Systemic immune-inflammation index and neutrophil-to-lymphocyte ratio predict treatment responses in elderly patients with profound sudden deafness

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Received October 16, 2025; Accepted February 6, 2026

DOI: 10.3892/etm.2026.13156

Abstract. The aim of the present study was to evaluate the potential role of the neutrophil-to-lymphocyte ratio (NLR) and the systemic immune-inflammation index (SII) in predicting hearing recovery among elderly patients with profound sudden sensorineural hearing loss (SSNHL) following steroid treatment. The present retrospective study analyzed data from 186 elderly patients with profound SSNHL. Clinical characteristics and laboratory parameters were assessed to identify independent predictors of hearing outcomes using logistic regression and receiver operating characteristic (ROC) analyses. Baseline characteristics were generally comparable across groups; however, NLR, SII, total bilirubin (TBIL) and C-reactive protein (CRP) were significantly elevated in the non-recovery group (P<0.001). Multivariate logistic regression analysis further demonstrated that elevated NLR and SII were independent risk factors for poor hearing recovery; notably, increased CRP and TBIL levels were also independently associated with a higher likelihood of no recovery. ROC analysis demonstrated that both the NLR [area under the curve (AUC)=0.809] and SII (AUC=0.862) possessed a strong discriminatory ability for identifying non-recovery. In an exploratory analysis, the combined use of CRP, TBIL, SII and NLR achieved the highest predictive performance for distinguishing no recovery from complete recovery, with an AUC of 0.951 (95% CI, 0.907-0.996; P<0.001). Overall, elevated NLR and SII were independent predictors of poor hearing recovery in elderly patients with profound SSNHL. These readily available inflammatory markers may serve as useful prognostic tools for outcome stratification in clinical practice.

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Abbreviations: SSNHL, sudden sensorineural hearing loss; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; PTA, pure-tone average; TBIL, total bilirubin; Hb, hemoglobin; TP, total protein; Alb, albumin; Cr, creatinine; OR, odds ratio; ROC, receiver operating characteristic; AUC, area under the curve

Key words: profound sudden deafness, elderly, SII, NLR, hearing recovery

Introduction

Sudden sensorineural hearing loss (SSNHL) is clinically defined as a rapid, unexplained loss of hearing, typically ≥30 dB across ≥3 contiguous frequencies within 72 h (1). As a time-sensitive neuro-otologic emergency, SSNHL may result in permanent hearing loss, markedly affecting communication and quality of life, especially when diagnosis or treatment is delayed (2). Although its diagnostic criteria are well established (1), the underlying pathophysiology remains unclear and is likely multifactorial. Proposed mechanisms include viral infection (3), immune-mediated inner ear damage (4) and vascular insufficiency leading to cochlear ischemia (5). The heterogeneity in both clinical presentation and etiology makes SSNHL a diagnostic and therapeutic challenge. A number of cases do recover spontaneously, while others suffer irreversible hearing loss even despite timely treatment (6). This variability highlights the need for early, reliable and accessible prognostic indicators. However, current predictors, primarily clinical features, such as initial hearing level, vertigo, and treatment delay, lack sufficient accuracy (5). Therefore, there is growing interest in identifying biological markers that can more effectively predict treatment response and long-term outcomes in SSNHL.

In recent years, increasing evidence has indicated that systemic inflammation may play a contributory role in the progression of SSNHL (7,8). Inflammatory mediators may promote vascular dysfunction, microcirculatory disturbances and direct cochlear damage, thereby impairing auditory recovery (7,8). This has led to an increase in research regarding the use of systemic inflammatory markers as accessible and cost-effective prognostic indicators. Among these, the neutrophil-to-lymphocyte ratio (NLR) and the systemic immune-inflammation index (SII), which incorporates neutrophil, lymphocyte and platelet counts, have gained attention due to their potential to reflect the balance between pro-inflammatory and immune-regulatory processes (9-11). Numerous studies have demonstrated the prognostic utility of the NLR and SII in varying clinical conditions, including malignancies (9), cardiovascular (12) and cerebrovascular (13)

diseases, as well as autoimmune disorders (14). In the context of SSNHL, emerging data suggest that elevated baseline levels of these markers may be associated with poorer hearing outcomes (15,16). However, the majority of available studies (9,12) have focused on general adult populations with variable severity of hearing loss, and data specific to cases with profound SSNHL remain sparse.

The applicability of NLR and SII in elderly patients has yet to be adequately addressed. Aging is associated with a wide array of physiological changes, including immune senescence, chronic low-grade systemic inflammation, endothelial dysfunction and a higher prevalence of metabolic and vascular comorbidities such as hypertension, diabetes mellitus and atherosclerosis (17-19). These age-related alterations may exacerbate cochlear vulnerability and impair the recovery potential following auditory insult (20). In addition, older individuals frequently exhibit atypical clinical presentations and may have delayed access to care or limited responsiveness to standard therapies due to pharmacodynamic changes or comorbid disease (21-23). Therefore, accurate and objective prognostic tools are particularly valuable in this population, where clinical decision-making is often complicated by overlapping risk factors and reduced physiological reserve.

Despite their clinical application, the prognostic importance of NLR and SII in elderly patients with profound SSNHL treated with systemic steroids, with or without intratympanic methylprednisolone injection, remains to be further investigated. Therefore, the present study aimed to explore the predictive value of the NLR and SII for recovery outcomes in elderly patients diagnosed with profound sudden deafness who were treated with systemic steroids, with or without intratympanic methylprednisolone injection.

