433 (7.42)	370 (8.46)	63 (9.31)	
Body mass index, kg/m^2				0.320
<25.0	1498 (25.66)	1278 (28.85)	220 (25.64)	
25.0–29.9	1687 (28.9)	1422 (28.49)	265 (29.64)	
>29.9	2652 (45.43)	2288 (42.66)	364 (44.72)	
Physical activity, %				<0.001
Inactive	1655 (28.35)	1229 (21.05)	426 (48.20)	
Insufficiently active	2075 (35.55)	1843 (39.78)	232 (27.53)	
Active	2107 (36.1)	1916 (39.17)	191 (24.27)	

Energy intake, kcal/day	1944.00 [1459.00, 2565.00]	1987.00 [1483.00, 2601.98]	1618.00 [1297.00, 2154.00]	<0.001
Serum albumin, g/L	43.00 [40.00, 45.00]	43.00 [40.00, 45.00]	41.00 [39.00, 44.00]	<0.001
Total cholesterol, mg/dL	190.00 [164.00, 219.00]	190.00 [164.00, 218.00]	197.00 [163.00, 230.00]	0.020
NLR	2.00 [1.54, 2.65]	1.97 [1.52, 2.59]	2.34 [1.74, 3.44]	<0.001
LMR	3.83 [3.00, 4.80]	4.00 [3.00, 5.00]	3.20 [2.29, 4.33]	<0.001
NPS, %				<0.001
0 point	986 (16.89)	902 (17.21)	84 (10.52)	
1-2 points	4012 (68.73)	3465 (71.26)	547 (64.36)	
3-4 points	839 (14.37)	621 (11.53)	218 (25.13)	

Table 2. Characteristics of adult with asthma in NHANES 1999–2018. *Normally distributed continuous variables are described as means ± SEs, and continuous variables without a normal distribution are presented as medians [interquartile ranges]. Categorical variables are presented as numbers (percentages). N reflect the study sample while percentages reflect the survey-weighted. PIR, poverty income ratio; NLR, neutrophil-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio*

had a greater significance than other indicators (Figure S1).

Sensitivity analyses

In sensitivity analyses, upon excluding participants who died within 2 years of follow-up and performing Cox regression analysis again, we confirmed the persistence of the aforementioned relationship (Table S7). Adjusting further for medication use (oral glucocorticoids and statins), or adjusting for major noncommunicable diseases (cardiovascular, emphysema, cancer, or diabetes) for the full model showed similar results (Table S8).

DISCUSSION

This study analyzes data from the NHANES database, which is representative of the US population from 1999 to 2018. To the best of our knowledge, this is the first investigation into the relationship between NPS and asthma prevalence. Our findings indicate that patients with asthma exhibited higher NPS levels relative to those without asthma. After adjusting for relevant factors, we observed a significant positive correlation between NPS and the risk of all-cause and cause-specific mortality in asthma patients. Furthermore, our machine learning analysis demonstrated that NPS is a more accurate predictor than a single marker. Our study provides promising results for the investigation of the association between NPS and asthma prognosis in the future.

Asthma is a chronic inflammatory disease of the airways involving multiple cells, including eosinophils, neutrophils, lymphocytes, and macrophages.[27] Timely assessment of asthma inflammation is crucial for controlling its progression and selecting appropriate treatment plans.[7] Recently, markers such as NLR and LMR, which reflect the immune and chronic inflammatory states of the body, have been studied,[28,29] but their role in the diagnosis and prognosis of asthma remains unclear. A meta-analysis showed that NLR values are a useful and easy-to-use marker for asthma and its exacerbations.[13] Shi et al also demonstrated that NLR, as a non-specific inflammatory index, effectively diagnoses patients with acute asthma attacks and is related to the severity of the disease.[30] In our study, we found that NLR was significantly

