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Research article

Postoperative SIRS after thermal ablation of HCC: Risk factors and short-term prognosis

Xiaorong Peng [a,1], Jibin Xing [a,1], Hao Zou [b,1], Mengya Pang [c], Qiannan Huang [d], Shaoli Zhou [a], Kai Li [d,**], Mian Ge [a,*]

[a] *Department of Anesthesiology, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*
[b] *Department of Anesthesiology, Foshan Women and Children Hospital, Foshan, China*
[c] *Department of Anesthesiology, Shenzhen Children's Hospital, Shenzhen, China*
[d] *Department of Ultrasound, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

A R T I C L E I N F O

Keywords:
SIRS
Hepatocellular carcinoma
Thermal ablation
Risk factors
Short-term prognosis

A B S T R A C T

Background: We aimed to explore the potential risk factors and short-term prognosis for SIRS after thermal ablation of hepatocellular carcinoma (HCC).
Methods: Data from patients with HCC who underwent thermal ablation in the Third Affiliated Hospital of Sun Yat-sen University between January 2015 and August 2021 were retrieved from the perioperative database. Pre-, intra- and postoperative data between SIRS group and non-SIRS group were compared and multivariate logistic regression analysis was performed to identify the risk factors for SIRS after thermal ablation.
Results: A total of 1491 patients were enrolled and 234 (15.7 %) patients developed SIRS after thermal ablation. Compared with those without SIRS, patients with SIRS had a longer hospital stay, higher hospitalization costs and higher risk of more severe postoperative complications. In the multivariate logistic regression analysis, current smoking (OR 1.58, 95 %CI 1.09–2.29), decreased HCT (OR 1.51,95 %CI 1.11–2.04), NEUT $< 1.5 \times 10^9$/L(OR 1.74, 95 %CI 1.14–2.65), NEUT% < 0.5 or > 0.7 (OR 1.36, 95 %CI 1.01–1.83) and PT > 16.3s (OR 2.42, 95 %CI 1.57–3.74) were significantly associated with postoperative SIRS.
Conclusions: Current smoking, decreased HCT, neutropenia, abnormal percentage of neutrophils and prolonged PT are the independent risk factors for SIRS after thermal ablation of HCC, which worsens outcomes of patients. This study can help identify high-risk population and guide appropriate care so as to reduce the incidence of postoperative SIRS.

1. Introduction

Hepatocellular carcinoma (HCC) is the sixth common cancer worldwide [1]. Thermal ablations (including microwave ablation and radiofrequency ablation), with the advantages of minimally invasive, low cost and short hospital stay, have been recommended as one of the first-line curative treatment for early-stage HCC [2–4]. The complications after thermal ablations are usually mild compared to

* Corresponding author.
** Corresponding author.
E-mail addresses: likai@mail.sysu.edu.cn (K. Li), gemiansums@163.com (M. Ge).
[1] These authors contributed equally to the work.

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surgical resection, but system inflammatory response commonly occurs, featured in a significant increase of plasma inflammatory cytokines such as TNF-α and IL-6 [5], which are essential mediators of systemic inflammatory response syndrome (SIRS) [6].

SIRS is widely recognized as a potential warning of impending severe conditions such as sepsis, multiple organ dysfunction syndrome and multiple organ failure [7–9]. We have reported that 14.4 % cases occur postoperative SIRS after thermal ablation of liver tumor and postoperative SIRS was a major risk factor associated with major complications [10]. Previous studies have shown that systemic inflammation is a hallmark of acute decompensation of cirrhosis, and presented that systemic inflammation through dysfunction of one or more of the major organ systems may be involved in the development of acute decompensation of cirrhosis [11]. Much evidence suggested that SIRS had a negative effect on the outcome of cirrhotic patients [12–14]. Given that the great majority of HCC cases arise in a background of cirrhosis [15], postoperative SIRS after thermal ablation may aggravate the diseases. Early identification is crucial to decision-making and improving prognosis. However, there are limited investigations on the postoperative SIRS after thermal ablation of HCC. Therefore, we sought to assess the incidence and risk factors of SIRS after thermal ablation of HCC and further evaluate the impact of postoperative SIRS on the short-term prognosis.

