BMC Urology

RESEARCH

Open Access

Relationship between albumin-globulin ratio and prostate-specific antigen: a cross-sectional study based on NHANES 2003–2010

Simeng Gao[1†], Shaojie Li[2†], Baofang Wu[2], Jiayin Wang[2], Sijuan Ding[1] and Zhaohui Tang[1*]

Abstract

Purpose The albumin-globulin ratio (AGR) influences the development of prostate cancer; however, the relationship between AGR and prostate-specific antigen (PSA) has not been reported.

Methods This cross-sectional investigation used comprehensive AGR versus PSA data from men with 40 years of age and older, who participated in the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2010, spanning 4 investigation cycles, as only these cycles contained complete PSA data. To evaluate the nonlinear relationship between the ARG and PSA level, a regression utilizing smoothed curve fitting (penalized spline approach) and a generalized additive model (GAM) were employed. A two-segment linear regression model was used to conduct threshold effect evaluations. Lastly, subgroup analyses were carried out along with interaction tests.

Results This study included 5,376 subjects, whose total serum PSA (mean ± standard deviation) was 1.83 ± 3.34, and its level decreased roughly with increasing quartiles of AGR. In the fully-adjusted model, AGR was negatively correlated with the likelihood of PSA, and this relationship persisted across subgroups (trend > 0.05). The PSA was characterized by an "L"-shaped curve with an inflection point. On the left side of the inflection point (K = 1.32), there was a negative relationship between AGR and PSA.

Conclusion In the United States, among men over 40 years of age without prostate diseases, AGR demonstrated a nonlinear relationship with PSA, negatively correlating when AGR was below 1.32.

Clinical trial number Not applicable.

Keywords Albumin-globulin ratio, Prostate-specific antigen, NHANES, Cross-sectional study

†Simeng Gao and Shaojie Li are co-first authors.

*Correspondence:
Zhaohui Tang
tangzhaohui2023@163.com
[1]The Central Hospital of Yongzhou, Yongzhou, Hu Nan 425000, China
[2]The Second Affiliated Hospital of Fujian Medical University, Quanzhou, Fujian, 362000, China

Introduction

Prostate cancer is expected to be the second most common type of cancer and the fifth largest cause of cancer-related mortality among males by 2020, according to the World Cancer Statistics [1]. Almost all reputable clinical guidelines from the past few decades have suggested using prostate-specific antigen (PSA) to identify prostate cancer [2]. However, PSA is characterized by its high sensitivity and low specificity, which often lead to diagnostic biases [3]. Many factors are known to affect the PSA level, such as age, prostatitis, certain medications and prostate size [4].

The albumin-globulin ratio (AGR), as everyone knows, is calculated by dividing the serum albumin count by the globulin count [5]. Albumin responds to the nutritional state of human body while globulin responds to its immunoinflammatory state [6]. There is a significant controversy around the link between the level of albumin and PSA. It has been observed that middle-aged males with a lower serum albumin level have higher PSA readings [7]. Similar to this, a different study found a nonlinear relationship between the level of serum albumin and PSA, with a negative relationship observed between them when the serum albumin level was over 41 g [8]. In contrast, a cross-sectional study noted that dietary protein intake was positively associated with an elevated PSA level when dietary protein intake exceeded a threshold of 181.8 g [9]. A growing body of research suggests that immune inflammation plays an important role in the development of prostate cancer. Previous studies have shown that platelet-lymphocyte ratio (PLR) seems to have a higher accuracy in screening for prostate cancer, which, together with neutrophil-lymphocyte ratio (NLR), has significant predictive value for the development of metastatic prostate cancer [10]. However, there is still no consensus on the relationship between AGR and prostate. It has been noted that a lower level of AGR before treatment is strongly associated with poorer pathologic outcomes; AGR may be a reliable serologic marker for prostate cancer [11]. A retrospective analysis noted that patients suffering prostate cancer with a lower preoperative AGR level had a worse tumor recurrence-free survival [12]. However, a meta-analysis of studies noted a failure to demonstrate a potential predictive role of AGR in the prognosis of non-metastatic prostate cancer [13].

In conclusion, the purpose of this study was to investigate the relationship between the level of serum AGR and PSA among American males of over 40, who had non-prostate cancer.

Methods

Survey description

The National Center for Health Statistics (NCHS) performed the National Health and Nutrition Examination Survey (NHANES), a population-based cross-sectional survey, to gather information about Americans' health and nutritional status. It is conducted on a two-year cycle using complex multi-stage stratified probability sampling; hence, the study samples are representative.

