Observational Study

Relationship Between Preoperative Serum Albumin and Uric Acid and One-year Cure Rate in Patients With Herpes Zoster

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Background: Herpes zoster (HZ) is a common condition that causes severe pain mostly in middle-aged and older adults. It is currently treated with a combination of medication and surgery. However, some patients do not experience complete pain relief even after surgery and often experience a period of mild pain until a complete cure. Some studies suggest that the development of HZ is markedly associated with antioxidant factors; however, the relationship between preoperative antioxidant factors and the prognosis of HZ remains undetermined.

Objectives: Our study aimed to investigate the relationship between preoperative antioxidant factors and the one-year cure rate in patients with HZ.

Study Design: A retrospective, observational study.

Setting: The study was carried out in the Pain Department of the First Hospital Affiliated to Jiaxing College in Jiaxing, People's Republic of China.

Methods: The clinicopathological data of the patients who were admitted with HZ neuralgia at the First Hospital of Jiaxing from October 2021 through October 2022 were retrospectively analyzed, and their pain cure was followed up over the telephone. Furthermore, the optimal cut-off value of the antioxidant factor was assessed via the receiver operating characteristic (ROC) curve, whereas to evaluate the relationship between the antioxidant factor and various clinicopathologic characteristics of the patient, a χ^2 was performed. The Kaplan-Meier method was utilized to estimate the cure rate at one year. Moreover, the Cox regression model was used to assess the association of antioxidant factors with the prognosis of patients with HZ neuralgia. Lastly, ROC curves were generated to predict the effect of albumin (ALB), uric acid (UA), and combined ALB-UA (Co ALB-UA) on the patient's prognosis.

Results: A total of 225 patients were included in this study: 138 women and 87 men, with the median age of 62 years. The cure rate at one year was significantly higher in the ALB, UA, total bilirubin level (TBL), and homocysteine (HCY) groups than in the low value group (83.1%vs 41.6%, 73.7% vs 55.0%, 70.4% vs 52.1%, 71.3% vs 57.3% respectively, $P < 0.05$). The multifactorial Cox regression model indicated that the preoperative Numeric Rating Scale pain score (hazard ratio [HR] = 0.630; 95% CI, 0.437-0.907; $P < 0.05$), ALB (HR = 3.221; 95% CI, 2.212-4.690; $P < 0.05$), and UA (HR = 1.691; 95% CI, 1.182-2.419; $P < 0.05$) were identified as independent protective factors for a complete cure. An ROC curve analysis showed that the area under the curve of ALB, TBL, UA, HCY, and Co ALB-UA was 0.731 (95% CI, 0.658-0.805), 0.597 (95% CI, 0.518-0.675), 0.704 (95% CI, 0.633-0.774), 0.587 (95% CI, 0.508-0.666), and 0.777 (95% CI, 0.716-0.837) respectively. Additionally, the Co ALB-UA was more important than the individual antioxidant factors in evaluating a prognosis.

Limitations: Major limitations of this study are its nonrandomized, single-center, and retrospective design.

Conclusions: ALB and UA are independent risk factors and reflect the prognosis of patients with HZ neuralgia. Furthermore, their combined application may improve prediction accuracy.

Key words: Antioxidant factors, prognostic factors, joint assessment index, cure rate, herpes zoster

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Herpes zoster (HZ), commonly called shingles, is a common disease characterized by the presence of herpes on the skin and severe pain due to varicella-zoster virus reactivation because of decreased immunity. Furthermore, its incidence increases with age and is accompanied by many sequelae, such as postherpetic neuralgia (PHN) (1).

Herpetic neuralgia can be categorized into acute and subacute phases. If the infection occurs within a month, it is considered as the acute phase and is accompanied by hyperalgesia, allodynia, burning, tingling, and stabbing sensations or sensations similar to electric shocks. The pain may disappear as the herpes subsides. It has been observed that 60%-70% of patients report persistent pain after one month, which is the subacute phase of shingles (2). PHN is diagnosed when the pain persists for 3 months after the herpes has subsided. Currently, treating HZ neuralgia and PHN is based on a combination of antiviral drugs nutritive nerve medications, and surgical procedures, including pulsed radiofrequency and paravertebral nerve block (3).

If HZ is not diagnosed at early onset, then patients lose precious time for treatment, often resulting in poor clinical outcomes (4). Therefore, it is particularly important to explore models that effectively predict the prognosis of patients with HZ neuralgia so that individualized treatment plans can be developed.

Recent studies have indicated oxidative stress imbalance in the developmental stages of HZ. Furthermore, the total antioxidant capacity and total polyphenol content are also significantly lower in patients with HZ neuralgia than in healthy individuals, while the total oxidant status and oxidative stress index were higher than in healthy patients. Human antioxidant capacity weakening is closely related to the reactivation of the HZ virus, acute nerve injury, and PHN (5). Albumin (ALB), uric acid (UA), total bilirubin level (TBL), homocysteine (HCY), melatonin, indole-dioxygenase, vitamin C, vitamin D, and others are all involved in the body's oxidative-antioxidant system (6). It has been shown that the levels of all these biomarkers in patients with HZ neuralgia differ from healthy individuals (7-9).

Methods

Patients

In this retrospective study, we analyzed the clinical data of 225 patients with HZ neuralgia admitted to the Affiliated Hospital of Jiaxing University from October 2021 through October 2022. All the patients underwent computed tomography-guided pulsed radiofrequency surgery and conventional drug therapy, indicated acceptable results, and were discharged. There were no fatalities.

Study inclusion criteria were: 1) patients clinically diagnosed with HZ neuralgia, 2) aged between 18 and 80, and 3) were not systematically treated.