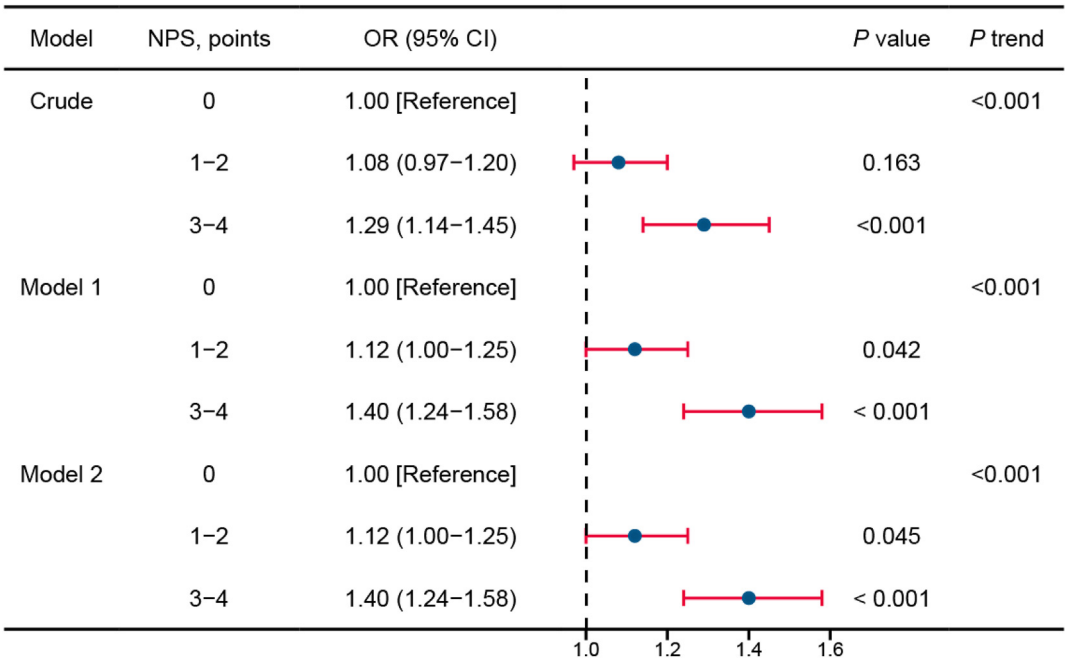

Fig. 2 ORs (95% CIs) of the prevalence of asthma according to the Naples prognostic score (NPS) among adults in the NHANES 1999–2018 (n = 44,601)

associated with the prevalence of asthma and increased the risk of all-cause and respiratory disease mortality in patients with asthma.

Nutrition is also believed to play a critical role in disease progression by changing the metabolic state of tissues.[31] Nutritional markers such as albumin and cholesterol have been shown to be effective predictors of disease progression.[32] Changes in serum albumin concentration have been reported in patients with asthma[14] and can potentially affect the unbound drug concentrations, especially for drugs with low hepatic clearance.[33] Cholesterol also plays a crucial role in asthma development through inflammatory responses and oxidative stress.[34] Su et al found that TC levels were higher in patients with asthma than in non-asthmatic patients,[15] and hypercholesterolemia can be a potential risk factor for asthma independent of obesity.[35] In our study, we found that albumin and TC were significantly associated with the prevalence of asthma. Furthermore, albumin was significantly associated with a higher risk of all-cause and cardiovascular mortality in asthma patients.

Systemic inflammation and nutrition are closely related,[36] and abnormal nutritional status can destroy the body's inflammatory regulation system.[37] Combining systemic inflammatory and nutritional markers to predict disease progression and prognosis has been widely used. NPS reflects systemic inflammation, malnutrition, and survival for various conditions and is related to the outcome of multiple diseases.[38–40] Although research on NPS is primarily focused on tumor-related diseases, its role in non-tumor diseases remains unclear.[41–43] Erdogan et al found an association between NPS and in-hospital and follow-up outcomes in ST-segment elevation myocardial infarction (STEMI) patients.[44] They identified NPS as an independent predictor of all-cause mortality in STEMI patients. In our study, we found that a higher NPS was associated with a higher prevalence of asthma, and NPS showed superior prognostic value for mortality prediction than a single factor in patients with asthma.

