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Associations of Naples prognostic score with stroke in adults and all cause mortality among stroke patients

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This study seeks to assess the associations of Naples Prognostic Score with stroke in adults and all cause mortality among stroke patients. We analyzed data from 44,601 participants in the 2005–2018 National Health and Nutrition Examination Survey (NHANES). The Naples Prognostic Score (NPS) was derived from total cholesterol, serum albumin, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR). Participants were classified into three groups based on their NPS. Stroke incidence was determined through self-reported questionnaires, and mortality data were diligently tracked using the National Death Index. We investigated the relationship between NPS and stroke prevalence using multiple logistic regression analysis. To explore the association between NPS and all cause mortality in stroke survivors, we applied Kaplan–Meier survival analysis and Cox proportional hazards models. Furthermore, we conducted a detailed subgroup analysis to assess interaction effects on all cause mortality risk within this population. The median age of the participants was 50.00 years [interquartile range: 35.00–64.00], with males comprising 49.36% of the study. The overall stroke prevalence was 3.93%. Participants were categorized into three groups based on their NPS: 6,328 (18.1%) in Group 0 (NPS 0), 24,015 (68.8%) in Group 1 (NPS 1 or 2), and 4,580 (13.1%) in Group 2 (NPS 3 or 4). After adjusting for covariates, individuals in Group 2 exhibited a significantly higher stroke prevalence compared to Group 0, with an odds ratio (OR) of 1.82 [95% confidence interval: 1.48–2.23]. Among the 1372 patients with a history of stroke, with a median follow-up duration of 5.94 years, we utilized Cox proportional hazards models to assess the relationship between NPS and all cause mortality risk. The analysis revealed that, after adjusting for covariates, stroke patients in Group 2 faced a significantly elevated risk of all cause mortality (hazard ratio [HR] = 2.21 [95% confidence interval: 1.44–3.11]) compared to those in Group 0. Subsequent subgroup analyses to explore interaction effects on all cause mortality risk among stroke patients shown no significant interactions (p for interaction > 0.05). This study indicate a positive correlation between NPS and the risk of stroke in adults, as well as all cause mortality in stroke patients.

Keywords Stroke, Naples prognostic score, Mortality, NHANES

Stroke is a major global health issue, ranking as the second leading cause of death[1], with direct and indirect costs exceeding US$891 billion annually[2]. In the U.S., approximately 610,000 people experience a first stroke each year, about 185,000 have a recurrent stroke, and stroke causes 162,890 deaths, making it the fifth leading cause of death[3]. In 2019, the U.S. had 7.09 million prevalent stroke cases. Despite a decline in age-standardized incidence rates, the absolute burden of stroke continues to rise[4], prompting ongoing research to improve prognosis by targeting key risk factors[5]. Clinically, stroke is characterized by sudden neurological impairments, leading to varying degrees of physical and cognitive disabilities, which impact daily activities and quality of life for survivors[6]. Given the substantial impact of stroke on individual health and socio-economic well-being, understanding and

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managing these risk factors is of paramount importance. Researchers are focusing on identifying new risk factors and delving into the mechanisms of known ones to develop more effective prevention and treatment strategies[1]. These efforts aim not only to reduce the incidence of stroke but also to improve long-term outcomes for patients, enhancing their quality of life.

The Naples Prognostic Score (NPS) is a novel scoring system that combines inflammatory and nutritional markers, including total cholesterol, serum albumin, neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR)[7]. Initially used to assess the prognosis of colorectal cancer patients[8], NPS has since been extended to various malignancies[9–11] and recently applied to nonalcoholic fatty liver disease[12] and asthma[13]. Both the occurrence and prognosis of stroke are affected by nutritional status and inflammation[14,15]. However, the association between NPS and stroke patients remains unexplored.

Utilizing data from NHANES (2005–2018), this study systematically evaluates the relationship between NPS and stroke prevalence. Additionally, it undertakes a comprehensive examination of the correlation related to NPS and all cause mortality in stroke patients. The aim is to establish the associations of Naples Prognostic Score with stroke and all cause mortality in adults.

Methods

Study participants

All data used in this study were publicly available through the National Center for Health Statistics (NCHS), which provides comprehensive medical information from NHANES, including nutritional assessments, physical exams, and health interviews. NHANES data has been approved by the NCHS Ethics Review Board (details available at: https://www.cdc.gov/nchs/nhanes/). Mortality data were obtained from the National Death Index, tracked through December 31, 2019.

Sample size

This study analyzed data from seven NHANES cycles between 2005 and 2018 to explore the relationship between NPS and stroke and all cause mortality in stroke patients. Exclusion criteria included: (1) participants under 18 years old; (2) missing stroke status data; (3) pregnant women; (4) missing data on total cholesterol, serum albumin, neutrophil count, lymphocyte count, or monocyte count. Initially, 70,190 participants were enrolled. After excluding those under 18 ($n = 28{,}047$), missing stroke status data ($n = 2{,}454$), pregnant women ($n = 682$), and those missing relevant biomarkers ($n = 4{,}084$). The final sample included 34,923 participants after the exclusions, out of which 1374 had stroke.Two participants lost to follow-up for all cause mortality were excluded.This sample of 1372 stroke participants was used for the survival analysis (Fig. 1).

