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ORIGINAL ARTICLE

Correlation of Serum Oxidative Stress with the Effect of Initial Induction Chemotherapy in Acute Myeloid Leukemia

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SUMMARY

Background: **Achieving first complete remission with induction chemotherapy (ICT) for acute myeloid leukemia (AML) correlates with patient's prognosis. This study aimed to determine the correlation between oxidative stress and the outcome of ICT in AML patients.**
Methods: **A total of 195 AML patients underwent initial ICT at the Longyan First Affiliated Hospital of Fujian Medical University from 06-11-2018 to 12-30-2023. Three weeks after ICT, patients were divided into two groups, CR (complete remission) and PR (partial remission), by detecting blood parameters and bone marrow cells. Serum oxidative stress-related factors, malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), total antioxidant capacity (T-AOC), and growth/differentiation factor-15 (GDF15) activities or levels were measured to assess the diagnostic value of these factors as a means of diagnosing the efficacy of ICT in patients. Factors affecting PR after initial ICT were analyzed.**
Results: **Patients in the PR group had higher levels of oxidative stress three weeks after initial ICT. Compared with the CR group, patients in the PR group had elevated levels of MDA and GDF15 and reduced activities of SOD, GSH-Px, and T-AOC. Serum MDA levels (AUC 0.709; 95% CI. 0.618 - 0.781) and the combination of multiple indicators (AUC 0.791; 95% CI. 704 - 0.851) had diagnostic value for the efficacy of AML patients undergoing ICT. Serum MDA and GDF15 exceeding cutoff values were risk factors for PR in AML patients undergoing ICT, as were serum SOD and T-AOC below cutoff values. Preoperative malnutrition was associated with PR in patients.**
Conclusions: **Serum oxidative stress-related factors in AML patients are helpful in detecting the efficacy of ICT. Oxidative stress in response to ICT is useful for characterizing the efficacy in AML patients after ICT.**
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KEYWORDS

oxidative stress, MDA, GDF15, acute myeloid leukemia, complete remission

INTRODUCTION

Acute myeloid leukemia (AML) is a hematopoietic malignancy originating from myeloid stem and progenitor cells [1]. It is the most common acute leukemia in adults, and only 20% of patients are expected to survive more than 5 years after diagnosis [2]. Most of the clinical manifestations of AML reflect an accumulation of malignant myeloid cells in the bone marrow and peripheral blood, with the majority of patients exhibiting signs

of leukocytosis and bone marrow failure such as anemia and/or thrombocytopenia [3]. The first complete remission (CR1) is achieved in 70 - 80% of AML patients treated with 1 - 2 courses of induction chemotherapy (ICT), although some patients relapse after remission [4]. However, it has been shown that in AML patients, CR1 after ICT is strongly associated with survival and a risky prognosis for transplanted AML patients. Partial remission (PR) is associated with poorer 3-year survival [5]. In addition, patients with AML who did not have a CR1 had a shortened time to CR after intensive therapy. Patients with sustained CR after first induction benefited the most, with a long-term survival rate of 36% [6]. Therefore, improving the CR1 rate with ICT is a challenge in the treatment of AML to achieve disease-free long-term survival.

Oxidative stress is related to the pathogenesis of AML [7]. Reactive oxygen species (ROS) play a dual role in tumorigenicity, especially in hematological malignancies. Oxidative stress promotes proliferation, differentiation, genomic and epigenetic alterations, immune evasion, and survival of leukemic cells [8]. However, in chemotherapy and radiotherapy, ROS can occur by inducing activation of cancer cell death processes, including apoptosis, which provides a mechanism for cancer therapy [9,10]. Oxidative stress is usually defined as an imbalance between ROS production and impaired antioxidant defenses [11]. Proper redox homeostasis is maintained through the combined action of antioxidant enzymes, in which antioxidant defense parameters, including total antioxidant capacity (T-AOC), glutathione S-transferase (GST), and superoxide dismutase (SOD), play a particularly important role [12]. Impaired antioxidant defense systems are widely believed to be responsible for the accumulation of oxidative damage in cells [13]. Malondialdehyde (MDA) is one of the most popular markers designed to indicate lipid peroxidation [14]. Current treatment of leukemia consists mainly of high-dose cytotoxic chemotherapy with or without allogeneic stem cell transplantation [15]. Although chemotherapy is usually accompanied by elevated levels of ROS and exerts cytotoxic effects by inducing oxidative stress, it can also and accordingly lead to drug intolerance or resistance [16]. Most clinicians are skeptical about the use of antioxidants in cancer chemotherapy or radiotherapy. This is because both chemotherapy and radiation therapy for cancer utilize the production of excess free radicals during chemotherapy and radiation therapy to kill and inhibit cancer cells. It is possible that antioxidants could make cancer cells resistant to chemotherapy and radiotherapy. However, this is not the case. Cancer patients who receive standard cancer treatment along with vitamins, antioxidants, and cell-supporting nutrients have significantly better outcomes than those who do not take nutrients and antioxidants [17]. Glutathione (GSH) is an antioxidant supplement in combination with chemotherapy or radiotherapy for various cancer treatments [18]. Although antioxidant therapy is now approved for relapse prevention in AML, it is still not a standard treatment strategy in clinical practice. New clinical trials are currently underway for a variety of antioxidants that are expected to be absorbed and become new standard treatment strategies.