The exclusion criteria were: 1) those who were lost to follow-up, 2) had a history of diabetes mellitus, 3) had a malignant tumor or tumors, 4) had other diseases that caused acute or chronic pain, 5) had hepatic or renal insufficiencies, 6) had acute or chronic inflammatory diseases at the time of hospitalization, and 7) had any ALB, UA, TBL, or HCY level outside the normal range.

The initial blood test data of hospitalized patients were acquired, and ALB, UA, TBL, and HCY were grouped according to their optimal cut-off values, and their relationships with clinicopathological factors were analyzed. Patients were regularly followed up by telephone at 3-month intervals. The follow-up data included the patient's current general condition, whether there had been a recurrence, complications, and the degree of pain relief. Recurrence was defined as an increase in pain score of > 25% or a Numeric Rating Scale (NRS-11) score ≥ 4. The postoperative period was indicated by pain relief of < 25% and NRS-11 ≥ 4, whereas the preoperative period was defined at postdischarge follow-up in patients with effective treatment. Treatment effectiveness was defined as a degree of pain relief ([a-b]/a, where a = patient's preoperative NRS-11 score and b = patient's NRS-11 score at postoperative follow-up) $\geq 25\%$. Time to cure was defined as the first postoperative day until the patient was cured or the follow-up cutoff, which was October 2023, or the patient was cured.

Statistical Analysis

Data were statistically analyzed using IBM SPSS Statistics 25.0 (IBM Corporation), GraphPad Prism 8.0 (GraphPad Software) and R 4.1.0 (The R Foundation) and expressed as n (%).

The intergroup comparisons and relationship between ALB, UA, TBL, and HCY and the clinicopathological features of HZ were assessed using the χ^2 test. Spearman correlation was used to analyze the correlation between ALB, UA, TBL, HCY, and admission NRS-11 score. Using the receiver operating characteristic curve (ROC), the optimal critical values of ALB, UA,

TBL, and HCY were determined. Patients were categorized into high and low groups based on the critical values. Kaplan-Meier estimates and log-rank tests were performed to compare the cumulative incidence of a complete cure. The Cox regression model was used for multifactorial analysis. Furthermore, the hazard ratios and corresponding 95% CIs were also calculated. For the outcome indicator, a complete cure was used; the difference was considered statistically significant at $P < 0.05$.

Results

A total of 297 patients with HZ neuralgia were admitted to the Affiliated Hospital of Jiaxing University from October 2021 through October 2022. Of these, 65 were excluded, while 7 were lost to follow-up. Of the 225 patients who met the inclusion criteria, 138 (61.3%) were women and 87 (38.7%) were men; their median age was 62 (56-69 years).

The Spearmen correlation analysis showed that ALB, UA, TBL, and HCY were negatively correlated with the NRS-11 score at admission (ρ = -0.345, -0.420, -0.285, and -0.217, respectively; all $P < 0.05$). It was found that preoperative antioxidant factor levels correlated with pain levels in HZ neuralgia. Furthermore, using the ROC curves, the optimal cutoff values were assessed in order to predict the postoperative cure rate. For ALB, the cut-off value was 43.85 g/L, and the area under the curve (AUC) was 0.731 (95% CI, 0.658-0.805); for UA, the cutoff value was 285.4 μmol/L, and the AUC was 0.704 (95% CI, 0.633-0.774); for TBL, the cutoff value was 7.75 μmol/L, and the AUC was 0.597 (95% CI, 0.518-0.675); for HCY, the cutoff value was 9.25 μmol/L, and the AUC was 0.587 (95% CI, 0.508-0.666). Based on the cut-off value, the patients were divided into 2 groups for further analysis of clinicopathological characteristics: low ALB (≤ 43.85 g/L) and high ALB (> 43.85 g/L), low UA (≤ 285.4 μmol/L) and high UA (> 285.4 μmol/L), low TBL (≤ 7.75 μmol/L) and high TBL (> 7.75 μmol/L), as well as low HCY (≤ 9.25 μmol/L) and high HCY (> 9.25 μmol/L).

Preoperative ALB was associated if PHN occurred, length of hospitalization, admission NRS-11 score, and preoperative C-reactive protein (CRP) ($P < 0.05$) but was not associated with age, gender, disease duration, smoking, alcohol abuse, presence of hypertension, rash lateralization, ganglion involvement, number of involved ganglia, presence of preoperative numbness, and body mass index (BMI; kg/m^2) ($P > 0.05$).

Preoperative UA was associated with gender, if PHN occurred, length of hospitalization, and admission NRS-11 score ($P < 0.05$), but was not associated with age, disease duration, smoking, alcohol abuse, hypertension, rash lateralization, ganglionic segments involvement, number of involved ganglionic segments, preoperative numbness, preoperative CRP, and BMI ($P > 0.05$).

Preoperative TBL was associated with if PHN occurred, length of hospitalization, and admission NRS-11 score ($P < 0.05$), but was not correlated with age, gender, disease duration, smoking, alcohol abuse, hypertension, rash lateralization, ganglionic segments involvement, number of involved ganglionic segments, preoperative numbness, preoperative CRP, and BMI ($P > 0.05$).

Preoperative HCY was associated with age, if PHN occurred, and the preoperative numbness ($P < 0.05$), but was not correlated with gender, disease duration, length of hospitalization, smoking, alcohol abuse, hypertension, rash lateralization, involvement of ganglionic segments, number of involved ganglionic segments, admission NRS-11, preoperative CRP, and BMI ($P > 0.05$) (Table 1).

