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Splenic Radiofrequency Ablation with Splenic Artery Balloon Occlusion for Hypersplenism in Hepatocellular Carcinoma

Huiying Yan
Tianjin Medical University Cancer Institute & Hospital

Linze Xu
Tianjin Medical University Cancer Institute & Hospital

Junbo Cao
Tianjin Medical University Cancer Institute & Hospital

Rentao Li
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Xiaofeng Mu
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Qi Qi
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Xihao Zhang
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Junchao Yao
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Linlin Fu
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Luying Fan
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Xiaojing Xie
Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Di He

Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Wenxin Li

Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Mao Yang

Tianjin Medical University Cancer Institute & Hospital

Yong Xu

Tianjin Medical University Cancer Institute & Hospital

Tongguo Si

Tianjin Medical University Cancer Institute & Hospital

Xing Li

Tianjin Medical University Cancer Institute & Hospital

Huikai Li

Tianjin Medical University Cancer Institute & Hospital

Yang Liu

yang_liu@tmu.edu.cn

Tianjin Medical University Cancer Institute and Hospital: Tianjin Medical University Cancer Institute & Hospital https://orcid.org/0000-0001-6450-9509

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Title

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Authors:

Huiying Yan[1], Linze Xu[1], Junbo Cao[1], Rentao Li[2], Xiaofeng Mu[2], Qi Qi[2], Xihao Zhang[2], Junchao Yao[2], Linlin Fu[2], Luying Fan[2], Xiaojing Xie[2], Di He[2], Wenxin Li[2], Mao Yang[3,4], Yong Xu[5,6], Tongguo Si[3,4], Xing Li[5,6], Huikai Li[1,7], Yang Liu[1,7]

Affiliations:

[1] Department of Hepatobiliary Cancer, Liver Cancer Center, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China;

Hospital telephone: +86 22 2334 0123

[2] Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China;

Hospital telephone: +86 22 6017 7666

[3] Department of Interventional Therapy, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China;

Hospital telephone: +86 22 2334 0123

[4] Department of Interventional Therapy, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China;

Hospital telephone: +86 22 6017 7666

[5] Department of Ultrasound Diagnosis and Treatment, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China;

Hospital telephone: +86 22 2334 0123

[6] Department of Ultrasound Diagnosis and Treatment, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China;

Hospital telephone: +86 22 6017 7666

[7] Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

Hospital telephone: +86 22 6017 7666

Author degrees and e-mail addresses:

Huiying Yan: BM, yanhuiying@tmu.edu.cn

Linze Xu: BM, xulinze1002@tmu.edu.cn

Junbo Cao: BM, 1010894141@qq.com

Rentao Li: MD, 13821171879@163.com

Xiaofeng Mu: MMed, fenglei557@163.com

Qi Qi: MMed, qiqi@tmu.edu.cn

Xihao Zhang: MMed, zxh15510801035@163.com

Junchao Yao: MMed, yaojunchao.123@163.com

Linlin Fu: MMed, fulinlin2023@163.com

Luying Fan: MMed, fanluying20@163.com

Xiaojing Xie: BM, xxjfjxxjfj@163.com

Di He: MMed, hedi0606@163.com

Wenxin Li: MMed, Liwenxin1998@126.com

Mao Yang: MMed, matchym@126.com

Yong Xu: MD, xuyongcmu@126.com

Tongguo Si: MD, sitongguo@tjmuch.com

Xing Li: BM, ipcclx@163.com

Huikai Li: MD, lihuikai@tjmuch.com

Yang Liu: MD, yang_liu@tmu.edu.cn

Co-first authors:

Huiying Yan and Linze Xu contributed equally to this work.

Corresponding Authors: Xing Li, Huikai Li, and Yang Liu

Xing Li, BM.

Department of Ultrasound Diagnosis and Treatment, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China;

Department of Ultrasound Diagnosis and Treatment, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China;

E-mail: ipcclx@163.com

Tel: +86 13820344321

Huikai Li, MD.

Department of Hepatobiliary Cancer, Liver Cancer Center, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China; Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

E-mail: lihuikai@tjmuch.com

Tel: +86 18622228639

Yang Liu, MD.

Department of Hepatobiliary Cancer, Liver Cancer Center, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin 300060, China; Department of Hepatobiliary and Pancreatic Oncology, Tianjin Cancer Hospital Airport Hospital, National Clinical Research Center for Cancer, Tianjin 300308, China

E-mail: yang_liu@tmu.edu.cn

Tel: +86 17612261906

Abbreviations

HCC, hepatocellular carcinoma; RFA, radiofrequency ablation; PLT, platelet count; WBC, white blood cell; CTCAE, Common Terminology Criteria for Adverse Events; PFS, progression-free survival; OS, overall survival; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; RECIST, Response Evaluation Criteria in Solid Tumors; ANC, absolute neutrophil count; SAEs, serious adverse events; DVT, deep vein thrombosis; NA, not assessed; NE, not evaluable; NR, not reached; PSE, partial splenic embolization; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; CI, confidence interval; BMI, body mass index; KPS, Karnofsky Performance Status; ALBI, albumin–bilirubin; BCLC, Barcelona Clinic Liver Cancer; IQR, interquartile range; ORR, objective response rate; DCR, disease control rate

Abstract

Background: Cytopenias can complicate antitumor treatment in hepatocellular carcinoma (HCC) with portal hypertension-related hypersplenism. We examined treatment receipt, blood-count trajectories, and adverse events after splenic radiofrequency ablation (RFA) with splenic artery balloon occlusion.