All NHANES study protocols were approved by the NCHS Research Ethics Review Board, and each survey participant provided a signed informed permission. The public can access all comprehensive NHANES study designs and data at www.cdc.gov/nchs/nhanes/. The present investigation adhered to the cross-sectional research reporting criteria and guidelines of the Strengthening Norms for Reporting Observational Studies in Epidemiology (STROBE).

Study population

This study is based on 4 NHANES cycles from 2003 to 2010 because only those cycles contains complete PSA data.

In this analysis, participants with complete PSA and AGR data were included. The following exclusion criteria were applied to the subjects in this study: (1) age < 40 years, (2) lack of complete data on PSA and SII, and (3) factors affecting PSA (drug use such as 5-ARI, prostate hyperplasia, prostate infections and inflammation, undergoing prostate biopsy within 1 week, urological surgeries within 1 month and prostate cancer, etc.).

Definition of AGR and PSA

AGR is calculated using the formula: AGR = serum albumin/serum globulin. Serum specimens were processed, stored under proper refrigeration (2–8 °C), and shipped to Collaborative Laboratory Services for testing and analyses using the Beckman Synchron LX20 and Beckman UniCel DxC800® Synchron. In our analyses, the AGR served as the primary variable for investigation.

The total PSA was measured using the Hybritech PSA methods for recording serum total PSA concentrations (ng/mL) and the Beckman access, Department of Laboratory Medicine Immunology. Serum total PSA data was used as outcome variables in our analyses.

Covariate

Covariates that may influence the relationship between AGR and PSA were also included in this study, including demographic characteristics: age, ethnicity, education level, body mass index and alcohol use; laboratory indices: blood urea nitrogen (mmol/L), cholesterol (mg/dL), glucose, serum (mg/dL), lactate dehydrogenase (U/L), total bilirubin (mg/dL), triglycerides (mmol/L), serum uric acid (mg/dL), serum creatinine (mg/dL), alachlor aminotransferase (U/L) and alanine aminotransferase (U/L); history of chronic diseases: hypertension (yes/no), diabetes mellitus (yes/no/critical), coronary artery

disease (yes/no), angina pectoris (yes/no) and history of neoplastic diseases (yes/no);

Statistical analysis

This study additionally included covariates that might have an impact on the link between AGR and PSA. Percentages are used to indicate categorical data, while means and standard deviations are used to express continuous variables. Using student's t-tests for continuous variables or chi-square tests for categorical data, the differences among the AGR (quartiles) groups were evaluated. Multiple regression models were used to explore the relationship between AGR and PSA based on 3 different models. For Model 1, no adjustment was made for covariates. Model 2 was adjusted for age and race. Model 3 was adjusted for age, race, education, body mass index, drinking status, urea nitrogen, glutamic oxaloacetic transaminase, glutamic alanine aminotransferase, cholesterol, lactate dehydrogenase, total bilirubin, triglycerides, serum uric acid, serum creatinine, hypertension, diabetes mellitus, coronary artery disease, angina pectoris and history of neoplasia. Building on Model 3, subgroup studies on the relationship between ARG and PSA were carried out, utilizing age, BMI, diabetes and hypertension as stratification factors. In addition, an interaction test was added to this study as a way to test the heterogeneity of the associations among subgroups. The nonlinear connection between the ARG and PSA level was evaluated using the generalized additive model (GAM) regression and smoothed curve fitting (penalized spline approach). Finally, based on Model 3, the nonlinear relationship between AGR and PSA was further validated using a two-stage linear regression model for threshold effect analyses. $p<0.05$ was considered statistically significant. R version 4.3 and Empower software version 2.0 were used.

