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RESEARCH

# The value of plasma sCD25 in diagnosis, therapeutic efficacy, and prognosis of acute myeloid leukemia

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## Abstract

This study aims to investigate the clinical importance of soluble CD25 (sCD25) levels in diagnosing acute myeloid leukemia (AML), predicting patient outcomes, and monitoring treatment responses. Plasma sCD25 levels were measured in 190 AML patients and 47 healthy controls. AML patients were further divided into subgroups based on chemotherapy status, therapeutic response, and prognostic risk. Statistical analyses were performed to investigate the relationships between sCD25 levels and various clinical parameters, along with its potential diagnostic and prognostic significance. Plasma sCD25 levels were significantly elevated in AML patients compared to healthy controls ($p < 0.0001$). High sCD25 levels correlated positively with white blood cell count, age, and pulmonary infection ($p < 0.01$) and negatively with hemoglobin and platelet counts ($p < 0.01$). Logistic regression analysis identified sCD25 as a risk factor for both AML diagnosis (OR = 59.240, 95% CI: 11.14–315.0, $p < 0.0001$) and poor prognosis (OR = 1.651, 95% CI: 1.094–2.492, $p < 0.05$). ROC curve analysis demonstrated that sCD25 has high diagnostic accuracy for AML (AUC = 0.929, sensitivity = 86.44%, specificity = 93.62%) and moderate predictive value for chemotherapy non-remission (AUC = 0.66, $p < 0.05$). Plasma sCD25 levels are significantly elevated in AML and show potential as a diagnostic and prognostic biomarker. sCD25 may also be useful for monitoring treatment response in AML patients. Further studies are warranted to elucidate its role in AML pathogenesis.

**Keywords** sCD25 · AML · Diagnosis · Prognosis · Treatment efficacy

## Abbreviations

| | |
|---|---|
| AML | Acute myelocytic leukemia |
| sCD25 | Soluble CD25 |
| HC | Health control |
| WHO | World Health Organization |
| ELN | Uropean Leukemia-Net |
| ELISA | Enzyme-linked immunosorbent assay |
| Avidin-HRP | Avidin-horseradish peroxidase |
| TMB | Tetramethylbenzidine |
| CR | Complete remission |
| NR | Non-remission |
| WBC | White blood cell |
| HB | Hemoglobin |
| PLT | Platelets |
| ROC | Receiver operating characteristic curve |
| AUC | Area under the curve |
| OR | Odds ratio |
| CI | Confidence intreval |
| MRD | Minimal Residual Disease |
| ELN | Uropean Leukemia-Net |
| HLH | Hemophagocytic lymphohistiocytosis |
| Tregs | Regulatory T cells |

## Introduction

Acute myeloid leukemia is a diverse group of hematologic cancers, marked by the rapid expansion of abnormally differentiated precursor cells of the myeloid lineage. This pathological mechanism results in the build-up of immature progenitor cells within the bone marrow, peripheral blood, and/or various tissues, disrupting normal hematopoiesis. As a result, patients may suffer from severe infections, anemia, and bleeding complications [1]. Despite advances in

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treatment, AML prognosis remains poor, particularly in older adults or those with adverse genetic profiles [2]. Existing treatment approaches, such as chemotherapy and stem cell transplantation, frequently face challenges due to high relapse rates and resistance to therapy [3, 4]. Therefore, we hope to find novel markers and provide new directions for AML diagnosis and treatment to improve patient prognosis in clinical practice.

Soluble CD25, the soluble form of the interleukin-2 receptor, has been implicated in various malignancies, including AML [5–7]. Elevated levels of sCD25 in plasma may reflect the activity of T regulatory cells and the immune response to tumor burden. Recent research indicates that sCD25 may be a promising biomarker for diagnosing diseases, predicting outcomes, and monitoring treatment effectiveness [8–10]. sCD25 has been implicated in modulating immune responses and tumor burden in various malignancies [10], but its specific role in AML diagnosis, prognosis, and treatment response remains underexplored.