Materials and methods

Subjects. The present retrospective study was conducted at the Department of Otolaryngology, Emergency General Hospital (Beijing, China). Consecutive elderly patients aged ≥60 years (range, 60-86 years) who presented to the hospital and received treatment for profound sudden sensorineural hearing loss between February 2021 and March 2024 were included. A total of 186 patients met the eligibility criteria and were included for subsequent analysis. Since the present study was retrospective and no additional interventions were performed, the requirement for ethical approval for this study was waived by the Ethics Committee of the Emergency General Hospital (No. L24-1; Beijing, China), and the requirement for informed consent was also waived. The inclusion criteria (20) were: i) Age ≥60 years; ii) diagnosis of profound sudden deafness, defined as a ≥30 dB hearing loss across ≥3 consecutive frequencies within 72 h; and iii) complete clinical records, including demographics, audiological data and laboratory results. The exclusion criteria were: i) Pre-existing hearing loss, bilateral onset or concurrent ear disorders (such as Meniere's disease or otosclerosis); ii) systemic diseases affecting hearing (such as neurological or autoimmune disorders); iii) prior treatment for sudden deafness (such as corticosteroids or immunosuppressants); or iv) incomplete follow-up data.

All patients were initially treated with intravenous steroids for a duration of 7 days. In cases where no hearing recovery was observed, intratympanic methylprednisolone was administered at a concentration of 40 mg/m, with an injection volume of 0.5-0.7 ml per dose, once per day for 4 consecutive days.

Based on hearing recovery status, patients were classified (20) into the following groups: i) No recovery (n=92), where hearing improvement remained <50%; ii) partial recovery (n=62), representing gains of up to half the original loss relative to the unaffected ear; and iii) complete recovery (n=32), indicating hearing improvement to within 10 dB of the unaffected side.

Baseline clinical and laboratory data collection. For this retrospective study, clinical information documented at the time of admission was obtained from patients' electronic medical records. Collected data included age, sex, BMI, smoking and alcohol history, affected ear side, initial pure-tone average (PTA), and otologic symptoms (tinnitus, vertigo or aural fullness). Comorbidities (such as coronary artery disease, diabetes and hypertension) were also documented. PTA was calculated at 4, 2, 1 and 0.5 kHz, and reassessed after treatment (within 2-4 weeks). Laboratory parameters were measured within 24 h of admission, including C reactive protein (CRP), total bilirubin (TBIL), hemoglobin (Hb), total protein (TP), albumin (Alb), creatinine (Cr) and lipid levels. The NLR was calculated based on the following formula: Neutrophil count/lymphocyte count. The SII was calculated based on the following formula: Platelet count x neutrophil count/lymphocyte count. Peripheral venous blood samples (3-5 ml per patient) were collected at patient admission for routine laboratory testing, and all analyses were performed using standardized methods in the Clinical Laboratory of the Emergency General Hospital.

Statistical analysis. SPSS (version 26.0; IBM Corp.) was used for data analysis. $P<0.05$ was considered to indicate a statistically significant difference. Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. Variables that followed a normal distribution were expressed as the mean ± standard deviation (SD) and analyzed using parametric tests, whereas variables that did not conform to a normal distribution were presented as the median (interquartile range) and analyzed using non-parametric methods. Group comparisons of continuous variables were conducted using one-way ANOVA, followed by the Bonferroni post hoc test for multiple pairwise comparisons. Fisher's exact or χ^2 tests were performed for comparisons of categorical variables. Variables with significant intergroup differences were included in logistic regression models to identify independent predictors of hearing outcomes. Comorbidities, including hypertension, diabetes mellitus and coronary artery disease, were excluded from the multivariate analysis as they did not demonstrate statistical significance in the univariate comparison ($P>0.05$). This selection strategy was intentionally employed to maintain model parsimony and stability, thereby minimizing the risk of overfitting and ensuring the reliability of the identified predictors within this specific elderly cohort. Stepwise logistic regression analysis (LRA) was conducted separately for partial vs. complete recovery and no recovery vs. complete recovery, with odds ratios (ORs) and 95% CIs reported. To assess the potential issue of multicollinearity among predictor variables, variance inflation factor (VIF) analysis was performed for

all variables included in the multivariate logistic regression models. A VIF value >10 was considered indicative of significant multicollinearity. Receiver operating characteristic (ROC) curves were generated to evaluate the predictive value of CRP, TBIL, SII and NLR. The area under the curve (AUC), optimal cut-off value (based on Youden's index), specificity and sensitivity were calculated for individual markers and their combinations. Notably, the analysis of the combined biomarker model was treated as exploratory rather than definitive, acknowledging the potential for optimistic performance estimates given the sample size of the complete recovery subgroup. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics of elderly patients with profound sudden deafness. A total of 186 elderly patients with profound sudden deafness were stratified into three outcome groups: Complete (n=32), partial (n=62) and no recovery (n=92). Baseline demographics, including age, sex, BMI, smoking status and alcohol consumption, did not significantly differ among groups (P>0.05). Similarly, clinical features such as initial PTA thresholds, ear laterality, tinnitus, vertigo, aural fullness and comorbidities (hypertension, diabetes mellitus and coronary artery disease) were comparable (P>0.05). However, the PTA-after differed significantly among the complete recovery, partial recovery and no recovery groups (overall P<0.001, one-way ANOVA). Post-hoc pairwise analyses demonstrated that the complete recovery group achieved significantly better hearing outcomes than both the partial and no recovery groups (all pairwise P<0.001). Similarly, CRP and TBIL levels showed significant overall differences among the three groups (overall P<0.001, one-way ANOVA), with the lowest levels observed in the complete recovery group, intermediate levels in the partial recovery group and the highest levels in the no recovery group (post-hoc pairwise comparisons, all P<0.001). Notably, SII and NLR increased progressively across outcome groups, from complete recovery to partial recovery and no recovery (SII: 869.38±140.20, 972.15±152.34 and 1,090.24±148.65, respectively; NLR: 2.79±0.52, 3.08±0.47 and 3.43±0.50, respectively; overall P<0.001, one-way ANOVA; post-hoc pairwise comparisons, all P<0.001). Other routine parameters (Hb, TP, Alb, Cr and lipids) exhibited no significant differences (P>0.05; Table I).