Table 1. *Correlations between the albumin (ALB), uric acid (UA), total bilirubin level (TBL), homocysteine (HCY) and clinicopathological variables in patients with herpes zoster neuralgia.*

Variables	ALB			UA			TBL			HCY		
	High (n = 124)	Low (n = 101)	*P* Value	High (n = 114)	Low (n = 111)	*P* Value	High (n = 152)	Low (n = 73)	*P* Value	High (n = 115)	Low (n = 110)	*P* Value
Age												
≤ 65	85	58	0.085	72	71	0.900	102	41	0.110	62	81	0.002
> 65	39	43		42	40		50	32		53	29	
Gender												
Men	49	38	0.772	60	27	0.00	62	25	0.345	56	31	0.002
Women	75	63		54	84		90	48		59	79	

Table 1 cont. *Correlations between the albumin (ALB), uric acid (UA), total bilirubin level (TBL), homocysteine (HCY) and clinicopathological variables in patients with herpes zoster neuralgia.*

Variables	ALB			UA			TBL			HCY		
	High (n = 124)	Low (n = 101)	*P* Value	High (n = 114)	Low (n = 111)	*P* Value	High (n = 152)	Low (n = 73)	*P* Value	High (n = 115)	Low (n = 110)	*P* Value
Course of disease (mos)												
≤ One	118	93	0.081	106	105	0.617	86	90	0.629	110	101	0.234
> One	6	8		8	6		5	7		5	9	
Smoker												
Yes	10	8	0.968	9	9	0.953	11	7	0.543	11	7	0.376
No	114	93		105	102		141	66		104	103	
Alcoholism												
Yes	6	8	0.331	5	9	0.255	7	7	0.140	9	5	0.309
No	118	92		108	102		145	65		106	105	
High blood pressure												
Yes	26	28	0.238	29	25	0.609	39	15	0.149	27	27	0.851
No	98	73		85	86		113	58		88	83	
Lesion location												
Right	66	47	0.318	62	51	0.206	73	40	0.401	55	58	0.462
Left	58	54		52	60		79	33		60	52	
Ganglion segment												
Cervical ganglia	15	24	0.082	20	19	0.768	23	16	0.446	18	21	0.318
Thoracic ganglia	95	61		82	74		105	51		85	71	
Lumbar ganglia	11	10		9	12		17	4		7	14	
Sacral ganglia	1	2		1	2		2	1		1	2	
Trigeminal ganglia	2	4		2	4		5	1		4	2	
Postherpetic neuralgia												
Yes	20	58	0.000	22	56	0.000	42	37	0.001	30	48	0.006
No	104	43		92	55		110	36		85	62	
Numbness												
Yes	23	23	0.435	18	28	0.079	28	18	0.278	15	31	0.005
No	101	78		96	83		124	55		100	79	
Length of Hospitalization (days)												
≤ 7	120	84	0.000	108	96	0.033	142	62	0.040	107	97	0.210
> 7	4	17		6	15		10	11		8	13	
Number of segments involved												
≤ 3	100	89	0.128	97	92	0.652	127	62	0.792	99	90	0.383
> 3	24	12		17	19		25	11		16	20	
Body mass index (kg/m^2)												
≤ 23.9	77	64	0.845	73	68	0.667	94	47	0.712	68	73	0.262
> 23.9	47	37		41	43		58	26		47	37	
Numeric Rating Scale score on admission												
≤ 6	78	47	0.014	82	43	0.000	95	30	0.002	70	55	0.101
> 6	46	54		32	68		57	43		45	55	
C-reactive protein level												
≤ 8	121	92	0.031	107	106	0.585	146	67	0.182	109	104	0.937
> 8	3	9		7	5		6	6		6	6	

The median and mean follow-up times were 240 days and 252.71 days, respectively. Figure 1 indicates the correlation between antioxidant factors and the one-year cure rate of patients with HZ neuralgia. The cure rate in the high ALB group was greater than in the low ALB group (83.1% vs 41.6%; $P < 0.05$; Fig. 1); the cure rate in the high UA group was greater than in the low UA group (73.7% vs 55.0%; $P < 0.05$; Fig. 2); the

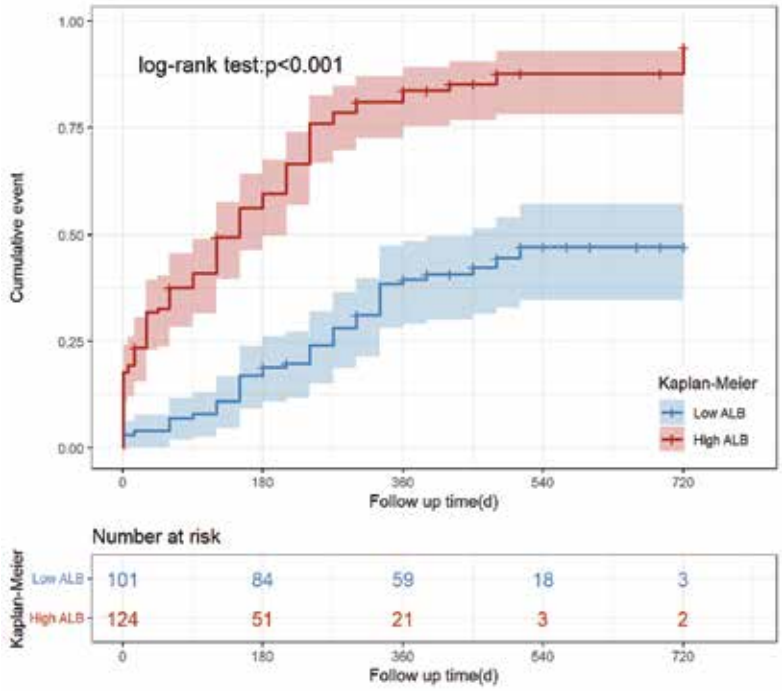

Fig. 1. *Kaplan-Meier estimation of 95% CIs for albumin (ALB) levels in patients with herpes zoster neuralgia for postoperative cumulative cured rate plots. Patients with a > 43.85 g/L preoperative ALB level had a better prognosis than those with < 43.85 g/L (P < 0.05).*

