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Baseline characteristics of people living with HIV with different CD4+ T cell depletion

Peipei Luo[1], Juan Jin[2], Dingsheng Kong[3], and Guoxiang Yang[4]*

[1]Department of Emergency; [2]Antiviral Clinic; [3]Department of Surgery; [4]Department of Pharmacy. Xi'an Eighth Hospital, Xi'an, China

Abstract

HIV-1 infection can easily cause CD4+ T cell depletion. To investigate the impact of CD4+ T cell depletion on the health of people living with HIV-1 (PLWH), we collected and analyzed baseline data from 5139 volunteers who had never received any treatment. The results showed that as CD4+ T cells were depleted, the volunteers were more likely to suffer from anemia, liver and kidney dysfunction, and blood glucose abnormalities, which were more pronounced in elderly PLWHs. In addition, there was a low correlation between dyslipidemia and CD4+ depletion. CD4+ T cell depletion increases the likelihood of HIV-1 carriers developing anemia, liver and kidney dysfunction, and blood glucose abnormalities, making elderly PLWHs more susceptible to these effects. Relatively speaking, the correlation between dyslipidemia and CD4+ depletion is low.

Keywords: *HIV-1. CD4+ T cell depletion. Aging. Baseline characteristics.*

***Correspondence:**
Dingsheng Kong
E-mail: 15389282218@163.com

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Introduction

After HIV infection, the steady-state mechanism of T lymphocyte count in the human body is disrupted, leading to the gradual loss of CD4+ T cells and systemic immune activation. A major direct consequence of untreated pathogenicity in HIV-1-infected populations is the depletion of CD4+ T cells, which is largely caused by apoptosis[1-3]. Furthermore, CD4+ T cell depletion can affect disease progression[4]. Therefore, here we retrospectively analyzed the baseline data from 5139 people living with HIV-1 (PLWH) to explore the effects of increasing CD4+ T cell depletion and aging.

Methods

In this cross-sectional study, we have adhered to the relevant EQUATOR guidelines to collect and analyze laboratory test data of PLWHs who were preparing for treatment at the Eighth Hospital of Xi'an, China, from March 2010 to December 2024. Everyone has signed an informed consent form.

Participants included

Inclusion criteria

(1) Diagnosed as a carrier of HIV-1. (2) Data integrity: It has a complete baseline laboratory index record (including white blood cell count, platelets, hemoglobin, blood creatinine, triglycerides, total cholesterol, blood glucose, glutamate aminotransferase, aspartate aminotransferases (AST), and total bilirubin [TBIL]). (3) Age: ≥ 18 years. (4) PLWHs have never received any treatment. (5) Time range: including PLWHs from March 2010 to December 2024.

Exclusion criteria

(1) Data missing: PLWHs with a lack of key indicators (such as core laboratory parameters and diagnostic results). (2) Comorbidity interference: merging other diseases (such as malignant tumors, end-stage nephropathy, rheumatoid arthritis, systemic lupus erythematosus, hepatitis, autoimmune nephritis, leukemia, pulmonary tuberculosis, liver cirrhosis, diabetes, congenital obesity, and metabolic disorders).

Statistical analysis

We used Statistical Package for the Social Sciences 26.0 statistical software to analyze the data, using the Chi-square test or Fisher's exact test for categorical variables (anomaly rate). Continuous variables are tested using the t-test/Mann-Whitney U-test. Logistic regression was used to explore the related factors of abnormal indicators (such as age and complications). $p < 0.05$ indicates a statistically significant difference.

Abnormality percentage calculation: (1) Abnormality percentage of creatinine (%) = Number of PLWHs with creatinine < 44 (μmol/L) or > 106 (μmol/L)/Total number of PLWHs × 100. (2) Abnormality percentage of platelet (%) = Number of PLWHs with platelet < 100 × 10^9/L/Total number of PLWHs × 100. (3) Abnormality percentage of hemoglobin (%) = Number of PLWHs with hemoglobin < 110 g/L/Total number of PLWHs × 100. (4) Abnormality percentage of leukocyte (%) = Number of PLWHs with leukocyte < 4 × 10^9/L/Total number of PLWHs × 100. (5) Abnormality percentage of triglyceride (%) = Number of PLWHs with triglycerides > 1.7mmol/L/Total number of PLWHs × 100. (6) Abnormality percentage of total cholesterol (%) = Number of PLWHs with total cholesterol > 5.2 mmol/L/Total number of PLWHs × 100. (7) Abnormality percentage of alanine aminotransferase (ALT) (%) = Number of PLWHs with ALT activity > 40 (U/L)/Total number of PLWHs × 100. (8) Abnormality percentage of AST (%) = Number of PLWHs with AST activity > 40 (U/L)/Total number of PLWHs × 100. (9) Abnormality percentage of TBIL (%) = Number of PLWHs with TBIL > 17.1 μmol/L/Total number of PLWHs × 100. (10) Abnormality percentage of blood sugar (%) = Number of PLWHs with blood sugar > 6.1 mmol/L/Total number of PLWHs × 100.