Identification of independent predictors of partial recovery using LRA in elderly patients with profound sudden deafness. To identify independent risk factors for partial vs. complete recovery in elderly patients with profound sudden deafness, stepwise LRA was performed. Variables identified as significant in the baseline characteristics analysis (Table I), including CRP, TBIL, SII and NLR, were subsequently entered into the univariate analysis. Univariate analysis results indicated that higher CRP (95% CI, 1.003-1.344; OR, 1.161; P=0.046), SII (95% CI, 1.002-1.010; OR, 1.006; P=0.003) and NLR (95% CI, 1.454-11.457; OR, 4.082; P=0.008) were significantly associated with partial recovery. TBIL was not significantly associated with partial recovery (P=0.668) and was therefore excluded from subsequent analyses. Variables with P<0.05 in univariate analysis were included in the multivariate model. CRP (95% CI, 1.011-1.412; OR, 1.195; P=0.037), SII (95% CI, 1.001-1.010; OR, 1.005; P=0.016) and NLR (95% CI, 1.580-15.174; OR, 4.897; P=0.006) remained independently significant. The present findings demonstrated that elevated CRP, SII and NLR were independent risk factors of partial recovery, underscoring their potential as prognostic markers in elderly patients with profound sudden deafness. Additionally, VIF analysis was performed to assess multicollinearity among these variables. The VIF values for CRP, SII and NLR were 1.073, 1.060 and 1.056, respectively, indicating that multicollinearity was not a concern in this model. Detailed information is shown in Table II.

Evaluation of the predictive performance of the SII and NLR in differentiating elderly patients with profound sudden deafness who achieved partial recovery from those with complete recovery. As the aforementioned multivariate LRA identified CRP, SII and NLR as independent risk factors for partial recovery, ROC curve analysis was conducted to assess their predictive value in differentiating elderly patients with profound sudden deafness who achieved partial recovery from those with complete recovery (Fig. 1; Table III). Among individual markers, NLR demonstrated moderate discriminatory performance (AUC=0.663; 95% CI, 0.538-0.788; P=0.010). At a cut-off value of 2.58, the sensitivity and specificity were 90.3 and 46.9%, respectively. The SII showed the strongest predictive ability (95% CI, 0.551-0.808; AUC=0.679; P=0.005), with a cut-off of 890.96 yielding a sensitivity of 75.8% and a specificity of 65.6%. CRP did not reach statistical significance (95% CI, 0.496-0.732; AUC=0.614; P=0.071), although it showed a trend toward predictive relevance. Notably, the combined use of the NLR and SII improved diagnostic accuracy, yielding the highest AUC of 0.718 (95% CI, 0.604-0.833, P=0.001), with a sensitivity of 88.7% and a specificity of 46.9%. Detailed information is presented in Table III.

Identification of independent predictors of no recovery using LRA in elderly patients with profound sudden deafness. To explore the risk factors associated with poor prognosis, LRA was conducted to compare elderly patients with no recovery with those with complete recovery from profound sudden deafness. Based on variables exhibiting significant differences in the analysis of baseline characteristics (Table I), CRP, TBIL, SII and NLR were included in the univariate LRA. The results revealed that all four variables were significantly associated with increased odds of no recovery. Specifically, elevated CRP levels were associated with a higher risk (P<0.001), with an OR of 1.462 (95% CI, 1.225-1.745). TBIL also showed a significant association (95% CI, 1.104-1.600; OR, 1.329; P=0.003). The SII exhibited a strong association with non-recovery (95% CI, 1.006-1.014; OR, 1.010; P<0.001), as did the NLR, which exhibited the highest effect size (95% CI, 4.713-41.804; OR, 14.037; P<0.001). In the multivariate LRA model, all four variables remained independently significant. TBIL (95% CI, 1.042-2.023; OR, 1.452; P=0.028), SII (95% CI, 1.004-1.013; OR, 1.008; P<0.001), CRP (95% CI, 1.185-2.018; OR, 1.547; P=0.001) and NLR (95% CI, 4.391-145.089; OR, 25.239; P<0.001) were each independently associated with no recovery. The VIF values for CRP, TBIL, SII and NLR

Table I. Comparison of baseline characteristics among elderly patients with profound sudden deafness according to recovery outcomes.

