The prognostic value of the controlling nutritional status score in patients with myelodysplastic syndrome

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Abstract

Purpose To evaluate the prognostic value of the controlling nutritional status score (CONUT) in patients with myelodysplastic syndrome (MDS).

Methods The clinical data of 81 newly diagnosed MDS patients treated with decitabine in the hematology ward of our hospital from October 2009 to September 2020 were analyzed retrospectively. According to the ROC curve of overall survival (OS), the best cutoff value of CONUT was obtained. MDS patients were divided into high CONUT score group and low CONUT score group according to the best cut-off value, and their clinical characteristics and survival were analyzed.

Results Among the 81 patients with MDS, there were 32 cases in the high CONUT score group and 49 cases in low CONUT score group. Compared with the low CONUT group, the high CONUT group had lower levels of hemoglobin, lymphocyte count, albumin, and total cholesterol ($P=0.037$, $<0.001$, $0.009$, $<0.001$). The median OS of low and high CONUT groups were 17.2 and 11.0 months ($P=0.017$). According to the results of univariate and multivariate survival analysis of OS, thrombocytopenia, high CONUT score, and medium and high risk IPSS-R score were independent prognostic factors.

Conclusion High CONUT score is associated with low hemoglobin in patients with MDS. High CONUT score indicates poor OS and it is an independent prognostic factor in patients with MDS.

Keywords Myelodysplastic syndrome · CONUT score · Prognosis · Nutrition

Myelodysplastic syndromes (MDS) are a heterogeneous group of bone marrow disorders associated with ineffective hematopoiesis with an increased risk of transforming into acute myeloid leukemia(AML), manifesting as morphologic dysplasia in hematopoietic elements and peripheral cytopenia. The median age of MDS patients is about 70 years old, and the incidence rate increases with age. The incidence rate of people over 60 years old reached 35/100,000 [1].

Patients with MDS are highly heterogeneous, so it is particularly important to classify the prognosis of the disease. The traditional risk stratification of MDS is based on disease-related factors, such as cytogenetics, percentage of bone marrow primordial cells, hemoglobin, platelet, and neutrophil count. Some prognostic risk scores, such as the World Health Organization classification-based Prognostic Scoring System (WPSS) and the revised International Prognostic Scoring System (IPSS-R), have been used to stratify related risks. Clinically, appropriate treatment is often selected according to this.

However, considering the prognosis, only according to the IPSS-R score will ignore the basic function of the patient, so there is an urgent need for a scoring standard to evaluate the patient’s own conditions and prognosis, so as to formulate a more comprehensive treatment plan.

In patients with MDS, the prognostic value of nutritional status has not been paid attention to. The controlling nutritional status score (CONUT), counted from total lymphocyte counts, serum albumin, and total cholesterol levels, is an easy-to-use tool to assess nutritional status and has been confirmed to have an inversely correlated prognostic value for several solid tumors, heart diseases, and hematological malignancies [2–5].

This study retrospectively analyzed the initial CONUT score and clinical characteristics of 81 patients with MDS.
and discussed the prognostic value of CONUT score in the survival of patients with MDS. We further analyze the prognostic factors based on OS with other prognostic factors, in order to provide basis for a new prognostic model of MDS.

**Research object and research method**

**Patients**

This study enrolled 81 patients with MDS in the Hematology Department of our hospital from October 2009 to September 2020. The patients were classified according to the MDS classification standard revised by WHO in 2016. Inclusion criteria: ① MDS patients newly diagnosed by hemogram, myelogram, and cytogenetics; ② Age $\geq 18$ years old; ③ the first-line treatment was decitabine alone or decitabine combined with chemotherapy, and at least two courses of treatment were completed.

The baseline clinical data of patients were recorded, including age, gender, WHO classification, hemoglobin (Hb), platelet count (PLT), absolute neutrophil count (ANC), total lymphocyte count (TLC), albumin (Alb), total cholesterol (T-Cho), and IPSS-R score.

**CONUT score**

The CONUT score is calculated by serum albumin, total cholesterol, and total lymphocyte count (Table 1). The total score is 0–12, 0–1 is normal, 2–4 is mild, 5–8 is moderate and 9–12 is severe.

