Quantitative tumor burden imaging parameters of the spleen at MRI for predicting treatment response in patients with acute leukemia

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ABSTRACT

Objectives: To study the value of standardized volume and intravoxel incoherent motion (IVIM) parameters of the spleen based on tumor burden for predicting treatment response in newly diagnosed acute leukemia (AL).

Methods: Patients with newly diagnosed AL were recruited and underwent abdominal IVIM diffusion-weighted imaging within one week before the first induction chemotherapy. Quantitative parameters of magnetic resonance imaging (MRI) included the standardized volume (representing volumetric tumor burden) and IVIM parameters (standard apparent diffusion coefficient [sADC]; pure diffusion coefficient [D]; pseudo-diffusion coefficient [D^*]; and pseudo-perfusion fraction [f], representing functional tumor burden) of the spleen. Clinical biomarkers of tumor burden were collected. Patients were divided into complete remission (CR) and non-CR groups according to the treatment response after the first standardized induction chemotherapy, and the MRI and clinical parameters were compared between the two groups. The correlations of MRI parameters with clinical biomarkers were analyzed. Multivariate logistic regression was performed to determine the independent predictors for treatment response. Receiver operating characteristic curves were used to analyze the predicted performance.

Results: 76 AL patients (CR: n = 43; non-CR: n = 33) were evaluated. Standardized spleen volume, sADC, D, f, white blood cell counts, and lactate dehydrogenase were significantly different between CR and non-CR groups (all $p < 0.05$). Standardized spleen volume, sADC, and D were correlated with white blood cell and lactate dehydrogenase, and f was correlated with lactate dehydrogenase (all $p < 0.05$). Standardized spleen volume (hazard ratio = 4.055, $p = 0.042$), D (hazard ratio = 0.991, $p = 0.027$), and f (hazard ratio = 1.142, $p = 0.008$) were independent predictors for treatment response, and the combination of standardized spleen volume, D, and f showed more favorable discrimination (area under the curve = 0.856) than individual predictors.

Conclusion: Standardized volume, D, and f of the spleen could be used to predict treatment response in newly diagnosed AL, and the combination of morphological and functional

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parameters would further improve the predicted performance. IVIM parameters of the spleen may be viable indicators for evaluating functional tumor burden in AL.

Abbreviations

ADC	apparent diffusion coefficient
AL	acute leukemia
AUC	area under the curve
CI	confidence interval
CR	complete remission
D	pure diffusion coefficient
D^*	pseudo-diffusion coefficient
DWI	diffusion-weighted imaging
f	pseudo-perfusion fraction
ICC	interclass correlation coefficient
IVIM	intravoxel incoherent motion
LDH	lactate dehydrogenase
NEX	number of excitations
PET-CT	positron-emission tomography-computed tomography
ROC	receiver operating characteristic
ROI	region of interest
sADC	standard apparent diffusion coefficient
SUV	standardized uptake value
SV	spleen volume
WBC	white blood cell

1. Introduction

Leukemia can be considered a highly efficient metastatic cancer, and its treatment has been challenging [1]. Splenic infiltration occurs in up to 80% of patients with leukemia, commonly accompanied by splenomegaly [2–4]. Leukemia cells enter the spleen through sinusoidal vessels in the red pulp and result in increased cellularity with more blasts, pathological angiogenesis, and the expansion of the white pulp [1,5]. Recent evidences also suggested that the spleen could be a sanctuary site for residual disease after treatment and an important source for relapse [6,7]. Thus, splenomegaly was identified as an important clinical indicator of high tumor burden, which was related to poor overall survival in acute leukemia (AL) [8–10]. Some researchers have proposed that early splenectomy based on decreased tumor burden might be considered as a promising adjunct to the treatment for AL [5,11].