Clinical indices	Complete recovery (n=32)	Partial recovery (n=62)	No recovery (n=92)	P-value
Demographic characteristics				
Age, years	63.72±4.77	64.82±4.60	64.63±4.85	0.548
Sex, n (%)				0.941
Male	13 (40.63)	28 (45.16)	41 (44.57)	
Female	19 (59.38)	34 (54.84)	51 (55.43)	
BMI, kg/m^2	25.39±2.57	25.23±2.74	25.07±1.95	0.781
Smoking status, n (%)				>0.999
Current	5 (15.63	9 (14.52)	14 (15.22)	
Former	8 (25.00)	16 (25.81)	24 (26.09)	
Never	19 (59.38)	37 (59.68)	54 (58.70)	
Alcohol consumption, n (%)				0.992
Current	3 (9.38)	7 (11.29)	11 (11.96)	
Former	10 (31.25)	21 (33.87)	31 (33.70)	
Never	19 (59.38)	34 (54.84)	50 (54.35)	
Clinical presentation and history				
PTA-initial, dB	102.97±13.06	102.97±9.04	103.72±10.53	0.889
PTA-after, dB	59.56±9.01	84.76±7.92	99.89±10.67	<0.001
Affected ear, n (%)				0.738
Right	18 (56.25)	37 (59.68)	49 (53.26)	
Left	14 (43.75)	25 (40.32)	43 (46.74)	
Tinnitus, n (%)	23 (71.88)	45 (72.58)	68 (73.91)	>0.999
Vertigo, n (%)	12 (37.50)	22 (35.48)	37 (40.22)	0.844
Aural fullness, n (%)	4 (12.50)	11 (17.74)	14 (15.22)	0.801
HTN, n (%)	7 (21.88)	12 (19.35)	24 (26.09)	0.638
DM, n (%)	13 (40.63)	22 (35.48)	32 (34.78)	0.859
Coronary artery disease, n (%)	9 (28.13)	17 (27.42)	23 (25.00)	0.925
Laboratory indices				
CRP, mg/l	13.67±3.14	15.03±2.94	16.67±2.56	<0.001
TBIL, μmol/l	13.63±2.07	13.40±2.61	15.14±2.34	<0.001
Hb, g/l	138.25±11.05	135.30±10.98	138.29±12.90	0.281
TP, g/l	67.89±3.10	68.09±2.60	68.45±2.82	0.548
Alb, g/l	41.17±3.76	41.73±3.66	42.35±3.67	0.253
Cr, μmol/l	66.36±2.89	66.60±3.94	66.96±3.57	0.673
Cholesterol, mmol/l	4.87±0.29	4.89±0.32	4.82±0.30	0.356
TG, mmol/l	1.20±0.13	1.22±0.14	1.18±0.12	0.122
HDL, mmol/l	1.30±0.12	1.32±0.15	1.28±0.15	0.263
LDL, mmol/l	3.19±0.30	3.21±0.27	3.20±0.32	0.957
SII	869.38±140.20	947.55±92.79	1,090.24±148.65	<0.001
NLR	2.79±0.52	3.07±0.40	3.43±0.50	<0.001

CRP, C reactive protein; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglyceride; Cr, creatinine; Alb, albumin; TP, total protein; Hb, hemoglobin, TBIL, total bilirubin; DM, diabetes mellitus; HTN, hypertension; PTA, pure-tone average.

were 1.145, 1.078, 1.221 and 1.143, respectively, demonstrating that multicollinearity was not a concern and the stability of the model was maintained. Detailed information is shown in Table IV.

Evaluation of the predictive performance of the SII and NLR in differentiating elderly patients with profound sudden deafness who experienced no recovery from those with complete recovery. Since the aforementioned multivariate LRA showed