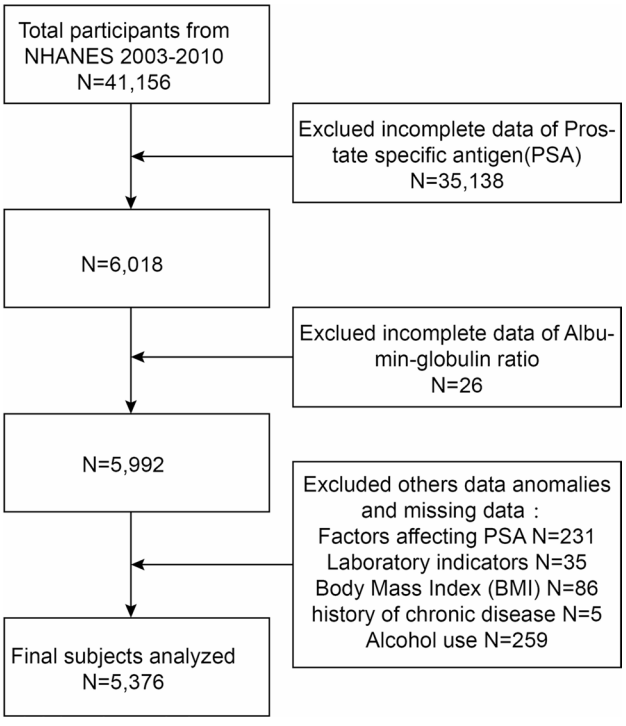

Fig. 1 Flow chart for NHANES 2003–2010 sample selection

Results

Baseline characteristics of participants

In this study, a total of 41,156 participants were initially recruited. Exclusions were made for missing data on PSA (35,138 participants), albumin (11), globulin (15), factors affecting PSA (231), laboratory indices (35), body mass index (86), chronic diseases (5) and alcohol consumption history (259). Ultimately, 5,376 eligible individuals aged over 40 years were included for analyses. The mean age of these subjects was 59.56 years, with a standard deviation of 12.54 (Fig. 1). The interquartile range of AGRs 1–4 was 0.26–1.3, 1.30–1.48, 1.48–1.66 and 1.67–4.5 respectively. The participants had a total serum PSA (mean±standard deviation) of 1.83±3.34, whose level decreased roughly with increasing quartiles of AGR (Q1: 2.31±5.15; Q2: 1.79±2.60; Q3: 1.61±2.36; Q4: 1.63±2.37, $P=0.003$). Participants in the lower quartiles of the AGR tended to exhibit a higher serum total PSA level (Table 1). Higher AGR levels are primarily associated with the following characteristics: younger ages, lower levels of ALT, AST, blood glucose, uric acid, lactate dehydrogenase, creatinine, BMI, as well as higher levels of urea nitrogen and bilirubin. Additionally, higher AGR levels are linked to a history of cancer, alcohol consumption as well as the absence of diabetes and hypertension histories.

Relationship between AGR and PSA

A significant negative relationship between AGR and serum total PSA was observed in models 1 and 2. (Model 1: β =-0.92, 95%CI:-1.23, -0.60; Model 2: β =-0.34, 95%CI: -0.67, -0.02). Fully multivariate model (Model 3), PSA levels were reduced by 0.4 (ng/mL) with every 1 unit increase in AGR. (Model 3: β = -0.40, 95% CI:-0.74, -0.06). The results showed a negative relationship between AGR and serum PSA. Additionally, the relationship between AGR and PSA is stronger compared to other continuous variables (Supplementary Table 1). To further explore the relationship between AGR and PSA, we transformed AGR into categorical variables (quartiles) for analyses. In the fully-adjusted model, the trend of effect value differences among AGR quartiles was non-isometric (Q2:β =-0.29; Q3:β =-0.34; Q4:β =-0.23)(Table 2). The correlation results suggest that there may be a nonlinear relationship between the level f AGR and PSA.