2. Materials and methods

2.1. Study design and population

This retrospective study was approved by the Ethical Committee of The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China ([2021]02-379-01). Data of patients with HCC who underwent thermal ablation in the Third Affiliated Hospital of Sun Yat-sen University from January 2015 to August 2021 were retrieved from the Electronic Health Record system. Some patients underwent thermal ablation many times for tumor recurrence in our hospital, with only the first procedure included in the final analysis for the statistical independence. Patients with preoperative SIRS, undergoing thermal ablation combined with liver resection or with incomplete clinical data were excluded.

2.2. Thermal ablation

All thermal ablations, including microwave ablation (MVA) and radiofrequency ablation (RFA), were performed under ultrasound guidance by senior interventional sonographers with six years or more of experience performing this procedure. Ablation was performed under tracheal general anesthesia. RFA or MWA was selected according to tumor size, location and patient status. RFA was preferred for lesions directly adjacent to critical organs and structures, such as major hepatic vessel, diaphragm, gastrointestinal tract, gallbladder, and major intrahepatic bile duct, or in difficult puncture locations. MWA was preferred among patients with tumors $>$ 3 cm in maximum diameter, distance to critical organs and structures $>$ 5 mm, or abnormal coagulation function. All the ablation procedures were aimed for complete ablation. Patients underwent a multidisciplinary board assessment for deciding on thermal ablation.

2.3. Data collection

Based on previous studies, the preoperative data collected as follows: age, gender, body mass index (BMI), smoking history; ASA score (ASA II, patients with mild systemic diseases; ASA III, patients with severe systemic diseases; ASA IV, patients with severe systemic disease that is a constant threat to life; ASA V, moribund patients who are not expected to survive without surgery; ASA VI, brain-dead patients whose organs are being removed for donor purposes) [16]; Child-Pugh grade; albumin-bilirubin (ALBI) score [was calculated by serum bilirubin and albumin: $\log_{10}$ bilirubin(μmol/L) $\times$ 0.66 $-$ 0.085 $\times$ albumin(g/L); grade I, II, III were ≤ -2.60, -2.60 to ≤ -1.39, > -1.39, respectively] [17]; comorbidities (cirrhosis and diabetes), previous surgical history, antibiotic use (referring to preoperative therapeutic antibiotic use during hospital stay and excluding preoperative antibiotic prophylaxis on the day of surgery); number of lesions; BCLC grade; Maximum tumor size,; AFP level; and preoperative laboratory tests, including white blood cell (WBC), red blood cell (RBC), platelet count (PLT), hematocrit (HCT), hemoglobin (HGB), neutrophils (NEUT), blood urea nitrogen (BUN), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin (ALB), total bilirubin (TBILI), direct bilirubin (DBILI), indirect bilirubin (IBILI), creatinine (CREAT), activated partial thromboplastin time (APTT), prothrombin time (PT), prothrombin time-international normalized ratio (PT-INR) and fibrinogen (Fib).

The intraoperative data included operative duration, medicine use including intravenous anesthetics (propofol and etomidate), opioids (fentanyl, sufentanil, remifentanil and oxycodone), cisatracurium, non-steroidal anti-inflammatory drugs (parecoxib and flurbiprofen axetil), steroids, and ulinastatin, and fluid therapy (including crystal solution, colloid solution, red blood cells as well as sodium bicarbonate).