Definition of stroke

Stroke was determined based on self-reported diagnoses collected during structured, face-to-face interviews. Participants were classified as having a stroke if they answered "yes" to the question: "Has a doctor or other health professional ever told you that you had a stroke?". It is important to acknowledge the potential for recall bias in self-reported data, which may affect the accuracy and interpretation of the findings[16].

Assessment of NPS

According to previous research[7], the Naples Prognostic Score is calculated using four specific criteria: serum albumin (normal level: ≥4 g/dL), total cholesterol (normal level: >180 mg/dL), lymphocyte-to-monocyte ratio (LMR) (normal level: ≤2.96), and neutrophil-to-lymphocyte ratio (NLR) (normal level: >4.44). Individuals with all four parameters within the normal range score 0 points and belong to group 0 or the low NPS group. Those with 1 or 2 parameters outside the normal range belong to group 1 or the medium NPS group. Those with 3 or 4 parameters outside the normal range belong to group 2 or the high NPS group (Table 1).

Assessment of all cause mortality

The primary survival outcome in our analysis was all cause mortality. Death records were tracked through December 31, 2019, by linking the NHANES database with the National Death Index (NDI) using the unique participant identifier. This linkage is based on the most recent data provided by the National Center for Health Statistics (NCHS), as done in previous studies[17]. Participants were followed from the date of survey participation until the date of death or the end of the follow-up period, whichever occurred first.

Covariates

A variety of covariates were introduced into our study according to previous research[18]. These covariates are considered to have an association with stroke: sex (male or female), race (Mexican American, non-Hispanic White, non-Hispanic Black, or other race), age (≥ 18 years), body mass index (BMI), education level (Below high School, High School or above), poverty–income ratio (< 1 and ≥ 1), smoking (yes or not), marital status(Married/living with partner or Widowed/divorced/separated/never married), drinking, chronic conditions including hypertension and diabetes (was diagnosed with diabetes or Subcutaneous injection of insulin or oral hypoglycemic drugs or the value of fasting glycated hemoglobin more than 6.4).

Statistical analysis

Continuous variables are represented by median and interquartile ranges (IQRs), while categorical variables are represented by numbers and percentages. Wilcoxon rank-sum test is used for continuous variables. The pearson's Chi-square test is used for comparison of categorical variables.

We performed multivariate logistic regression analysis to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) to investigate the relationship between NPS and its components and the prevalence of