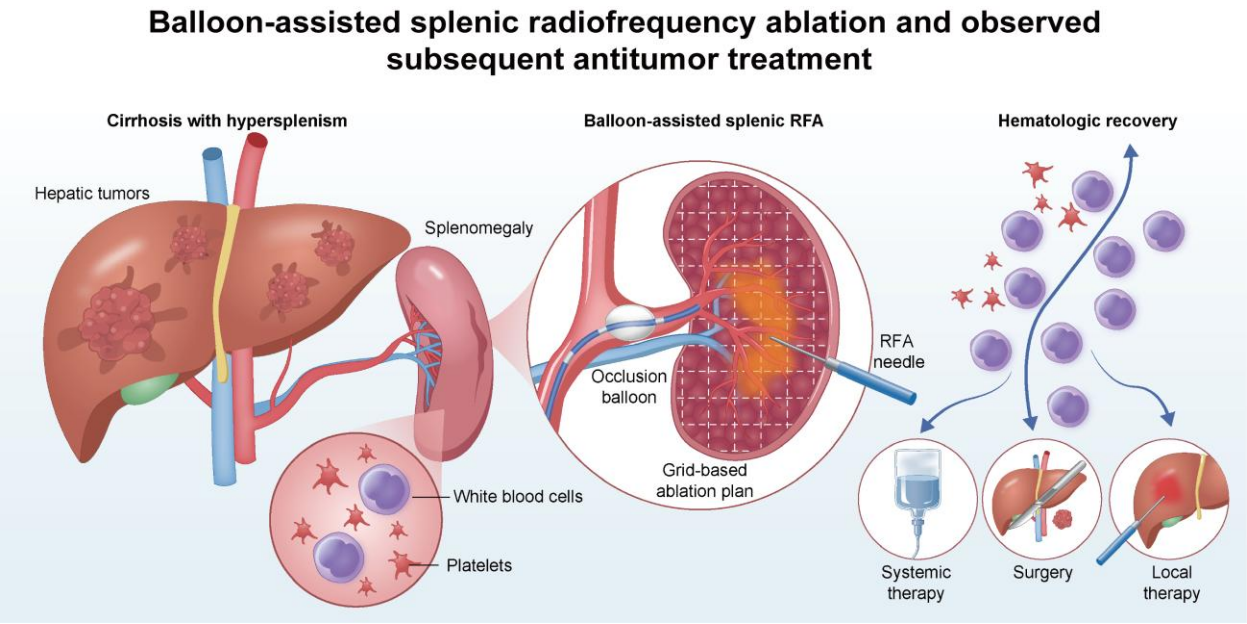
Methods: This single-center retrospective cohort included 36 patients treated between August 2023 and November 2025. The primary descriptive outcome was antitumor treatment receipt within 60 days, including treatment on the procedure date. Additional outcomes included blood-count threshold attainment, adverse events, and exploratory oncologic outcomes.

Results: Antitumor treatment was received by 21/36 patients (58.3%) within 60 days, including 8 treated on the procedure date, and by 28/36 (77.8%) during follow-up. Median platelet counts were 54.0 × 10^9/L at baseline and 176.0 × 10^9/L on day 7. Later laboratory observations were incomplete. Grade 3 adverse events were recorded in 15/36 patients (41.7%); no grade 4–5 events or procedure-attributed deaths were reported.

Conclusions: In this selected cohort, early platelet increases and antitumor treatment receipt were observed. Same-day treatment and the absence of a comparator prevent attributing treatment delivery to hematologic recovery. Comparative studies are needed to determine whether this approach facilitates treatment and to characterize thrombotic and other complications.

Keywords: Portal hypertension; Cytopenia; Thrombocytopenia; Leukopenia; Treatment delivery; Locoregional therapy; Systemic therapy; Hematologic recovery; Venous thrombosis; Patient selection

Graphical Abstract



Introduction

Hepatocellular carcinoma (HCC) management requires selection and sequencing of local and systemic therapies according to tumor burden and patient fitness [1,2,3]. In cirrhosis, thrombocytopenia and other cytopenias can complicate invasive procedures and treatment planning [4]. Hepatic reserve and portal hypertension create additional constraints [5]. For patients with hypersplenism, a clinically relevant outcome is whether antitumor treatment is delivered, not simply whether blood counts increase.

Splenectomy, partial splenic embolization (PSE), and splenic thermal ablation have been investigated for hypersplenism [6,7,8,9,10,11]. The potential to facilitate systemic treatment has also been discussed for splenectomy in advanced HCC [7]. For splenic ablation, treatment timing and complications need to be considered alongside hematologic response. Related reports include balloon-assisted splenic microwave ablation [12], an APASL conference abstract [13], and a Chinese-language spleen-ablation report [14]. The present analysis describes antitumor treatment receipt in an RFA cohort.

We therefore examined antitumor treatment receipt in a retrospective cohort of patients with HCC and portal hypertension-related hypersplenism who underwent ultrasound-guided percutaneous splenic RFA with splenic artery balloon occlusion. The primary descriptive outcome was treatment receipt within 60 days, including treatment on the procedure date. We also described treatment timing and type, blood-count trajectories and threshold attainment, adverse events, and exploratory oncologic outcomes.

Materials and methods

Study Design and Patient Assessment

This single-center retrospective cohort included patients with HCC and portal hypertension-related hypersplenism who underwent ultrasound-guided percutaneous splenic RFA combined with temporary splenic artery balloon occlusion at Tianjin Cancer Hospital Airport Hospital (August 2023–November 2025). Eligibility criteria were (1) histopathologically confirmed or clinically diagnosed HCC; (2) portal hypertension-related hypersplenism, defined as imaging-confirmed splenomegaly accompanied by one or more peripheral cytopenias in cirrhosis with portal hypertension, after excluding other major causes of cytopenias; (3) an inadequate or unsustained hematologic response after ≥2 weeks of pharmacologic supportive treatment or >3 repeated treatment courses. Exclusion criteria were: (1) a hematologic disorder or another predominant cause of cytopenias; (2) severe cardiac, pulmonary, or renal dysfunction precluding angiography, general anesthesia, or the planned procedure; (3) previous splenectomy, partial splenic embolization, splenic ablation, or another spleen-directed intervention.

Baseline assessments comprised the latest preprocedural laboratory and imaging examinations. Postprocedural laboratory assessments were assigned to days 1, 3, and 7, and these windows: 1 month (30 ± 14 days), 3 months (90 ± 30 days), 6 months (180 ± 45 days), 9 months (270 ± 45 days), and 12 months (365 ± 60 days). Within each window, the measurement closest to the target day was used. Patients were followed from the date of splenic RFA until death, loss to follow-up, or data cutoff (November 9, 2026), whichever occurred first.

Intervention

In all patients, ultrasound-guided percutaneous splenic RFA [11] was performed under temporary splenic artery balloon occlusion in the same session.

Under local anesthesia, right femoral arterial access was obtained, and a catheter was advanced into the celiac trunk using digital subtraction angiography. Splenic arteriography delineated splenic arterial anatomy and assessed splenic morphology and perfusion. A balloon catheter (diameter, 8 mm; length, 4 or 6 cm; U3513084; Bard Medical Technology [Shanghai] Co., Ltd., Shanghai, China) was positioned in the main splenic artery and inflated with ioversol until splenic arterial occlusion was confirmed angiographically.

Splenic RFA was performed under general anesthesia and real-time ultrasound guidance. When necessary, artificial pleural effusion was induced by instilling 1,500–2,000 mL of sterile saline into the left pleural cavity to improve visualization and protect adjacent structures. An RFA electrode (device model: R150E, consumable model: SS-RFAS1-2030/SS-RFAS1-1010/SS-RFAS1-2020; Surgnova Healthcare Technologies, China) was inserted into the planned ablation area, avoiding the splenic hilum and major vessels. After initial fixed-position ablation, incremental electrode redirection targeted ablation of 60–70% of the splenic parenchyma. Contrast-enhanced ultrasound then assessed the nonperfused area and excluded active bleeding. The balloon remained inflated, and the catheter and vascular sheath were retained for 48 h. After comprehensive bleeding-risk assessment by the interventional team and other relevant clinicians, the catheter and sheath were removed, followed by arterial access site compression.