Spleen palpation can only detect splenomegaly when the spleen volume (SV) is 2–3 times larger than normal [12]. Some cross-sectional imaging techniques (CT, MRI) have been used to measure two-dimensional spleen size. Three-dimensional quantitative volume assessment considering the spleen's irregular shape can calculate SV coherently and accurately [13,14]. However, standardized SV is deemed as the most accurate parameter to evaluate spleen size, which excludes the effect of age, gender, and body size [15,16]. So, we could try to use quantitatively standardized SV to assess tumor burden and prognosis in AL patients.

Functional tumor burden assessed by imaging methods is an effective supplement to volumetric tumor burden [17–19]. The standardized uptake value (SUV) of the spleen on positron-emission tomography-computed tomography (PET-CT) could be used to evaluate metabolic tumor burden in AL patients [20,21]. A recent study showed that reduced splenic ^{68}Ga-Pentixafor uptake was associated with shorter overall survival in patients with multiple myeloma [22]. Reduced signal intensity of the spleen on diffusion-weighted imaging (DWI) inverted greyscale images has also been linked to a high tumor burden and worse survival in multiple myeloma [23]. Intravoxel incoherent motion (IVIM) is a DWI method that uses a biexponential signal model to enable quantitative parameters that separately reflect tissue microcapillary perfusion and tissue diffusivity. The parameters include: pure diffusion coefficient [D] that reflects tissue cellularity, pseudo-perfusion fraction [f] that represents the fraction of vascular volume, pseudo-diffusion coefficient [D^*] that is related to blood flow velocity, and standard apparent diffusion coefficient (sADC) that is the ADC value derived from biexponential signal model [24–26]. IVIM parameters have been utilized in characterizing solid and hematologic tumors [25–28]. A study also confirmed that IVIM parameters were reliable imaging biomarkers for splenic changes in pancreatitis [29]. We hypothesized that IVIM parameters could be valuable factors to evaluate functional tumor burden based on the higher cellularity and increased angiogenesis of the spleen in patients with AL.

The treatment response to the first induction chemotherapy has been linked to the overall survival for AL patients, early prediction of treatment response facilitates timely regimen adjustment [30]. The purpose of our study is to determine whether the quantitative tumor burden imaging parameters of the spleen are more valuable for assessing treatment response in newly diagnosed AL.

2. Methods

2.1. Study participants

This prospective study was approved by the review board of our institution, and all patients provided the written informed consent. Between April 2020 and June 2022, patients with newly diagnosed AL as determined by the WHO classification of hematopoietic tissue [31,32] were enrolled consecutively in the study. Inclusion criteria were patients who had no known history of splenic disease, splenic surgery or other diseases which may lead to splenic involvement (including immune system diseases, chronic liver disease and cirrhosis), had not previously received any treatment, and were eligible for MRI. Exclusion criteria included refusal of standardized chemotherapy and poor IVIM images quality. The characteristics and baseline clinical biomarkers of patients with AL (e.g., age, sex, peripheral white blood cell [WBC] counts, lactate dehydrogenase [LDH] and bone marrow blasts) were collected. All patients underwent abdominal MRI within one week before the first induction chemotherapy, and recieved standardized chemotherapy according to the National Comprehensive Cancer Network guidelines [33,34]. The treatment responses of AL patients were evaluated after the first induction chemotherapy in accordance with the conventional criteria [33–35]. Complete remission (CR) was defined as normalization of the marrow and peripheral blood with $\leq$5% marrow blasts, a granulocyte count higher than $10^3/\mu L$, a platelet count higher than $100 \times 10^3/\mu L$ and normal differential [35]. Patients who did not achieve CR were divided into non-CR group.

2.2. MRI acquisition

All patients underwent abdominal IVIM DWI in the supine position with a 3.0T MRI scanner (Discovery 750w, GE Healthcare, Waukesha, WI). IVIM DWI was performed using a respiratory-triggered single-shot spin echo-planar imaging pulse sequence, and a spectral spatial excitation pulse was used for fat suppression. The imaging parameters of IVIM DWI were: b = 0, 10, 20, 30, 40, 50, 100 (number of excitations [NEX] = 1), 200 (NEX = 2), 400 (NEX = 3), 800 s/mm^2 (NEX = 4), repetition time = 6000 to 10,000 ms depending on the number of slices to adequately cover the anatomy, echo time = 69.7 ms, slice thickness = 6.0 mm, slice spacing = 2.0 mm, field of view = 40cm × 40 cm, matrix = 128 × 128. The acquisition time was approximately 4 min, depending upon the breathing.