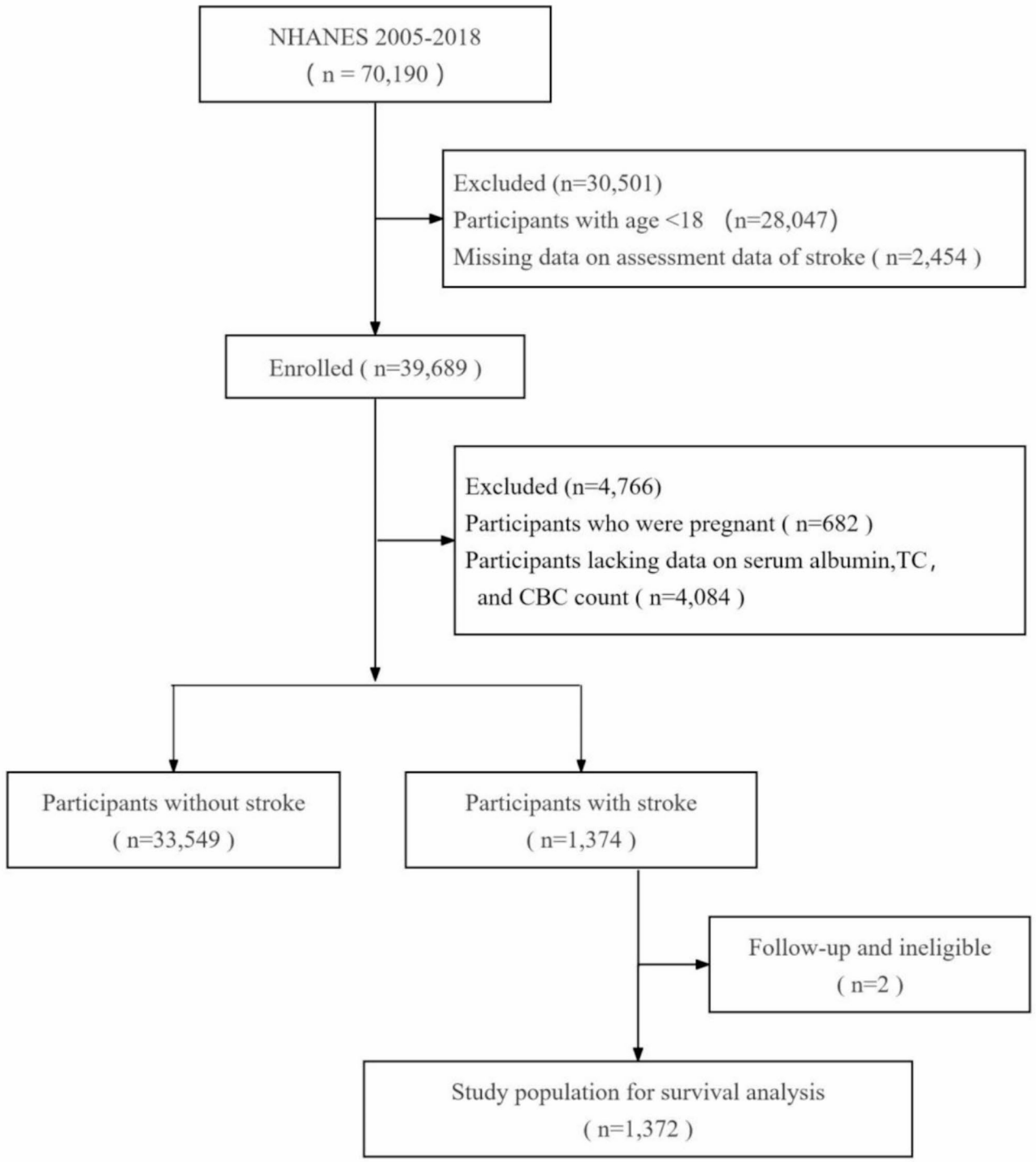

Fig. 1. Flowchart of study participants.

stroke. We calculated cumulative survival rates using the Kaplan–Meier method and log-rank test, and compared the three groups based on NPS. The adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of all cause mortality in stroke patients were calculated using Cox regression analysis. Subgroup analysis was conducted to evaluate the interaction effect on all cause mortality risk among stroke patients. Inverse Probability Weighting (IPW) was applied to adjust for potential bias resulting from the exclusion of participants with missing NPS scores. Additionally, a sensitivity analysis was performed using weighted multivariate logistic regression and Cox regression analyses to assess the robustness of the findings. All statistical analyses were performed using R software (version 4.4.0).

Characteristic	Total	NPS, points			p-value[2]
		0	1–2	3–4	
Participants, N	34,923[1]	6328[1]	24,015[1]	4580[1]	
Age, years	50.00 [35.00, 64.00]	48.00 [36.00, 59.00]	49.00 [34.00, 64.00]	61.00 [41.00,74.00]	< 0.001
Male, n (%)	17,238 (49.36%)	2,630 (41.56%)	12,245 (50.99%)	2,363 (51.59%)	< 0.001
Race, n (%)					< 0.001
Mexican American	5,505 (15.76%)	1,235 (19.52%)	3,677 (15.31%)	593 (12.95%)	
Non-Hispanic White	14,846 (42.51%)	2,053 (32.44%)	10,562 (43.98%)	2,231 (48.71%)	
Non-Hispanic Black	7,249 (20.76%)	1,397 (22.08%)	4,873 (20.29%)	979 (21.38%)	
Other race	7,323 (20.97%)	1,643 (25.96%)	4,903 (20.42%)	777 (16.97%)	
Education level, n (%)					0.007
Below high school	8,720 (24.97%)	1,587 (25.08%)	5,906 (24.59%)	1,227 (26.79%)	
High school or above	26,203 (75.03%)	4,741 (74.92%)	18,109 (75.41%)	3,353 (73.21%)	
Marital status, n (%)					< 0.001
Married/living with partner	20,845 (59.69%)	4,010 (63.37%)	14,374 (59.85%)	2,461 (53.73%)	
Widowed/divorced/separated/never married	14,078 (40.31%)	2,318 (36.63%)	9,641 (40.15%)	2,119 (46.27%)	
Family PIR, n (%)					0.250
< 1	6,674 (19.11%)	1,171 (18.51%)	4,598 (19.15%)	905 (19.76%)	
≥ 1	28,249 (80.89%)	5,157 (81.49%)	19,417 (80.85%)	3,675 (80.24%)	
Smoking, n (%)	15,643 (44.79%)	2,589 (40.91%)	10,700 (44.56%)	2,354 (51.40%)	< 0.001
Drinking, n (%)	23,742 (67.98%)	4,118 (65.08%)	16,526 (68.82%)	3,098 (67.64%)	< 0.001
BMI (kg/m^2)	28.07 [24.38, 32.60]	28.03 [24.52, 32.20]	27.92 [24.30, 32.40]	28.93 [24.70,34.60]	< 0.001
Obesity, n (%)	17,469 (50.02%)	3,176 (50.19%)	11,837 (49.29%)	2,456 (53.62%)	< 0.001
Diabetes, n (%)	6,291 (18.01%)	900 (14.22%)	3,991 (16.62%)	1,400 (30.57%)	< 0.001
Hyptersion, n (%)	14,971 (42.87%)	2,410 (38.08%)	9,966 (41.50%)	2,595 (56.66%)	< 0.001
SBP (mmHg)	121.33 [111.33, 134.00]	120.67 [111.33, 133.33]	121.33 [111.33, 134.00]	124.00 [112.67,138.00]	< 0.001
DBP (mmHg)	70.67 [63.33, 78.00]	72.00 [65.33, 79.33]	70.67 [63.33, 78.00]	68.00 [59.33,76.00]	< 0.001
Total cholesterol (mg/dL)	189.00 [164.00, 218.00]	215.00 [197.00, 238.00]	188.00 [163.00, 215.00]	160.00 [142.00,174.00]	< 0.001
Serum albumin (g/L)	42.00 [40.00, 45.00]	43.00 [42.00, 45.00]	42.00 [40.00, 45.00]	39.00 [37.00,42.00]	< 0.001
Neutrophils (1000 cells/uL)	4.00 [3.10, 5.10]	3.60 [2.80, 4.60]	3.90 [3.10, 5.00]	5.00 [3.90,6.40]	< 0.001
Lymphocyte (1000 cells/uL)	2.10 [1.70, 2.50]	2.50 [2.00, 3.00]	2.00 [1.70, 2.50]	1.60 [1.30,2.00]	< 0.001
Monocyte (1000 cells/uL)	0.50 [0.40, 0.70]	0.40 [0.40, 0.50]	0.50 [0.40, 0.70]	0.60 [0.50,0.70]	< 0.001
Platelet (1000 cells/uL)	240.00 [203.00, 284.00]	247.00 [212.00, 291.00]	239.00 [203.00, 282.00]	234.00 [191.00,284.00]	< 0.001
LMR	4.00 [3.00, 5.00]	5.50 [4.88, 6.33]	3.75 [3.00, 4.50]	2.75 [2.13,3.40]	< 0.001
NLR	1.93 [1.45, 2.57]	1.48 [1.17, 1.87]	1.94 [1.50, 2.47]	3.27 [2.45,4.00]	< 0.001
NPS					< 0.001
0	6,328 (18.12%)	6,328 (100.00%)	0 (0.00%)	0 (0.00%)	
1	13,443 (38.49%)	0 (0.00%)	13,443 (55.98%)	0 (0.00%)	
2	10,572 (30.27%)	0 (0.00%)	10,572 (44.02%)	0 (0.00%)	
3	3,830 (10.97%)	0 (0.00%)	0 (0.00%)	3,830 (83.62%)	
4	750 (2.15%)	0 (0.00%)	0 (0.00%)	750 (16.38%)	
Stroke, n (%)	1,374 (3.93%)	148 (2.34%)	830 (3.46%)	396 (8.65%)	< 0.001