In this study, we sought to examine the clinical relevance of plasma sCD25 levels in patients with AML. Specifically, we assessed its diagnostic value, prognostic implications, and utility in monitoring response to chemotherapy. Our findings demonstrates that sCD25 is an important diagnostic and prognostic biomarker for AML, aiding in personalized treatment strategies and improving patient outcomes.

## Participants and methods

### Study population

This study included 190 participants, consisting of 143 newly diagnosed AML patients and 47 healthy controls. All patients were enrolled from the First Affiliated Hospital of Soochow University between December 2020 and May 2022, with diagnoses confirmed based on clinical, morphological, and immunophenotypic criteria following WHO guidelines. Patients with concurrent malignancies, autoimmune diseases, or other serious systemic conditions were excluded. The control group consisted of healthy individuals matched by age and sex to the AML cohort. All participants gave written informed consent, and the study received approval from the Clinical Research Ethics Committee of the First Affiliated Hospital of Soochow University.

### Study design and data collection

This is a retrospective, observational study designed to assess the clinical significance of sCD25 in AML patients. Peripheral blood samples were collected from all participants at baseline (i.e., at the time of diagnosis for AML patients) and after induction chemotherapy for those who underwent treatment. Plasma samples were collected and preserved from all AML patients and healthy controls on the same day of enrollment. Whole blood was collected and centrifuged at 2000 × g for 15 min. The supernatant plasma was then stored at − 80 °C until analysis. Plasma was preserved in sterilized EP tubes at − 80 °C and transferred to the central laboratory for sCD25 measurement.

Clinical and laboratory data, including white blood cell (WBC) count, hemoglobin (HB) concentration, platelet (PLT) count, and infection status, were obtained from the patients' medical records. Prognostic risk stratification was performed using cytogenetic and molecular data, and patients were classified into favorable, intermediate, or poor risk groups based on the European LeukemiaNet (ELN) criteria. Based on bone marrow morphology and MRD (Minimal Residual Disease) detection, chemotherapy-treated patients were divided into the complete remission (CR) group and the non-remission (NR) groups. CT imaging was used to detect pulmonary infections, and patients were categorized into the co-infection and non-co-infection groups. The flow diagram of our study is summarized in Fig. 1.

### sCD25 measurement

The plasma sCD25 concentration was measured using an ELISA kit (Guangke Xing Antibody Biotechnology Co., Ltd.). The coefficients of variation for intra-assay and inter-assay were both less than 5.00%. All samples were tested in the same batch to minimize assay variation.

### Statistical analysis

Continuous variables were reported as medians with interquartile ranges (IQR), and categorical variables were shown as percentages. Group differences were assessed using the Mann–Whitney U test or ANOVA test for non-normally distributed data and the chi-square test for categorical variables. Correlations between sCD25 levels and clinical parameters were evaluated using Spearman's rank correlation coefficient. Multivariate logistic regression analysis was utilized to determine independent factors related to AML diagnosis, prognosis, and treatment response. Receiver operating characteristic (ROC) curves were applied to evaluate the diagnostic and prognostic performance of sCD25, with the area under the curve (AUC) used to measure accuracy. A $p$ value of $< 0.05$ was deemed statistically significant. All analyses were performed using SPSS version 26 [Chicago, IL, USA] and GraphPad Prism version 9 [San Diego, California, USA].