According to the ROC curve of overall survival (OS), the best cutoff value of CONUT score was 5.5 (area under the curve [AUC]:0.604, 95% confidence interval [95% CI]: 0.456–0.753, sensitivity 44.4%, specificity 77.8%). According to the cutoff value, the patients were divided into 32 cases in high CONUT group (CONUT $> 5.5$) and 49 cases in low CONUT group (CONUT $< 5.5$).

**Efficacy evaluation and follow-up**

The curative effect was evaluated according to the curative effect standard of MDS international working group. Overall survival (OS) was defined as the time from diagnosis to death or to the end of follow-up. The deadline for follow-up is December 1, 2020. All patients are followed up from the date of diagnosis, and the dead patients are followed up to the date of death. Follow-up data were obtained from inpatient medical records or telephone contact with patients and their families.

**Statistical analysis**

Overall survival was analyzed using the Kaplan–Meier method and compared between groups through univariate analysis using the log-rank test. Cox proportional hazards regression model was used for multivariate analyses of the OS outcomes. Differences in treatment regimens were evaluated using the chi-square test. The cutoff point of $p$-value for statistical significance was set to 0.05. Statistical analyses were performed using IBM Corp. 2018. IBM SPSS Statistics for Windows, Version 21. Armonk, NY.

**Result**

**General clinical characteristics of patients**

Among 81 patients with MDS, there were 25 cases of MDS-EB-I, 30 cases of MDS-EB-II, 8 cases of MDS-SLD, 16 cases of MDS-MLD, and 2 cases of MDS-U. The median age was 64 (18–82) years, including 46 males and 35 females. The median number of ANC at initial diagnosis was 1.19 (0.08–66) $\times 10^9$ / L, median Hb was 76.5 (43.0–134.0) g/L, and median PLT was 47.5 (3.0–814.0) $\times 10^9$/L. The median Alb was 34.9 (20.8–48.1) g/L and the median TLC was 1.18 (0.21–23.62) $\times 10^9$/L, the median T-Cho was 3.3 (1.31–7.0) mmol/L. There were 13 patients with low risk IPSS-R score (1.5–3 points), 25 patients with medium risk (3.5–4.5 points), 26 patients with high risk (5–6 points) and 17 patients with very high risk (> 6 points). All patients received first-line treatment based on decitabine. The median follow-up time was 13.1 (2.1–115.7) months, and the median OS was 13.8 months (95% CI 9.2–18.5). Eighteen patients survived and 63 died. The clinical features are shown in Table 2.

**Clinical characteristics of each group after grouping according to CONUT score**

Among the 81 patients with MDS, there were 32 cases in the high CONUT score group and 49 cases in the low CONUT score group.
Among the 32 patients with high CONUT score, there were 11 cases of MDS-EB-I, 9 cases of MDS-EB-II, 4 cases of MDS-SLD, and 8 cases of MDS-MLD. The median age was 64 (18–80) years, including 20 males and 12 females. The median number of ANC at initial diagnosis was 1.06 \((0.08–66)\) × 10^9/L, median Hb was 81.5 (43.0–134.0) g/L, and median PLT was 58.0 (3.0–285.0) × 10^9/L. The median Alb was 31.35 (20.8–40.7) g/L and the median TLC was 0.805 (0.21–3.351) × 10^9/L; the median T-Cho was 2.86 (1.31–4.96) mmol/L. There were 3 low-risk patients, 9 medium-risk patients, 12 high-risk patients and 8 very high-risk patients with IPSS-R score.