Outcomes

The primary descriptive outcome was antitumor treatment receipt within 60 days of splenic RFA, including treatment on the procedure date (day 0). Inclusion of same-day treatment means that this outcome does not establish a sequence of hematologic recovery followed by treatment. Other outcomes comprised treatment receipt at 30, 90, and 180 days and during follow-up; first treatment type; hematologic trajectories; and attainment of PLT thresholds of ≥50, ≥75, and ≥100

× 10^9/L, WBC thresholds of ≥3 and ≥4 × 10^9/L, and ANC ≥1.5 × 10^9/L. These thresholds describe blood counts, not eligibility for a specific treatment regimen. Adverse events were graded using CTCAE version 6.0. Exploratory outcomes were associations with 60-day treatment receipt, tumor response assessed using RECIST 1.1, PFS, OS, and NLR, PLR, and SII.

Statistical Analysis

Continuous variables were summarized as medians with interquartile ranges or ranges; categorical variables as n/N (%). Follow-up hematologic parameters were compared with baseline using two-sided Wilcoxon signed-rank tests, with complete patient pairs for each parameter and time point and no imputation. Univariable logistic regression yielded unadjusted odds ratios (ORs) and 95% CIs. Categorical comparisons used Fisher's exact test. Given the small cohort, no multivariable model was fitted. Analyses were exploratory, with two-sided nominal P values and no correction for multiple comparisons. Lack of statistical significance was not interpreted as absence of association. Response rates used the response-evaluable subset as denominator. PFS and OS were estimated using Kaplan–Meier methods, and follow-up using reverse Kaplan–Meier estimation. The reported analyses used R 4.2.2.

Results

Cohort assembly and baseline characteristics

Of 45 patients assessed for eligibility, 36 were included in the analytic cohort; 4 were excluded because splenic artery balloon occlusion was not performed, and 5 because they underwent splenic microwave ablation rather than RFA (Fig. 1). Liver function was Child–Pugh class A in 22/36 (61.1%), class B in 13/36 (36.1%), and class C in 1/36 (2.8%). The median baseline PLT and WBC counts were 54.0 (42.5–70.0) × 10^9/L and 3.7 (2.8–5.3) × 10^9/L, respectively (Table 1).

Before spleen-directed therapy, prior antitumor therapy was documented in 27/36 patients (75.0%), including systemic therapy in 25/36 (69.4%), interventional therapy in 21/36 (58.3%), and surgery in 1/36 (2.8%). The most common recorded treatment-limiting conditions were esophagogastric varices (23/36, 63.9%), thrombocytopenia (16/36, 44.4%), ascites (15/36, 41.7%), leukopenia (10/36, 27.8%), and previous variceal bleeding (6/36, 16.7%). These non-mutually exclusive conditions frequently occurred concurrently (Fig. 2a, Table 2, Supplementary Fig. 1a, b).

Antitumor treatment timing and receipt

Hospital utilization was summarized separately from treatment receipt (Table 2). Hospitalization or readmission was recorded in 30/36 patients (83.3%); 28 had admissions for antitumor treatment and 2 had unplanned readmissions unrelated to antitumor treatment or splenic ablation. Recorded cumulative readmission proportions were 29/36 (80.6%) by 30 days and 30/36 (83.3%) by 90 days.

During follow-up, 28/36 patients (77.8%) received antitumor treatment. The first treatment was local therapy in 12 patients, systemic therapy in 12, and surgery in 4 (Fig. 2c). Cumulative treatment receipt at 30, 60, 90, and 180 days was 15/36 (41.7%), 21/36 (58.3%), 23/36 (63.9%), and 27/36 (75.0%), respectively (Fig. 2d). Cumulative counts included 8 patients treated on day 0. The reported median interval to first treatment was 21 days (range, 0–292). Eight patients (22.2%) received no antitumor treatment during follow-up.

Hematologic trajectories and threshold attainment

Median PLT counts at baseline and days 1, 3, and 7 were 54.0, 79.5, 101.0, and 176.0 × 10^9/L, respectively (Fig. 3a). At months 1, 3, 6, 9, and 12, the corresponding medians were 184.0, 131.0, 137.5, 126.0, and 109.0 × 10^9/L. Median WBC counts were 3.7, 11.5, 11.8, and

10.9 × 10^9/L at baseline and days 1, 3, and 7, and 6.5 × 10^9/L at month 1 (Fig. 3b). Median ANC increased from 2.5 × 10^9/L at baseline to 10.0, 9.6, and 9.6 × 10^9/L on days 1, 3, and 7 (Supplementary Table 1). Measurements were available in 36 patients at baseline and days 1 and 3, 30 at day 7, and 21, 13, 12, 7, and 7 at months 1, 3, 6, 9, and 12, respectively. Later medians describe the patients with available measurements rather than sustained within-patient improvement across the cohort.

At baseline, 20/36 (55.6%), 7/36 (19.4%), and 0/36 patients met PLT thresholds of ≥50, ≥75, and ≥100 × 10^9/L, respectively. The corresponding proportions were 34/36 (94.4%), 25/36 (69.4%), and 19/36 (52.8%) on day 3; 27/30 (90.0%), 27/30 (90.0%), and 26/30 (86.7%) on day 7; and 20/21 (95.2%), 18/21 (85.7%), and 16/21 (76.2%) at month 1 (Fig. 3c; Supplementary Table 2). All observed WBC counts on days 1, 3, and 7 were ≥3 × 10^9/L. ANC was ≥1.5 × 10^9/L in 33/36 (91.7%) at baseline, 36/36 (100.0%) on day 1, and 35/36 (97.2%) on day 3. Patient-level threshold status and exploratory laboratory comparisons are shown in Supplementary Figs. 1c and 2a. NLR, PLR, and SII varied over time (Supplementary Table 2).

Exploratory associations with antitumor treatment receipt within 60 days

Exploratory univariable logistic regression examined associations with treatment receipt within 60 days, including same-day treatment (Supplementary Fig. 2b). For baseline PLT as a continuous variable, each 10 × 10^9/L increase in PLT count was associated with higher odds of treatment receipt (OR, 1.79; 95% CI, 1.10–2.91; $P = 0.020$). In a categorical analysis, patients with a baseline PLT count ≥50 × 10^9/L had higher unadjusted odds of treatment receipt than those with <50 × 10^9/L (OR, 8.80; 95% CI, 1.92–40.30; $P = 0.005$). In group comparisons, 16 of 20 patients (80.0%) with a baseline PLT count ≥50 × 10^9/L received antitumor treatment within 60 days, compared with 5 of 16 patients (31.3%) with a PLT count <50 × 10^9/L ($P = 0.006$; Fig.