Table 1 Baseline characteristics of participants

AGR	Q1(0.26–1.3)	Q2(1.30–1.48)	Q3(1.48–1.66)	Q4(1.67–4.5)
	N **= 1335**	***N*** **= 1332**	***N*** **= 1322**	***N*** **= 1387**
Age, years	62.04 ± 12.53	59.85 ± 12.36	58.52 ± 12.42	57.87 ± 12.48
ALT(U/L)	29.26 ± 23.77	29.08 ± 27.11	28.21 ± 14.38	27.61 ± 13.47
AST(U/L)	30.93 ± 22.55	27.75 ± 15.35	26.83 ± 10.76	26.48 ± 8.47
Blood urea nitrogen (mmol/L)	14.87 ± 7.80	14.54 ± 5.87	14.67 ± 5.87	15.07 ± 5.41
Cholesterol (mg/dL)	194.54 ± 44.44	200.52 ± 42.36	200.93 ± 42.82	197.39 ± 40.74
Glucose, serum (mg/dL)	114.85 ± 52.27	110.12 ± 42.79	105.58 ± 37.89	101.10 ± 28.89
Lactate dehydrogenase (U/L)	137.20 ± 35.80	134.68 ± 42.09	132.02 ± 26.07	131.84 ± 27.01
Bilirubin, total	0.81 ± 0.32	0.81 ± 0.31	0.84 ± 0.28	0.87 ± 0.30
Triglycerides (mmol/L)	162.60 ± 139.68	171.15 ± 122.62	177.35 ± 132.38	177.07 ± 139.01
Uric acid (mg/dL)	6.29 ± 1.51	6.11 ± 1.34	6.02 ± 1.26	5.93 ± 1.23
Creatinine (mg/dL)	1.16 ± 0.93	1.05 ± 0.45	1.02 ± 0.27	1.02 ± 0.26
BMI(kg/m^2)	29.28 ± 7.13	29.33 ± 5.46	28.81 ± 5.11	28.02 ± 4.62
PSA(ng/mL)	2.31 ± 5.15	1.79 ± 2.60	1.61 ± 2.36	1.63 ± 2.37
Ethnicity, **%**				
Mexican American	21.42%	20.20%	18.46%	10.89%
Other Hispanic	7.79%	7.06%	6.51%	5.05%
Non-Hispanic White	35.21%	49.55%	58.85%	74.41%
Non-Hispanic Black	31.99%	20.20%	12.93%	6.63%
Other Races	3.60%	3.00%	3.25%	3.03%
Education level, **%**				
Less than junior high school	22.17%	19.14%	13.62%	10.31%
Middle to high school	19.40%	14.41%	13.62%	10.31%
High school graduate/GED or equivalent	24.12%	22.60%	24.96%	23.29%
Some College or AA degree	21.80%	24.25%	25.42%	26.24%
College Graduate or above	12.51%	19.59%	22.39%	29.85%
Diabetes mellitus, **%**				
No	78.20%	80.26%	82.30%	85.00%
Yes	20.07%	17.04%	15.28%	11.90%
Borderline	1.72%	2.70%	2.42%	3.10%
Hypertension, **%**				
No	48.61%	54.88%	57.41%	61.72%
Yes	51.39%	45.12%	42.59%	38.28%
Coronary heart disease, **%**				
No	90.26%	90.32%	92.44%	91.35%
Yes	9.74%	9.68%	7.56%	8.65%
Angina, **%**				
No	94.98%	95.50%	95.61%	95.31%
Yes	5.02%	4.50%	4.39%	4.69%
Tumor history, **%**				
No	91.39%	92.64%	92.21%	89.40%
Yes	8.61%	7.36%	7.79%	10.60%
Alcohol use, **%**				
No	20.52%	20.05%	15.96%	15.14%
At least 12 cups per year	79.48%	79.95%	84.04%	84.86%

Unless otherwise indicated, continuous values are shown as the mean ± standard deviation (SD)

The population classified as normal weight, overweight, and obese, respectively, had BMIs of < 25, 25–29.9, and ≥ 30 kg/m2

Nonlinear relationship between AGR and serum total PSA

To further characterize the nonlinear relationship between AGR and PSA, a smoothed curve was fitted in this study (Fig. 2). As shown in Fig. 2, there is a nonlinear relationship between AGR and PSA, which was confirmed by employing a two-stage linear regression model in this investigation. The findings revealed an L-shaped connection with an inflection point (K) of 1.32 between AGR and PSA. The relationship between AGR and PSA was negatively correlated to the left side of the

Table 2 Relationship between AGR and PSA

AGR	Univariable model (Model 1)		Minimally multivariable model (Model 2)		Fully multivariate model (Model 3)	
	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Continuous	-0.92 (-1.23, -0.60)	< 0.0001	-0.34 (-0.67, -0.02)	0.0378	-0.40 (-0.74, -0.06)	0.0209
Categories						
Q1	Reference		Reference		Reference	
Q2	-0.51 (-0.76, -0.26)	< 0.0001	-0.28 (-0.53, -0.03)	0.0264	-0.29 (-0.54, -0.04)	0.0246
Q3	-0.70 (-0.95, -0.44)	< 0.0001	-0.32 (-0.58, -0.07)	0.0117	-0.34 (-0.60, -0.08)	0.0096
Q4	-0.68 (-0.93, -0.43)	< 0.0001	-0.21 (-0.46, 0.05)	0.1168	-0.23 (-0.50, 0.04)	0.0900
P for trend	< 0.000001		0.1417		0.1126	

Model 1: variables were not adjusted

Model 2: age and ethnicity adjusted

Model 3: adjusted for Age, ethnicity, Education level, BMI, Blood urea nitrogen, Cholesterol, ALT, AST, Lactate dehydrogenase, Bilirubin, Triglycerides, Blood urea nitrogen, Creatinine, Glucose, Diabetes mellitus, Hypertension, Coronary heart disease, Angina, Tumor history, Alcohol use