Compared with previous studies, our study has several advantages. First, we used a nationally representative, relatively large sample, enabling us to discover the association between NPS and the prevalence of asthma, as well as mortality in adults with asthma. Second, we adjusted our analysis for primary factors affecting lung function, including age, smoking, BMI, physical activity, and other

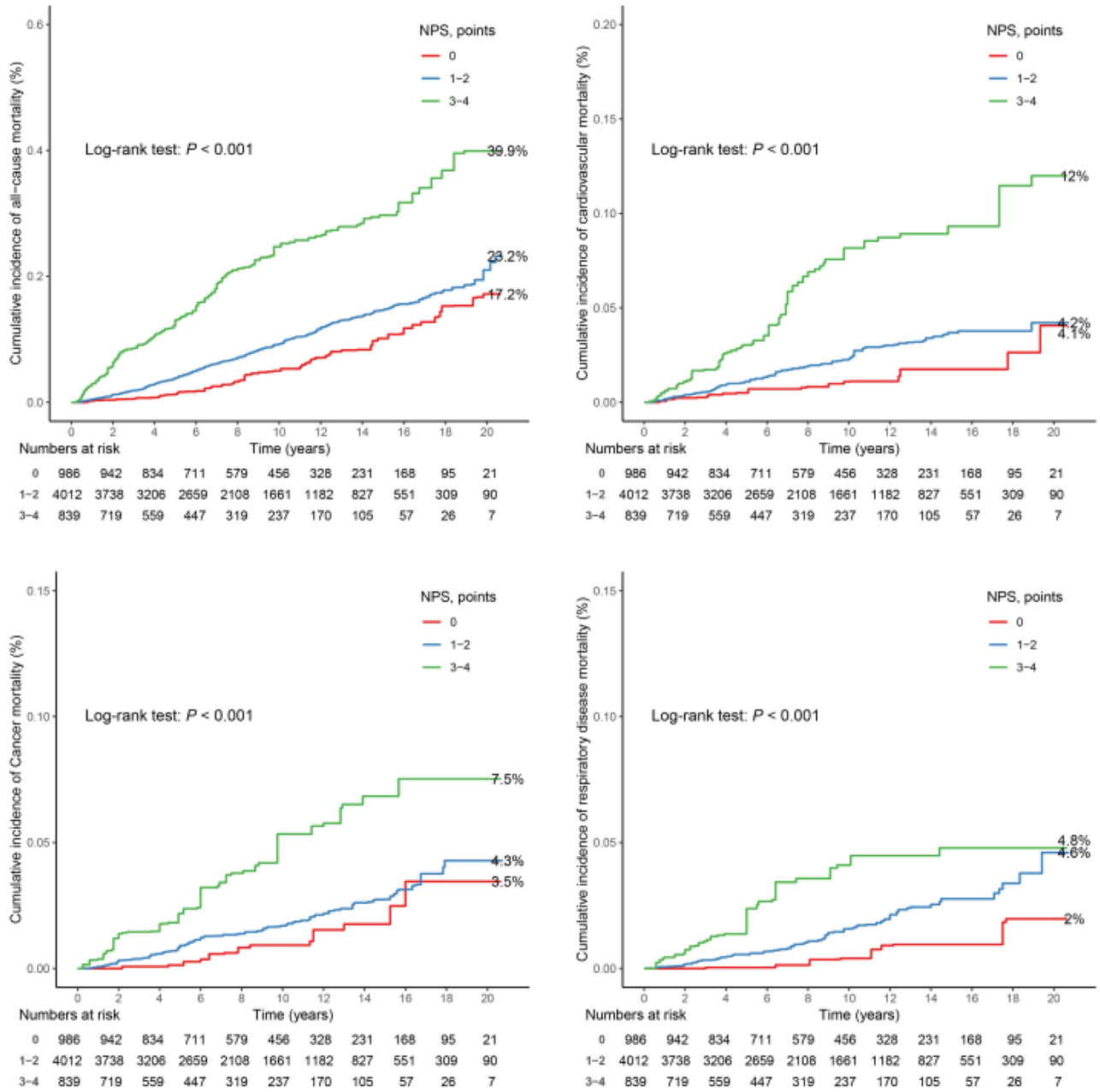

Fig. 3 Kaplan-Meier survival curves for all-cause and cause-specific mortality in adults with asthma grouped by Naples prognostic score (NPS)