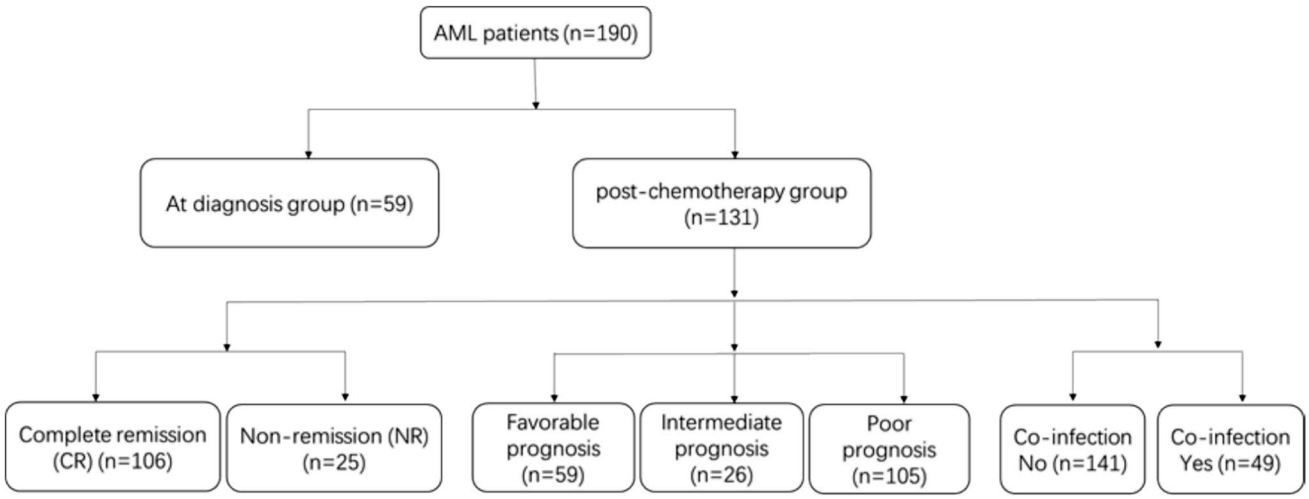


**Fig. 1** Flow diagram of the study process

## Results

### Baseline characteristics

A total of 190 AML patients (81 males, 109 females) and 47 healthy controls (27 males, 20 females) were included in this study. The AML group was divided based on whether patients had received chemotherapy into the diagnostic group (n = 59) and the chemotherapy group (n = 131). The chemotherapy group was further divided based on treatment response into the remission group (n = 106) and the non-remission group (n = 25). Additionally, the AML group was classified according to prognostic risk as per the guidelines into the good prognosis group (n = 59), intermediate prognosis group (n = 26), and poor prognosis group (n = 105). Based on the presence of pulmonary infections, the AML group was categorized into the infection group (n = 49) and the non-infection group (n = 141). No significant differences in age or sex distribution were found between AML patients and healthy controls ($p > 0.05$) as detailed in Table 1.

### Elevated plasma sCD25 Levels in AML patients and clinical correlations

As detailed in Table 1, plasma sCD25 levels were significantly elevated in the AML group [1.81 (1.26, 2.53) ng/mL] compared to healthy controls [0.85 (0.75, 1.07) ng/mL, $p < 0.0001$]. sCD25 levels in AML patients exhibited positive correlations with WBC count (r = 0.2347, $p < 0.01$), age (r = 0.1518, $p < 0.05$), and pulmonary infection (r = 0.2088, $p < 0.01$), while showing negative correlations with HB (r = − 0.4424, $p < 0.0001$) and PLT counts (r = − 0.1890, $p < 0.01$) as detailed in Fig. 2.

**Table 1** Basic clinical data of AML patients and healthy control group

| | HC n = 47 | AML n = 190 | *p* value |
|---|---|---|---|
| Age (years) | 40 (32, 50) | 42 (33, 53) | $p > 0.05$ |
| WBC(cells × $10^9$/L) | 5.73 (4.72, 7.12) | 4.1 (2.42, 7.36) | $p < 0.001$ |
| HB(g/L) | 144 (131, 155) | 93 (69, 114) | $p < 0.0001$ |
| PLT (cells × $10^9$/L) | 217 (187, 261) | 101 (31, 170.3) | $p < 0.0001$ |
| sCD25(ng/mL) | 0.85 (0.75, 1.07) | 1.81 (1.26, 2.53) | $p < 0.0001$ |
| Sex (%) | | | $p > 0.05$ |
| Male | 27 (57.45%) | 81 (42.63%) | |
| Female | 20 (42.55%) | 109 (57.37%) | |
| *Chemotherapy* | | | |
| Yes | NA | 131 (69%) | |
| No | NA | 59 (31%) | |
| *After chemotherapy* | | | |
| CR | NA | 106/131(81%) | |
| NR | NA | 25/131(19%) | |
| *Co-infection* | | | |
| Yes | NA | 49 (26%) | |
| No | NA | 141 (74%) | |
| *Prognostic risk* | | | |
| Favorable | NA | 59 (31%) | |
| Intermediate | NA | 26 (14%) | |
| Poor | NA | 105 (55%) | |