Table 1. Characteristics of adult participants in NHANES 2005–2018. *BMI* body mass index, *PIR* poverty income ratio, *NLR* neutrophil-to-lymphocyte ratio, *LMR* lymphocyte-to-monocyte ratio, *SBP* systolic blood pressure, *DBP* diastolic blood pressure. [1]n (%); Median [25%,75%]. [2]Pearson's Chi-squared test; Kruskal-Wallis rank sum test.

Results

Characteristics of study participants

A flow diagram of this research population is shown in Fig. 1. Information of 70,190 participants were sourced from the NHANES (2005–2018). The final sample included 34,923 participants after the exclusions, out of which 1374 had stroke. Two participants lost to follow-up for all cause mortality were excluded, 1372 patients with past histories of stroke were investigated. Baseline characteristics of the three NPS groups in NHANES from 2005 to 2018 was shown in Table 1. The median age of the study population was 50.00 [IQR 35.00, 64.00] years, with 49.36% being male. The prevalence of stroke was 3.93%. The median for serum albumin was 42.00 [IQR 40.00, 45.00] g/L, the medians for TC was 189.00 [IQR 164.00, 218.00] mg/dL, the medians for NLR was 1.93 [IQR 1.45, 2.57], and the medians for LMR was 4.00 [IQR 3.00, 5.00]. The number of participants with NPS = 0 was 6328 (18.12%), NPS = 1 was 13,443 (38.49%), NPS = 2 was 10,572 (30.27%), NPS = 3 was 3730 (10.97%), and NPS = 4

was 3830 (2.15%). Compared to Group 0 (NPS0), participants in Group 2 (NPS = 3, 4) were older, lower rates of marriage and non-drinkers, a higher prevalence of hypertension, diabetes and stroke.

In the all cause mortality outcomes with a median follow-up time of 5.94 years, among 1372 adult stroke patients, 504 cases (36.73%) experienced all cause mortality (Table 2). Compared to adult stroke survivors, stroke patients who experienced all cause mortality were characterized by older age, being non-Hispanic white males, lower education and income levels, and a higher prevalence of hypertension and diabetes. Additionally, they had significantly lower levels of serum albumin and LMR, and higher levels of TC and NLR ($p < 0.05$).

The relationship between NPS and stroke

In this study, NPS was classified into three groups, with Group 0 serving as the reference, as described in prior literature[13]. Logistic regression analysis was performed to examine the relationship between NPS and stroke prevalence (Table 3). The crude model revealed a strong positive association between NPS and stroke prevalence (OR = 3.95 [3.26, 4.79]). In Model 1, compared to the reference group, participants in Group 2 exhibited a markedly increased prevalence of stroke (OR = 2.13 [1.74, 2.61]). This link retained its statistical significance in Model 2 (OR = 1.82 [1.48, 2.23]). Further trend test results showed that as NPS levels increased, the risk of stroke significantly increased (trend $p < 0.001$).