2.4. Definition of outcomes

The primary outcome was SIRS during the first 7 postoperative days that defined by presence of two or more of the following criteria (1) body temperature $> 38\,^{\circ}$C or $< 36\,^{\circ}$C, (2) heart rate $>$ 90 bpm, (3) WBC count $>12 \times 10^9$/L or $< 4 \times 10^9$/L, (4) respiratory rate $>$ 20/min or $PaCO_2 < 32$ mmHg [18]. Secondary outcomes were also evaluated and included complications occurred within 7 days after surgery (including pneumonia, acute respiratory distress syndrome, acute left ventricular insufficiency, cardiac arrest, cerebral infarction, acute kidney injury, hyperkalemia and lactic acidosis), total cost of anesthesia, cost of hospitalization, total and postoperative length of hospital stay. Diagnostic criteria for these complications are listed in the supplemental data. Lenth of follow-up after surgery was also collected.

2.5. Statistical analysis

Statistical analysis was performed using R statistical software. Patients were grouped into SIRS group or non-SIRS group. Normally distributed and non-normally distributed variables were presented as mean ± standard deviation and as median (1st, 3rd quartiles), respectively. Categorical variables were shown as number and percentage. Student's *t*-test was used to compare normally distributed data and Mann-Whitney rank sum test was used to compare for skewed data. Chi-square test or Fisher's exact test was applied to analyze categorical variables.

As potentially non-linear associations between risk factors and outcome would conceal their underlying effects, we performed multivariate logistic regression analysis (stepwise backward) to adjust the effect of putative factors on SIRS and derived ORs (odds ratios). Based on the literatures, in addition to variables with potential significance ($P < 0.1$), demographic factors (including sex, age, smoking history and BMI classification), foci number and cirrhosis were also further subjected to stepwise multivariate logistic regression model. The final model was chosen according to Akaike Information Criterion in backward elimination. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Incidence of SIRS after thermal ablation

A total of 2027 cases undergoing thermal ablation for HCC were collected, of whom 536 were excluded according to exclusion criteria, leaving 1491 cases to be enrolled in the final analysis (Fig. 1). The baseline characteristics were shown in Table 1. The median (interquartile) age was 56.0 (47.3, 64.0) yr and majority of patients were male (1248, 83.7 %). 234 (15.7 %) patients developed SIRS within 7 days after surgery and the median length of follow-up after surgery is 5.0 days (Table 2).

3.2. Prognosis of patients with or without postoperative SIRS

Compare with non-SIRS group **(Table 2),** those with SIRS had a higher risk of postoperative pneumonia (8.1 % vs 1.8 %), acute respiratory distress syndrome (2.1 % vs 0.2 %), and lactic acidosis (3.4 % vs 0.3 %) ($P < 0.01$ for all). And two patients in the SIRS group suffered cardiac arrest. Patients with SIRS also had significantly higher hospitalization costs (4.2 vs 3.6, thousand yuan, $P < 0.01$) and a longer hospital stay (14.0 days vs 11.0 days, $P < 0.01$) **(Table 2).**

3.3. Univariate analysis

Preoperative characteristics of patients with or without SIRS were shown in Table 2 and 3. There was no significance in age, sex, BMI, BMI classification, ASA score, Child-Pugh grade, ALBI grade, comorbidities, previous surgical history, antibiotic use BCLC grade, maximum tumor size, AFP level or number of lesions between the two groups. The proportions of patients with fever in SIRS group was significantly higher than that in non-SIRS group ($P = 0.02$). As for preoperative laboratory data, non-SIRS and SIRS groups were