Results

Creatinine

As CD4+ T cell exhaustion worsened, the number of individuals with creatinine abnormalities increased, with the lowest proportion being 1.66% and the highest being 4.96%, PLWHs with CD4 < 200 presented with the most evident abnormalities (4.96%, 95% confidence interval [CI], 3.94-5.98%) ($p < 0.01$) (Fig. 1). Based on the comparison of different age groups, PLWHs over 60 years old had an utterly higher abnormality percentage (Highest value 5.94%, 95% CI, 4.83-7.05%) ($p < 0.01$) (Fig. 2).

Anemia-related indicators

With the increase in CD4+ T cell depletion, the abnormalities of hemoglobin, platelets, and leukocytes showed an upward trend. The most severe abnormality

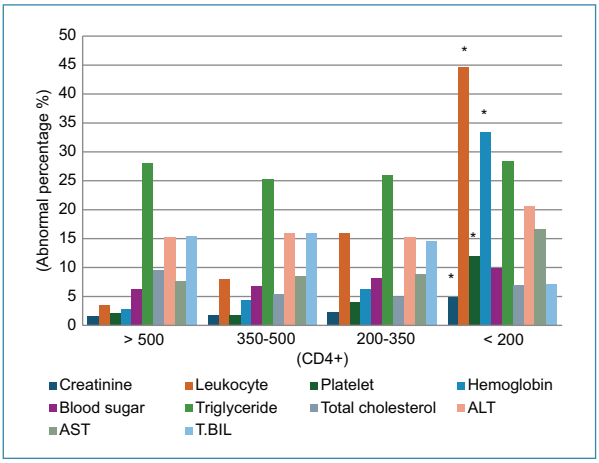

Figure 1. Changes of various indexes under different CD4+ T cell depletion conditions. *p < 0.01.

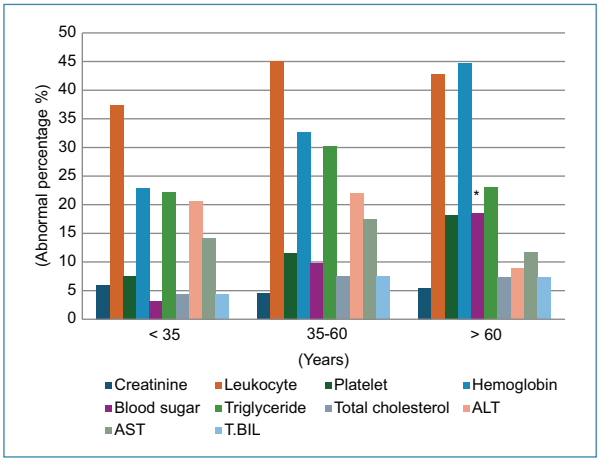

Figure 2. Comparison of indexes in different age groups (CD4 count < 200).*p < 0.01.

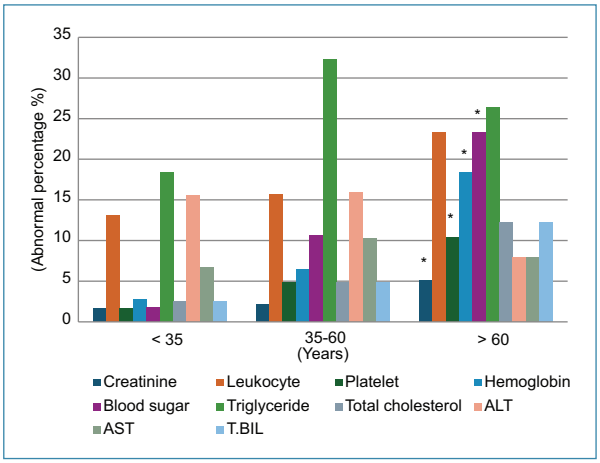

Figure 3. Comparison of indexes in different age groups (CD4 count: 200-350). *p < 0.01.