Characteristic	Total	All cause mortality		*p*-value[2]
		No	Events	
Participants, N	1372[1]	868[1]	504[1]	
Age, years	68.00 [59.00, 78.00]	64.00 [54.00, 73.00]	77.00 [68.00, 80.00]	< 0.001
Male, n (%)	669 (48.76%)	384 (44.24%)	285 (56.55%)	< 0.001
Race, n (%)				< 0.001
Mexican American	124 (9.04%)	87 (10.02%)	37 (7.34%)	
Non-Hispanic White	701 (51.09%)	378 (43.55%)	323 (64.09%)	
Non-Hispanic Black	368 (26.82%)	262 (30.18%)	106 (21.03%)	
Other Race	179 (13.05%)	141 (16.24%)	38 (7.54%)	
Education level, n (%)				0.001
Below high school	469 (34.18%)	269 (30.99%)	200 (39.68%)	
High School or above	903 (65.82%)	599 (69.01%)	304 (60.32%)	
Marital status, n (%)				0.014
Married/living with partner	697 (50.80%)	463 (53.34%)	234 (46.43%)	
Widowed/divorced/separated/never married	675 (49.20%)	405 (46.66%)	270 (53.57%)	
Family PIR, n (%)				0.013
< 1	312 (22.74%)	216 (24.88%)	96 (19.05%)	
≥ 1	1,060 (77.26%)	652 (75.12%)	408 (80.95%)	
BMI (kg/m^2)	29.00 [25.10, 33.50]	29.60 [25.58, 34.30]	27.94 [24.58, 31.90]	< 0.001
Obesity, n (%)	734 (53.50%)	507 (58.41%)	227 (45.04%)	< 0.001
Smoking, n (%)	831 (60.57%)	511 (58.87%)	320 (63.49%)	0.091
Drinking, n (%)	877 (63.92%)	587 (67.63%)	290 (57.54%)	< 0.001
Diabetes, n (%)	551 (40.16%)	332 (38.25%)	219 (43.45%)	0.058
Hypertension, n (%)	1,113 (81.12%)	684 (78.80%)	429 (85.12%)	0.004
Total cholesterol (mg/dL)	178.00 [151.00, 211.00]	182.00 [156.00, 211.00]	172.00 [144.00, 210.25]	0.003
Serum albumin (g/L)	41.00 [38.00, 43.00]	41.00 [39.00, 43.00]	41.00 [38.00, 43.00]	0.002
Neutrophils (1000 cells/uL)	4.30 [3.30, 5.50]	4.20 [3.20, 5.40]	4.50 [3.40, 5.60]	0.006
Lymphocyte (1000 cells/uL)	1.90 [1.50, 2.50]	2.00 [1.60, 2.50]	1.80 [1.30, 2.30]	< 0.001
Monocyte (1000 cells/uL)	0.60 [0.50, 0.70]	0.60 [0.40, 0.70]	0.60 [0.50, 0.70]	< 0.001
Platelet (1000 cells/uL)	228.50 [191.00, 275.00]	233.00 [196.00, 276.00]	221.50 [177.75, 272.00]	0.001
LMR	3.40 [2.50, 4.58]	3.67 [2.71, 4.75]	3.00 [2.17, 4.17]	< 0.001
NLR	2.23 [1.64, 3.07]	2.08 [1.55, 2.85]	2.47 [1.82, 3.51]	< 0.001
NPS				< 0.001
0	148 (10.79%)	115 (13.25%)	33 (6.55%)	
1–2	829 (60.42%)	555 (63.94%)	274 (54.37%)	
3–4	395 (28.79%)	198 (22.81%)	197 (39.09%)	

Table 2. Survey baseline demographic and medical characteristics of patients with stroke in the NHANES 2005–2018. *BMI* body mass index, *PIR* poverty income ratio, *NLR* neutrophil-to-lymphocyte ratio, *LMR* lymphocyte-to-monocyte ratio, *SBP* systolic blood pressure, *DBP* diastolic blood pressure. [1]n (%); Median [25%,75%]. [2]Pearson's Chi-squared test; Wilcoxon rank sum test.

Model	NPS, points	OR (95% CI)	*p* value	*p* for trend
Crude model	0	1.0 [Reference]		
	1–2	1.49 (1.25, 1.78)	< 0.001	< 0.001
	3–4	3.95 (3.26, 4.79)	< 0.001	
Model I	0	1.0 [Reference]		
	1–2	1.22 (1.01, 1.46)	0.035	< 0.001
	3–4	2.13 (1.74, 2.61)	< 0.001	
Model II	0	1.0 [Reference]		
	1–2	1.16 (0.96, 1.39)	0.127	< 0.001
	3–4	1.82 (1.48, 2.23)	< 0.001	

Table 3. ORs (95% CIs) of NPS among adults with stroke in NHANES 2005–2018 ($n = 34923$). Model I adjusted for age, sex, Race. Model II adjusted for age, sex, Race, Education level, poverty income ratio (PIR), Marital status, Obesity, Smoking, Drinking, Diabetes, Hypertension. *OR* odds ratio, *CI* confidence interval.