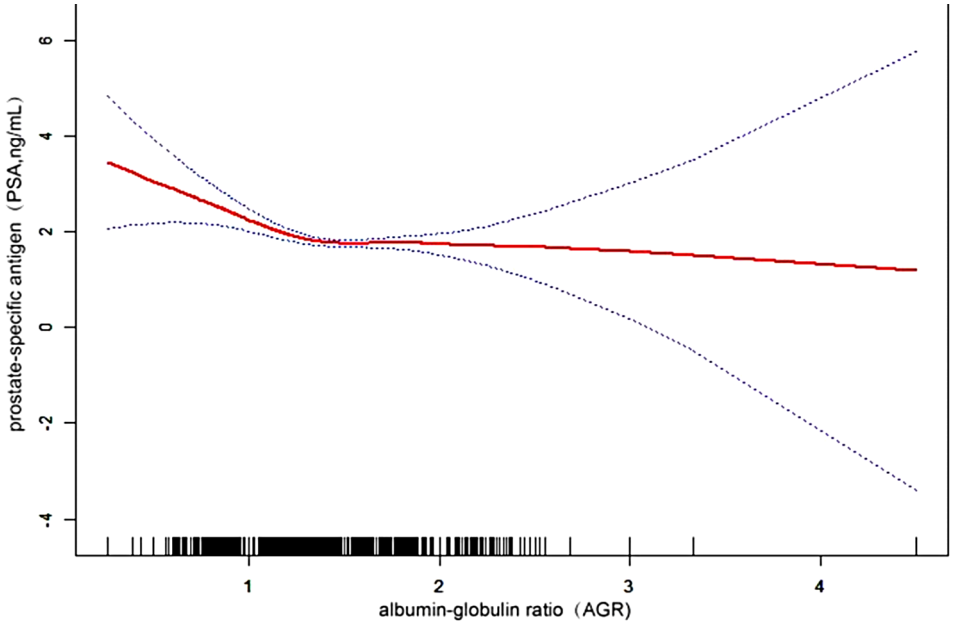

Fig. 2 Relationship between AGR and PSA. **a**. Each small line segment on the x-axis line represents a sample. **b**. The red solid line indicates a smooth curve fit between the variables. The blue dashed line indicates the 95% confidence interval of the fit

inflection point (β= -1.91, 95% CI -2.86, -0.95). Nevertheless, there was no statistically-significant relationship between AGR and PSA to the right side of the inflection point (β=0.05, 95% CI -0.38, 0.49). *P*-value for the log-likelihood ratio test was less than 0.001(Table 3).

Subgroup analysis

This study conducted subgroup analyses and further investigated interactions with age, BMI, diabetes as well as hypertension to determine the stability of the connection between AGR and PSA in various populations. Apart from participants aged 40 to 49 and those with diabetes, the relationship between AGR and PSA was generally negative across all other demographics. In the subgroups comprising age, BMI, hypertension and diabetes, as illustrated in Fig. 3, the interaction test for the link between AGR and PSA was not statistically significant ($P>0.05$),suggesting that the relationship between AGR and PSA was independent of age, BMI, hypertension and diabetes.

Discussion

This study included 5,736 participants from the NHANES database in a cross-sectional study, and we observed a nonlinear relationship between AGR and PSA, with AGR negatively correlated with PSA when AGR values were lower than 1.32. At the same time, this relationship remained stable across subgroups of age, BMI, hypertension and diabetes.

It has been demonstrated that the primary serum proteins albumin (ALB) and globulin (GLB) are linked to the onset of systemic inflammation. These proteins are also frequently used to evaluate the nutritional state and severity of cancerous patients' sickness [10]. Decreased

Table 3 Threshold effects between AGR on PSA

		Fully multivariate model
Model 1	β (95% CI)	-0.41 (-0.75, -0.07)
	P for trend	0.0167
Model 2	Breakpoint (K)	1.32
	β1 (< 1.32)	-1.91 (-2.86, -0.95)
	P for trend	< 0.0001
	β2 (> 1.32)	0.05 (-0.38, 0.49)
	P for trend	0.8172
	Logarithmic likelihood ratio test *P* value	< 0.001

Model 1: Standard linear model

Model 2: Two-piecewise linear model

β1:regression coefficient, represents the relationship between AGR and PSA to the left of the inflection point (K = 1.32)

β2:regression coefficient, Represents the relationship between AGR and PSA to the right of the inflection point (K = 1.32)