2.3. IVIM imaging analysis

All IVIM images were processed on the workstation (Advantage Windows Workstation 4.6; GE Healthcare) to produce the parameters (sADC, *D, D** and *f*). To reduce the effect of noise and overcome the mathematical instability of the IVIM model, a typical segmented fitting method was used for IVIM calculation, and the specific procedures were conducted as previously described [36–38]. The IVIM images were measured independently by two board-certified abdominal radiologists (with 7 and 3 years of abdominal imaging experience, respectively) who were blinded to clinical information. Regions of interest (ROIs) were manually delineated on each splenic slice of the b = 0 s/mm^2 images by tracing the outline of spleens with the freehand ROI tool. Large vessels as well as areas with gross artifacts were avoided. The ROIs were copied to the sADC, *D, D**, and *f* maps automatically, and the average parameter values and the number of voxels for each ROI were documented. Data for each spleen was expressed as the weighted average of IVIM parameters across all splenic sections.

2.4. Standardized SV calculation

The two abdominal radiologists who were blinded to clinical information performed splenic volume measurements using ITK-SNAP software (version 3.8.0, www.itksnap.org). The spleens were segmented manually by outlining each section of spleens on the b = 0 s/mm^2 images and the volumes were calculated automatically. This method has been validated in previous studies and shown optimal reproducibility [8,14]. In order to account for individual variations in spleen size, standardized SV was calculated using the following formula [39,40]:

$$\text{Standardized SV}(\text{cm}^3) = \frac{\text{SV}}{\text{Body surface area}} = \frac{\text{SV}(\text{cm}^3)}{\sqrt{\frac{\text{height(cm)} \times \text{weight(kg)}}{3600}}}$$

The values were divided just by the numerical value excluding units of body surface area for simplicity [40].

2.5. Statistical analysis

Interobserver agreements for SV and IVIM parameters were evaluated by calculating the interclass correlation coefficient (ICC). Categorical data were tested using the chi-square test. Independent *t*-test or Mann-Whitney *U* test was applied for continuous variables comparison between two groups, as appropriate. Correlation analyses were done using Spearman correlation. Area under the curve (AUC) of the receiver operating characteristic (ROC) analysis was used to evaluate the efficacy of different parameters in prognosis. The optimal cutoff values were determined by the Youden index. All variables with $p < 0.05$ in univariate analysis were incorporated in the multivariate logistic regression analysis, in which standardized SV was treated as a categorical variable according to the optimal threshold and other variables were included as continuous variables. DeLong test was applied to compare the AUC values between the different parameters. Statistical analyses were conducted using SPSS statistical software (version 26.0, IBM) and MedCalc statistical

software (version 20.0.22). $p < 0.05$ was considered statistically significant.

3. Results

3.1. Study participants

85 patients with AL underwent IVIM DWI in the abdomen. 4 patients who refused standardized chemotherapy and 5 patients with inferior quality of IVIM images were excluded. Ultimately, 76 patients with AL (mean age, 44 years $\pm$ 17 [standard deviation]; age range, 13–73 years) were enrolled in this study, including 54 patients with acute myeloid leukemia and 22 patients with acute lymphocytic leukemia. After the first standardized induction chemotherapy, 43 patients achieved CR to treatment, while the remaining 33 patients did not achieve CR (Table 1).

3.2. Inter-reader variability

The ICC values of IVIM parameters were 0.92(95% confidence interval [CI]: 0.88–0.95) for sADC, 0.88(95% CI: 0.80–0.93) for D, 0.65 (95% CI: 0.40–0.79) for D^*, and 0.85(95% CI: 0.77–0.91) for f, and the ICC value of SV was 0.97 (95% CI: 0.94–0.98) (all $p < 0.001$), indicating good or excellent agreement. As a consequence, only the results from the first reader were analyzed in our study.