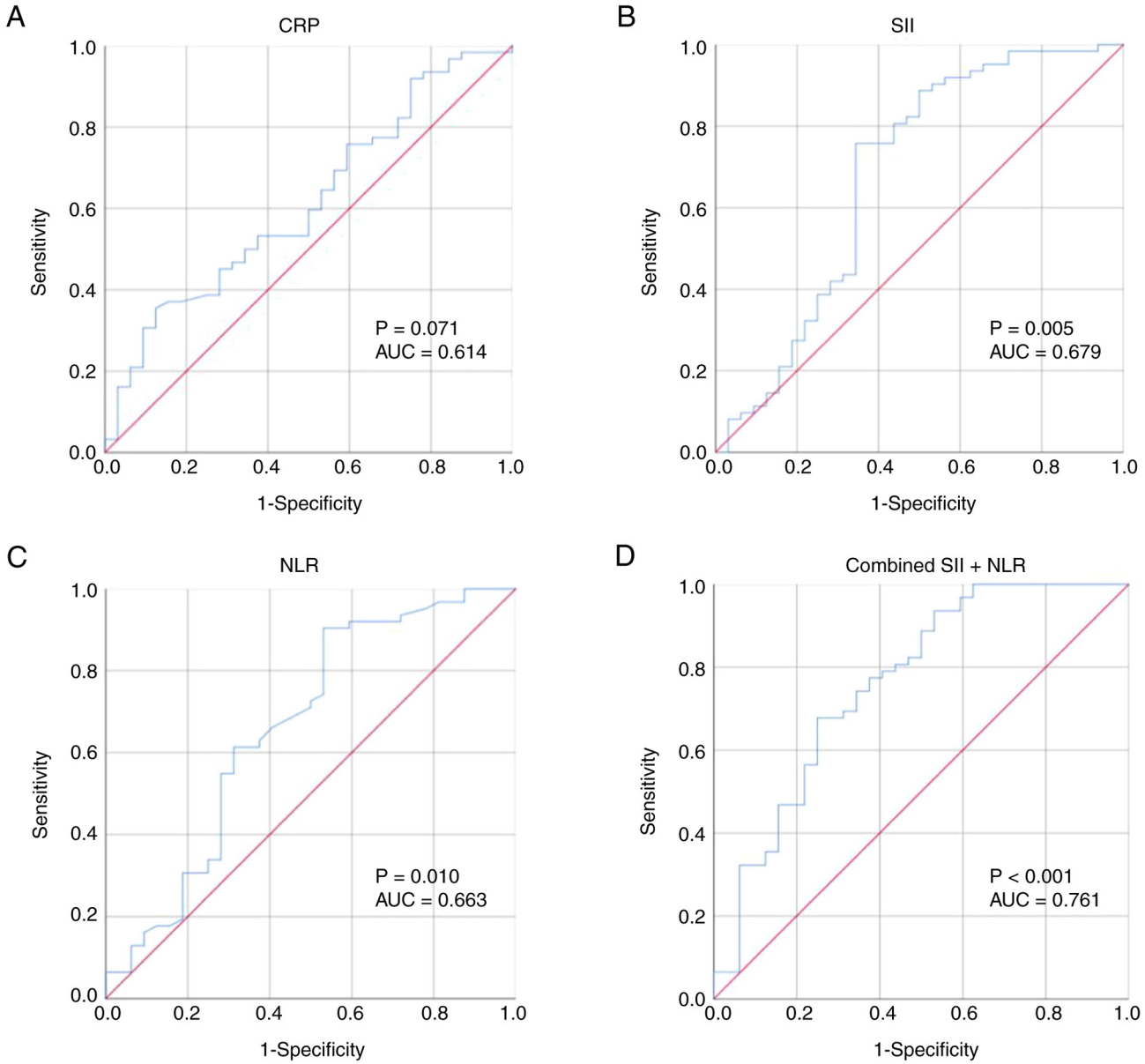

Figure 1. ROC analysis of CRP, SII, NLR and the combination of SII + NLR in distinguishing patients with partial recovery from patients with complete recovery in elderly patients with profound sudden deafness. (A) ROC curves of CRP; (B) ROC curves of the SII; (C) ROC curves of the NLR; and (D) ROC curves of the combined model incorporating SII and NLR. The AUC and corresponding P-values are indicated in each panel. CRP, C-reactive protein; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; AUC, area under the curve; ROC, receiver operating characteristic.

that CRP, TBIL, SII and NLR were independent risk factors for no recovery, ROC curve analysis was conducted to assess their predictive value in differentiating elderly patients with profound sudden deafness who experienced no recovery from those with complete recovery (Fig. 2; Table V). Among individual markers, the SII exhibited the strongest predictive performance (95% CI, 0.790-0.934; AUC=0.862; P<0.001), with a cut-off value of 893.78 yielding a sensitivity of 92.4% and a specificity of 65.6%. The NLR also showed high predictive value (95% CI, 0.720-0.898; AUC=0.809; P<0.001), with a cut-off of 2.98, sensitivity of 84.8% and specificity of 68.7%. TBIL exhibited an AUC of 0.691 (95% CI, 0.590-0.792; P=0.001), with a cut-off of 15.61 μmol/l, corresponding to a sensitivity of 51.1% and a specificity of 87.5%. CRP demonstrated moderate discrimination (95% CI, 0.678-0.864; AUC=0.771; P<0.001), with a cut-off of 16.83 mg/l, corresponding to a sensitivity of 53.3% and a specificity of 90.6%. In an exploratory analysis, the combined use of CRP, TBIL, SII and NLR demonstrated improved predictive performance, yielding an AUC of 0.951 (95% CI, 0.907-0.996; P<0.001), with a sensitivity of 87.0% and a specificity of 93.7%.

Discussion

The results of the present study provide evidence for the prognostic value of the NLR and SII in elderly patients with profound sudden deafness treated with systemic steroids, with or without intratympanic methylprednisolone injection. Elevated SII and NLR were independently associated with poor hearing recovery outcomes, and their predictive performance surpassed that of traditional inflammatory markers, such as CRP and TBIL, particularly when used in combination. To the

Table II. Univariate and multivariate LRA of potential factors associated with partial recovery compared with complete recovery in elderly patients with profound sudden deafness.

	Univariate LRA						Multivariate LRA						
Variable	β	SE	Wald χ^2	P-value	OR	95% CI	β	SE	Wald χ^2	P-value	OR	95% CI	VIF
CRP	0.149	0.075	3.974	0.046	1.161	1.003-1.344	0.178	0.085	4.364	0.037	1.195	1.011-1.412	1.073
TBIL	0.039	0.091	0.184	0.668	0.962	0.805-1.149							
SII	0.006	0.002	8.685	0.003	1.006	1.002-1.010	0.005	0.002	5.754	0.016	1.005	1.001-1.010	1.06
NLR	1.406	0.527	7.133	0.008	4.082	1.454-11.457	1.589	0.577	7.58	0.006	4.897	1.580-15.174	1.056

LRA, logistic regression analysis; CRP, C reactive protein; TBIL, total bilirubin; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; VIF, variance inflation factor; OR, odds ratio; SE, standard error.

Table III. Receiver operating characteristic curves of CRP, SII, NLR and their combination for predicting partial recovery vs. complete recovery in elderly patients with profound sudden deafness.

Variable	AUC	95% CI	Best cut-off value	Sensitivity, %	Specificity, %	P-value
CRP, mg/l	0.614	0.496-0.732	16.44	35.5	87.5	0.071
SII	0.679	0.551-0.808	890.96	75.8	65.6	0.005
NLR	0.663	0.538-0.788	2.58	90.3	46.9	0.010
Combined SII + NLR	0.718	0.604-0.833		88.7	46.9	0.001

CRP, C reactive protein; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; AUC, area under the curve.

Table IV. Univariate and multivariate LRA of potential factors associated with no recovery compared with complete recovery in elderly patients with profound sudden deafness.