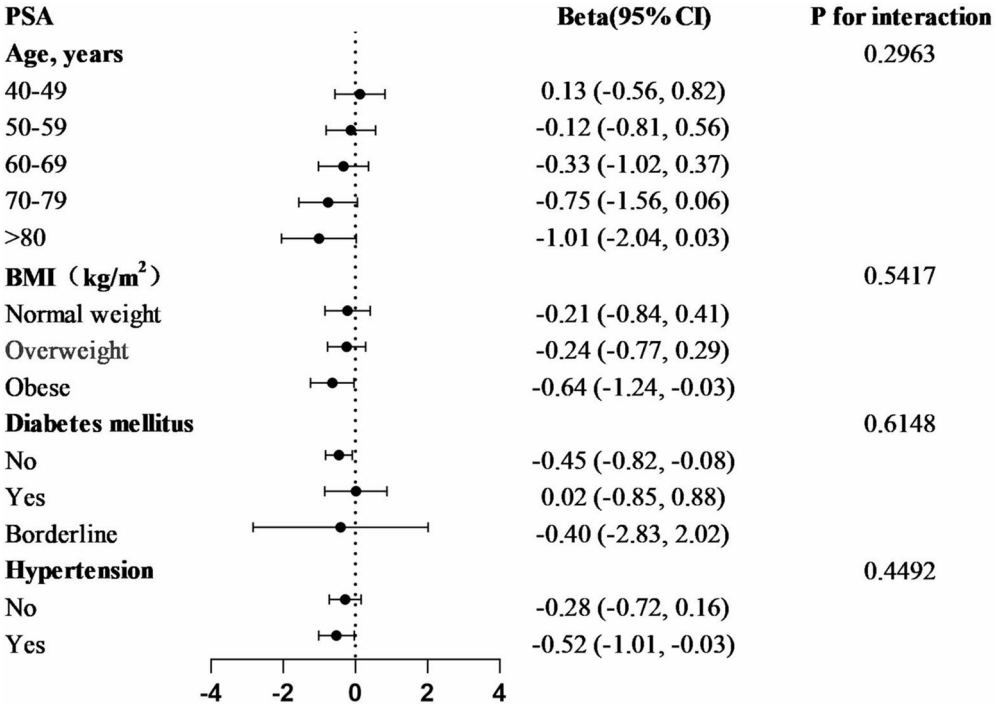

Fig. 3 Subgroup analysis of the relationship between AGR and PSA

ALB or increased GLB levels are frequently linked to increased death and recurrence rates in terms of many cancer types [14, 15]. Consequently, for cancerous patients, the combined effect of ALB and GLB can offer an accurate prognostic value [16]. Yakup Bozkaya et al. retrospectively analyzed patients diagnosed with metastatic gastric cancer from 2009−2006 and noted that AGR was an independent predictor of the overall survival (OS) and progression-free survival (PFS) [17]. A retrospective investigation revealed that a lower OS was linked to preoperative AGR < 1.43 among patients with metastatic renal cell carcinoma who had nephrectomy (HR: 1.51,95% CI: 1.23–1.85). A retrospective cohort analysis study showed that the relationship between AGR and OS among patients with advanced non-small cell lung cancer (NSCLC) treated with amrlotinib was nonlinear; while higher AGR levels were an independent protective factor for OS among patients with advanced NSCLC treated with amrlotinib [18]. A retrospective analysis made by Basem N Azab et al. indicated that the pretreatment AGR level was a significant predictor of mortality for patients with breast cancer [19]. In our study, a significant negative relationship was demonstrated between AGR and serum total PSA, with the PSA level decreasing by 0.4 (ng/mL) with every 1 unit increase in the AGR of a fully-adjusted covariate model. After fitting the smoothed curve, we found an L-shaped relationship between AGR and PSA with an inflection point (K) of 1.32. To the left side of the inflection point, there was a negative relationship between AGR and PSA. In summary, lower levels

of AGR values are associated with higher levels of PSA. Previous studies also supported our results, as Zhongyou Xia et al. noted that a low AGR level before treatment was associated with a poorer OS, cancer-specific survival (CSS), recurrence-free survival (RFS), PFS and biochemical recurrence-free survival (BRFS) in terms of urologic cancers [5]. AGR is used as a noninvasive, effective and cost-effective marker to predict the prognosis of patients with urologic cancers [5]. An analysis of data from a large multicenter Korean institution showed that lower AGR levels were strongly associated with poorer pathological outcomes; AGR may be a useful serological marker for further predicting the poor pathological outcomes of patients with non-metastatic PCA [11].