Growth/differentiation factor-15 (GDF15) is a distant member of the transforming growth factor β superfamily and is widely expressed in a variety of mammalian tissues. Its expression is highly regulated and is usually induced under conditions associated with cellular stress [19]. GDF15 is upregulated in a variety of cancers [20], and in addition, GDF has been reported to be associated with cancer prognosis. In clinical studies, serum GDF15 has been reported to be a potentially effective serum marker for detecting hepatitis B-associated hepatocellular carcinoma [21]. GDF15 can promote bone marrow adipocyte remodeling in response to leukemia cell proliferation [22].

Therefore, the present study hypothesized that oxidative stress after initial ICT for AML affects the efficacy of chemotherapy and provides theoretical data for the study of molecularly targeted drugs.

MATERIALS AND METHODS

Patients

A total of 213 patients (223 patients entered the eligibility assessment) who were initially diagnosed with AML (except acute promyelocytic leukemia) at the Longyan First Affiliated Hospital of Fujian Medical University from 06/11/2018 to 12/30/2023 were selected. Among them, 5 patients who refused chemotherapy and 13 patients who did not complete the data statistics or were lost to follow-up were excluded from the study. The rest of the patients were subjected to cytomorphology, immunology, genetic testing, and chromosome karyotype analysis, etc., and all of them completed the initial ICT with complete data. The study was reviewed and approved by the Ethics Committee of the Longyan First Affiliated Hospital of Fujian Medical University. All subjects participating in the study signed an informed consent form. Flowchart of clinical case inclusion is shown in Figure 1.

The diagnosis of AML in all patients was based on the 2016 World Health Organization criteria [23]. This study included 51 age- and gender-matched healthy volunteers of the same study period as a control group. Inclusion criteria: 1) age greater than 18 years; 2) meeting the World Health Organization diagnostic criteria for AML; 3) initial diagnosis with AML; 4) no previous history of other hematological diseases (e.g. myelodysplastic syndromes [MDS], paroxysmal nocturnal hemoglobinuria, etc.).

Exclusion criteria: 1) acute promyelocytic leukemia; 2) AML secondary to MDS or chronic myeloproliferative neoplasm; 3) history of AML-related treatment.

ICT regimen

All patients received the standard DA (3 + 7) regimen or MA (Homoharringtonine + Cytarabine), HA (Homoharringtonine + Cytarabine + Daunorubicin), and CAG (Cytarabine + aclarubicin free base + granulocyte colony-stimulating factor). All patients were guided by medical oncologists to receive the proper chemotherapy regimen based on NCCN Clinical Practice Guidelines in AML Oncology and to develop a standardized chemotherapy course [24].

Efficacy criteria

Patients were assessed following the conclusion of the 21-day initial induction therapy period. CR [25]: 1) clinical absence of signs and symptoms due to AML cell infiltration; 2) blood routine: hemoglobin > 100 g/L (male) or > 90 g/L (female), absolute neutrophil value > 1.5×10^9/L, platelets (PLT) > 100×10^9/L; and absence of AML cells in leukemic cells in the peripheral blood; and 3) bone marrow < 5%. PR: (1) bone marrow > 5% and ≤ 20%; and 2) one of the clinical or hematologic criteria was not fully met. Failure to remission in this study was also categorized in the PR group.