Among the 49 patients with low CONUT score, there were 14 cases of MDS-EB-I, 21 cases of MDS-EB-II, 4 cases of MDS-SLD, 8 cases of MDS-MLD, and 2 cases of MDS-U. The median age was 63 (28–82) years, including 26 males and 23 females. The median number of ANC at initial diagnosis was 1.34 (0.19–51.7) × 10^9/L, median Hb was 71.0 (45.0–116.0)g/L, and median PLT was 39.5 (10.0–814.0)× 10^9/L. The median Alb was 31.35 (20.8–40.7) g/L and the median TLC was 1.4 (0.38–23.62) × 10^9/L; the median T-Cho was 3.62 (2.4–7.0) mmol/L. There were 10 low-risk patients, 16 medium-risk patients, 14 high-risk patients, and 9 very high-risk patients with IPSS-R score. Compared with the low CONUT score group, Hb, T-Cho, TLC, and Alb in the high CONUT score group decreased significantly (P values were 0.037, < 0.001, 0.009, and < 0.001, respectively).

### Survival analysis

Among the 81 patients, 18 survived and 63 died. Fourteen patients (28.5%) survived in the low CONUT score group and 4 patients (12.5%) survived in the high CONUT score group; 35 cases (71.4%) died in the low score group and 28 cases (87.5%) died in the high CONUT score group \((\chi^2 = 2.893, P = 0.089)\).

The median overall survival time in the high CONUT score group was 11.0 months \((95\% CI 7.42–14.6)\), and the median OS in the low CONUT score group was 17.2 months \((95\% CI 13.3–21.1)\) \((\chi^2 = 5.745, P = 0.017)\) (Fig. 1).

### Analysis of prognostic factors

The age, gender, hemoglobin, platelet count, neutrophil count, IPSS-R score, and CONUT score of MDS patients at the initial diagnosis were included in the univariate prognosis analysis based on OS. The results showed that thrombocytopenia, high CONUT score, medium and high-risk IPSS-R score at the initial diagnosis were associated with poor OS \((P = 0.033, 0.018, 0.006\), respectively). Furthermore, the factors related to OS in univariate analysis were put into multivariate analysis. The results showed that the above three items were still poor prognostic factors of OS \((P = 0.026, 0.038\), and 0.016 respectively) (Table 3).

### Discussion

Myelodysplastic syndrome (MDS) is a clonal bone marrow stem cell disease, which has higher prevalence rate in elderly patients. It is often accompanied by comorbidities, organ dysfunction, and poor general conditions. Therefore, in MDS patients, it is not only necessary to carry out traditional prognosis grouping for patients, but also to individualized assessment of patients’ own conditions.
CONUT score is a simple and completely objective tool to evaluate nutritional status. It can be determined by routine measurement parameters. It includes albumin, lymphocyte count, and total cholesterol, reflecting the nutritional, immune, and caloric status of patients. It has been confirmed that CONUT score can indicate the prognosis of a variety of diseases, including solid tumors and hematological malignancies, such as diffuse large B-cell lymphoma, multiple myeloma, and adult T-cell leukemia/lymphoma [6–8]. There are few reports on the CONUT score in patients with MDS. Sakurai A’s study found that in patients treated with azacitidine, high CONUT score is closely related to the poor prognosis of MDS and AML with bone marrow dysplasia [9].

The CONUT score was composed of serum albumin, total cholesterol, and lymphocyte count. Albumin is often used as a general index of nutritional evaluation, which widely reflects the balance between protein synthesis and catabolism. A multicenter study showed that pre transplant hypoalbuminemia was associated with poor OS in AML and MDS patients undergoing allogeneic transplantation [10].

Dyslipidemia in MDS is characterized by tumor wasting diseases, and lipid reduction is associated with HMGCoAR and LDL-R gene expression [11]. Studies have shown that the cholesterol level in MDS patients is significantly lower than that in the normal control group and decreases progressively with the progress of the disease, especially in EB type [12], and the total cholesterol level is significantly lower in IPSS-R high-risk group or very high–risk group, while the TC level in patients relieved by demethylation treatment is significantly higher than that before treatment [13].

In tumor patients, the decrease of lymphocyte count is related to the impairment of immunity, which leads to tumor progression [14]. Previous studies have shown that the low lymphocyte count level at the initial diagnosis of low-risk MDS is associated with poor prognosis [15], and the decrease of NK cells in high-risk MDS patients is associated with poor prognosis [16]. In patients treated with decitabine, lymphocyte count can be used as the standard to evaluate the efficacy [17]. Although the mechanism of action remains to be further studied, there is more and more evidence that the immune homeostasis of patients with MDS has changed [16].