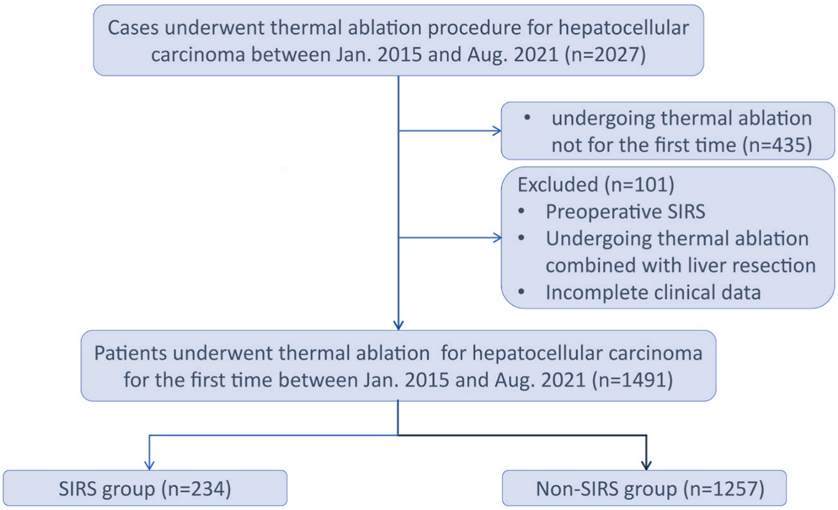

Fig. 1. Flowchart of study population screened and enrolled.

Table 1
Preoperative clinical characteristics of patients with or without postoperative SIRS.

Characteristics	All (n = 1491)	Non-SIRS (n = 1257)	SIRS (n = 234)	*P* value
Age	56.0(47.3, 64.0)	56.0(47.0, 64.0)	56.0(48.0, 64.0)	0.43
Sex, male	1248 (83.7 %)	1052 (83.7 %)	196 (83.8 %)	0.98
BMI, kg/m^2	22.9 (20.6, 25.2)	22.9 (20.6, 25.2)	22.6 (20.4, 25.0)	0.30
BMI classification				
< 18.5	116 (7.8 %)	97 (7.7 %)	19 (8.1 %)	0.76
18.5–23.9	821 (55.1 %)	686 (54.6 %)	135 (57.7 %)	
24–27.9	445 (29.8 %)	382 (30.4 %)	63 (26.9 %)	
≥ 28	109 (7.3 %)	92 (7.3 %)	17 (7.3 %)	
ASA score				
II	1259 (84.4 %)	1071 (85.2 %)	188 (80.3 %)	0.06
III/IV	232 (15.6 %)	186 (14.8 %)	46 (19.7 %)	
Child-Pugh grade				
A	1361 (91.3 %)	1143 (90.9 %)	218 (93.2 %)	0.27
B/C	130 (8.7 %)	114 (9.1 %)	16 (6.8 %)	
ALBI grade				
I	1425 (95.6 %)	1205 (95.9 %)	220 (94.0 %)	0.21
II/III	66 (4.4 %)	52 (4.1 %)	14 (6.0 %)	
Smoking history				
Never	1199 (80.4 %)	1024 (81.5 %)	175 (74.8 %)	0.05
Current	219 (14.7 %)	173 (13.8 %)	46 (19.7 %)	
Former	73 (4.9 %)	60 (4.8 %)	13 (5.6 %)	
Fever	102 (6.8 %)	78 (6.2 %)	24 (10.3 %)	0.02*
Cirrhosis	1219 (81.8 %)	1035 (82.3 %)	184 (78.6 %)	0.18
Diabetes	414 (27.8 %)	342 (27.2 %)	72 (30.8 %)	0.26
Previous surgical history	653 (43.8 %)	554 (44.1 %)	99 (42.3 %)	0.62
Antibiotic use	675 (45.3 %)	559 (44.5 %)	116 (49.6 %)	0.15
Number of lesions				
≤ 3	1425 (95.6 %)	1205 (95.9 %)	220 (94.0 %)	0.21
> 3	66 (4.4 %)	52 (4.1 %)	14 (6.0 %)	
BCLC grade				0.13
0	660 (44.3 %)	559 (44.5 %)	101 (43.2 %)	
A	466 (31.3 %)	381 (30.3 %)	85 (36.3 %)	
B	365 (24.5 %)	317 (25.2 %)	48 (20.5 %)	
Maximum tumor size				0.15
≤3 cm	961 (64.5 %)	800 (63.6 %)	161 (68.8 %)	
>3 cm	530 (35.5 %)	457 (36.4 %)	73 (31.2 %)	
AFP, ng/ml	8.5 (3.0, 72.0)	8.0 (2.9, 71.4)	11.2(3.7, 81.2)	0.13

*$P < 0.05$; BMI, body mass index; ASA, American Society of Anesthesiologists; ALBI, albumin-bilirubin.