3d). Higher baseline aspartate aminotransferase levels were also positively associated with treatment receipt, with each 10-U/L increase corresponding to higher odds of treatment receipt (OR, 2.05; 95% CI, 1.01–4.12; $P = 0.045$). In contrast, the proportion receiving treatment within 60 days did not differ significantly by baseline WBC count ($P = 0.260$; Supplementary Fig. 2c). No other nominal associations were reported (all $P > 0.05$). These unadjusted analyses do not identify independent predictors or establish a platelet threshold for treatment selection.

Safety and adverse events after spleen-directed therapy

The maximum recorded CTCAE grade was 0 in 4 patients (11.1%), 1 in 9 (25.0%), 2 in 8 (22.2%), and 3 in 15 (41.7%) (Fig. 4a; Supplementary Table 3). No grade 4–5 events or procedure-attributed deaths were reported. Recorded events included fever in 19/36 patients (52.8%), DVT in 8/36 (22.2%), bleeding in 4/36 (11.1%), renal failure and portal vein thrombosis in 3/36 each (8.3%), splenic vein thrombosis in 2/36 (5.6%), and splenic abscess and superior mesenteric vein thrombosis in 1/36 each (2.8%) (Fig. 4b). Among patients with DVT, grades 1, 2, and 3 were recorded in 2, 2, and 4 patients, respectively. One grade 3 DVT was pre-existing; these counts therefore do not represent the incidence of new postprocedural DVT. No deaths were attributed to DVT. Event categories overlapped within patients.

Exploratory oncologic outcomes after subsequent treatment

Tumor response after subsequent antitumor therapy was assessed exploratorily given treatment heterogeneity and incomplete response assessment. Of the 36 patients, 15 were evaluable for tumor response, including 2 with partial response, 3 with stable disease, and 10 with progressive disease. Among the remaining 21 patients, 10 had no post-treatment tumor assessment (not assessed, NA), whereas 11 underwent post-treatment imaging but could not be

evaluated according to the response criteria used for this analysis (not evaluable, NE; Fig. 4c and Supplementary Table 4).

Among the 15 response-evaluable patients, the objective response rate was 13.3% (2/15), and the disease control rate was 33.3% (5/15). Changes in target-lesion size among patients with measurable disease and adequate post-treatment imaging are presented in the waterfall plot (Fig. 4d). Because these responses followed heterogeneous subsequent treatments, they were summarized descriptively and were not used to estimate the antitumor efficacy of spleen-directed therapy. Representative imaging findings are shown in Supplementary Fig. 3.

From splenic RFA, median OS was not reached (NR) (95% CI, 19.0–NR; Fig. 4e) and median PFS was 7.3 months (95% CI, 4.9–NR; Fig. 4f). Median follow-up was 27.6 months (95% CI, 24.7–30.0). At cutoff, 15/36 patients had died (41.7%) and 24/36 had a recorded PFS event (66.7%; Supplementary Table 5). These estimates are descriptive and do not establish a survival benefit of spleen-directed therapy.

Discussion

This cohort describes antitumor treatment delivery in patients with HCC and hypersplenism selected for splenic RFA with balloon occlusion. Early platelet increases were observed, and treatment was received by 21/36 patients within 60 days and 28/36 during follow-up. Reporting treatment receipt alongside blood counts addresses a clinical outcome not captured by threshold attainment alone. However, the inclusion of 8 patients treated on the procedure date prevents interpreting the 60-day proportion as a measure of treatment enabled by hematologic recovery.

Platelet increases are consistent with the hematologic rationale for spleen-directed treatment, but blood counts are only one component of treatment planning. Liver function, bleeding risk, tumor status, and regimen-specific requirements remain relevant. Early WBC and

ANC elevations may also reflect postprocedural inflammation, while incomplete later measurements limit conclusions about durability. Splenectomy, PSE, and splenic ablation have already been investigated for hypersplenism [6,7,8,9,10,11,12]. Combining RFA with balloon occlusion is intended to control splenic perfusion during ablation while retaining nonablated tissue. Prior balloon-occlusion hemodynamic work was performed in a different procedural setting [15]. The present study does not isolate the contribution of balloon occlusion or establish superiority over alternative interventions.

Complications are central to the clinical interpretation of these findings. Grade 3 events were recorded in 15/36 patients, with thromboses, bleeding, renal failure, and a splenic abscess. No grade 4–5 events or procedure-attributed deaths were reported, but this does not establish safety. The zero recorded serious-event count does not resolve this concern: CTCAE grade describes severity, not seriousness, and event ascertainment was retrospective. DVT counts included a pre-existing event and do not represent new-event incidence. Infection and thrombosis after splenectomy in other populations [16,17] and complications after PSE [18,19,20] provide clinical context, not comparative risk estimates for this cohort.

Oncologic outcomes describe the subsequent clinical course under heterogeneous antitumor treatments. Only 15/36 patients were response-evaluable, and ORR and DCR used this subset as the denominator. Incomplete imaging and the absence of a comparator prevent attribution of response or survival to splenic RFA. Similarly, exploratory changes in NLR, PLR, and SII do not establish an immune mechanism or a validated prognostic marker.

Important limitations are the small sample, single-center retrospective design, and lack of a comparator. Selection for splenic intervention and later cancer treatment depended on clinical judgment, leaving substantial potential for confounding. Same-day treatment limits the temporal

interpretation of the primary outcome. Unadjusted exploratory associations, incomplete laboratory follow-up, limited response evaluation, and retrospective safety ascertainment further constrain inference. Future comparative studies should define treatment eligibility before intervention, document treatment decisions and timing, and use standardized follow-up and safety adjudication.

In summary, early platelet increases and antitumor treatment receipt were observed around splenic RFA with balloon occlusion in selected patients with HCC and hypersplenism. These findings warrant comparative evaluation of treatment delivery and complications; they do not establish that the procedure enabled treatment or improved survival.

Declarations

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Competing Interests

The authors have no conflicts of interest to declare.

Author contributions

Huiying Yan: investigation, methodology, formal analysis, and writing – original draft. Linze Xu: methodology, formal analysis, and writing – original draft. Junbo Cao: investigation, methodology, and formal analysis. Rentao Li, Xiaofeng Mu, and Qi Qi: methodology and investigation. Xihao Zhang, Junchao Yao, Linlin Fu, and Luying Fan: investigation and formal

analysis. Xiaojing Xie, Di He, and Wenxin Li: data analysis and methodology. Mao Yang, Yong Xu, and Tongguo Si: operation. Xing Li: operation, investigation, and data analysis. Huikai Li: conceptualization, methodology, and data analysis. Yang Liu: conceptualization, methodology, and supervision. All authors contributed to critical review and revision of the manuscript.