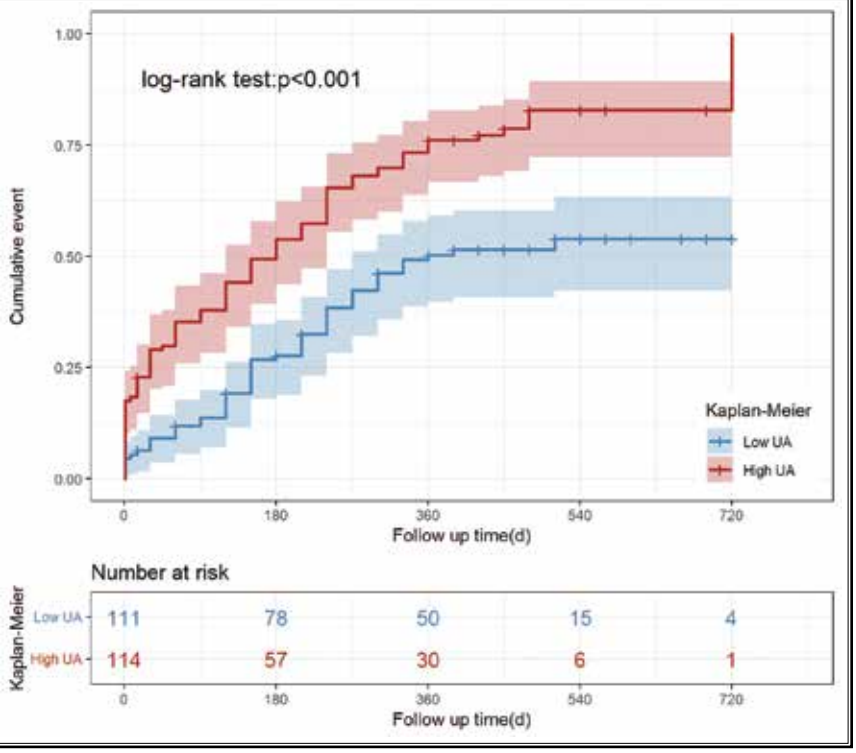

Fig. 2. *Kaplan-Meier estimation of 95% CIs for uric acid (UA) levels in patients with herpes zoster neuralgia for postoperative cumulative cured rate plots. Patients with a > 285.4 μmol/L preoperative UA level had a better prognosis than those with < 285.4 μmol/L (P < 0.05).*

cure rate in the high TBL group was greater than in the low TBL group (70.4% vs 52.1%; $P < 0.05$; Fig. 3); and the cure rate in the high HCY group was greater than in the low HCY group (71.3% vs 57.3%; $P < 0.05$; Fig. 4).

A Cox univariate analysis revealed that numbness in the affected area, length of hospitalization, as well as preoperative NRS-11, ALB, UA, TBL, and HCY levels were significant factors affecting the postoperative