Data are expressed as median [interquartile range] or percentage in parentheses; *WBC* White blood cell count; *HB* Hemoglobin count; *PLT* Platelet count; *AML* Acute myeloid leukemia patients; *sCD40L* Soluble CD40L; *sCD25* Soluble CD25; *Sex* Gender; *After Chemotherapy* Post-chemotherapy; *Co-infection* Concurrent infection; *Prognostic risk* Prognostic risk; *Favorable* Good prognosis; *Intermediate* Intermediate prognosis; *Poor* Poor prognosis

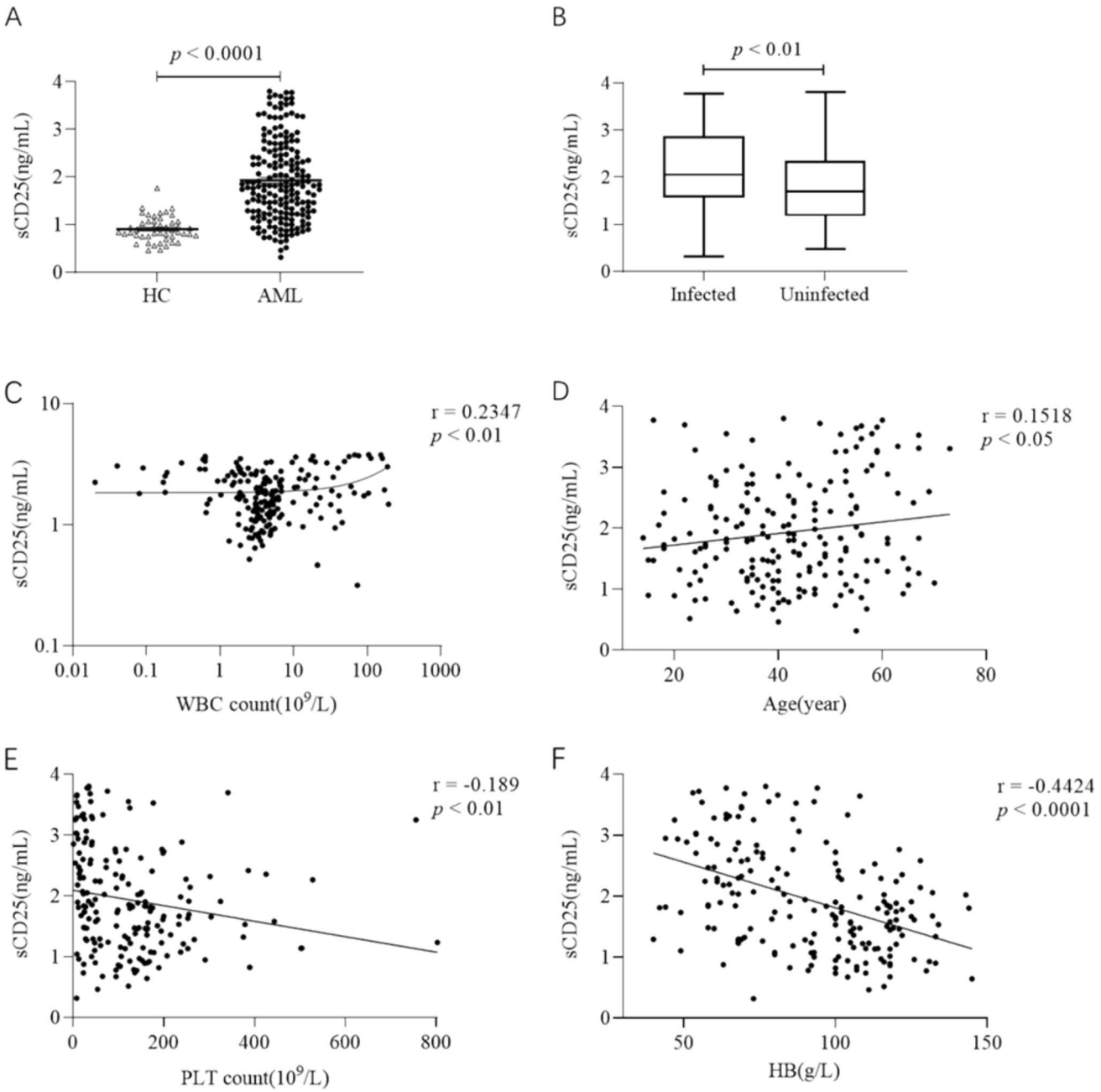


**Fig. 2** Clinical Correlation Analysis of Plasma sCD25 in AML Patients. **A** showed the comparison of sCD25 in the HC group and the AML group. **B** showed the comparison of sCD25 in the Infected group and the Uninfected group. Group differences were assessed using the Mann–Whitney U test. **C**–**F** Correlation analysis between WBC, Age, PLT, HB and sCD25 using Spearman's rank correlation coefficient. The X and Y axes of Fig. C are processed with log10

**Table 2** Logistic analysis of risk factors in newly diagnosed AML patients

| Parameters | $\beta$ | SE | Wald $X^2$ | $p$ value | OR | 95%CI |
|---|---|---|---|---|---|---|
| Sex (Male) | −0.402 | 0.394 | 1.042 | 0.307 | 1.495 | 0.691–3.233 |
| Age | 0.014 | 0.016 | 0.749 | 0.387 | 1.014 | 0.983–1.045 |
| WBC | 0.137 | 0.046 | 8.962 | 0.003 | 1.147 | 1.049–1.255 |