	Univariate LRA						Multivariate LRA						
Variable	β	SE	Wald χ^2	P-value	OR	95% CI	β	SE	Wald χ^2	P-value	OR	95% CI	VIF
CRP	0.38	0.09	17.711	<0.001	1.462	1.225-1.745	0.436	0.136	10.318	0.001	1.547	1.185-2.018	1.145
TBIL	0.284	0.095	9.013	0.003	1.329	1.104-1.600	0.373	0.169	4.842	0.028	1.452	1.042-2.023	1.078
SII	0.01	0.002	26.339	<0.001	1.01	1.006-1.014	0.008	0.002	12.172	<0.001	1.008	1.004-1.013	1.221
NLR	2.642	0.557	22.511	<0.001	14.037	4.713-41.804	3.228	0.892	13.089	<0.001	25.239	4.391-145.089	1.143

LRA, logistic regression analysis; CRP, C reactive protein; TBIL, total bilirubin; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; VIF, variance inflation factor; OR, odds ratio; SE, standard error.

Table V. Receiver operating characteristic curves of CRP, TBIL, SII, NLR and their combination for predicting no recovery vs. complete recovery in elderly patients with profound sudden deafness.

Variable	AUC	95% CI	Best cut-off value	Sensitivity, %	Specificity, %	P-value
CRP, mg/l	0.771	0.678-0.864	16.83	53.3	90.6	<0.001
TBIL, μmol/l	0.691	0.590-0.792	15.61	51.1	87.5	0.001
SII	0.862	0.790-0.934	893.78	92.4	65.6	<0.001
NLR	0.809	0.720-0.898	2.98	84.8	68.7	<0.001
Combined	0.951	0.907-0.996		87.0	93.7	<0.001

CRP, C reactive protein; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; AUC, area under the curve; TBIL, total bilirubin.

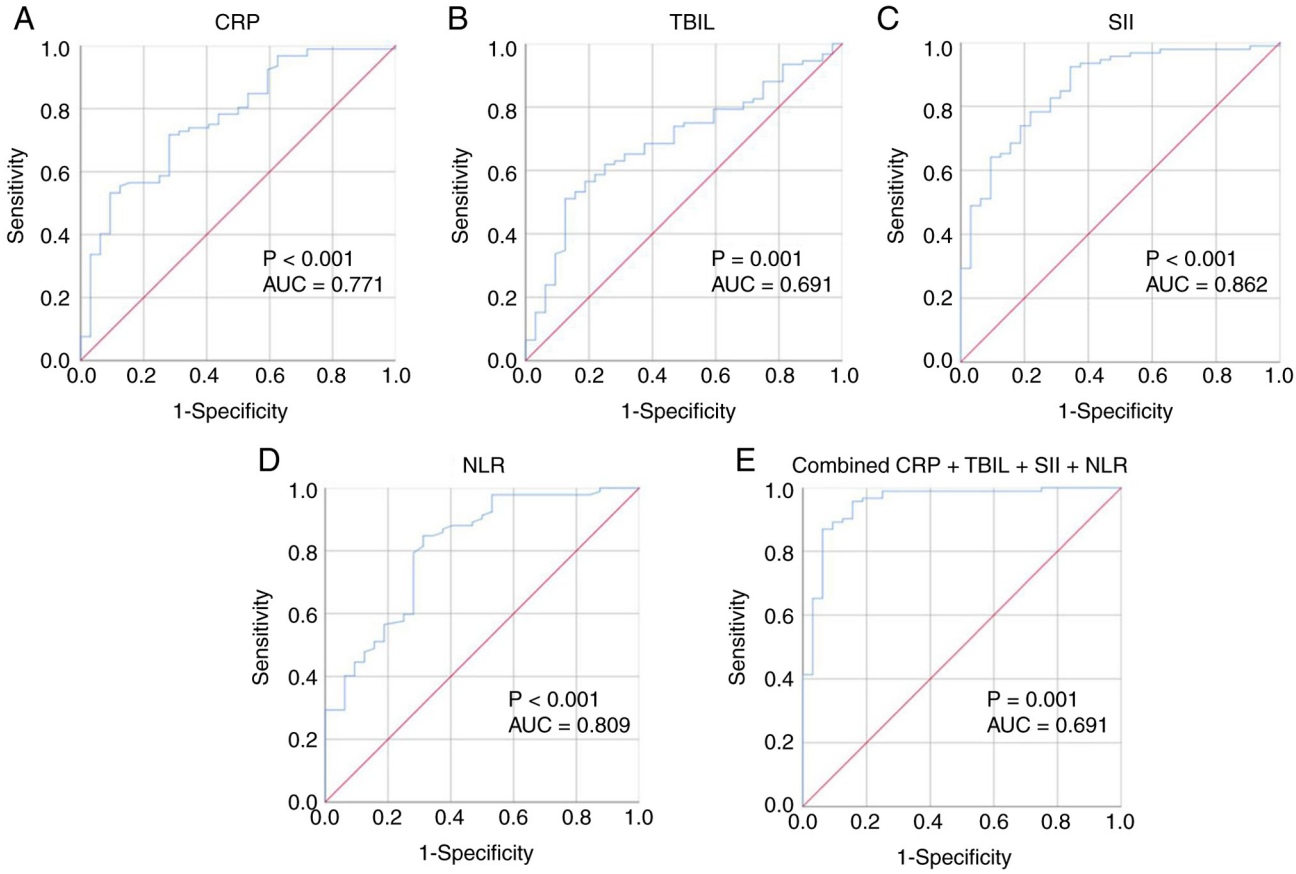

Figure 2. Receiver operating characteristic curves of CRP, TBIL, SII, NLR and their combination for predicting no recovery vs. complete recovery in elderly patients with profound sudden deafness. (A) ROC curves of CRP; (B) ROC curves of TBIL; (C) ROC curves of SII; (D) ROC curves of NLR; and (E) ROC curves of the combined model incorporating CRP, TBIL, SII and NLR. The AUC and corresponding P-values are indicated in each panel. CRP, C-reactive protein; TBIL, total bilirubin; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; AUC, area under the curve; ROC, receiver operating characteristic.

best of our knowledge, the present study is among the first to specifically focus on inflammatory biomarkers in an elderly subset of patients with profound sudden deafness, a population with distinct immunosenescence-related vulnerabilities.