confounding factors. Third, NPS is superior to other single inflammatory or nutritional markers, as it takes into account the impact of systemic inflammation and nutritional status on disease prognosis.

There are several limitations to this study that should be acknowledged. Firstly, the findings from the NHANES relied on patient self-reports, which could be susceptible to recall bias. Secondly, while the study controlled for various potential confounding factors such as age, sex, and smoking status, there may still be unmeasured confounders that could impact the analyses. Lastly, although this study had a national scope, the data were primarily obtained from the US population, and there remains a lack of data on populations from countries with less developed economies. Further global clinical studies are needed to verify our conclusions. These limitations should be taken into consideration when interpreting the results of this study.

	NPS, points			P_{trend}
	0	1-2	3-4	
All-cause mortality				
Crude	1 [Reference]	1.56 (1.14-2.14)	4.30 (3.02-6.11)	<0.001
Model 1	1 [Reference]	1.38 (0.99-1.92)	2.49 (1.77-3.49)	<0.001
Model 2	1 [Reference]	1.40 (1.01-1.94)	2.42 (1.67-3.50)	<0.001
Cardiovascular mortality				
Crude	1 [Reference]	1.86 (1.13-3.06)	5.65 (3.26-9.79)	<0.001
Model 1	1 [Reference]	1.53 (0.92-2.55)	2.79 (1.57-4.96)	<0.001
Model 2	1 [Reference]	1.53 (0.92-2.54)	2.68 (1.50-4.79)	<0.001
Cancer mortality				
Crude	1 [Reference]	2.68 (1.50-4.79)	3.74 (1.79-7.82)	<0.001
Model 1	1 [Reference]	1.25 (0.62-2.51)	2.19 (1.03-4.63)	0.030
Model 2	1 [Reference]	1.26 (0.65-2.48)	2.10 (1.00-4.45)	0.043
Respiratory disease mortality				
Crude	1 [Reference]	2.75 (1.23-6.18)	6.39 (2.44-16.74)	<0.001
Model 1	1 [Reference]	2.29 (1.01-5.24)	3.28 (1.26-8.50)	0.019
Model 2	1 [Reference]	2.27 (1.06-4.87)	3.00 (1.18-7.65)	0.033

Table 3. HRs (95% CIs) of mortality according to three groups based on the Naples prognostic score (NPS) among adults with asthma in NHANES 1999-2018 (n = 5837). *Model 1 was adjusted for age (continuous), sex (male or female), and race (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black or Other);Model 2 was adjusted for Model 1 plus education level (below high school, high school, or above high school), family income-to-poverty ratio (≤1.0, 1.1-3.0, or >3.0), smoking status (never smoker, former smoker, or current smoker), drinking status (nondrinker, low-to-moderate drinker, or heavy drinker), BMI (<25.0, 25.0-29.9, or >29.9), energy intake levels (tertiles), physical activity (inactive, insufficiently active, or active)*