| HB | −0.241 | 0.080 | 9.122 | 0.003 | 0.786 | 0.672–0.919 |
| PLT | −0.019 | 0.003 | 31.322 | 0.000 | 0.981 | 0.975–0.988 |
| sCD25 | 4.082 | 0.853 | 22.917 | 0.000 | 59.240 | 11.14–315.0 |

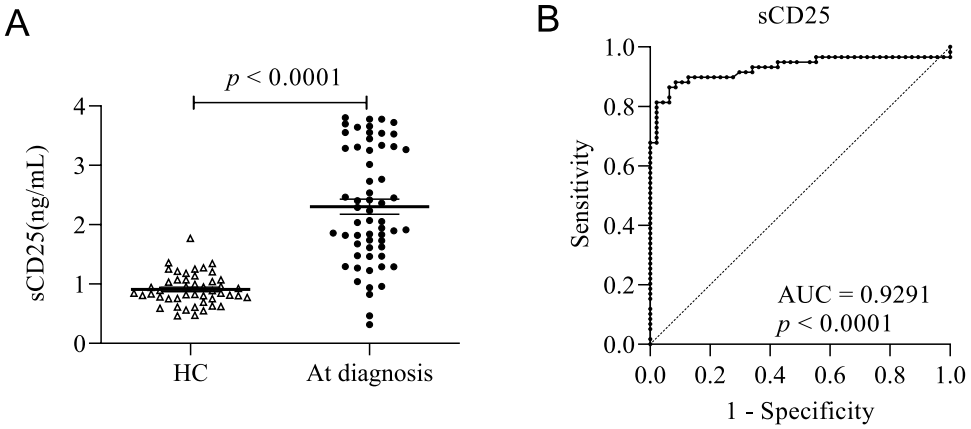


**Fig. 3** Diagnostic Value of sCD25 for Newly Diagnosed AML. **A** showed the comparison of sCD25 in the HC group and the At diagnosis group. Group differences were assessed using the Mann–Whitney U test. **B** ROC curve analysis showed that sCD25 has a high diagnostic value for newly diagnosed AML. AUC = 0.929, sensitivity = 86.44%, specificity = 93.62%, cut-off > 1.282 ng/mL, $p < 0.0001$. At diagnosis: Newly Diagnosed AML Patients; Healthy control: Healthy Control

## Significantly elevated plasma sCD25 levels in newly diagnosed AML and clinical correlations

Newly diagnosed AML patients showed significantly elevated sCD25 levels [2.07 (1.61, 3.31) ng/mL] compared to healthy controls [0.85 (0.75, 1.07) ng/mL, $p < 0.0001$] as detailed in Table 2, Fig. 3A. Logistic regression analysis identified sCD25 as a risk factor for AML diagnosis (OR = 59.240, 95% CI: 11.14–315.0, $p < 0.0001$) as detailed in Table 2. ROC curve analysis demonstrated that sCD25 had high diagnostic accuracy (AUC = 0.929, sensitivity = 86.44%, specificity = 93.62%, cut-off > 1.282 ng/mL, $p < 0.0001$) as detailed in Fig. 3B.