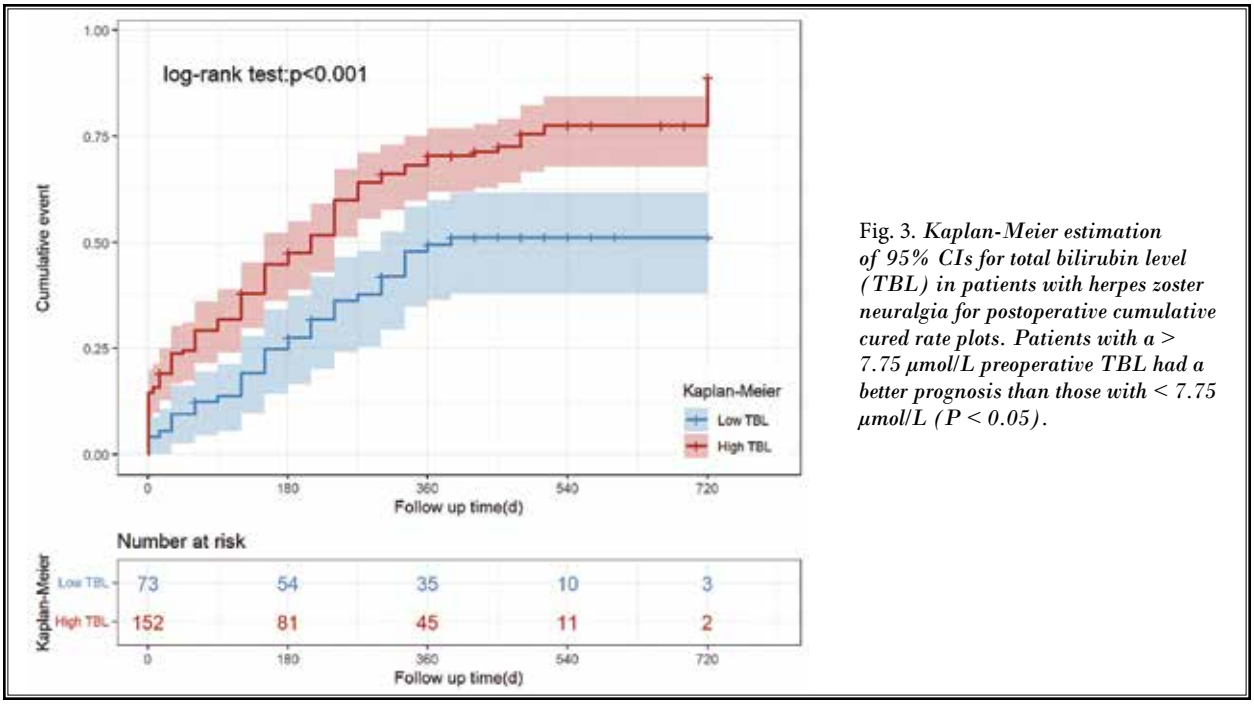

Fig. 3. *Kaplan-Meier estimation of 95% CIs for total bilirubin level (TBL) in patients with herpes zoster neuralgia for postoperative cumulative cured rate plots. Patients with a > 7.75 μmol/L preoperative TBL had a better prognosis than those with < 7.75 μmol/L ($P < 0.05$).*

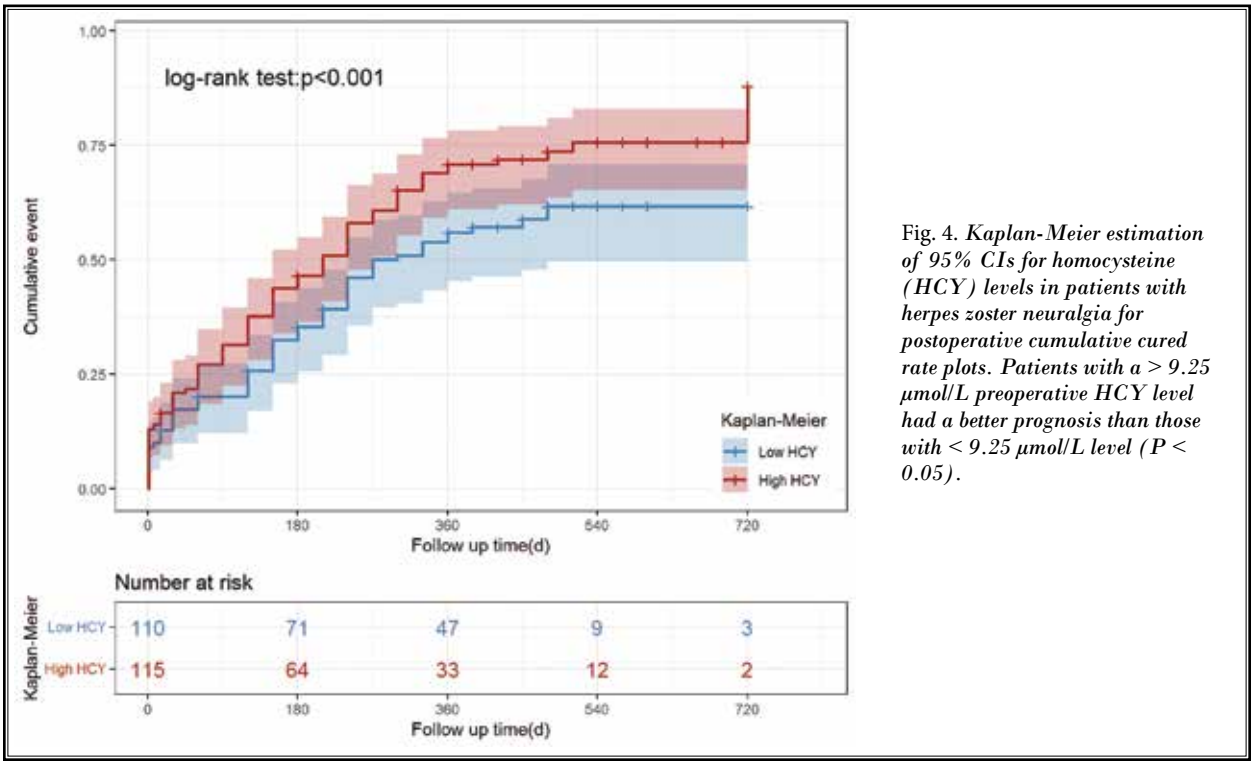

Fig. 4. *Kaplan-Meier estimation of 95% CIs for homocysteine (HCY) levels in patients with herpes zoster neuralgia for postoperative cumulative cured rate plots. Patients with a > 9.25 μmol/L preoperative HCY level had a better prognosis than those with < 9.25 μmol/L level ($P < 0.05$).*

cure rate. Multifactorial Cox regression modeling indicated that preoperative NRS-11 (hazard ratio [HR] = 0.630; 95% CI, 0.437-0.907; $P < 0.05$), ALB (HR = 3.221; 95% CI, 2.212-4.690; $P < 0.05$), and UA (HR = 1.691; 95% CI, 1.182-2.419; $P < 0.05$) were independent protective factors for a complete cure (Table 2).