3.3. Comparisons of MRI and clinical parameters between CR and non-CR groups

In the univariable analysis, the standardized SV, sADC, D, f, WBCs and LDH were associated with treatment response. Standardized SV ($Z = -3.453$, $p = 0.001$), f value ($t = -4.361$, $p < 0.001$), WBC ($Z = -2.924$, $p = 0.005$), and LDH ($Z = -2.835$, $p = 0.003$) of non-CR group were significantly higher than those of CR group, while sADC value ($t = 2.104$, $p = 0.039$) and D value ($t = 3.666$, $p < 0.001$) of non-CR group were significantly lower than those of CR group. Sex ($\chi^2 = 2.204$, $p = 0.138$), age ($t = 0.013$, $p = 0.989$), bone marrow blasts ($Z = -0.157$, $p = 0.875$), and D^* value ($t = 1.175$, $p = 0.244$) showed no significant difference between the two groups (Table 1). Fig. 1 shows the representative IVIM images of the spleen in AL patients from CR Group (a-d) and non-CR Group (e-h).

3.4. Correlations of MRI parameters with clinical biomarkers

Standardized SV showed positive correlation with WBC counts ($r = 0.397$, $p < 0.001$) and LDH ($r = 0.495$, $p < 0.001$). The sADC and D values of the spleen were negatively correlated with WBC counts ($r = -0.414$, $p < 0.001$; $r = -0.489$, $p < 0.001$, respectively) and LDH ($r = -0.232$, $p = 0.044$; $r = -0.235$, $p = 0.041$, respectively), and D value was also negatively correlated with bone marrow blasts ($r = -0.251$, $p = 0.029$). f value showed positive correlation with LDH ($r = 0.567$, $p < 0.001$), while D^* value exhibited no correlation with any clinical biomarker of tumor burden (Table 2).

Standardized SV was negatively correlated with sADC ($r = -0.615$, $p < 0.001$), D ($r = -0.551$, $p < 0.001$) and D^* ($r = -0.412$, $p < 0.001$) values, while positively correlated with f value ($r = 0.396$, $p < 0.001$) (Table 2).

**Table 1**
Participant characteristics and group differences.

Variable	CR (n = 43)	Non-CR (n = 33)	p Value
Sex			0.138[a]
Men	20(46.5%)	21(63.6%)	
Women	23(53.5%)	12(36.4%)	
Age (y)	44 $\pm$ 17	44 $\pm$ 19	0.989[b]
Standardized SV (cm^3)	184.5(122.0–265.6)	266.3(186.0–409.4)	0.001[c]
Threshold of standardized SV			<0.001[a]
Standardized SV $\leq$ 217.9 cm^3	29(67.4%)	8(24.2%)	
Standardized SV > 217.9 cm^3	14(32.6%)	25(75.8%)	
IVIM parameters			
sADC (10^{-3} mm^2/s)	0.95 $\pm$ 0.20	0.86 $\pm$ 0.18	0.039[c]
D (10^{-3} mm^2/s)	0.76 $\pm$ 0.17	0.64 $\pm$ 0.10	<0.001[b]
D^* (10^{-3} mm^2/s)	136.5 $\pm$ 48.0	124.1 $\pm$ 42.7	0.244[b]
f (%)	22.9 $\pm$ 5.9	29.3 $\pm$ 6.9	<0.001[b]
WBC counts ($\times$ 10^9)	5.73(2.49–28.71)	22.29(9.58–96.38)	0.005[c]
LDH (U/L)	319(200–604)	554(313–1036)	0.003[c]
Bone marrow blasts (%)	70.0(48.8–83.0)	73.3(30.4–89.3)	0.875[c]

Data are shown in counts and percentages for categorical data and mean $\pm$ standard deviation or median (interquartile range) for continuous data. AL, acute leukemia; CR, complete remission; D, diffusion coefficient; D^*, pseudo-diffusion coefficient; f, pseudo-perfusion fraction; IVIM, Intravoxel incoherent motion; LDH, lactate dehydrogenase; sADC, standard apparent diffusion coefficient; SV, spleen volume; WBC, white blood cell.