Ethics approval and consent to participate

The study protocol was approved by the Medical Ethics Committee of Tianjin Cancer Hospital Airport Hospital and conformed to the ethical guidelines of the 1975 Declaration of Helsinki (approval date: August 14, 2026; approval no.: LWK-2026-0035). The requirement to obtain informed consent from patients was waived by the committee due to the retrospective nature of this study.

Data Availability

Summary data are provided in the article and supplementary material. Requests for additional de-identified data may be directed to the corresponding authors and will be considered subject to institutional requirements, ethics approval, and applicable privacy restrictions.

AI-assisted editing: OpenAI Codex (OpenAI) was used to assist with scientific and language editing, cross-document consistency checks, and verification of reported aggregate counts. No patient-level observations were generated or imputed by the tool. Responsibility for the data, analyses, references, and final manuscript remains with the authors.

References

1 Yang X, Yang C, Zhang S, et al. Precision treatment in advanced hepatocellular carcinoma. Cancer Cell. 2024;42(2):180–197. https://doi.org/10.1016/j.ccell.2024.01.007

2 Vogel A, Meyer T, Sapisochin G, et al. Hepatocellular carcinoma. Lancet. 2022;400(10360):1345–1362. https://doi.org/10.1016/S0140-6736(22)01200-4

3 Du JJ, Yang F, Dong W, et al. Revisiting the role of local treatments in the era of targeted therapy and immunotherapy for hepatocellular carcinoma. World J Surg Oncol. 2025;23(1):323. https://doi.org/10.1186/s12957-025-03963-3

4 Gallo P, Terracciani F, Di Pasquale G, et al. Thrombocytopenia in chronic liver disease: physiopathology and new therapeutic strategies before invasive procedures. World J Gastroenterol. 2022;28(30):4061–4074. https://doi.org/10.3748/wjg.v28.i30.4061

5 Zhang N, Lu L, Cao B, et al. Liver protection of CACA technical guidelines for holistic integrative management of cancer. Holist Integr Oncol. 2025;4:28. https://doi.org/10.1007/s44178-025-00157-5

6 Beji H, De La Fouchardière C, Desseigne F, et al. Thrombocytopenia due to hypersplenism in oncological disease: partial splenic embolization during palliative treatment. Diagn Interv Imaging. 2015;96(4):383–386. https://doi.org/10.1016/j.diii.2014.08.005

7 Zhang EL, Zhang ZY, Huang ZY. Splenectomy may facilitate systemic therapy for advanced hepatocellular carcinoma with hypersplenism. Hepatobiliary Surg Nutr. 2023;12(1):137–139. https://doi.org/10.21037/hbsn-22-545

8 Liang P, Gao Y, Zhang H, et al. Microwave ablation in the spleen for treatment of secondary hypersplenism: a preliminary study. Am J Roentgenol. 2011;196(3):692–696. https://doi.org/10.2214/AJR.10.4193

9 Liu Q, Ma K, Song Y, et al. Two-year follow-up of splenic radiofrequency ablation in patients with cirrhotic hypersplenism: does increased hepatic arterial flow induce liver regeneration? Surgery. 2008;143(4):509–518. https://doi.org/10.1016/j.surg.2007.11.016

10 Martins GL, Bernardes JP, Rovella MS, et al. Radiofrequency ablation for treatment of hypersplenism: a feasible therapeutic option. World J Gastroenterol. 2015;21(20):6391–6397. https://doi.org/10.3748/wjg.v21.i20.6391

11 Feng K, Ma K, Liu Q, et al. Randomized clinical trial of splenic radiofrequency ablation versus splenectomy for severe hypersplenism. Br J Surg. 2011;98(3):354–361. https://doi.org/10.1002/bjs.7367

12 Gao X, Ou Y, Xu Y, et al. [Analysis of the efficacy and safety of splenic artery balloon occlusion combined with splenic microwave ablation in the treatment of hepatocellular carcinoma complicated with cirrhosis and hypersplenism]. Chin J Hepatobiliary Surg. 2025;31(1):49–53. Chinese. https://doi.org/10.3760/cma.j.cn113884-20240826-00256

13 Xu Y, Li H, Si T, et al. Mobile ablation for secondary hypersplenism in hepatocellular carcinoma patients with liver cirrhosis: a safety and efficacy study. Hepatol Int. 2026;20(Suppl 1):S704. https://doi.org/10.1007/s12072-026-11095-3

14 Qi Q, Wang Z, Guo Y, et al. [Efficacy analysis of spleen ablation in hepatocellular carcinoma with portal hypertension and hypersplenism]. Chin J Hepatobiliary Surg. 2026;32(9):641–644. Chinese. https://doi.org/10.3760/cma.j.cn113884-20260323-00098

15 Yoshimatsu R, Yamagami T, Tanaka O, et al. Hemodynamic changes after balloon occlusion of the splenic artery during balloon-occluded retrograde transvenous obliteration for gastric varices. J Vasc Interv Radiol. 2012;23(9):1207–1212. https://doi.org/10.1016/j.jvir.2012.06.010

16 Ogbue OD, Bahaj W, Kewan T, et al. Splenectomy outcomes in immune cytopenias: treatment outcomes and determinants of response. J Intern Med. 2024;295(2):229–241. https://doi.org/10.1111/joim.13742

17 Boyle S, White RH, Brunson A, et al. Splenectomy and the incidence of venous thromboembolism and sepsis in patients with immune thrombocytopenia. Blood. 2013;121(23):4782–4790. https://doi.org/10.1182/blood-2012-12-467068

18 Hayashi H, Beppu T, Okabe K, et al. Therapeutic factors considered according to the preoperative splenic volume for a prolonged increase in platelet count after partial splenic embolization for liver cirrhosis. J Gastroenterol. 2010;45(5):554–559. https://doi.org/10.1007/s00535-009-0185-9

19 Cai M, Huang W, Lin C, et al. Partial splenic embolization for thrombocytopenia in liver cirrhosis: predictive factors for platelet increment and risk factors for major complications. Eur Radiol. 2016;26(2):370–380. https://doi.org/10.1007/s00330-015-3839-4

20 Zhang L, Zhang ZG, Long X, et al. Severe complications after splenic artery embolization for portal hypertension due to hepatic cirrhosis. Risk Manag Healthc Policy. 2020;13:135–140. https://doi.org/10.2147/RMHP.S234628