## Monitoring sCD25 expression levels has clinical significance for AML chemotherapy efficacy

sCD25 levels were significantly lower in the complete remission (CR) group [1.55 (1.13, 2.16) ng/mL] compared to both the newly diagnosed [2.07 (1.61, 3.31) ng/mL, $p < 0.0001$] and non-remission (NR) groups [2.30 (1.50, 2.75) ng/mL, $p < 0.05$]. However, there was no significant difference in sCD25 levels between the newly diagnosed AML patients and the NR (non-remission) group ($p > 0.05$) as detailed in Fig. 4A. Logistic regression analysis identified sCD25 as a risk factor for non-remission (NR) (OR = 2.175, 95% CI: 1.931–3.946, $p < 0.05$) as detailed in Table 3. ROC analysis revealed moderate discriminatory power for sCD25 in distinguishing NR patients (AUC = 0.66, sensitivity = 52%,

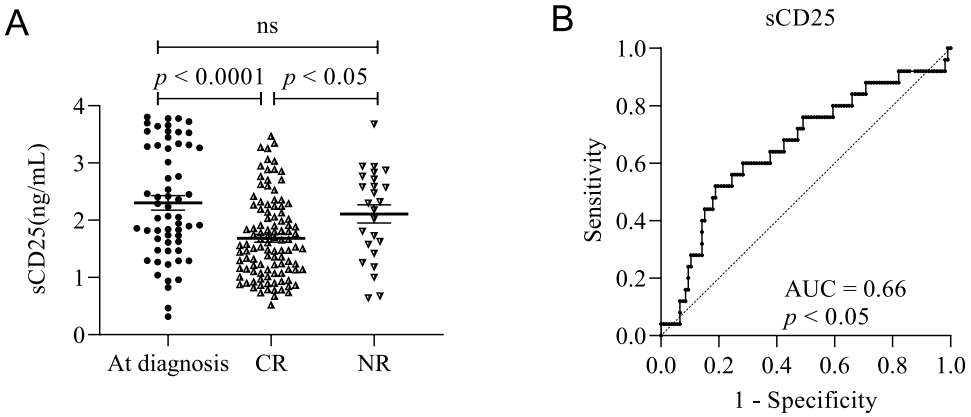


**Fig. 4** Expression Levels of sCD25 in Newly Diagnosed AML Patients, AML Patients in Complete Remission, and AML Patients Not in Remission. **A** Comparison of sCD25 levels between the three groups was performed by ANOVA test and Bonferroni correction was used for post hoc tests. **B** ROC analysis revealed moderate discriminatory power for sCD25 in distinguishing NR patients (AUC = 0.66, sensitivity = 52%, specificity = 81.13%, cut-off > 2.294 ng/mL, $p < 0.05$). At diagnosis: Newly Diagnosed AML Patients; CR: AML Patients in Complete Remission After Chemotherapy; NR: AML Patients Not in Remission After Chemotherapy; ns: $p > 0.05$

**Table 3** Logistic regression analysis of risk factors for non-remission in AML patients after treatment

| Parameters | $\beta$ | SE | Wald $X^2$ | $p$ value | OR | 95%CI |
|---|---|---|---|---|---|---|
| Sex (Male) | −1.197 | 0.537 | 4.974 | 0.026 | 0.302 | 0.106–0.865 |
| Age | 0.001 | 0.017 | 0.007 | 0.933 | 1.001 | 0.969–1.035 |
| WBC | 0.003 | 0.041 | 0.007 | 0.934 | 1.003 | 0.926–1.087 |
| HB | −0.032 | 0.010 | 11.317 | 0.001 | 0.968 | 0.950–0.987 |
| PLT | −0.016 | 0.004 | 15.058 | 0.000 | 0.984 | 0.977–0.992 |
| sCD25 | 0.777 | 0.306 | 6.430 | 0.011 | 2.175 | 1.193–3.946 |
| Coinfection | 0.012 | 0.556 | 0.000 | 0.983 | 1.012 | 0.340–3.010 |