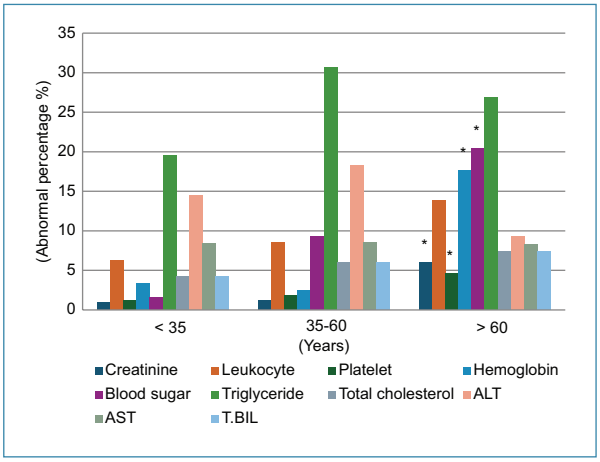

Figure 4. Comparison of indexes in different age groups (CD4 count: 350-500). *p < 0.01.

occurred in PLWHs with CD4 < 200 (leukocyte 44. 68%, 95% CI, 42.34-47.02%) (hemoglobin 33.37%, 95% CI, 31.15-35.59%) (platelets 12.03%, 95% CI, 10.5-13.56%) (p < 0.01) (Fig. 3).

Further testing the impact of aging on these indicators under the same CD4+ T cell depletion (CD4 < 200, CD4: 200-350, CD4: 350-500, respectively) showed that the anomalies of the three indicators increased with aging (Figs. 4-6).

Blood sugar

When CD4+ T cell depletion progressed, blood glucose abnormalities presented a slight increasing trend (Fig. 7), and with age, the abnormal rate of blood sugar increased several times (highest value 23.31%, 95% CI, 21.32-25.3%) (Fig. 8).

Blood lipids

The abnormal percentages of triglycerides and total cholesterol did not show differential fluctuations with CD4+ T cell depletion (Fig. 9). Within the same range of CD4+ T cell depletion, there was no statistical difference in triglycerides among PLWHs of different age groups (Fig. 10), and cholesterol abnormalities mildly increased with age (Fig. 11).

Hepatic function

As for hepatic function, we focused on detecting ALT, aspartate aminotransferase, and TBIL. The results showed that PLWHs with CD4 < 200 had elevated levels of ALT (20.61%, 95% CI, 18.71-22.52%) and aspartate transaminase (16.57%, 95% CI,

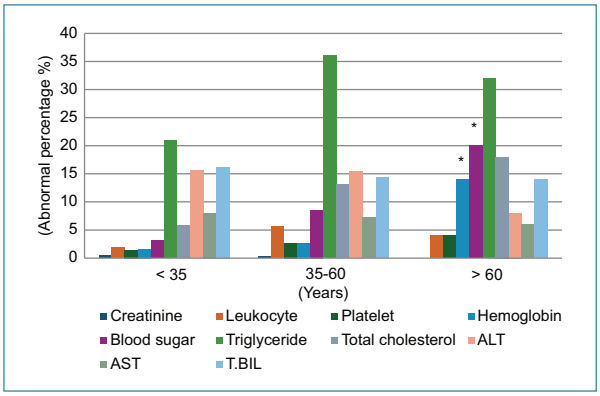

Figure 5. Comparison of indexes in different age groups (CD4 count > 500). *p < 0.01.

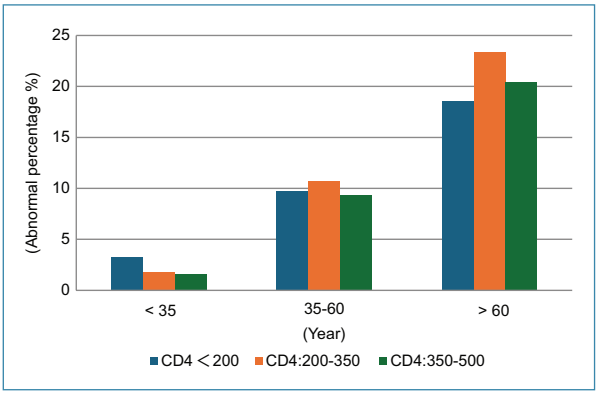

Figure 8. Proportion of abnormal blood glucose in PLWHs of different age groups (within the same range of CD4+ depletion).