Figure Legends

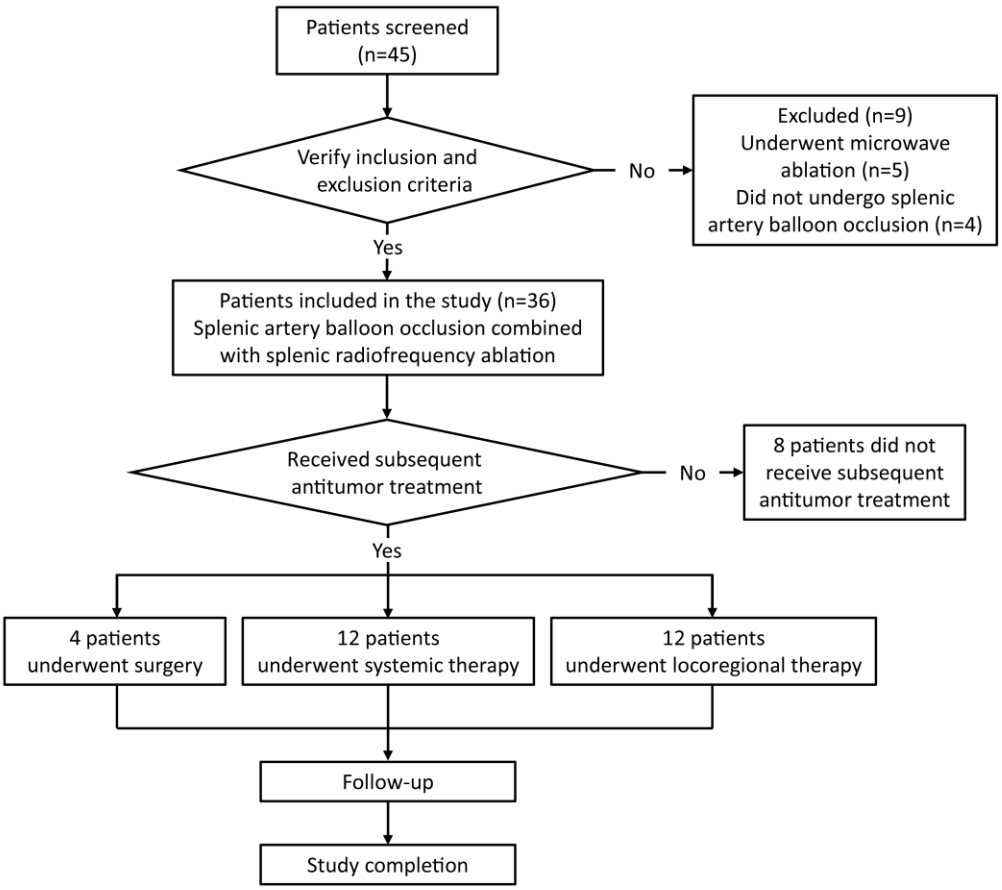

Fig. 1 Flow diagram of participant selection

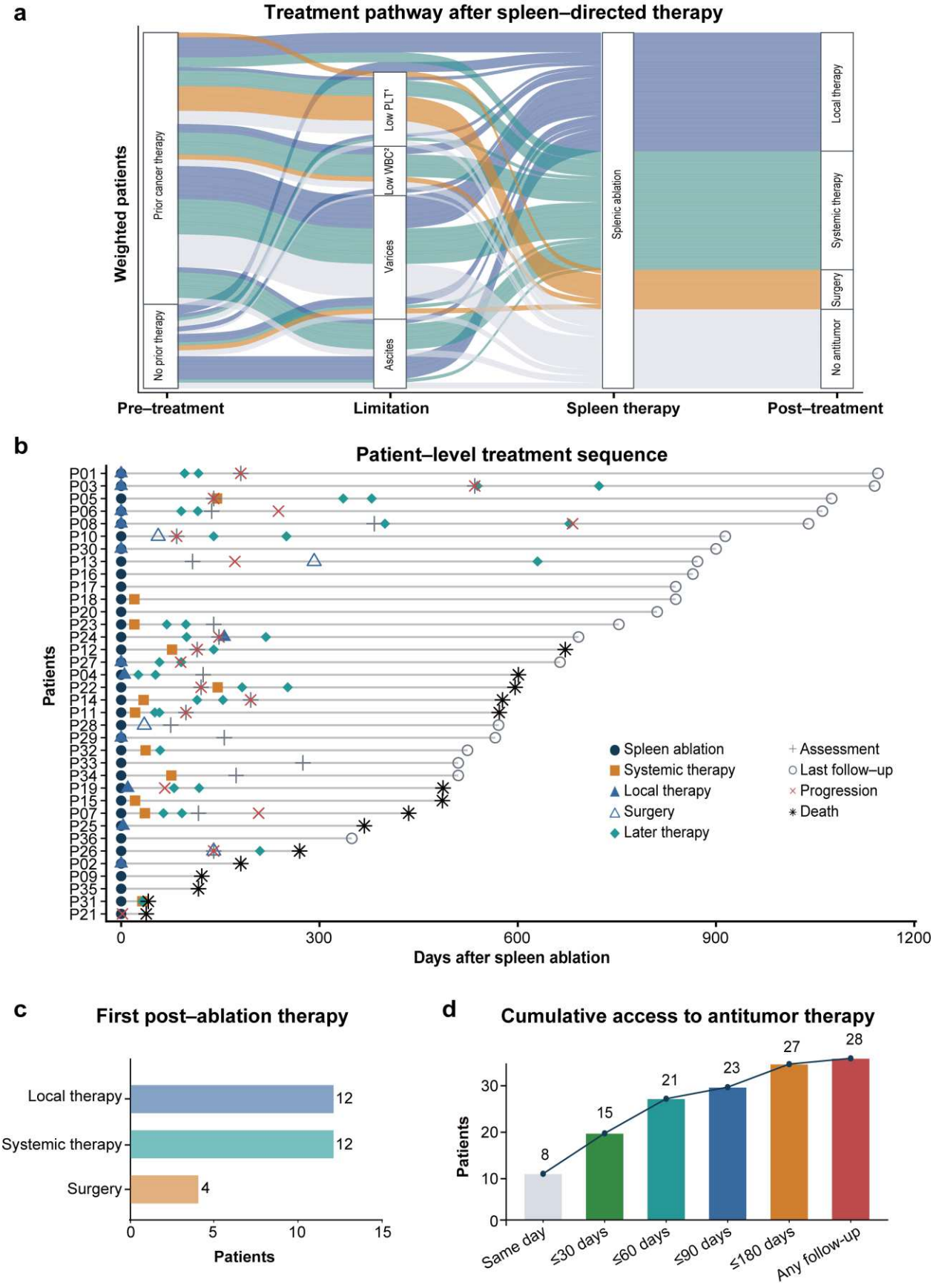
a
Treatment pathway after spleen–directed therapy
Weighted patients
Prior cancer therapy
No prior therapy
Low PLT¹
Low WBC²
Varices
Ascites
Splenic ablation
Local therapy
Systemic therapy
Surgery
No antitumor
Pre–treatment
Limitation
Spleen therapy
Post–treatment
b
Patient–level treatment sequence
Patients
P01
P03
P05
P06
P08
P10
P30
P13
P16
P17
P18
P20
P23
P24
P12
P27
P04
P22
P14
P11
P28
P29
P32
P33
P34
P19
P15
P07
P25
P36
P26
P02
P09
P35
P31
P21
Spleen ablation
Systemic therapy
Local therapy
Surgery
Later therapy
Assessment
Last follow–up
Progression
Death
0
300
600
900
1200
Days after spleen ablation
c
First post–ablation therapy
Local therapy
Systemic therapy
Surgery
12
12
4
0
5
10
15
Patients
d
Cumulative access to antitumor therapy
Patients
0
10
20
30
8
15
21
23
27
28
Same day
≤30 days
≤60 days
≤90 days
≤180 days
Any follow-up