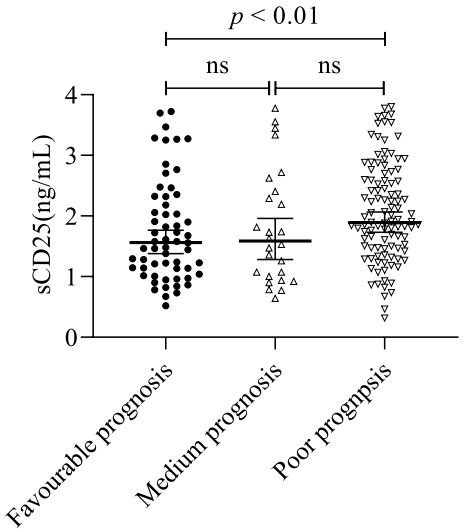


**Fig. 5** Comparison of sCD25 levels between the three groups was performed by ANOVA test and Bonferroni correction was used for post hoc tests. ns: $p > 0.05$

specificity = 81.13%, cut-off > 2.294 ng/mL, $p < 0.05$) as detailed in Fig. 4B.

### sCD25 expression levels have clinical significance in AML prognostic grouping

AML patients with poor prognosis exhibited significantly higher sCD25 levels [1.91 (1.47, 2.65) ng/mL] compared to those with favorable prognosis [1.56 (1.13, 2.31) ng/mL, $p < 0.01$] as detailed in Fig. 5. Logistic regression confirmed that sCD25 was a predictor of poor prognosis in AML (OR = 1.651, 95% CI: 1.094–2.492, $p < 0.05$) as detailed in Table 4.

## Discussion

AML is a heterogeneous hematologic malignancies, with the tumor microenvironment playing a key role in its pathogenesis and progression [1, 11]. Cytokines, as critical components of the tumor microenvironment, contribute to cancer progression and therapies through both immune and non-immune mechanisms [12]. The binding of sCD25 to its ligand, cytokine IL-2, can modulate the immune response, either enhancing or suppressing it. Elevated sCD25 levels may also originate from the tumor itself, serving as a potential marker of tumor burden [10]. This study investigates the association of sCD25 levels with the diagnosis, prognosis, and response to chemotherapy in AML patients.

Our results demonstrate that plasma sCD25 levels are significantly higher in AML patients compared to healthy controls. Elevated sCD25 levels correlate positively with WBC count, age, and pulmonary infection, and negatively with HB and PLT count. This is consistent with the clinical manifestations of AML, where impaired hematopoiesis leads to infection, anemia, and thrombocytopenia. As high WBC count and age ≥ 60 years are established poor prognostic factors in AML, our findings suggest that sCD25 expression may also be linked to these adverse prognostic indicators.

Previous studies have identified elevated sCD25 as a diagnostic marker for hemophagocytic

**Table 4** Logistic regression analysis of risk factors for poor prognosis in AML patients

| Parameters | $\beta$ | SE | Wald $X^2$ | $p$ value | OR | 95%CI |
|---|---|---|---|---|---|---|
| Sex (Male) | −0.501 | 0.333 | 2.268 | 0.132 | 0.606 | 0.316–1.163 |
| Age | 0.018 | 0.012 | 2.183 | 0.140 | 1.018 | 0.994–1.042 |
| WBC | 0.011 | 0.007 | 2.632 | 0.105 | 1.011 | 0.998–1.025 |
| HB | −0.013 | 0.007 | 3.799 | 0.051 | 0.987 | 0.974–1.000 |
| PLT | −0.002 | 0.001 | 3.353 | 0.067 | 0.998 | 0.995–1.000 |
| sCD25 | 0.501 | 0.210 | 5.694 | 0.017 | 1.651 | 1.094–2.492 |
| Coinfection | −0.939 | 0.403 | 5.416 | 0.20 | 0.391 | 0.177–0.862 |