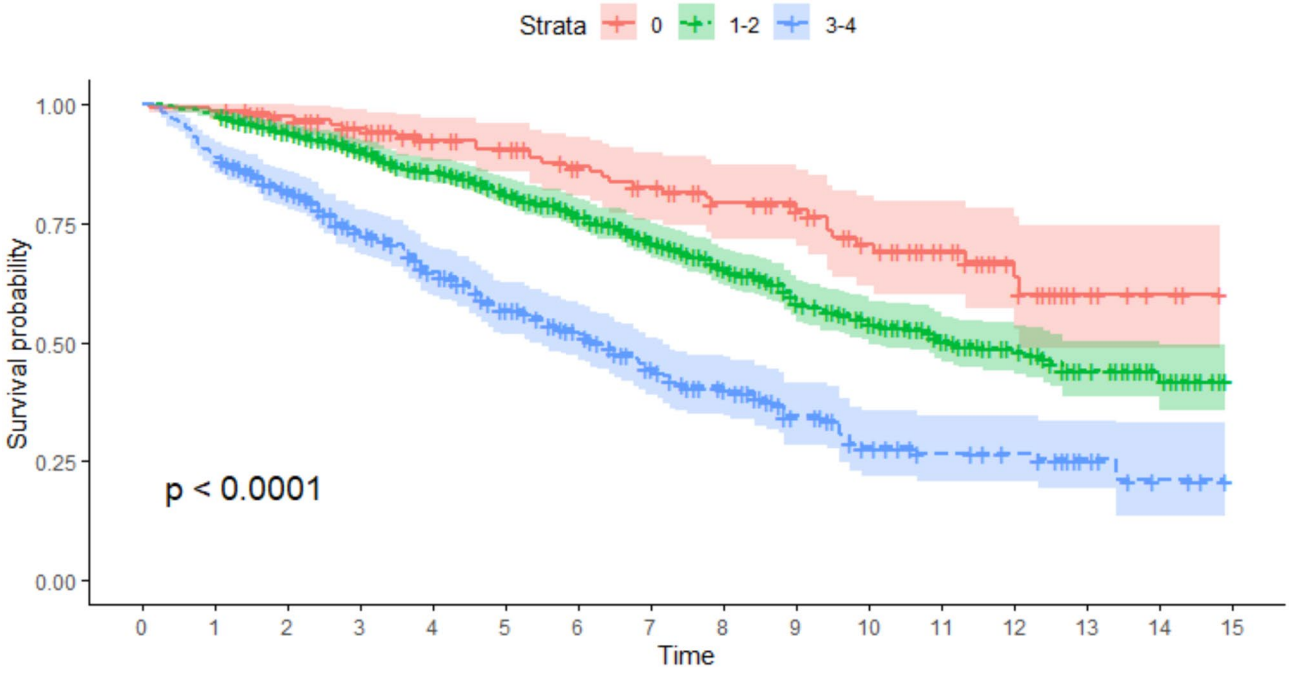

Fig. 2. Kaplan-Meier survival curves for all cause mortality in stroke patients based on Naples Prognostic Score, with a median follow-up time of 5.94 years. Strata 0 represents an NPS = 0, shown in red in the figure, with the red line indicating the Survival Probability and the red shaded area representing the 95% confidence interval. Strata 1–2 represents an NPS = 1–2, shown in green in the figure, with the green line indicating the Survival Probability and the green shaded area representing the 95% confidence interval. Strata 3–4 represents an NPS = 3–4, shown in blue in the figure, with the blue line indicating the Survival Probability and the blue shaded area representing the 95% confidence interval.

The relationship between NPS and mortality participants with stroke

The relationship between NPS and mortality in stroke participants was evaluated using Kaplan-Meier curves (Fig. 2). The results revealed that NPS = 3–4, shown in blue in the figure had the highest risk of all cause mortality when compared to the other two groups stratified based on NPS (log-rank test $P < 0.001$). Among the 1,372 patients with a history of stroke, with a median follow-up duration of 5.94 years, we utilized Cox proportional hazards models to assess the relationship between NPS and all cause mortality risk. The analysis revealed that, after adjusting for covariates, stroke patients in Group 2 faced a significantly elevated risk of all cause mortality (hazard ratio [HR] = 2.21 [95% confidence interval: 1.44–3.11]) compared to those in Group 0 (Table 4). Subsequent subgroup analyses to explore interaction effects on all cause mortality risk among stroke patients shown no significant interactions (p for interaction > 0.05) (Fig. 3).

Sensitivity analyses

In sensitivity analyses, We compared the baseline characteristics of the 4,085 participants excluded due to missing NPS variables with the 34,923 included participants (eTable 1). Inverse Probability Weighting (IPW) was then

Outcome	Crude model		Model I		Model II	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
NPS, points						
0	Reference		Reference		Reference	
1–2	1.74 (1.21, 2.50)	0.003	1.22 (0.85, 1.76)	0.289	1.19 (0.82, 1.72)	0.360
3–4	4.00 (2.76, 5.79)	< 0.001	2.20 (1.50, 3.23)	< 0.001	2.21 (1.44, 3.11)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	

Table 4. HRs (95% CIs) of mortality s according to three groups based on NPS among adults with stroke in NHANES 2005–2018 ($n = 1372$). Model I adjusted for age, sex, Race, Education level. Model II adjusted for age, sex, Race, Education level, Marital status, Obesity, Diabetes, Hypertension, Smoking, Drinking. *CI* confidence interval.