[a] Determined with chi-square test.
[b] Determined with independent t-test.
[c] Determined with Mann-Whitney U test.
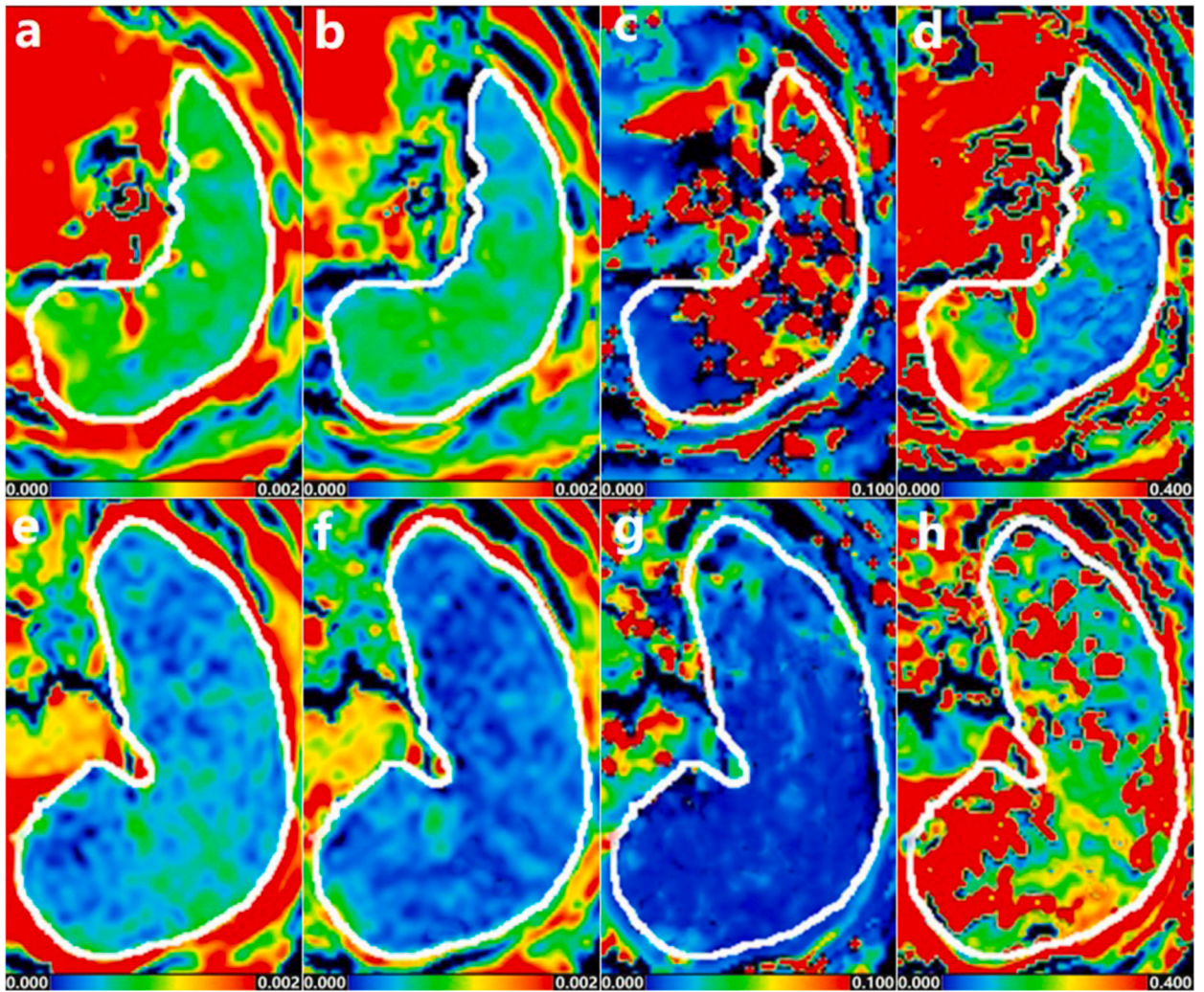
Fig. 1. IVIM parametric maps of the spleen in a representative AL patient who achieved CR after the first induction chemotherapy (top row; a-d, standardized SV = 214.0 cm^3) and another representative AL patient whose treatment response was non-CR (bottom row; e-h, standardized SV = 431.0 cm^3). In the top row, the maps show (a) high value for sADC (0.91×10^{-3} mm^2/s), (b) high value for D (0.67×10^{-3} mm^2/s), (c) high value for D^* (141×10^{-3} mm^2/s), and (d) low value for f (17.5%). In the bottom row, the maps show (e) low value for sADC (0.51×10^{-3} mm^2/s), (f) low value for D (0.32×10^{-3} mm^2/s), (g) low value for D^* (28×10^{-3} mm^2/s), and (h) high value for f (39.4%). IVIM, Intravoxel incoherent motion; AL, acute leukemia; CR, complete remission; SV, spleen volume.