This study found that ALB and UA had high accuracy in predicting a one year cure rate after HZ surgery; there-

Table 2. *Univariate and multivariate Cox proportional hazards regression models for overall patients with herpes zoster neuralgia survival.*

	Univariate analysis		Multivariate analysis	
	Hazard Ratio (95% CI)	***P* Value**	**Hazard Ratio (95% CI)**	***P* Value**
Age				
≤ 65	1			
> 65	0.844 (0.600-1.188)	0.3332		
Gender				
Women	1			
Men	1.256 (0.904-1.745)	0.173		
Course of disease (mos)				
≤ 1	1			
> 1	0.870 (0.426-1.776)	0.702		
Smoker				
No	1			
Yes	0.591 (0.290-1.207)	0.149		
Alcoholism				
No	1			
Yes	0.668 (0.295-1.512)	0.333		
High blood pressure				
No	1			
Yes	0.831 (0.564-1.225)	0.349		
Lesion location				
Right	1			
Left	0.992 (0.717-1.373)	0.962		
Ganglion segment				
Cervical ganglia	1	0.587		
Thoracic ganglia	1.479 (0.916-2.386)	0.109		
Lumbar ganglia	1.522 (0.778-2.975)	0.220		
Sacral ganglia	1.110 (0.259-4.753)	0.888		
Trigeminal ganglia	1.260 (0.430-3.688)	0.673		
Numbness				
No	1		1	
Yes	0.625 (0.403-0.970)	0.036	0.641 (0.409-1.004)	0.052
Length of hospitalization (days)				
≤ 7	1		1	
> 7	0.341 (0.159-0.729)	0.006	0.526 (0.241-1.149)	0.107
Number of segments involved				
≤ 3	1			
> 3	1.062 (0.685-1.646)	0.789		
Body mass index (kg/m^2)				
≤ 23.9	1			
> 23.9	1.207 (0.866-1.683)	0.266		
Numeric Rating Scale score on admission				
≤ 6	1		1	
> 6	0.485 (0.345-0.683)	0.000	0.630 (0.437-0.907)	0.013
Albumin level				
Low	1		1	
High	3.780 (2.626-5.441)	0.000	3.221 (2.212-4.690)	0.000
uric acid level				
Low	1		1	
High	2.207 (1.577-3.091)	0.000	1.691 (1.182-2.419)	0.004
Total bilirubin level				
Low	1		1	
High	1.942 (1.331-2.832)	0.001	1.308 (0.885-1.935)	0.178
Homocysteine level				
Low	1		1	
High	1.460 (1.051-2.028)	0.024	1.074 (0.762-1.516)	0.683
C-reactive protein level (mg/L)				
≤ 8	1			
> 8	0.436 (0.161-1.178)	0.102		

fore, the prognostic value of combined ALB-UA (Co ALB-UA) use was evaluated. Patients with high ALB and UA levels scored 2, those with low ALB and high UA or low UA and high ALB scored one, whereas those with low ALB and low UA scored 0. Kaplan-Meier analyses and log-rank tests indicated that the cure rates for patients with combined ALB-UA (Co ALB-UA) = 0, 1, and 2 were 90.1, 61.5, and 37.9%, respectively, and that the higher the score, the shorter the recovery time (Fig. 5).

The predictive accuracy of ALB, UA, TBL, Hcy, and Co ALB-UA for cure rate was compared by an ROC curve analysis. Furthermore, the AUC values for ALB, UA, TBL, HCY, and Co ALB-UA were 0.731 (95% CI, 0.658-0.805), 0.704 (95% CI, 0.633-0.774), 0.597 (95% CI, 0.518-0.675), 0.587 (95% CI, 0.508-0.666), and 0.777 (95% CI, 0.716-0.837), respectively., This suggests that Co ALB-UA was the most accurate prognostic indicator among these inflammatory markers for predicting a cure, and can be used as a tool for assessing the prognosis of patients with HZ neuralgia (Fig. 6).

Discussion

Recently, multiple studies have indicated that the imbalance between oxidation and antioxidants plays an important role in the onset, progression, and metastasis of various diseases and affects host immunomodulation (10-15). In our investigation, the clinical and prognostic value of preoperative antioxidant markers, including ALB, UA, TBL, and HCY levels, were assessed in patients with HZ neuralgia and compared with their predictive accuracy. The results suggest that high preoperative levels of ALB and UA are independent predictors of the postoperative cure rate in patients with HZ neuralgia. Per our knowledge, this is the first study in which these 4 antioxidant indices have been compared for their prognostic value in patients with HZ neuralgia.

This investigation assessed the optimal cutoff values of ALB, UA, TBL, and HCY using ROC curves, based on whether the patients were divided into high or low cohorts. The analysis of the relationship between the above antioxidant and clinicopathological factors revealed that the preoperative ALB level was related to the occurrence of PHN, length of hospitalization, admission NRS-11, and preoperative CRP ($P < 0.05$). Furthermore, the preoperative UA level was related to gender, the occurrence of PHN, length of hospitalization, and admission NRS-11 score ($P < 0.05$); TBL was associated with if PHN was present, length of hospitalization, and admission NRS-11 score ($P < 0.05$); whereas the preoperative HCY level was linked with age, PHN occurrence, and preoperative numbness ($P < 0.05$). Our study found that both high and low levels of preoperative antioxidant factors were