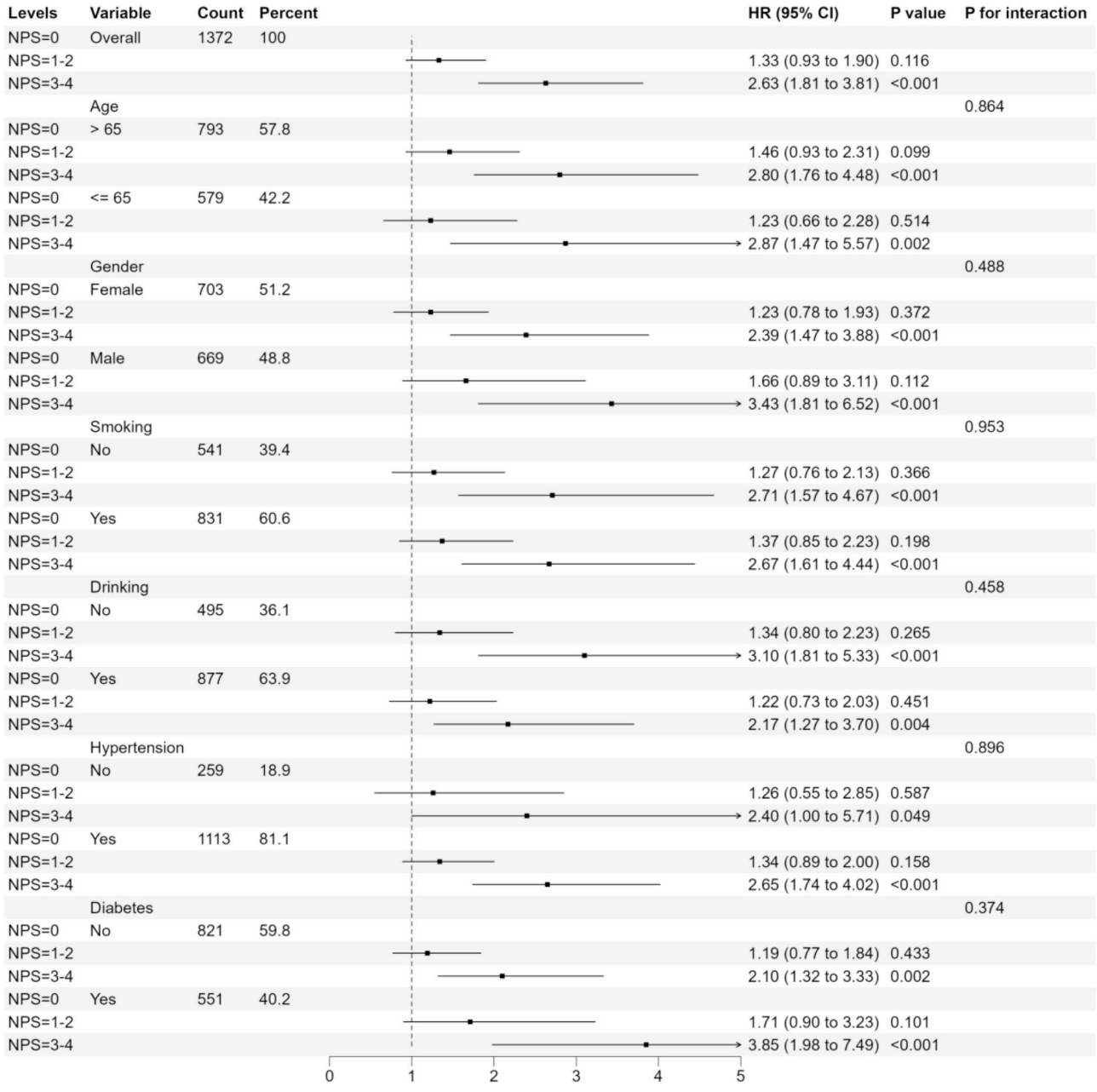

Fig. 3. Subgroup analyses of the associations (HRs, 95% CIs) between the NPS score and all cause mortality among patients with stroke in NHANES 2005–2018 ($n = 1372$).

applied in multivariate logistic and Cox regression analyses to validate the stability of these relationships (eTable 2, 3).

Discussion

This study, using NHANES 2005–2018 data, is the first to explore the relationship between the Naples Prognostic Score (NPS) and stroke in Adults, as well as all cause mortality among stroke patients. Logistic regression analysis revealed a strong positive association between NPS and stroke prevalence, with a significantly increased risk of stroke as NPS levels rose. Kaplan-Meier curve analysis indicated that the NPS = 3–4 group had the highest risk of all cause mortality compared to the other 2 groups. Cox regression analysis, after adjusting for covariates, showed that stroke patients in the NPS = 2 group had a significantly higher risk of all cause mortality. Sensitivity analyses confirmed the robustness of these findings.