The mechanisms associated with low AGR levels and tumor development are unclear. Some studies have pointed out that serum albumin and globulin respond to the body's nutritional and immune-inflammatory status respectively [20]. The albumin-to-globulin ratio is more reflective of the physiologic and pathologic state of the body. Albumin is closely related to the globulin level. When the body is in an inflammatory state, cytokines associated with the inflammatory response inhibit albumin synthesis [20]. At the same time, inflammation can cause changes in the permeability of blood vessels, and serum albumin can then leak through blood vessels into the intercellular matrix, resulting in lower levels [17]. Moreover, research findings indicate that the serum albumin level serves as an indicator of inflammation severity [21]. When immune cells become activated as a result of inflammation, they generate an increased quantity of cytokines, consequently causing a transition in the liver's protein synthesis from the production of albumin towards that of other acute-phase proteins [21]. In addition to this, the chronic inflammatory state is thought to produce an inflammatory microenvironment that predisposes individuals to cancers [22], and inflammatory substances secreted by cells in such an inflammatory microenvironment can induce cancer cell proliferation as well as survival, thereby promoting cancer metastasis and angiogenesis [23]. The specific mechanism still needs to be verified by a large number of basic experiments.

This study has the following advantages. First of all, NHANES data served as the foundation for our investigation, and the large number of samples obtained were analyzed to provide a scientific basis for quantifying the relationship between PSA and AGR. Thirdly, based on previous studies and biological indicators that may affect PSA, this study incorporated as many confounders as possible to ensure more reliable results. The smoothed curve fitting model was utilized to confirm the nonlinear relationship between PSA and AGR, and the threshold analysis was employed to validate the AGR threshold level.

However, this study has some limitations, which may affect its results. First of all, because this study was based on a cross-sectional design, it was not possible to determine a causal relationship between AGR and PSA. Although we observed an association between them, the influence of reverse causality or other potential covariates could not be ruled out. Secondly, the NHANES study population was limited to Americans, so the generalisability of our results was geographically limited. Thirdly, 41,156 participants were initially included in this study, and the final retained 5,376 samples were rigorously screened. Although the above screening ensured data integrity, it might have also resulted in less representative samples, limiting the extrapolation of results. Finally, although we controlled for many covariates in our multivariate regression models, there might still be unmeasured or unknown covariates that affected the accuracy of the results.

Conclusion

This study demonstrated a significant non-linear relationship between AGR and PSA among men aged over 40 years in the United States who were free of prostate diseases, with a negative relationship, particularly at AGRs of below 1.32. This finding suggests that a low AGR may be associated with higher PSA levels. However, because the cross-sectional design of this study limits the confirmation of causality, more prospective research and clinical trials are needed in the future to validate these results, as well as to explore the specific mechanisms linking AGR to prostate cancer development and progression.

Author Contributions: S.G., S.L., B.W. and J.W designed the study and supervised the completion, S.G., SL, and S.D. contributed to data collection and analysis, S.G. and S.L. wrote the manuscript, Z.T. reviewed the background and edited the manuscript. All the authors approved the final version of the manuscript.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12894-024-01687-2.

Supplementary Material 1

Author contributions

S.G. , S.L., B.W. and J.W designed the study and supervised the completion, S.G., SL, and S.D. contributed to data collection and analysis, S.G. and S.L. wrote the manuscript, Z.T. reviewed the background and edited the manuscript. All the authors approved the final version of the manuscript.

Funding

This research received no external funding.

Data availability

All data are available at NHANES website https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate
This study involving human participants were reviewed and approved by the Ethics Review Board of the National Center for Health Statistics. The patients/participants provided their written informed consent to participate in this study.

Consent for publication
Not applicable.

Statement of agree publication
All authors have read this manuscript and agree to publish this manuscript.

Competing interests
The authors declare no competing interests.

Received: 3 April 2024 / Accepted: 25 December 2024
Published online: 07 January 2025