Table 2
Prognosis of patients with or without postoperative SIRS.

	All (n = 1491)	Non-SIRS (n = 1257)	SIRS (n = 234)	*P* value
Pneumonia	41 (2.7 %)	22 (1.8 %)	19 (8.1 %)	<0.01*
Acute respiratory distress syndrome	7 (0.5 %)	2 (0.2 %)	5 (2.1 %)	<0.01*
Acute left cardiac insufficiency	8 (0.5 %)	5 (0.4 %)	3 (1.3 %)	0.09
Cardiac arrest	2(0.1 %)	0(0.0 %)	2 (0.9 %)	0.01*
Cerebral infarction	10 (0.7 %)	7 (0.6 %)	3 (1.3 %)	0.21
Acute kidney injury	16 (1.1 %)	13 (1.0 %)	3 (1.3 %)	0.74
Hyperkalemia	11 (0.7 %)	7 (0.6 %)	4 (1.7 %)	0.06
Lactic acidosis	12 (0.8 %)	4 (0.3 %)	8 (3.4 %)	<0.01*
Cost of anesthesia, thousand yuan	2.5(2.2, 2.7)	2.5(2.2, 2.7)	2.5(2.1, 2.7)	0.55
Hospitalization costs, thousand yuan	3.6(2.9, 4.6)	3.6 (2.9, 4.4)	4.2(3.4, 5.6)	<0.01*
Length of hospital stay	11.0 (8.0, 16.0)	11.0 (7.0, 15.0)	14.0 (9.0, 21.0)	<0.01*
Postoperative length of hospital stay	5.0 (3.0, 6.0)	4.0 (3.0, 6.0)	6.0(4.0, 11.0)	<0.01*
Length of follow-up after surgery	5.0 (3.0, 6.0)	4.0 (3.0, 6.0)	6.0(4.0, 7.0)	<0.01*

*$P < 0.05$.

significantly different with regard to the following: WBC $< 4 \times 10^9$/L or $> 10 \times 10^9$/L, decreased RBC, PLT $< 100 \times 10^9$/L, decreased HCT, NEUT $< 1.5 \times 10^9$/L, NEUT% < 0.5 or > 0.7, AST $>$ 40U/L, ALB $<$ 35 g/L, TBILI $>$ 17.1umol/L, DBILI $>$ 6.8umol/L, IBILI $>$ 10.2umol/L, APTT $>$ 44.5s, PT $>$ 16.3s, Fib $<$ 2 g/L (all $P < 0.05$).

In terms of intraoperative data (Table 4), the operative duration of those with SIRS was significantly longer than those without SIRS ($P = 0.04$). However, there were no significant differences in medicine use and fluid therapy between the two groups.

Table 3
The preoperative laboratory data patients with or without postoperative SIRS.