Malnutrition and its impact on prognosis in stroke patients has emerged as a critical and highly discussed issue in recent medical literature[19,20]. Clinically, various biomarkers are used to assess the nutritional status of stroke patients[14]. Serum albumin levels, a common indicator of nutritional status, are closely associated with increased stroke risk[21,22]. Total cholesterol levels are another nutritional status indicator; their relationship with stroke remains uncertain[23], with total cholesterol possibly positively associated with ischemic stroke and negatively associated with hemorrhagic stroke risk[24–26]. Malnutrition can trigger systemic inflammation[27], which increases the risk of stroke[28] and worsens outcomes[29]. NLR and LMR are potential novel biomarkers of systemic inflammation[30,31], systemic inflammation exacerbates atherosclerosis, thereby increasing the risk of stroke. Post-stroke inflammation can lead to significant long-term sequelae[32]. Inflammatory cytokines exacerbate malnutrition in stroke patients by increasing metabolic demands, reducing appetite, affecting digestion and absorption, and breaking down muscle and fat[33,34], creating a vicious cycle[35]. This creates a vicious cycle, underscoring the need for indicators that assess both nutritional status and systemic inflammation.

NPS is an innovative scoring system that integrates key inflammatory and nutritional markers[36,37]. This integrated approach allows NPS to demonstrate superior predictive accuracy when compared to other scoring systems, such as the Controlling Nutritional Status (CONUT) score, Nutritional Risk Index (NRI), and Prognostic Nutritional Index (PNI)[38,39]. Additionally, as a categorical scoring system, NPS offers greater consistency across studies, making it easier for clinicians and patients to interpret and apply, in contrast to the more complex and variable scoring systems[40,41]. Our results indicate a positive correlation between NPS and the risk of stroke in adults, as well as all cause mortality in stroke patients, thereby further extending the application of NPS.

Our study has the following strengths, first, we used a nationally representative and relatively large sample to investigate the significantly increased NPS levels in adult stroke patients and further elucidate the relationship between NPS and stroke mortality, enhancing the generalizability and credibility of our findings. Secondly, we meticulously adjusted our analyses for key factors affecting stroke, thereby improving the reliability and scientific rigor of our results. We included an average of 5.94 years of follow-up data, elucidating the correlation between NPS and all cause mortality in stroke patients. Third, NPS, a composite indicator of nutrition and inflammation, has been linked to various diseases and outcomes in prior studies. Given the critical role of nutritional and inflammatory factors in stroke and its prognosis, our study expands the use of NPS, showing its association with both stroke incidence and all cause mortality in stroke patients. Notably, NPS is a simple and practical tool that can be incorporated into health management monitoring indicators. It is not only applicable in hospital settings but can also be used in primary care environments, facilitating stratified management of stroke patients and warranting further investigation through interventional studies.

Despite the strengths of our study, several limitations warrant attention. Stroke diagnoses were based on self-reports, which may introduce bias, although this method is commonly employed in similar studies[16,42], future studies using more objective clinical assessments, may help overcome these limitations. The NHANES database also lacks critical details on stroke type, onset time, severity, neurological function scores, and treatment, limiting our ability to incorporate these key mortality-related factors into the analysis. Future research incorporating more detailed stroke data would be valuable for better understanding the association with the outcomes studied. Additionally, as the NHANES data predominantly represent the U.S. population, the findings may have limited applicability to economically underdeveloped regions. Most notably, although we employed the NHANES database and its associated mortality data to establish a prospective cohort when investigating the relationship between NPS and all cause mortality in stroke patients, a cross-sectional study design was used to analyze the association between NPS and stroke, we were unable to infer a causal relationship between NPS and stroke risk. These limitations must be fully considered when interpreting the study results, highlighting the necessity of conducting further randomized controlled trials to validate this association and explore its mechanisms. Future studies exploring the causal relationship between NPS and stroke risk, or interventional research, would help clarify the underlying mechanisms and establish NPS as an important tool for stroke prevention and management.

Conclusions

This study analyzed data from NHANES (2005–2018) to evaluate the associations of Naples Prognostic Score with stroke and all cause mortality in adults. The results indicate that NPS is significantly associated with stroke incidence and all cause mortality risk in adults stroke patients. These findings have clinical significance, suggesting that monitoring Naples Prognostic Score levels may be a valuable tool for detecting stroke patients and their all cause mortality.

Data availability

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.

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Author contributions
ZQ.X. performed data acquisition and drafted the main manuscript text. MY.P performed data analysis. XQ.Y. assisted in data acquisition. LX.X. and DY. Z. prepared Figs. 1, 2 and 3. XC. L. and CH.H. prepared Tables 1 and 2, JJ. Z. and RL. G. prepared Tables 3 and 4. WZ. X. and GQ. Y. contributed to the conception and design of the study and supervised the research process. All authors reviewed the manuscript.

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Declarations

Competing interests
The authors declare no competing interests.

Ethical 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. Details on Institutional Review Boards of the CDC and NCHS are available at (http://www.cdc.gov/nchs/nhanes/irba98.htm).

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

Additional information
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