Blood sample collection

Blood samples were collected in all subjects after an overnight fast and processed within 2 hours. In control subjects, blood samples were collected at the time of blood draw for other specified medical reasons. Blood was collected into tubes containing and not containing ethylenediamine tetraacetic acid, and 10 mL samples were centrifuged separately at 1,300 g for 20 minutes at 4°C. Serum was then aliquoted into tubes and stored at -80°C until analyzed.

Clinical characterization and laboratory testing

Clinical characteristics and anthropometric measurements were taken during clinical visits or by reviewing medical records. Clinical information included gender, age, clinical presentation, blood parameters, risk stratification for AML, and chemotherapy regimen. Risk stratification for AML was assessed based on cytogenetics and molecular genetics in accordance with the NCCN Clinical Practice Guidelines for AML Oncology (version 1.2015).

The samples were tested by the laboratory of Longyan First Hospital. PLT, neutrophils, white blood cell (WBC), red blood cell (RBC), and hemoglobin (HGB) were measured by a fully automated hematology analyzer (Sysmex XN9000, Japan). Serum albumin, MDA, SOD, GSH-Px, T-AOC, and lactate dehydrogenase (LDH) activities were measured by Beckman Coulter AU5800 automated biochemical analyzer (USA). Serum GDF15 (R&D Systems, USA) was determined by specific enzyme-linked immunoassay. Serum cytokine levels were expressed in picograms per milliliter (pg/mL). All samples were duplicated in a single assay to avoid interassay variation. The intra-assay variation was less than 3%.

Sample size estimation

The sample size for the study was estimated by using G*Power software version 3.1.9.2, with a significance level of $\alpha = 0.05$, power of $1-\beta = 0.8$, effect size of $d = 0.5$, and a bilateral test. Each group was determined to require a minimum of 64 participants, with a final sample size of 68 participants per group to account for a potential 5% loss to follow-up.

Data statistics

Continuous variables for clinical, anthropometric, and biochemical analyses are presented as mean ± standard deviation, whereas categorical variables are presented as frequencies (%). Shapiro-Wilk analysis was conducted to check data normality. For variables with normally distributed parameters, comparisons between groups were made by using independent Student's *t*-test or one-way ANOVA or analysis with Bonferroni correction, depending on the number of groups considered. Comparisons between two groups for non-normally distributed parameters were performed using the Mann-Whitney U test for comparisons followed by Bonferroni correction. $p < 0.05$ was considered statistically significant. The diagnostic value of efficacy after initial ICT was assessed by receiver operating characteristic (ROC) curve analysis, and the area under the ROC curve (AUC) was calculated. Multivariate logistic regression analyses were used to assess predictors of poor outcome. Analyses were performed using SPSS software 22.0, and figures were drawn by using GraphPad Prism 8.3.0.

RESULTS

General clinical characteristics of patients

A total of 195 AML patients, 103 males and 92 females, with an age range of 19 - 76 years, were included in this study. Based on the results after initial ICT, we categorized AML patients into a CR group (113 cases) and a PR group (82 cases). As shown in Table 1, we observed significant differences in age ($p = 0.041$), PLT ($p = 0.017$), bone marrow blasts ($p = 0.037$), and albumin ($p = 0.001$) between the two groups at the time of initial diagnosis. There were 52 patients, 63.4% (52/82), in the PR group whose age at the time of initial diagnosis was greater than 55 years. PLT was higher than 50×10^9 L in 40 patients (48.78%, 40/82), bone marrow blasts were higher than 50 in 45 patients (54.87%, 45/82), and albumin was lower than 3.0 g/dL in 38 patients (46.34%, 38/82). However, other clinical characteristics, gender, clinical symptoms, WBC, LDH, NCCN risk stratification, and initial ICT regimen, did not differ significantly between the two groups ($p > 0.05$).

Serum factor levels in AML patients with different efficacy after receiving initial ICT

As shown in Table 2, compared with controls, AML patients had higher levels of MDA and GDF15 ($p = 0.001$), and SOD, GSH-Px, and T-AOC activities were

Table 1. Clinical baseline of patients.