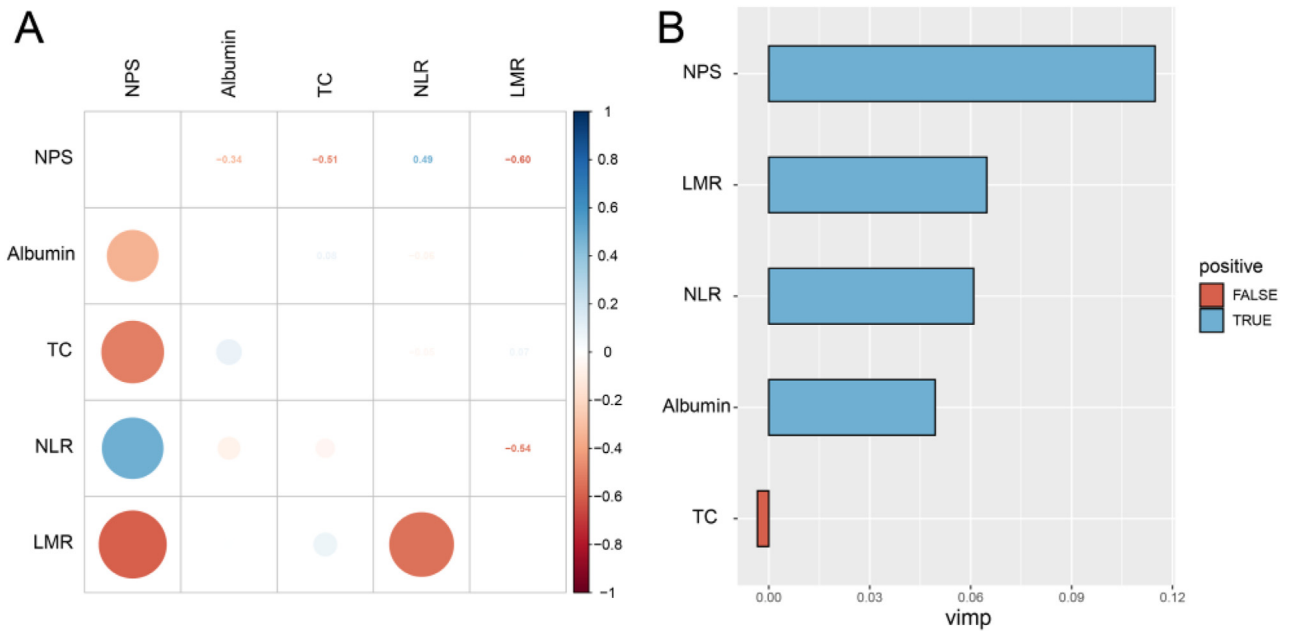

Fig. 4 Prognostic value of the Naples Prognostic Score (NPS) in adult asthma patients. **(A)** Spearman's correlation analysis was used to calculate the correlation coefficients among NPS and its components. **(B)** The random survival forest (RSF) was used to assess the prognostic importance of NPS and its components in predicting all-cause mortality in asthmatic patients

CONCLUSIONS

Our findings suggest that there is a positive association between a higher NPS and the prevalence of asthma. Furthermore, among participants with asthma, a higher NPS is associated with an increased risk of all-cause mortality and cause-specific mortality. These findings are of clinical significance and suggest that monitoring NPS levels may be a useful tool for identifying individuals at increased risk for adverse asthma outcomes. Further investigation is necessary to confirm these associations and elucidate the underlying mechanisms.

Abbreviations

NPS, Naples Prognostic Score; NLR, Neutrophil-to-lymphocyte Ratio; LMR, Lymphocyte-to-monocyte Ratio; RSF, Random Survival Forest; CDC, Centers for Disease Control and Prevention; MEC, Mobile Examination Center; NCHS, National Center for Health Statistics; NDI, National Death Index; NHANES, National Health and Nutrition Examination Survey.

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Availability of data and materials

The datasets analyzed during the current study are publicly available in the National Health Nutrition Survey (NHANES), https://www.cdc.gov/nchs/nhanes/index.htm.

Author contributions

ZN, CC, LS and HW conceived and designed the study. ZN, YH and LF extracted the data and analyzed and interpreted the data. ZN, CC and LS contributed to drafting and editing the paper and full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors have given the final approval of the manuscript.

Ethics approval

Data analyzed in this study were obtained from the NHANES. The protocols involved were approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB), and informed consent from all participants was documented.

Consent for publication

The authors provide their consent for the publication of the study results.

Declaration of competing interest

The author reports no conflicts of interest in this work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2023.100825.

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