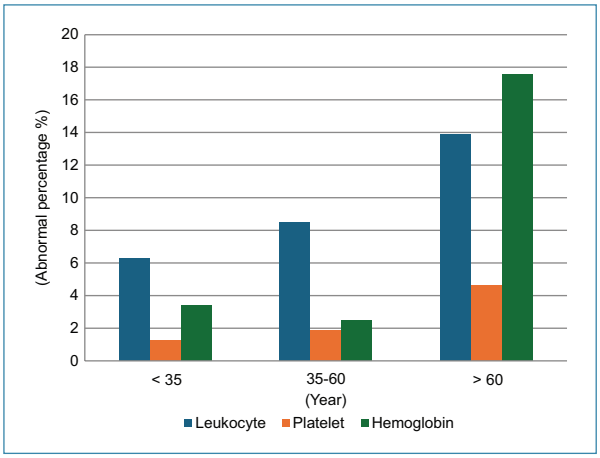

Figure 6. Abnormal rates of anemia-related indicators in PLWHs of different age groups (CD4: 350-500).

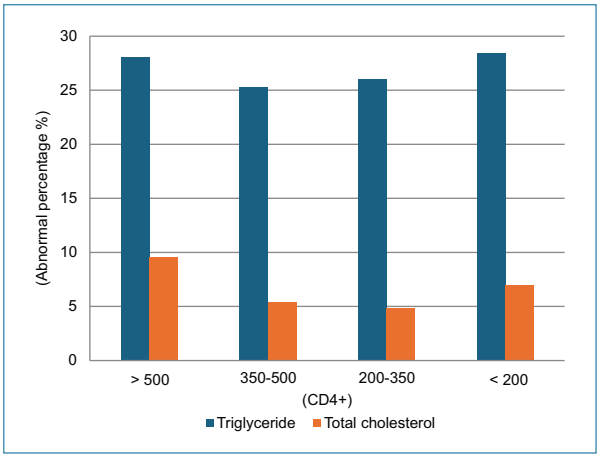

Figure 9. Abnormal rates of triglycerides and total cholesterol in PLWHs with different CD4+ T cell depletion.

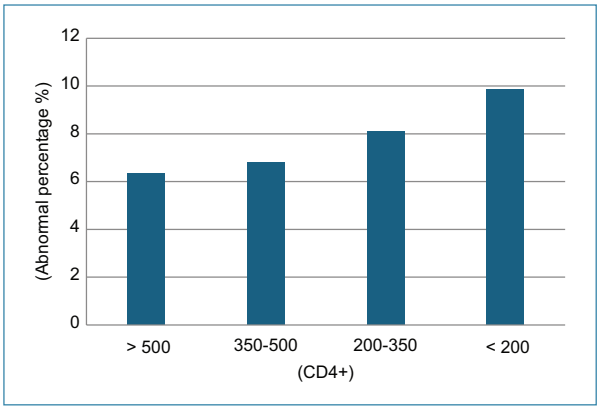

Figure 7. Abnormal proportion of blood sugar in PLWHs with different CD4+ T cell depletion.

14.82-18.32%) ($p < 0.05$) (Fig. 12), and under the same immunodeficiency conditions, there was no age-related difference in hepatic function (Figs. 13 and 14).

Discussion

HIV-1 can infect renal epithelial cells, and multiple copies of HIV-1 from each cell can be transferred from infected T cells to renal epithelial cells[5]. As the disease progressed, the proportion of people with abnormal creatinine increased, with the highest abnormality rate of 4.97% (2-3 times higher than other groups) when CD4+ T cells were < 200 (Fig. 1). Based on age