Variable	CR	PR	p-value
	(n = 113)	(n = 82)	
Age, years, median (range)			**0.041**
< 55	**58 (51.33)**	**30 (36.59)**	
≥ 55	**55 (48.67)**	**52 (63.41)**	
Gender			**0.067**
Male	**66 (58.41)**	**37 (45.12)**	
Female	**47 (41.59)**	**45 (54.88)**	
Clinical presentation			**0.586**
Fever	**40 (35.40)**	**23 (28.05)**	
Fatigue	**20 (17.7)**	**19 (23.17)**	
Bleeding	**34 (30.09)**	**22 (26.83)**	
Leukocytosis	**10 (8.85)**	**12 (14.63)**	
Extra medullary involvement	**9 (7.96)**	**9 (10.98)**	
PLT (× 10^9L)			**0.017**
< 25	**27 (23.89)**	**20 (24.39)**	
25 - 50	**51 (45.13)**	**22 (26.83)**	
> 50	**35 (30.97)**	**40 (48.78)**	
WBC at diagnosis			**0.071**
< 50 × 10^9L	**90 (79.65)**	**56 (68.29)**	
≥ 50 × 10^9L	**23 (20.35)**	**26 (31.71)**	
Bone marrow blasts			**0.037**
20 - 50	**68 (60.18)**	**37 (45.12)**	
> 50	**45 (39.82)**	**45 (54.88)**	
Albumin, g/dL			**0.001**
≥ 3.0	**86 (76.11)**	**27 (32.93)**	
< 3.0	**44 (38.94)**	**38 (46.34)**	
LDH, IU/L	**929 [209 - 11,035]**	**985 [365 - 10,258]**	**0.058**
NCCN risk stratification			**0.187**
Favorable risk	**16 (14.16)**	**16 (19.51)**	
Intermediate risk	**70 (61.95)**	**40 (48.78)**	
Adverse risk	**27 (23.89)**	**26 (31.71)**	
First line chemotherapy protocol			**0.272**
DA (3 + 7)	**63 (55.75)**	**40 (48.78)**	
MA	**38 (33.63)**	**25 (30.49)**	
HA	**8 (7.08)**	**12 (14.63)**	
Other chemotherapy protocols	**4 (3.54)**	**5 (6.10)**	

Categorical values were expressed as frequencies and tested for comparison using the chi-squared test. Measurements are expressed as mean ± standard deviation and were tested by using Student's *t*-test.

lower ($p < 0.001$). Before ICT, these serum markers were not different between the two groups ($p > 0.05$). As shown in Table 3, after ICT, we observed a decrease in serum oxidative stress levels in patients in the CR group; i.e., with the exception of GSH-Px, there was a decrease in the levels of MDA ($p = 0.005$) and GDF15 ($p < 0.001$) and an increase in the activities of SOD ($p = 0.004$) and T-AOC ($p = 0.032$), as compared to the pre-ICT period. Notably, blood oxidative stress levels did not appear to be improved in patients in the PR group,

Table 2. Serum factor levels in healthy control and AML groups (patients before chemotherapy).

Variable	AML (n = 195)	Control (n = 51)	p-value
MDA, nmol/mL	1.45 ± 0.28	0.93 ± 0.25	0.001
SOD, U/mL	0.83 ± 0.30	2.60 ± 0.44	< 0.001
GSH-Px, IU/mL	0.073 ± 0.25	0.095 ± 0.025	< 0.001
T-AOC, U/mL	5.72 ± 2.28	6.88 ± 2.57	< 0.001
GDF15, pg/Ml	70.97 ± 11.86	46.9 ± 15.35	< 0.001

p-values of < 0.05 were considered statistically significant.

Table 3. Serum factor levels in patients with different efficacy after initial induction chemotherapy.

Variable	CR (n = 113)		p-value	PR (n = 82)		p-value
	Pre. ICT	Pos. ICT		Pre. ICT	Pos. ICT	
MDA, nmol/mL	1.46 ± 0.30	1.34 ± 0.35	0.005 **	1.42 ± 0.25	1.61 ± 0.43 #	0.002 **
SOD, U/mL	0.83 ± 0.31	0.93 ± 0.25	0.004 **	0.83 ± 0.27	0.81 ± 0.31 #	0.832
GSH-Px, IU/mL	0.072 ± 0.021	0.079 ± 0.027	0.098	0.074 ± 0.030	0.071 ± 0.022#	0.53
T-AOC, U/mL	5.77 ± 2.45	6.56 ± 2.03	0.032 *	5.61 ± 1.90	5.39 ± 2.13 #	0.186
GDF15, pg/Ml	70.89 ± 12.30	62.81 ± 17.03	<0.001 ****	71.14 ± 10.94	68.64 ± 14.58 #	0.62

*** p < 0.05, pre. ICT vs. pos. ICT; # p < 0.05, CR group (pos. ICT) vs. PR group (pos. ICT). p-values of < 0.05 were considered statistically significant.**

Table 4. Sensitivity, specificity, AUC, and cutoff values of ROC curves for each factor.