Table 2
Correlations among standardized SV, IVIM parameters and clinical biomarkers in patients with AL.

Parameters	WBC counts		LDH		Bone marrow blasts		Standardized SV	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Standardized SV	0.397	<0.001	0.495	<0.001	0.039	0.740		
sADC	−0.414	<0.001	−0.232	0.044	−0.117	0.314	−0.615	<0.001
D	−0.489	<0.001	−0.235	0.041	−0.251	0.029	−0.551	<0.001
D^*	−0.077	0.510	−0.217	0.060	−0.022	0.847	−0.412	<0.001
f	0.161	0.164	0.567	<0.001	0.011	0.924	0.396	<0.001

AL, acute leukemia; D, diffusion coefficient; D^*, pseudo-diffusion coefficient; f, pseudo-perfusion fraction; IVIM, Intravoxel incoherent motion; LDH, lactate de hydrogenase; sADC, standard apparent diffusion coefficient; SV, spleen volume; WBC, white blood cell.

Table 3
ROC analyses of MRI parameters in predicting treatment response.

Parameters	AUC (95%CI)	Cutoff value	Sensitivity (%)	Specificity (%)	Accuracy (%)	p value
Standardized SV (cm^3)	0.732(0.618, 0.827)	217.9	75.8	69.8	72.4	0.001
sADC (10^{-3} mm^2/s)	0.650(0.523, 0.777)	0.96	78.8	55.8	65.8	0.026
D (10^{-3} mm^2/s)	0.713(0.598, 0.811)	0.83	97.0	34.9	61.8	0.001
f (%)	0.763(0.651, 0.853)	22.8	87.9	55.8	69.7	<0.001
Combined parameter (Standardized SV+ D + f)	0.856(0.756, 0.926)		87.9	72.1	78.9	<0.001

AL, acute leukemia; CI, confidence intervals; D, diffusion coefficient; f, pseudo-perfusion fraction; IVIM, Intravoxel incoherent motion; MRI, magnetic resonance imaging; ROC, Receiver operating characteristic; sADC, standard apparent diffusion coefficient; SV, spleen volume.
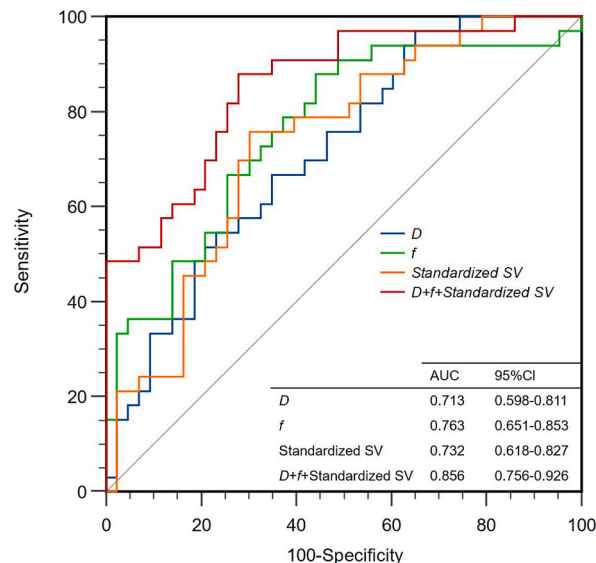
Fig. 2. Receiver operating characteristic curves of D (AUC = 0.713), f (AUC = 0.763), standardized SV (AUC = 0.732), and the combined parameter ($D + f$ + standardized SV, AUC = 0.856) for predicting treatment response in patients with newly diagnosed AL. The combination of D, f, and standardized SV demonstrated better diagnostic performance than the individual predictors. AL, acute leukemia; SV, spleen volume.