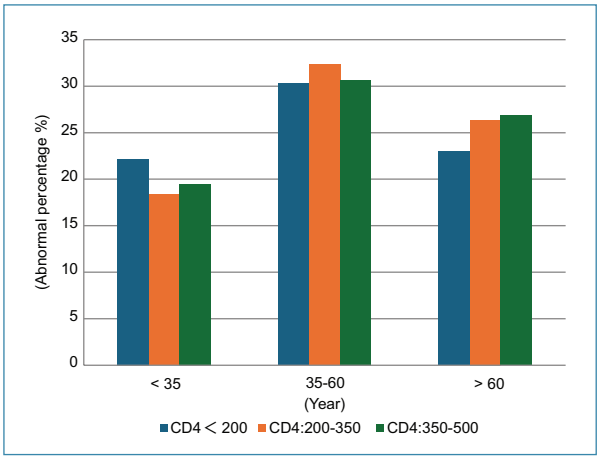

Figure 10. Proportion of PLWHs with abnormal triglycerides in different age groups (within the same range of CD4+ depletion).

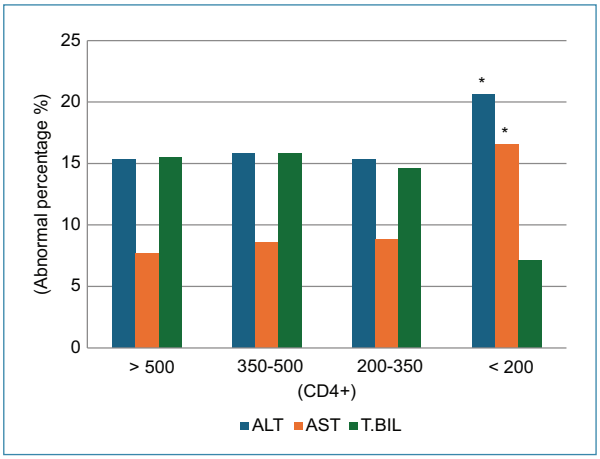

Figure 12. Abnormal proportion of hepatic function-related indicators under different CD4+ T cell depletion. *p < 0.05.

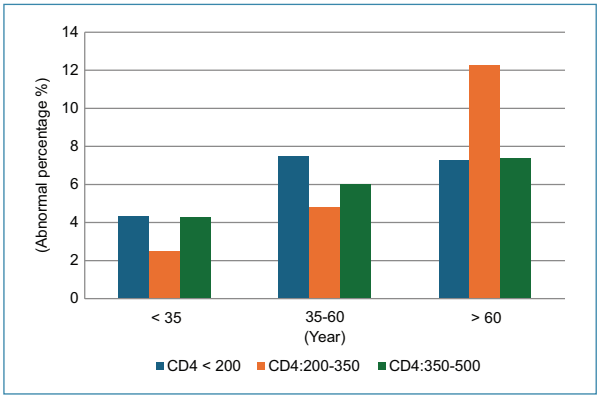

Figure 11. Proportion of PLWHs with abnormal cholesterol in different age groups (within the same range of CD4+ depletion).

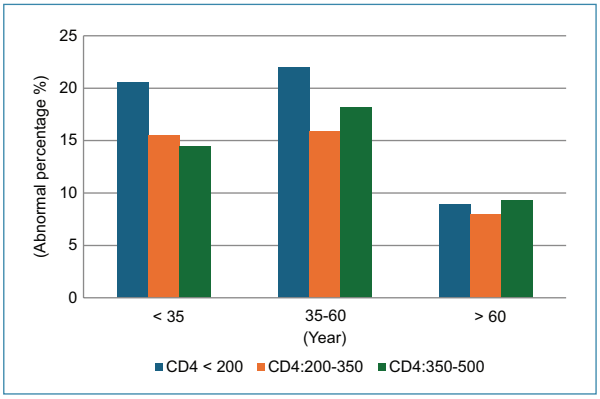

Figure 13. Proportion of PLWHs with abnormal alanine aminotransferase in different age groups (within the same range of CD4+ depletion).

comparison, it was found that older PLWHs were more likely to experience creatinine abnormalities, especially those over 60 years old, whose abnormality rate increased several times compared to other groups (Fig. 2), proving that the destruction of kidneys by HIV-1 virus may be a slow process, but elderly PLWHs would be more susceptible to kidney damage.