Fig. 2 Recorded treatment-limiting conditions and treatment trajectories. **a** Pathways from recorded baseline conditions to antitumor treatment. **b** Patient-level treatment sequences. c Type of first antitumor treatment on or after the splenic RFA date. d Cumulative treatment receipt, including day 0, at the reported time points and during follow-up. Same-day treatment was recorded in 8 patients and does not establish that postprocedural blood-count recovery enabled treatment. [1]PLT <50 × 10⁹/L. [2]WBC <3 × 10⁹/L. PLT, platelet count; WBC, white blood cell count.

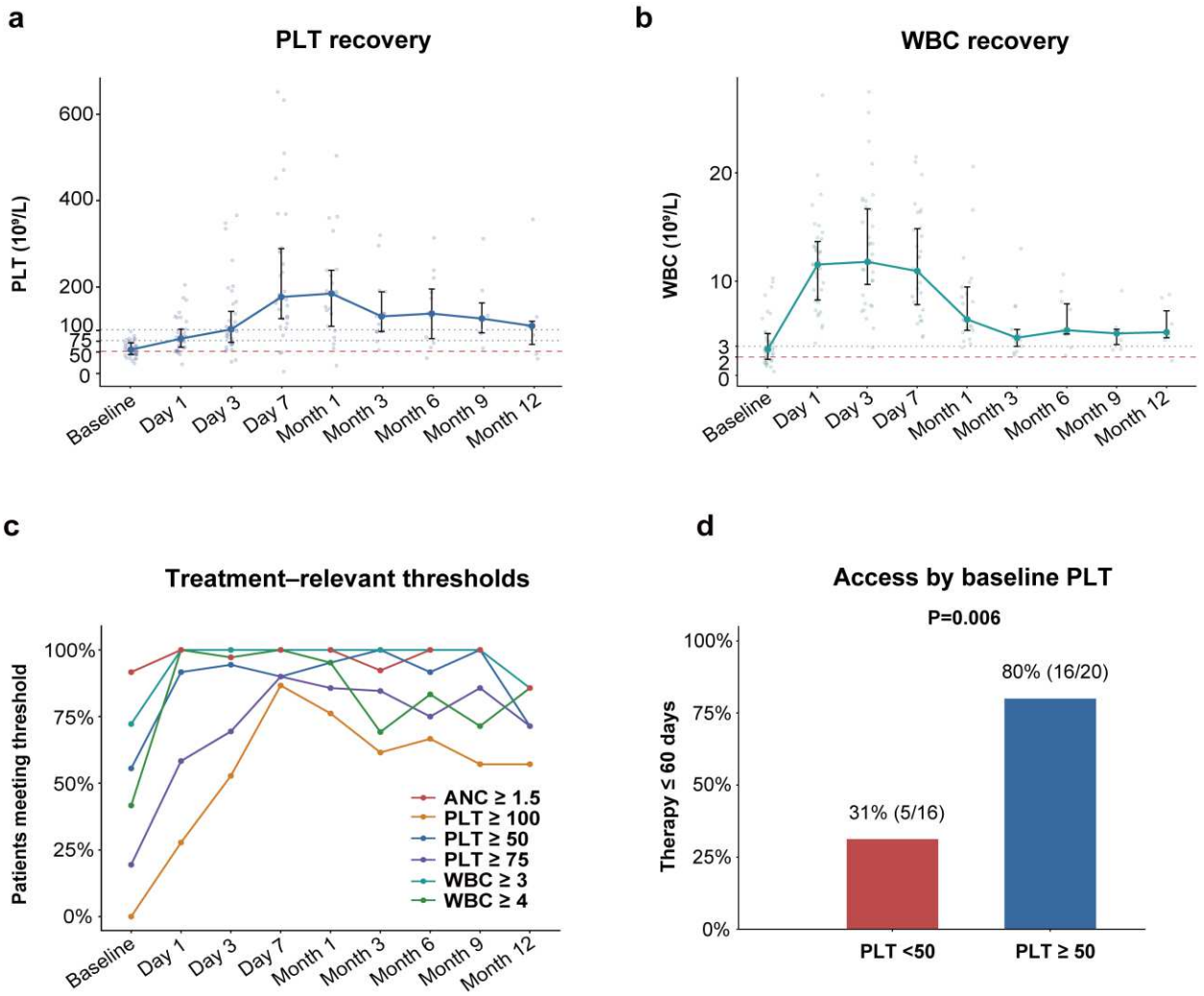

Fig. 3 Hematologic trajectories and threshold attainment after spleen-directed therapy. **a** PLT count over time. **b** WBC count over time. **c** Proportions of patients meeting reported hematologic

thresholds at each time point. **d** Proportions receiving antitumor treatment within 60 days (including day 0), stratified by baseline platelet count. Dots in (**a**) and (**b**) represent individual measurements; connected points and error bars indicate median values and interquartile ranges. Dashed lines indicate the blood-count thresholds used in this analysis. ANC, absolute neutrophil count.