3.5. The prognostic values of quantitative tumor burden MRI parameters

In the ROC analyses for evaluating the treatment response in patients with AL, standardized SV demonstrated an AUC of 0.732, with the cutoff of 217.9 cm^3. The AUC values for sADC, D, and f were 0.650, 0.713, and 0.763, respectively. The sensitivity, specificity, accuracy, and corresponding optimal cut-off value of each parameter are summarized in Table 3.

The standardized SV (>217.9 cm^3 or ≤217.9 cm^3), sADC, D, f, WBC, and LDH were incorporated into multivariate logistic regression analysis, and the result showed that standardized SV (hazard ratio, 4.055; 95% CI: 1.052, 15.627; p = 0.042), D value (hazard ratio, 0.991; 95% CI: 0.983, 0.999; p = 0.027), and f value (hazard ratio, 1.142; 95% CI: 1.036, 1.258; p = 0.008) were independent predictors for treatment response. In the ROC analyses, the combination of D, f, and standardized SV demonstrated better diagnostic efficacy than the single indicator D (Z = 2.702, p = 0.007), f (Z = 2.011, p = 0.044) and standardized SV (Z = 2.532, p = 0.011), with an AUC value of 0.856 (Table 3, Fig. 2).

4. Discussion

Splenomegaly is an important clinical indicator of high tumor burden in AL patients [8–10]. Our results showed that increased standardized volume (SV > 217.9 cm^3), lower sADC, lower D, and higher f values of the spleen were associated with unfavorable treatment response in patients with AL. Moreover, the combination of standardized volume and IVIM parameters of the spleen can further improve the prediction performance of treatment response.

Achieving CR after the first induction chemotherapy has been linked to a longer overall survival for AL patients [30]. In our study, 43/76 patients achieved CR. Splenomegaly is considered a qualitative indicator of high tumor burden in AL for prognostic evaluation [8–10]. Although one-dimensional, two-dimensional caliper-based, and three-dimensional quantitative volume techniques have been used as tools reflecting tumor burden for assessing overall survival in patients with AL [8,9], SV hinges upon individual factors, such as age, gender, and body size. Thus, standardized SV that accounts for the individual difference is needed to accurately evaluate the severity of splenomegaly. The results showed that increased standardized SV was linked to an unfavorable treatment response with a

standardized SV cutoff of 217.9 cm^3, which would provide reliable parameters for precisely evaluating the effect of spleen size on the prognosis of AL. In addition, our study showed standardized SV was correlated with lower *D* (cellularity) and higher *f* (angiogenesis) values, the result could indirectly reflect the pathological changes of splenomegaly in AL patients : (1) increased cellularity with more blasts which enter the spleen through large and fenestrated sinusoidal vessels in the red pulp [1]; and (2) pathological angiogenesis of leukemic spleen, which can promote the rapid expansion of malignant blasts in the spleen and the progression of the disease [5].

sADC and *D* values were associated with treatment response after the first induction chemotherapy in our study. Reduced splenic signal intensity on DWI inverted greyscale images has been revealed to be correlated with a worse prognosis in multiple myeloma [23]. Compared with conventional ADC acquired from DWI, the sADC was calculated from multiple b-values and *D* was the pure diffusion coefficient excluding the effect of microcirculation. Therefore, both sADC and *D* can more precisely reflect water diffusion in tissues and evaluate cellularity. The lower sADC and *D* values indicated an unfavorable treatment response, which may reflect the higher tumor burden based on hypercellularity.