Factors	cutoff value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	p-value
MDA, nmol/mL	1.505	0.709 (0.618 - 0.781)	64.62	70.23%	< 0.001
SOD, U/mL	0.61	0.619 (0.551 - 0.707)	43.85	92.31	0.013
GSH-Px, IU/mL	0.0535	0.602 (0.538 - 0.695)	43.83	83.08	0.037
T-AOC, U/mL	0.505	0.661 (0.604 - 0.738)	50.08	77.69	< 0.001
GDF15, pg/mL	66.54	0.644 (0.573 - 0.716)	66.15	62.31	0.002
Combination	/	0.791 (0.704 - 0.851)	78.46	81.54	< 0.001

p-values of < 0.05 were considered statistically significant (* p < 0.05, ** p < 0.01, *** p < 0.001).

while MDA levels were increased after ICT (p = 0.002). In addition, serum oxidative stress levels were significantly alleviated in patients in the CR group compared to the PR group, serum MDA and GDF15 levels were decreased (p < 0.05), and the activities of SOD, GSH-Px, and T-AOC were increased (p < 0.05).

Diagnostic value of serum oxidative stress levels for efficacy after initial ICT in AML patients

We evaluated the diagnostic value of these indicators on the efficacy of initial ICT by ROC curve. As shown in Figure 2, the ROC curve for serum MDA distinguished patients between CR and PR groups, with an AUC of 0.709 (95% CI. 0.618 - 0.781; p < 0.001). When the cutoff value was 1.505 nmol/mL, the sensitivity and specificity for MDA were 64.62% and 70.23% (Table