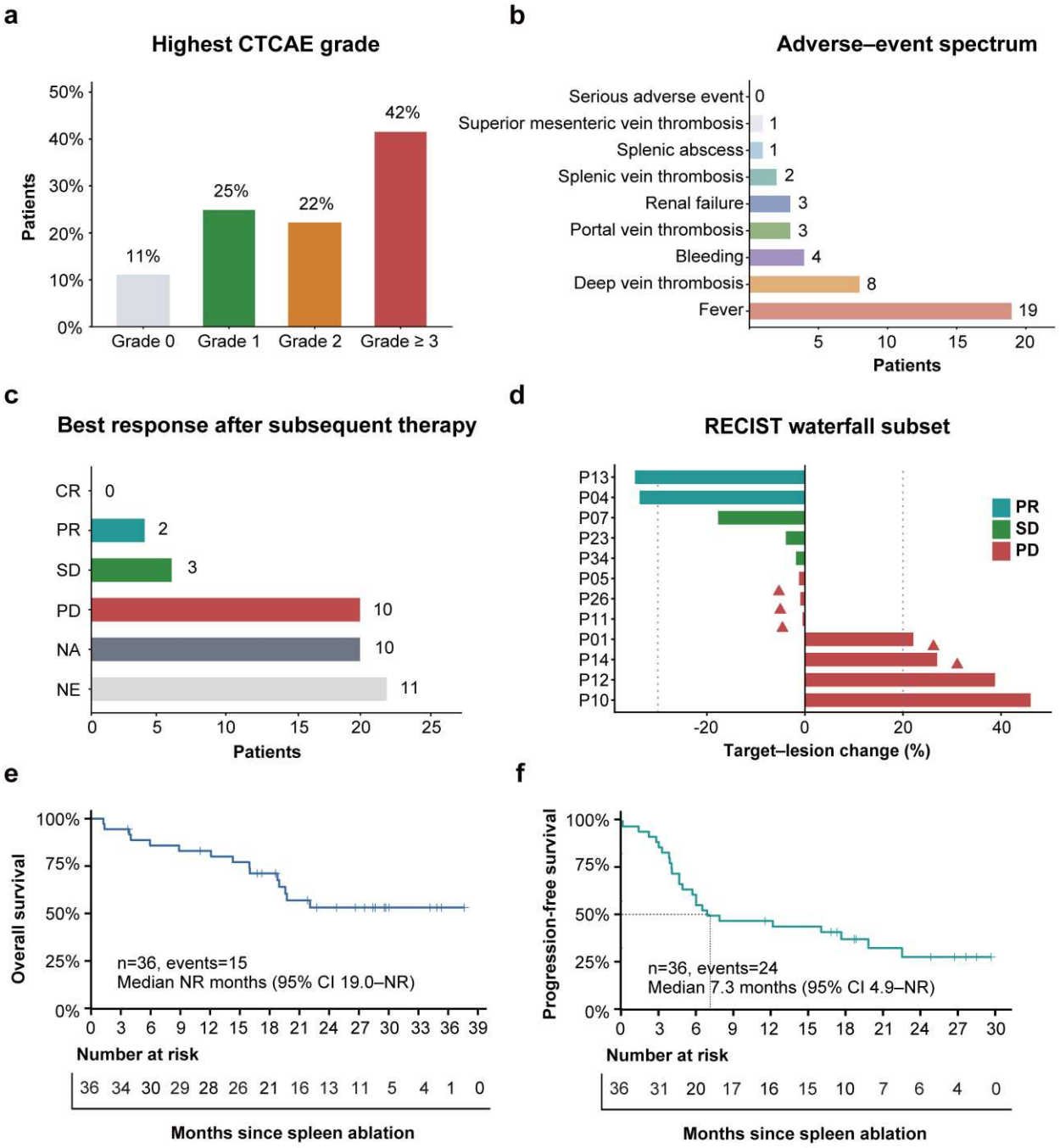

Fig. 4 Recorded adverse events and exploratory oncologic outcomes. **a** Maximum CTCAE grade per patient. **b** Frequencies of recorded events; categories overlap, and DVT counts include one pre-existing grade 3 event. The serious-event count is shown as recorded. c Response categories in the full cohort: 15 patients were response-evaluable, 10 were not assessed (NA), and 11 were

not evaluable (NE). d Target-lesion changes in the 12 patients included in the waterfall plot; this subset is not the denominator for ORR or DCR. **e** Overall survival and f progression-free survival, both from splenic RFA. Tick marks indicate censoring. CI, confidence interval; CR, complete response; CTCAE, Common Terminology Criteria for Adverse Events; DVT, deep vein thrombosis; NR, not reached; P, patient; PD, progressive disease; PR, partial response; SD, stable disease.

Table

Table 1 Baseline characteristics of patients

Characteristic	Patients (N=36)
Age, years, median (IQR)	56.0 (51.0–64.0)
Sex, n (%)	
Male	23/36 (63.9%)
Female	13/36 (36.1%)
BMI, median (IQR)	22.9 (20.4–25.5)
KPS, median (IQR)	90 (90–90)
Child-Pugh score, n (%)	
A	22/36 (61.1%)
B	13/36 (36.1%)
C	1/36 (2.8%)
ALBI grade, n (%)	

Characteristic	Patients (N=36)
1	9/36 (25.0%)
2	26/36 (72.2%)
3	1/36 (2.8%)
BCLC stage, n (%)	
A	9/36 (25.0%)
B	10/36 (27.8%)
C	17/36 (47.2%)
Maximum tumor diameter, cm, median (IQR)	5.2 (2.5–9.4)
Macrovascular invasion, n (%)	4/36 (11.1%)
Lymph-node metastasis, n (%)	5/36 (13.9%)
Portal vein diameter, mm, median (IQR)	13.0 (11.0–15.0)
Prior antitumor therapy, n (%)	27/36 (75.0%)
Prior systemic therapy, n (%)	25/36 (69.4%)
Prior interventional therapy, n (%)	21/36 (58.3%)
Prior surgery, n (%)	1/36 (2.8%)
Pre-ablation PLT, 109/L, median (IQR)	54.0 (42.5–70.0)
Pre-ablation WBC, 109/L, median (IQR)	3.7 (2.8–5.3)

Data are presented as median (IQR) or n/N (%). Twenty patients had previously received both systemic and interventional therapies. ALBI, albumin–bilirubin; BCLC, Barcelona Clinic Liver

Cancer; BMI, body mass index; IQR, interquartile range; KPS, Karnofsky Performance Status; PLT, platelet; WBC, white blood cell.

Table 2 Treatment-limiting conditions and antitumor treatment receipt around splenic ablation

Characteristic	Value
Treatment limitations	
Low PLT count[1]	16/36 (44.4%)
Low WBC count[2]	10/36 (27.8%)
Varices	23/36 (63.9%)
Variceal bleeding	6/36 (16.7%)
Ascites	15/36 (41.7%)
Others[3]	4/36 (11.1%)
Readmission	30/36 (83.3%)
Non-antitumor treatment	2/36 (5.6%)
Antitumor treatment	28/36 (77.8%)
Local therapy	12/36 (33.3%)
Surgery	4/36 (11.1%)
Systemic therapy	12/36 (33.3%)
Timing of first treatment	
Same day[4]	8/36 (22.2%)
Within 30 days	15/36 (41.7%)

Characteristic	Value
Within 60 days	21/36 (58.3%)
Within 90 days	23/36 (63.9%)
Within 180 days	27/36 (75.0%)
Median time, days (range)	21 (0–292)

Data are presented as n/N (%) unless otherwise indicated. Some patients had more than one treatment-limiting factor. Percentages may not sum to 100% because of rounding. [1]PLT <50 × 10^9/L. [2]WBC <3 × 10^9/L. [3]Others included patients who, after multidisciplinary team discussion, were considered eligible for splenic ablation and balloon occlusion. [4]Antitumor treatment administered on the same day as splenic ablation.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Graphicalabstract.pdf
- SupplementaryMaterial.docx