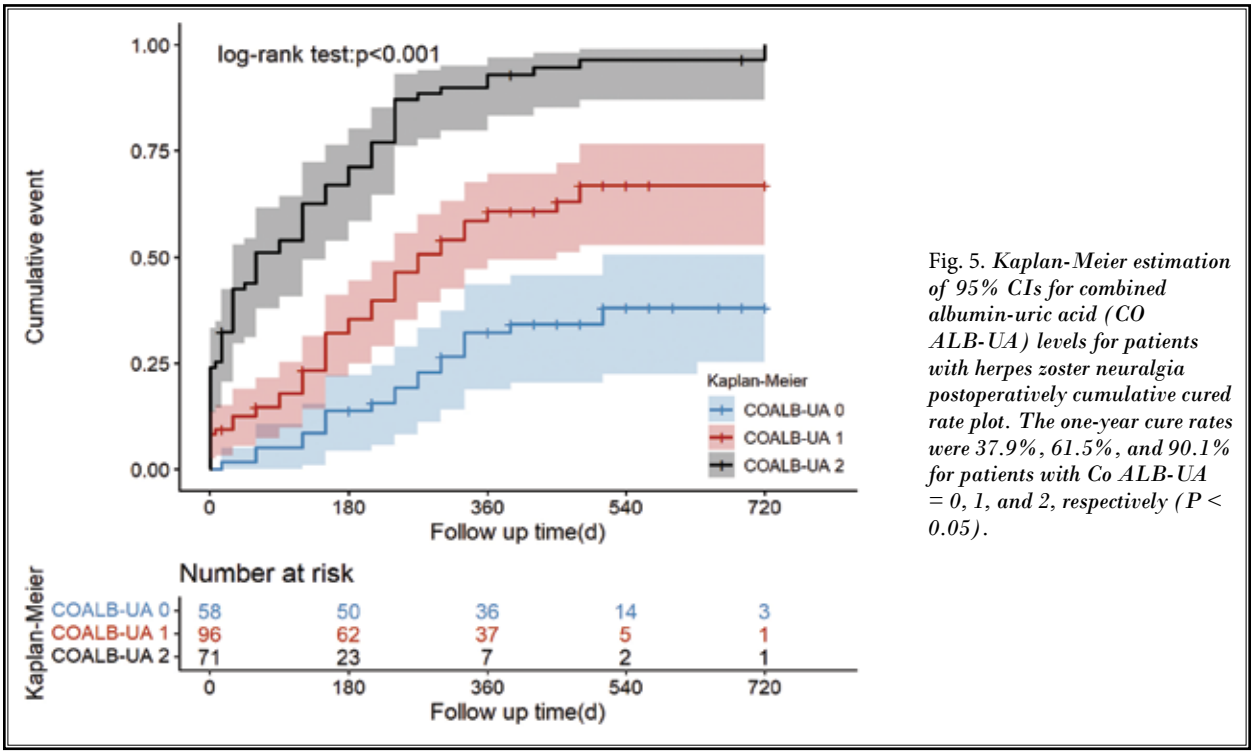

Fig. 5. *Kaplan-Meier estimation of 95% CIs for combined albumin-uric acid (CO ALB-UA) levels for patients with herpes zoster neuralgia postoperatively cumulative cured rate plot. The one-year cure rates were 37.9%, 61.5%, and 90.1% for patients with Co ALB-UA = 0, 1, and 2, respectively (P < 0.05).*

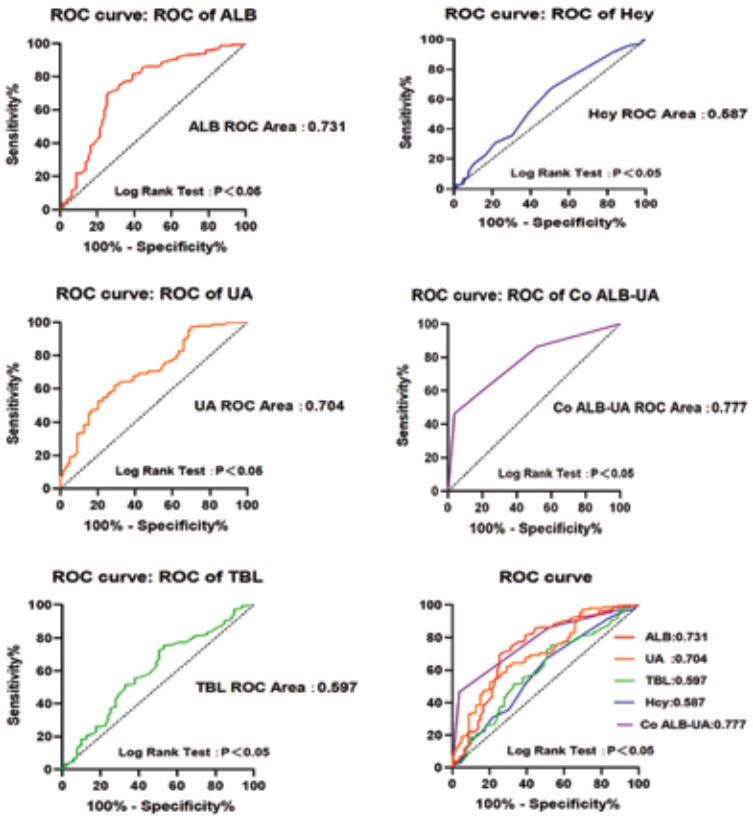

Fig. 6. *The area under the curve (AUC) of albumin (ALB), uric acid, total bilirubin level, homocysteine, and combined albumin-uric acid (Co ALB-UA) were 0.731 (95% CI,0.658-0.805), 0.704 (95% CI, 0.633-0.774), 0.597 (95% CI, 0.518-0.675), 0.587 (95% CI, 0.508-0.666), and 0.777 (95% CI, 0.716-0.837) respectively. Compared with UA or ALB alone, we found that CO ALB-UA has the highest AUC, which indicates that CO ALB-UA is the most accurate prognostic indicator for predicting the cure rate among these inflammatory indicators, and can be used as a tool for evaluating the prognosis of patients with herpes zoster neuralgia.*

associated with the development of PHN, providing a path to explore the relationship between the imbalance of antioxidant capacity and HZ prognosis.

Furthermore, the preoperative NRS-11 score, and ALB and UA levels were identified as independent protective factors for a complete cure ($P < 0.05$) according to Cox's regression model and multivariate analyses.

Moreover, the relationship between the preoperative ALB level and an HZ neuralgia patient's prognosis was assessed; it indicated that the time to cure was significantly shorter in patients with a preoperative ALB level higher than 43.85 g/L, and the cure rate was as high as 83.1% within one year, which was much higher than that of the other group (40.6%).