Baseline demographic and clinical characteristics, including age, sex, comorbidities (such as diabetes and hypertension), and otologic symptoms (for example, tinnitus, vertigo and aural fullness) did not significantly differ among the recovery groups, suggesting that traditional clinical parameters have limited prognostic value in elderly patients with profound sudden deafness. Collectively, these results highlight the complexity of the underlying disease mechanisms, which are likely influenced by heterogeneous pathophysiological processes, such as subclinical systemic inflammation, microvascular dysfunction and immune-mediated injury, which are not adequately captured by routine demographic or clinical assessments. By contrast, both the SII and NLR progressively increased from the complete to no recovery groups, reflecting systemic inflammatory burden. The SII captures both innate immune activation and adaptive suppression, while the NLR serves as a simpler marker of inflammatory imbalance. Their elevation in poorer outcome groups may indicate a hyperinflammatory state that compromises cochlear perfusion, promotes endothelial dysfunction and impairs auditory nerve repair (10). These findings exhibit further importance when interpreted within the broader context of aging-related immune alterations.

The elderly population with profound SSNHL presents unique challenges that differentiate it from younger cohorts, necessitating a more nuanced understanding of prognostic markers such as the NLR and SII. While a number of studies (9,15) have demonstrated the predictive value of these markers in SSNHL across different age groups, the association between systemic inflammation and hearing recovery in elderly patients may not be directly extrapolated from younger cohorts. This is primarily due to the complex interplay of factors specific to aging, which can markedly influence the clinical course and recovery process. Aging is associated with a range of physiological changes, including altered immune function, reduced cellular regeneration and decreased auditory nerve function, which may affect the ability to recover from SSNHL (21-23). Furthermore, elderly individuals are more likely to present with multiple comorbidities, such as cardiovascular disease, diabetes and hypertension, which can exacerbate the inflammatory response and complicate recovery (5,24).

In addition, elderly patients often experience frailty, which further exacerbates their vulnerability to poor health outcomes (25,26). Frailty, characterized by a decline in physical strength, endurance and physiological function, can

negatively influence the body's response to systemic inflammation (27,28), potentially altering the prognostic value of inflammation-related markers such as the NLR and SII. Furthermore, the elderly population frequently faces a higher burden of social and health-related challenges, including limited access to timely healthcare, reduced social support and impaired mobility (29,30), which can further impact recovery from SSNHL. These age-specific factors make it important to assess the prognostic markers within the context of the unique health profiles of the elderly. Given these complexities, the association between the NLR/SII and hearing recovery in the elderly population may differ from that reported in younger or general SSNHL cohorts. Previous research (31) on predominantly younger or mixed-age SSNHL populations has indicated that the elevated NLR is associated with poorer hearing recovery, whereas the prognostic value of SII has been less consistently reported, likely reflecting differences in age distribution, disease severity, and underlying inflammatory and vascular profiles across study populations. While the present study demonstrated the predictive value of the NLR and SII in elderly patients with profound SSNHL, it is important to recognize that these markers may be part of a broader spectrum of clinical factors that must be considered when evaluating prognosis in elderly patients.

Multivariate logistic regression analysis demonstrated that both SII and NLR were independently associated with partial and no recovery outcomes. Compared with SII and the other covariates included in the multivariate model, NLR exhibited a stronger association with poor hearing outcomes, particularly no recovery (OR=25.239), suggesting that neutrophil-dominant inflammation may be particularly detrimental in profound sudden deafness in elderly patients. This aligns with reports that age-related shifts toward myeloid-biased hematopoiesis can exacerbate pro-inflammatory responses and delay resolution of injury (32-34). Recent studies (9,10) have increasingly highlighted the potential role of the NLR as an accessible and valuable biomarker in the prognosis and pathophysiology of SSNHL. The NLR, a marker of systemic inflammation, has been shown to be associated with hearing recovery outcomes in both adult and pediatric populations. A previous study has demonstrated a non-linear relationship between the NLR and the recovery rate in SSNHL, identifying a threshold effect with an NLR value of ~3, where recovery was improved in patients with an NLR <3, but plateaued or diminished at higher values, indicating complex immunological interactions that may influence cochlear repair capacity (35).