Anemia and hypoalbuminemia are very common complications in HIV-1-infected individuals[6]. Among HIV-1 infected people, the prevalence of anemia ranges from 10% of asymptomatic HIV infected PLWHs to 92% of AIDS patients[7]. The underlying mechanisms include malnutrition, reduced hematopoietic cell production, reduced responsiveness of hematopoietic matrix to

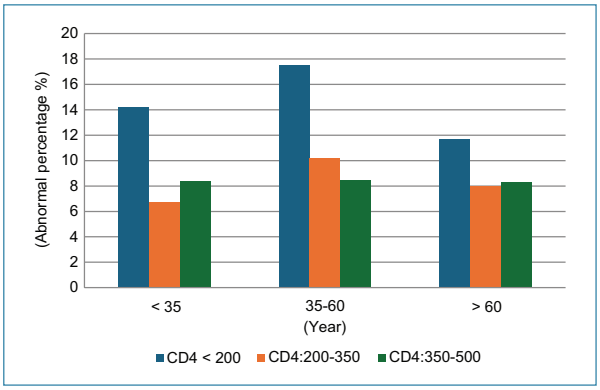

Figure 14. Proportion of PLWHs with abnormal aspartate aminotransferases in different age groups (within the same range of CD4+ depletion).

increased demand, and impaired erythropoietin feedback caused by excessive inflammatory cytokines[7-9]. CD4+ T cell depletion led to an exponential increase in the anomalies of anemia-related indicators (hemoglobin, platelets, and leukocytes) (Fig. 3), with the increase becoming more pronounced in older PLWHs (Figs. 4-6), indicating a higher risk of anemia in PLWHs as the condition worsens and age increases.

Compared with healthy individuals, diabetes is more common in people infected with HIV, and the incidence rate of diabetes in HIV infected people is 4 times higher than that in non-HIV-infected people[10]. With the occurrence of CD4+ T cell depletion, we detected that there was only a slight increase in abnormal blood glucose (up to 9.85%) (Fig. 7), but about a quarter of PLWHs aged 60 and above had abnormal blood glucose when their CD4+ count was < 200 (Fig. 8), suggesting that elderly PLWHs would be more susceptible to diabetes.

Several studies have shown that adults and children infected with HIV have an increased risk of developing cardiovascular disease[11,12]. Dyslipidemia is an important determinant of atherosclerosis and cardiovascular disease[13]. Our blood lipid survey results showed that approximately one-quarter of PLWHs in each group had abnormal triglycerides (Fig. 9), but the abnormal rates of triglycerides and cholesterol did not aggravate with the worsening of CD4+ T cell depletion. Under the same CD4+ depletion, aging did not have a noticeable impact on the abnormal rate of triglycerides (Fig. 10), the slight increase in abnormal cholesterol levels may be due to the decrease in metabolic efficiency and the weakened ability of the liver to clear cholesterol as age increases (Fig. 11). Therefore, we believe that there may not be an obvious correlation between dyslipidemia and CD4+ depletion, and even when CD4+T cells were < 200, dyslipidemia did not significantly worsen.

The abnormal rate of ALT and AST in PLWHs with CD4 < 200 was much higher than that in other groups, and little difference in TBIL was observed among the groups (Fig. 12). Meanwhile, aging did not lead to increases in the abnormalities of ALT and AST (Figs. 13 and 14), suggesting that CD4+ depletion rather than aging primarily may affect the hepatic function of PLWHs.

Conclusion

The primary factor affecting the health of PLWHs is the depletion of immune cells caused by HIV-1, with aging also playing a significant role. These two factors are closely related to anemia, followed by liver and kidney dysfunction and abnormal blood sugar levels. There is little correlation between CD4+ T cell depletion and dyslipidemia.

Limitations of this study: (1) The volunteers included were mainly male, making it difficult to distinguish gender differences in the impact of CD4+ depletion. (2) Lack of racial diversity, with almost all participants being Han Chinese. (3) It cannot be absolutely ruled out that certain undetected comorbidities may cause bias in the analysis of results. (4) Due to the small number of patients aged 60 and above, there may be some misjudgments in statistical analysis. (5) Elevated creatinine levels in some PLWHs aged 60 and above may be due to aging, which may have some impact on the analysis of results.

Author contributions

P. Luo and J. Jin: responsible for conducting research, collecting data, analyzing/interpreting data, designing research, and writing drafts; Others, collecting data, analyzing/interpreting data, and conducting clinical follow-up.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study. This study was approved by the Ethics Committee of Xi'an Eighth Hospital (NO.20230606)

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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