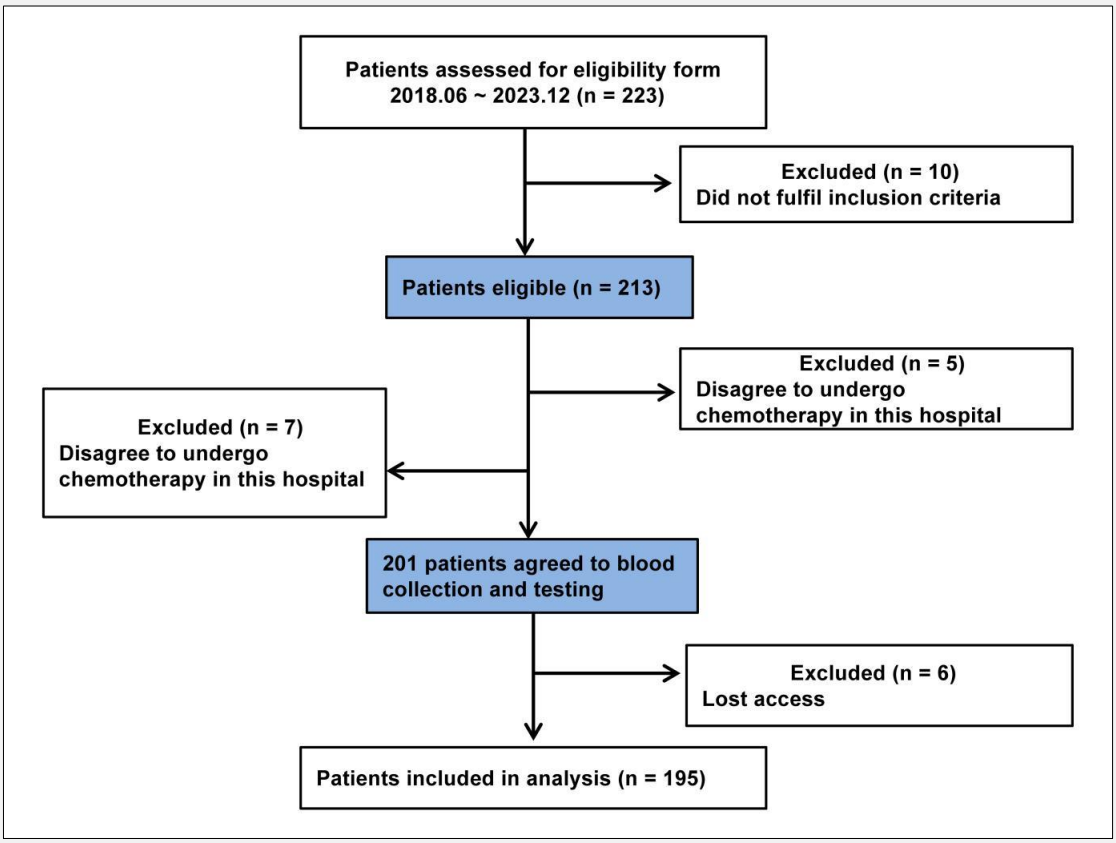

Figure 1. Flowchart of clinical case inclusion.

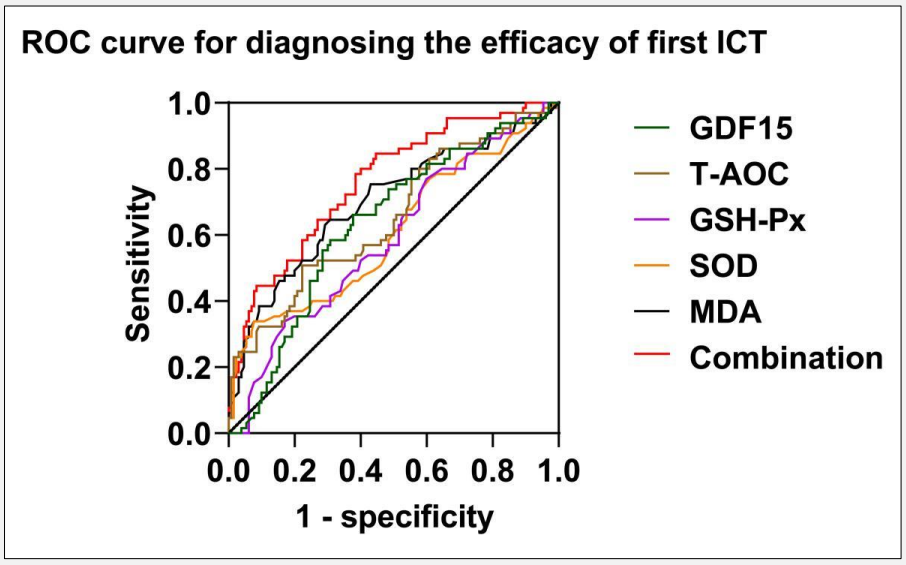

Figure 2. ROC curves analyzing the diagnostic value of patient serum factors for efficacy after initial ICT.