By contrast, an additional investigation reported a linear inverse association between the NLR and hearing gain in idiopathic SSNHL, with increased NLR values predicting poorer recovery across numerous frequencies, thereby supporting the utility of the NLR as a quantitative prognostic indicator (35). Furthermore, evidence from pediatric patients with SSNHL reinforced the inflammatory etiology hypothesis: Affected children exhibited markedly higher NLR values compared with matched healthy controls, and elevated NLR was positively associated with worse initial hearing thresholds (36). However, in the present study, it should be noted that the wide CI for the OR of the NLR in the no recovery vs. complete recovery model (95% CI, 4.391-145.089) reflected significant variability, primarily due to a small number of patients with extremely high NLR values. These outliers influence the model, resulting in a broader CI and increased uncertainty in the effect size. While the association between the NLR and no recovery was statistically significant, the wide CI highlights the uncertainty of the true effect, suggesting that the predictive value of the NLR may vary across different patient subsets. This reinforced the need for cautious interpretation and further research to refine the model and clarify the prognostic value of the NLR. Collectively, these findings suggested that an elevated NLR reflects an underlying inflammatory burden that may impair inner ear microcirculation or exacerbate immune-mediated cochlear damage, thus providing not only diagnostic insight but also prognostic value in the clinical management of SSNHL across age groups. Finally, it should be noted that intratympanic steroid therapy was administered as a salvage treatment for non-responders. While this led to differential treatment exposure, the baseline NLR and SII were measured prior to any intervention. The present findings suggested that elevated inflammatory marker levels are indicative of a severe, refractory inflammatory state that is associated with poor prognosis, even when maximal medical therapy (systemic plus intratympanic steroids) is employed.

The role of TBIL warrants further exploration. While TBIL was not predictive of partial recovery, it was independently associated with no recovery in the present multivariate logistic regression analysis. Given that bilirubin has recognized antioxidant and anti-inflammatory properties at physiological concentrations (37-39), the relatively lower TBIL levels in the partial recovery group may reflect reduced oxidative stress or a more favorable redox balance in these individuals. By contrast, higher TBIL levels in the no-recovery group may indicate a compensatory response to increased oxidative or inflammatory burden. However, the mechanistic importance of TBIL in inner ear pathology remains speculative and merits further investigation. ROC curve analyses supported the clinical utility of the NLR and SII. For partial recovery, the SII yielded the AUC of 0.679, while the NLR demonstrated superior sensitivity (90.3%) in detecting poor hearing recovery, and its lower specificity indicated a trade-off between sensitivity and discriminatory precision, reflecting the value of combining NLR with other inflammatory markers to enhance overall prognostic accuracy. For no recovery, the SII, in terms of predictive capacity, exhibited an AUC of 0.862, followed by the NLR (AUC=0.809). The combination of the SII and NLR significantly improved overall predictive accuracy, emphasizing the benefit of a multiparametric approach. When combined with CRP and TBIL, the AUC reached 0.951, suggesting that a composite biomarker panel may offer near-optimal discrimination of outcomes in clinical practice.

Elevated NLR and SII have shown potential as prognostic markers for poor recovery in elderly patients with profound SSNHL. While not yet tied to specific treatments, these markers may aid in patient stratification and clinical decision-making. Elderly patients with high NLR and SII may be at greater risk of poor recovery, influencing the intensity and type of care. Overall, while high NLR and SII alone should not dictate treatments, these parameters help guide management decisions and patient stratification. Further research is needed to explore their role in inflammation-targeted therapies and assess their clinical impact.

The present study exhibits a number of limitations. Critically, the present study relied solely on baseline measurements; the absence of longitudinal monitoring of the SII and NLR precluded the analysis of their dynamic trajectory during and after treatment, thereby limiting the ability to gain deeper insights into the specific disease process and recovery mechanisms. Additionally, the present findings may not be generalizable to younger populations or those with milder hearing loss. The primary aim was to investigate the short-term prognostic value of the NLR and SII, and their long-term prognostic value remains undetermined. Future prospective studies with extended follow-up and biomarker tracking are needed to address long-term outcomes. Furthermore, studies with mechanistic endpoints, such as cytokine profiling and cochlear perfusion imaging, are warranted. In addition, the present study does not propose a formalized risk score or clinical algorithm for immediate bedside application, therefore bridging the gap to practical clinical integration requires further development and calibration in future research. Finally, the high predictive performance of the combined model (AUC=0.951) should be interpreted as exploratory, as it was derived from a single-center cohort without external validation. Given the limited sample size, particularly the few 'complete recovery' cases (n=32), the risk of overfitting and overly optimistic estimates remains. Thus, validation in larger, independent cohorts is key in determining the robustness of the model.

In summary, the present study demonstrated the role of the NLR and SII in predicting treatment responsiveness in elderly patients with profound sudden deafness following systemic corticosteroid therapy, either alone or in combination with intratympanic methylprednisolone injection. Elevated levels of these markers were strongly associated with a poor therapeutic response and resistance to therapy, suggesting that heightened systemic inflammation may compromise the efficacy of both systemic steroids and salvage intratympanic injections. While the combined use of these markers offers potential for enhanced accuracy in identifying patients at risk of treatment failure, it is important to note that the present findings are specific to elderly patients with profound SSNHL and their applicability to younger populations or those with milder degrees of hearing loss remains uncertain. While promising, further research is needed to determine the broader applicability of systemic inflammatory indices in guiding personalized therapeutic strategies for SSNHL across varying patient demographics.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XW conceptualized the study, designed the overall methodology (including study design and statistical strategy), supervised the research process and contributed to manuscript writing, critical revision, and editing. XW also facilitated access to clinical resources, laboratory data and analytical tools required for the study. CL performed data validation by cross-checking raw clinical and laboratory records against the final analytical dataset, conducted the formal statistical analysis and led the investigation, including data extraction and organization. CL also drafted the original version of the manuscript. HW, HC, YL, SH and ZS participated in the investigation by collecting and curating clinical data, assisted with data verification, and contributed to manuscript review and editing. CL and XW confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The requirement for ethical approval for this study was waived by the Ethics Committee of the Emergency General Hospital (Beijing, China; approval no. L24-1) due to the retrospective nature of the study and the absence of any additional interventions beyond routine clinical care. The procedures used in the present study were performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The requirement for written informed consent was also waived by the Ethics Committee of the Emergency General Hospital.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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