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and Mortality Worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209–49.
2. Leapman MS, Wang R, Park H, Yu JB, Sprenkle PC, Cooperberg MR, et al. Changes in prostate-specific Antigen Testing relative to the Revised US Preventive Services Task Force Recommendation on prostate Cancer screening. JAMA Oncol. 2022;8:41–7.
3. Zhang M, Zhang J, Xing Z. Association of TyG index with prostate-specific antigen (PSA) in American men: results from NHANES, 2003–2010. Ir J Med Sci. 2023. https://doi.org/10.1007/s11845-023-03431-5.
4. Etzioni RD, Howlader N, Shaw PA, Ankerst DP, Penson DF, Goodman PJ, et al. Long-term effects of finasteride on prostate specific antigen levels: results from the prostate cancer prevention trial. J Urol. 2005;174:877–81.
5. Xia Z, Fu X, Yuan X, Li J, Wang H, Sun J, et al. Serum albumin to globulin ratio prior to treatment as a potential non-invasive prognostic indicator for urological cancers. Front Nutr. 2022;9:1012181.
6. Meyer EJ, Nenke MA, Rankin W, Lewis JG, Torpy DJ. Corticosteroid-binding globulin: a review of Basic and clinical advances. Horm Metab Res. 2016;48:359–71.
7. Lin H-Y, Zhu X, Aucoin AJ, Fu Q, Park JY, Tseng T-S. Dietary and Serum Antioxidants Associated with prostate-specific Antigen for Middle-aged and older men. Nutrients. 2023;15:3298.
8. Xu K, Yan Y, Cheng C, Li S, Liao Y, Zeng J, et al. The relationship between serum albumin and prostate-specific antigen: a analysis of the National Health and Nutrition Examination Survey, 2003–2010. Front Public Health. 2023;11:1078280.
9. Song J, Chen C, He S, Chen W, Su J, Yuan D, et al. Is there a non-linear relationship between dietary protein intake and prostate-specific antigen: proof from the national health and nutrition examination survey (2003–2010). Lipids Health Dis. 2020;19:82.
10. Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J. 2010;9:69.
11. Chung J-W, Ha Y-S, Kim SW, Park SC, Kang TW, Jeong YB, et al. The prognostic value of the pretreatment serum albumin to globulin ratio for predicting adverse pathology in patients undergoing radical prostatectomy for prostate cancer. Investig Clin Urol. 2021;62:545–52.
12. Aydh A, Mori K, D'Andrea D, Motlagh RS, Abufaraj M, Pradere B, et al. Prognostic value of the pre-operative serum albumin to globulin ratio in patients with non-metastatic prostate cancer undergoing radical prostatectomy. Int J Clin Oncol. 2021;26:1729–35.
13. Salciccia S, Frisenda M, Bevilacqua G, Viscuso P, Casale P, De Berardinis E, et al. Prognostic value of albumin to globulin ratio in non-metastatic and metastatic prostate Cancer patients: a Meta-analysis and systematic review. Int J Mol Sci. 2022;23:11501.
14. Li Q, Meng X, Liang L, Xu Y, Cai G, Cai S. High preoperative serum globulin in rectal cancer treated with neoadjunctive chemoradiation therapy is a risk factor for poor outcome. Am J Cancer Res. 2015;5:2856–64.
15. Ikeda S, Yoshioka H, Ikeo S, Morita M, Sone N, Niwa T, et al. Serum albumin level as a potential marker for deciding chemotherapy or best supportive care in elderly, advanced non-small cell lung cancer patients with poor performance status. BMC Cancer. 2017;17:797.
16. Li J, Zhu N, Wang C, You L, Guo W, Yuan Z, et al. Preoperative albumin-to-globulin ratio and prognostic nutritional index predict the prognosis of colorectal cancer: a retrospective study. Sci Rep. 2023;13:17272.
17. Bozkaya Y, Erdem GU, Demirci NS, Yazıcı O, Özdemir NY, Köstek O, et al. Prognostic importance of the albumin to globulin ratio in metastatic gastric cancer patients. Curr Med Res Opin. 2019;35:275–82.
18. Chen J, Xie C, Yang Y, Yang S, Huang J, Ye F, et al. Association between albumin-to-globulin ratio and the risk of overall survival in advanced non-small cell lung cancer patients with anlotinib treatment: a retrospective cohort study. BMC Pulm Med. 2023;23:275.
19. Azab BN, Bhatt VR, Vonfrolio S, Bachir R, Rubinshteyn V, Alkaied H, et al. Value of the pretreatment albumin to globulin ratio in predicting long-term mortality in breast cancer patients. Am J Surg. 2013;206:764–70.
20. Pfensig C, Dominik A, Borufka L, Hinz M, Stange J, Eggert M. A New Application for Albumin Dialysis in extracorporeal organ support: characterization of a putative Interaction between Human Albumin and Proinflammatory cytokines IL-6 and TNFα. Artif Organs. 2016;40:397–402.
21. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999;340:448–54.
22. Asegaonkar SB, Asegaonkar BN, Takalkar UV, Advani S, Thorat AP. C-Reactive protein and breast Cancer: New insights from Old Molecule. Int J Breast Cancer. 2015;2015:145647.
23. Kim E-S, Kim SY, Moon A. C-Reactive protein signaling pathways in Tumor Progression. Biomol Ther (Seoul). 2023;31:473–83.

Publisher's note