lymphohistiocytosis (HLH), with sensitivity reaching 100% and specificity around 70% in adult patients [13, 14]. Additionally, elevated sCD25 has been reported as a biomarker for immune checkpoint inhibitor-induced nephritis [15]. In this study, we found that sCD25 levels were markedly elevated in AML patients, and Logistic Regression analysis identified sCD25 as a risk factor for AML diagnosis, with a high diagnostic accuracy (AUC = 0.929). Therefore, plasma sCD25 is serve as a potential diagnostic biomarker for AML.

Beyond its diagnostic utility, sCD25 may also be valuable for monitoring disease activity. Previous reports have linked sCD25 levels to disease activity scores in autoimmune disorders [16–19], as well as tuberculosis and sarcoidosis [20–24]. sCD25 levels typically decrease following successful treatment but remain elevated compared to normal values. Our study revealed that sCD25 levels significantly decreased in the CR group, aligning with previous findings that suggest sCD25 reduction correlates with chemotherapy response [9]. Furthermore, sCD25 was identified as a risk factor for non-remission following chemotherapy, with a moderate diagnostic accuracy for predicting non-remission (AUC = 0.66). Although the AUC of 0.66 does not indicate exceptional diagnostic performance, sCD25 provides important insights into chemotherapy response, serving as an additional reference for clinicians when assessing ambiguous treatment outcomes.

The role of sCD25 in AML remains controversial, as its function may vary depending on its source. sCD25 derived from effector T cells may indicate an anti-tumor immune response, while sCD25 from regulatory T cells (Tregs) may be associated with immune tolerance [10]. High levels of sCD25 may also reflect tumor burden, with previous studies in T-cell lymphomas showing that elevated sCD25 levels predict shorter median survival [25, 26]. Similarly, in B-cell lymphomas, elevated sCD25 is associated with increased tumor burden and poor progression-free survival [27–31]. Interestingly, elevated sCD25 levels have also been linked to poor outcomes in various non-lymphoid malignancies [32–35]. Consistent with these findings, we observed significantly higher sCD25 levels in AML patients with poor prognosis. Logistic regression analysis confirmed that sCD25 is a risk factor for poor prognosis in AML, suggesting its potential value in prognostic assessment.

This study has several limitations. Firstly, we did not perform long-term follow-up to assess changes in sCD25 levels during disease progression or relapse. Additionally, the high heterogeneity of AML and variation in individual chemotherapy regimens may have impacted the reliability of our findings. Future studies should include larger cohorts, more standardized treatment protocols, and further exploration of the immune mechanisms involving sCD25 in AML to better understand its role in AML diagnosis, prognosis, and therapy.

## Conclusion

In summary, our study demonstrates that plasma sCD25 levels are significantly elevated in patients with newly diagnosed AML compared to healthy controls. sCD25 exhibits high sensitivity and specificity as a diagnostic biomarker for AML. Furthermore, it serves as a valuable prognostic indicator, correlating with treatment response and overall patient outcomes. These findings underscore the potential of plasma sCD25 as a critical tool in guiding therapeutic decisions and improving management strategies for AML patients. Future investigations should focus on elucidating the molecular mechanisms underlying sCD25's role in AML to enhance its clinical applicability.

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**Author contributions** JYW, YLZ, JX and WW analyzed data and wrote the manuscript. JYW reviewed that data and edited the manuscript. CPL and MJ guided the study, proposed the study protocol, supervised its implementation, and provided funding. All authors approved the final manuscript prior to submission.

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**Data availability** Data and materials are available from the corresponding author upon request.

## Declarations

**Conflict of interest** The authors declare no competing interests.

**Ethical approval** The study was approved by the Ethics Review Board of the First Affiliated Hospital of Soochow University (Ethical No.2020105) and informed consent was obtained.

**Consent to participate** The study was approved by the Ethics Review Board of the First Affiliated Hospital of Soochow University (Ethical No.2020105) and informed consent was obtained.

**Consent for publication** Not applicable.

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