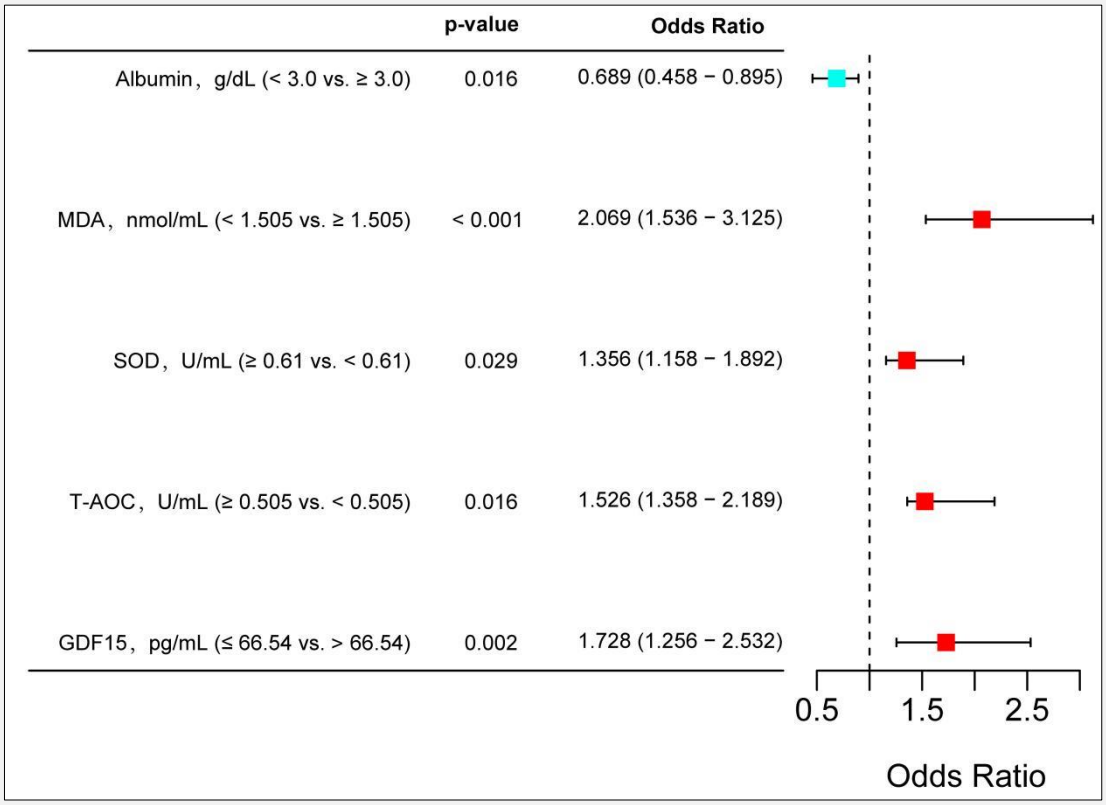

Figure 3. Multifactorial logistic regression analysis of patients' risk factors for PR after initial ICT.

p-values of < 0.05 were considered statistically significant.

4). Serum SOD, GSH-Px, T-AOC, and GDF15 had low value for the diagnostic efficacy. However, the predictive value of efficacy for initial ICT was improved by combined multimetric prediction with an AUC of 0.791 (95% CI. 0.704 - 0.851; p < 0.001) and sensitivity and specificity of 78.46% and 81.54%, respectively (Table 4).

Analysis of risk factors for PR after initial ICT in AML patients

Logistic regression analysis (Figure 3) was used to consider potential confounders affecting patient outcomes in the analysis, including age, gender, PLT, bone marrow blasts, albumin, and NCCN risk and serum factor. The results showed that albumin higher than 3.0 g/dL was an independent protective factor for reducing PR after initial ICT in AML patients, and MDA > 1.505 nmol/mL, SOD < 0.61 U/mL, T-AOC < 0.505 U/mL, and GDF15 > 66.54 pg/mL were independent risk factors.

DISCUSSION

AML is an aggressive hematologic neoplastic disease, and the clinical outcome of patients with AML can currently be highly heterogeneous in terms of surviving only a few days or being cured [26]. The rapid and convenient detection of serum factor levels offers a distinct advantage. The development of novel, sensitive serum biomarkers can enhance the ability to predict therapeutic efficacy in acute myeloid leukemia (AML) patients following induction chemotherapy. This study describes serum oxidative stress factor levels after initial ICT and risk factors for poor outcome. Overall, 195 AML patients achieved CR in 57.95% (113/195) and PR in 42.05% (82/195) of patients after initial ICT. Three weeks after initial ICT, serum oxidative stress levels were reduced in AML patients who achieved a CR relative to AML patients.

Currently, risk stratification of AML patients receiving chemotherapy relies heavily on pre-treatment disease characteristics. The current updated NCCN and European Leukemia Net risk classification systems consider

AML-specific molecular biology and cytogenetic abnormalities to be major determinants of disease prognosis [27]. Allogeneic hematopoietic cell transplantation during CR1 of AML reduces the risk of relapse and improves relapse-free survival in intermediate-risk and low-risk AML [28]. Breems et al. reported that a second CR was an independent factor influencing prognosis in 667 adults aged less than 60 years [29]. Prior research has consistently shown that the initial complete response rate following initial chemotherapy treatment is a significant factor in determining patient prognosis, for example: patients with CR1 had a lower relapse rate (25%) and relapse-free mortality (35%) [30].

GSH-Px and SOD are the major antioxidant enzymes in the human antioxidant system that protect against oxidative stress [31]. MDA is an endogenous product produced by lipid peroxidation of unsaturated fatty acids in phospholipids [32].

Chemotherapy for AML relies heavily on oxidative stress, and chemicals promote ROS production that is associated with cytotoxicity. However, oxidative stress can also lead to chemotherapeutic drug intolerance or drug resistance, which reduces the efficacy of chemotherapy. To our knowledge, this is the first relevant study to predict the efficacy of initial ICT in AML patients by serum oxidative stress factor levels. In this study, CR1 and no remission were used as chemotherapeutic effects.