Our study suggested that higher *f* value tended to indicate an unfavorable treatment response in AL. The parameters of contrast-enhanced CT and dynamic contrast-enhanced MRI, which may be indicators of increased angiogenesis, have been used to access splenic perfusion and infiltration of hematologic malignancies in several studies [41–43]. IVIM provides an alternative way to estimate the degree of perfusion without the use of contrast agents by measuring the fast diffusion component in tissues. Previous studies showed that *f* value of bone marrow was positively correlated with microvessel density in AL patients, while *f* could reflect the difference in vascularity between benign and malignant hematological disease [44,45]. In our study, *f* value showed moderately positive correlation with LDH, which is one of the factors promoting tumor angiogenesis [46]. Therefore, higher *f* value in the spleen of AL patients may reflect the higher tumor burden based on increased angiogenesis. *D** is another perfusion-related parameter that represents the rate of vascular flow [24–26]. However, *D** value was not associated with treatment response, which might be due to the errors and instability in the *D** determination. *D** values in our study showed relatively lower interobserver agreement compared with other IVIM parameters. Previous studies also demonstrated poor measurement reproducibility and high variation for *D** [38,47,48], which may be affected by respiratory trigger techniques, distribution of b values, fitting methods, and other factors [36,37,49]. Thus, further technical improvements, such as the Bayesian-Probability algorithm [50], which accounts for measurement uncertainty, are needed to strengthen the robustness of *D** and obtain more meaningful findings.

In our study, standardized SV, *f*, and *D* values of the spleen were independent predictors of treatment response in AL, and the combination of them could further improve the predictive performance of treatment response with a higher AUC than the individual predictors. The result suggested that combined morphological (standardized SV) and functional (*f* and *D*) indicators could be beneficial to predict prognosis more precisely.

Elevated LDH and high WBC counts are clinical markers of high tumor burden other than splenomegaly, which are related to poor prognosis in AL. Our study demonstrated that a larger standardized SV was correlated with higher WBC counts and LDH. Additionally, sADC, *D*, and *f* values showed significant correlation with clinical biomarkers of tumor burden. The findings provide viable imaging markers for the evaluation of tumor burden based on abnormal tumor function.

There were several limitations in the current study. First, the association of IVIM parameters and histologic features would aid in validating the pathophysiologic meanings of the splenic IVIM parameters. Second, the sample size was small, and further studies need to be performed to explore the differences in subgroups of AL, such as acute lymphoblastic leukemia and acute myelocytic leukemia. Third, splenomegaly was also an immunological phenomenon in AL, although this effect was small [41]. Finally, the study evaluated only the therapeutic efficacy of first induction chemotherapy, and the longer-term prognostic value of quantitative tumor burden imaging parameters of the spleen in AL will be explored in the next study.

In conclusion, standardized volume and IVIM parameters of the spleen were associated with treatment response in AL patients. The combination of morphological and functional parameters would predict the treatment response more precisely. IVIM parameters of the spleen may be viable markers for tumor burden evaluation in AL.

Ethics statement

This study was reviewed and approved by [Ethics Committee of the Second Hospital of Shanxi Medical University], with the approval number: [2020YX037].

All participants/patients (or their proxies/legal guardians) provided informed consent to participate in the study.

All participants/patients (or their proxies/legal guardians) provided informed consent for the publication of their anonymised case details and images.

Author contribution statement

Wenjin Bian: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper. Jianling Zhang, Qianqian Huang, Jianting Li: Performed the experiments; Contributed reagents, materials, analysis tools or data. Weiran Niu, Xiaoli Song, Sha Cui, Qian Zheng: Analyzed and interpreted the data; Wrote the paper. Jinliang Niu: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper. Xiaohong Joe Zhou: Conceived and designed the experiments; Wrote the paper.

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