ALB is a powerful diagnostic and prognostic marker that has multiple functions in the body, such as antioxidant capacity (16,17). ALB protects cells from oxidative stress by trapping free radicals and scavenging oxidants (18). Furthermore, its ability to bind to oxidizing substances can reduce cellular damage caused by oxidative stress, thereby protecting cellular functional and structural integrity (19). In addition, ALB promotes the production and regeneration of other antioxidants and enhances the antioxidant capacity of cells (20). Moreover, the HZ virus reactivates because of immunocompromised conditions; ALB maintains the normal functioning of the body's immune system (21). ALB also acts as an antioxidant and anti-inflammatory agent in the nervous system, where it reduces nerve cell damage and inflammatory responses (22). Hypoalbuminemia is a symptom of malnutrition and is a biomarker for a poor prognosis due to infections associated with edema. This may be the reason for the high cure rate in patients with high ALB levels. The healing time of patients may be shortened by increasing the patient's serum ALB level to the high end of the normal range through ALB supplementation.

Our investigation shows that patients in the high preoperative UA level group had a significantly shorter time to cure and a substantially higher one-year cure rate than those in the low UA group (73.7% vs 55.0%; $P < 0.05$), suggesting that a high UA level that is still within the normal range is crucial for the postoperative recovery of patients with HZ neuralgia. This is consistent with previous studies, including Oskay, et al (8),who reported that serum UA

was lower in patients with HZ than in healthy individuals. Additional studies have also linked UA to pathologic neuralgia. Chang, et al (23) noted that high or low UA levels directly affect the risk of trigeminal neuralgia. Zhang, et al (24) found that decreased serum UA affects peripheral neuropathy damage, especially nerve motor conduction velocity. Furthermore, UA levels have also been studied as a biomarker for neurocognitive dysfunction (25). Patients with HZ neuralgia have pathologic nerve damage that is associated with oxidative stress, and UA directly scavenges free radicals, binds to metal ions, and inhibits oxidative enzyme activity, thereby reducing the production of free radicals. Early intervention with UA, such as optimizing it by eating purine-rich foods, might speed up a patient's recovery and improve a patient's cure rate.

Bilirubin, in the physiological range, has many biological activities, such as anti-inflammatory, antioxidant, immunomodulatory, neuroprotective, and antiviral properties (26). Kong, et al (27) found that in mice, bilirubin modulates pain threshold by activating 5-hydroxytryptamine receptors and acting on gamma-aminobutyric acid (GABA) receptors; this explains the pain desensitization in many patients with cholestasis. Low serum bilirubin is also a potential risk factor for many neurological and immune system disorders, such as multiple sclerosis, myasthenia gravis, desiccation syndrome, and psoriasis (28-30). Our study shows that patients in the high preoperative TBL group had a better postoperative recovery process than those in the low preoperative TBL group (70.4% vs 52.1%; $P < 0.05$).

HCY is not an antioxidant; however, it can indirectly achieve antioxidant effects through glutathione synthesis. Chiang, et al (31) found that circulating cysteine may be used to mediate glutathione-associated antioxidant capacity and may also increase oxidative stress in tumors and adjacent normal tissues. Furthermore, Ye, et al (32) showed that HCY and its precursor methionine significantly reduced reactive oxygen species (ROS) production in erythrocytes induced by ROS-positive controls and inhibited the increase in erythrocyte osmotic fragility and methemoglobin formation induced by ROS-positive controls, suggesting that HCY may be a complementary protective factor for erythrocytes against ROS damage. &&&In our study, we show that patients in the high HCY level group recovered better than those in the low HCY group (71.3% vs 57.3%; $P < 0.05$). Although it has also been documented that greater than normal values of HCY can induce oxidative stress, if the level is within the normal range, it might be a major contributor to the antioxidant system.

Our study reviewed the clinical and prognostic value of preoperative oxidative stress markers (ALB, UA, TBL, and HCY) in patients with HZ neuralgia and revealed that ALB and UA were independent protective factors for a complete cure of the disease; therefore, it was further evaluated if the combination of ALB and UA could improve the prognostic value for these patients. The evaluation showed that patients with high ALB and UA levels had the best prognosis, whereas patients with low ALB and UA had the worst prognosis. An ROC curve analysis showed that Co ALB-UA had the highest AUC, suggesting that Co ALB-UA levels more accurately predicts an HZ cure within one year after receiving computed tomography-guided pulsed radiofrequency therapy than either ALB or UA alone.

Limitations

This investigation has certain limitations. 1) The indicators that directly reflect the antioxidant capacity of the body, such as superoxide dismutase, catalase, glutathione peroxidase, and total antioxidant capacity were not included. 2) Only a few pathologic indicators were studied, and only one inflammatory indicator, CRP, was included. 3) A subgroup analysis for the effect of gender on UA and HCY levels was not performed. 4) This was a small-sample retrospective analysis, and there may be a retrospective bias. 5) The patients were included with indices within the physiological range; it is not known whether exceeding the range of normal values would have consistent results. Therefore, more samples, larger prospective studies, and subgroup analyses are required to confirm the conclusions of this study and to include more antioxidant indices to complement and improve our joint assessment index.

Conclusions

In summary, ALB and UA are biochemical indicators that need routine blood collection for preoperative testing and have the advantages of easy operation, low price, and versatility, and are expected to become indicators for assessing the prognosis of patients with HZ neuralgia. Furthermore, combined ALB and UA levels can improve the prediction accuracy of the one-year cure rate of patients with HZ neuralgia.

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