Oxidative stress is characterized by a decrease in T-AOC and in the activity of antioxidant enzymes [33]. Hematopoietic cell differentiation is accompanied by changes in oxidative metabolism and an increase in ROS levels. Leukemic stem cells, which initiate and maintain the leukemic process, exhibit specific metabolic properties because they are more dependent on oxidative respiration than glycolysis and more sensitive to oxidative stress [34]. In the present study, we also demonstrated that *in vivo* oxidative stress occurs in AML patients compared to healthy controls, as evidenced by elevated MDA levels and reduced SOD, GSH-Px, and T-AOC activities. Furthermore, serum levels of GDF15, a marker of cellular stress, are elevated in AML patients [35]. GDF15 is not only a stress mitogenic factor, but it can also act as an inflammatory factor to regulate cancer development and progression [36]. After initial ICT in AML patients, serum oxidative stress appeared to be alleviated in AML patients in the CR group compared to the pre-ICT period, whereas the AML patients in the PR group still maintained high levels of oxidative stress. Notably, AML patients in the CR group had decreased serum MDA and GDF15 levels and increased activities of SOD, GSH-Px, and T-AOC. This suggested that PR of initial ICT in AML patients was associated with oxidative stress. Furthermore, we obtained the cutoff values for distinguishing the efficacy of these serum factors after chemotherapy through the ROC curve and the area under the curve. MDA as one of the end products of lipid peroxidation has a typical and reliable biomarker of oxidative stress [37]. Therefore, it has an outstanding diagnostic value relative to other indicators in this study. Finally, by correcting for confounders, albumin higher than 3.0 g/dL was an independent protective factor for reducing PR after initial ICT in AML patients, and MDA > 1.505 nmol/mL, SOD < 0.61 U/mL, T-AOC < 0.505 U/mL, and GDF15 > 66.54 pg/mL were independent risk factors for PR in AML patients. It is well known that serum albumin is one of the indicators commonly used in clinical practice to evaluate protein nutritional status and can be used to evaluate the degree of malnutrition [38]. Malnutrition in tumor patients decreases the tolerance to treatment and is associated with reduced response to treatment, prolonged treatment period, and poor prognosis [39]. Although the risk classification of AML is a major determinant of patient prognosis, in the present study, which mainly investigated the outcome of AML patients who received initial ICT, we did, however, not find a difference in the risk classification of AML between patients in the CR and PR groups. Long-term follow-up of these patients may be needed to obtain more prognostic information for further analysis. This study lays the foundation for further research on the correlation between oxidative stress levels and prognosis in patients after initial induction chemotherapy.

Limitations

This study has some limitations. Considering the paradoxical role of oxidative stress in chemotherapy, the serum factor levels of patients at the conclusion of initial ICT were not examined, thus precluding the determination of the post-chemotherapy dynamic changes in serum factor levels. Second, following up patients after initial ICT would be more useful to understand the impact of CR1 on patients' prognosis. Finally, this study only supports the correlation between oxidative stress and outcome in AML patients 3 weeks after receiving initial ICT. In future studies, it is necessary to follow up on the changes in stress levels and patient prognosis after ICT.

CONCLUSION

In summary, oxidative stress after initial ICT in AML patients was associated with PR. The high levels of serum MDA and GDF15 and the decreased activities of SOD, SOD, and T-AOC in AML patients 3 weeks after ICT suggested that the patients were not in CR. Following the evaluation of the remission rate and its contributing elements post-initial ICT, understanding the effectiveness traits of AML patients, and elucidating different influencing factors, we can administer tailored treatment more precisely. This approach is beneficial for enhancing chemotherapy remission rates, supplying theoretical information for molecular targeting drug research, and creating favorable circumstances for the future amalgamation of chemotherapy and bone marrow transplants in AML patients. Of course, clinical analysis

of larger cases is still needed to completely confirm the effect and safety of oxidative stress and ICT in AML patients.

Availability of Data and Materials:
The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Ethical Approval Statement:
The present study was approved by the Ethics Committee of Longyan First Affiliated Hospital of Fujian Medical University, and written informed consent was provided by all patients prior to the study start. All procedures were performed in accordance with the ethical standards of the Institutional Review Board and the Declaration of Helsinki and its later amendments or comparable ethical standards.

Declaration of Interest:
The authors have no conflicts of interest to declare.

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