In this study, according to the ROC curve, we determined that the cutoff value of CONUT score was 5.5, and the patients were divided into two groups, including 32 cases with high CONUT score and 49 cases with low CONUT score. There was no significant difference in WHO classification between the two groups. Compared with the low score group, the hemoglobin, total cholesterol, lymphocyte count, and albumin in the high CONUT score group were closely related to the poor prognosis of MDS and AML with bone marrow dysplasia [9].

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In this study, according to the ROC curve, we determined that the cutoff value of CONUT score was 5.5, and the patients were divided into two groups, including 32 cases with high CONUT score and 49 cases with low CONUT score. There was no significant difference in WHO classification between the two groups. Compared with the low score group, the hemoglobin, total cholesterol, lymphocyte count, and albumin in the high CONUT score group were significantly reduced. A meta-analysis showed that BMI and albumin, prealbumin, hemoglobin, total cholesterol, and total protein are useful biomarkers of adult malnutrition, which is consistent with previous studies [18]. In addition, we found that high CONUT score

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**Table 3** Univariate and multivariate prognostic analysis of MDS patients based on OS

| Risk factors | Univariate analysis | Multivariate analysis |
|--------------|---------------------|----------------------|
|              | HR (95% CI)         | P                    | HR (95% CI)         | P            |
| Age > 60 years | 0.933 (0.555–1.569) | 0.794                |                      |              |
| Gender       | 0.870 (0.517–1.463) | 0.599                |                      |              |
| Hb < 100 g/L | 0.919 (0.483–1.748) | 0.797                |                      |              |
| PLT ≤ 100×10^9/L | 0.537 (0.303–0.952) | 0.033                | 0.546 (0.313–0.953) | 0.026        |
| ANC ≤ 0.8×10^9/L | 1.359 (0.701–2.636) | 0.364                |                      |              |
| CONUT < 5.5  | 1.828 (1.108–3.018) | 0.018                | 0.52 (0.292–0.926)  | 0.038        |
| Low-risk IPSS-R | 3.086 (1.387–6.862) | 0.006                | 2.715 (1.208–6.106) | 0.016        |
was associated with poor OS. The median overall survival time in the high CONUT score group was 11.0 months and 17.2 months in the low CONUT score group.

Our results showed that thrombocytopenia, high CONUT, and medium and high risk IPSS-R scores at initial diagnosis were associated with poor OS. In previous studies, thrombocytopenia was associated with decreased overall survival [19], and high CONUT score was associated with poor nutritional status, resulting in poor prognosis, which is consistent with other results [20–22].

The traditional risk stratification of MDS is based on disease-related factors and does not include the patient’s physical fitness and tolerance to drug treatment into the score. The CONUT score evaluates the patient’s nutritional status, and it plays an important role in establishing a more detailed prognosis evaluation for MDS patients. As one of the few studies to explore the relationship between CONUT score and MDS, this study first paid attention to the prognostic role of CONUT score in MDS patients, and compared the relationship between CONUT score and clinical prognostic parameters for the first time, so as to understand the prognostic value of CONUT score in MDS patients.

However, our study has certain limitations. First of all, it was a single-center retrospective study with a small sample capacity, and it needs a larger sample capacity in the future. Secondly, we are targeted at hospitalized patients and lack comprehensive data of relatively low-risk patients. Finally, we refer to the data of patients at the initial diagnosis, and there is a lack of evaluation of the change of CONUT score after treatment. We are looking forward to a more standard system for the prognosis evaluation of MDS patients.

Author contribution Xin Zhou and Hong-feng Guo provided the conception of the study and Jun Xia provided the design of the study. Jin Qian collected and assembled the data and wrote the article. Jing Wang and Feng Cheng participated in the data analysis and interpretation. All authors finally approved the manuscript.

Data availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Ethics approval The Institutional Review Board of the Wuxi People’s Hospital approved this study in accordance with the Helsinki Declaration. The requirement for informed consent was waived owing to the retrospective design of data collection.

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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