Characteristics	All (n = 1491)	Non-SIRS (n = 1257)	SIRS (n = 234)	*P* value
WBC < 4 or > 10, 10^9/L	430 (28.8 %)	340 (27.0 %)	90 (38.5 %)	<0.01*
Decreased RBC[a]	279(18.7 %)	220(17.5 %)	59(25.2 %)	<0.01*
PLT < 100, 10^9/L	434(29.1 %)	340(27.0 %)	94(40.2 %)	<0.01*
Decreased HCT[b]	616(41.3 %)	487(38.7 %)	129(55.1 %)	<0.01*
Decreased HGB[c]	262(17.6 %)	211(16.8 %)	51(21.8 %)	0.07
NEUT < 1.5, 10^9/L	149 (10.0 %)	105 (8.4 %)	44 (18.8 %)	<0.01*
NEUT% < 0.5 or > 0.7	757 (50.8 %)	669 (53.2 %)	88 (37.6 %)	<0.01*
BUN > 7.1, mmol/L	169 (11.3 %)	141 (11.2 %)	28 (12.0 %)	0.74
AST > 40, U/L	388 (26.0 %)	304 (24.2 %)	84 (35.9 %)	<0.01*
ALT > 40, U/L	377 (25.3 %)	306 (24.3 %)	71 (30.3 %)	0.05
ALB < 35, g/L	218(14.6 %)	164(13.0 %)	54(23.1 %)	<0.01*
TBILI > 17.1, umol/L	436(29.2 %)	352(28.0 %)	84(35.9 %)	0.01*
DBILI > 6.8, umol/L	372(24.9 %)	292(23.2 %)	80(34.2 %)	<0.01*
IBILI > 10.2, umol/L	516(34.6 %)	421(33.5 %)	95(40.6 %)	0.04*
CREAT > 106, umol/L	91(6.1 %)	82(6.5 %)	9(3.8 %)	0.12
Potassium < 3.5 or >5.5, mmol/L	189 (12.7 %)	162 (12.9 %)	27 (11.5 %)	0.57
APTT > 44.5s	145 (9.7 %)	107 (8.5 %)	38 (16.3 %)	<0.01*
PT > 16.3s	115 (7.7 %)	75 (6.0 %)	40 (17.2 %)	<0.01*
PT-INR < 0.9 or > 1.1	10 (0.7 %)	8 (0.6 %)	2 (0.9 %)	0.70
Fib < 2, g/L	173 (11.6 %)	133 (10.6 %)	40 (17.2 %)	<0.01*

*$P < 0.05$; [a] Decreased RBC was defined as a RBC of less than 3.5 × 10^{12}/L for women and less than 4.0 × 10^{12}/L for men; [b] Decreased HCT was defined as a hematocrit concentration of less than 37.0 % for women and less than 40.0 % for men; [c] Decreased HGB was defined as a hemoglobin concentration of less than 120 g/l for men and less than 110 g/L for non-pregnant women; WBC, white blood cell; RBC, red blood cell; PLT, platelet count; HCT, red blood cell volume; HGB, hemoglobin; NEUT, neutrophils; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALB, albumin; TBILI, total bilirubin; DBILI, direct bilirubin; IBILI, indirect bilirubin; CREAT, creatinine; APTT, activated partial thromboplastin time; PT, prothrombin time; PT-INR, prothrombin time-international normalized ratio; Fib, fibrinogen.

Table 4
The intraoperative data of patients with or without postoperative SIRS.

Characteristics	All(n = 1491)	Non-SIRS (n = 1257)	SIRS(n = 234)	*P* value
Operative duration, min	83.0 (58.0, 118.0)	81.0 (57.0, 116.0)	90.5 (63.2, 130.0)	0.04*
Medicine use				
Propofol	1151 (77.2 %)	970 (77.2 %)	181 (77.4 %)	0.95
Etomidate	305 (20.5 %)	261 (20.8 %)	44 (18.8 %)	0.49
Fentanyl	759 (50.9 %)	634 (50.4 %)	125 (53.4 %)	0.40
Sufentanil	404 (27.1 %)	346 (27.5 %)	58 (24.8 %)	0.39
Remifentanil	28 (1.9 %)	24 (1.9 %)	4 (1.7 %)	0.90
Oxycodone	75 (5.0 %)	63 (5.0 %)	12 (5.1 %)	0.94
Cisatracurium	878(58.9 %)	731(58.2 %)	147(62.8 %)	0.14
Parecoxib	213 (14.3 %)	183(14.6 %)	30(12.8 %)	0.45
Flurbiprofen axetil	600(40.2 %)	506(40.3 %)	94(40.2 %)	0.97
Steroids	206 (13.8 %)	177 (14.1 %)	29 (12.4 %)	0.49
Ulinastatin	63 (4.2 %)	55 (4.4 %)	8 (3.4 %)	0.50
Fluid therapy				
Crystal solution, ml/kg	7.4(1.8, 10.8)	7.4(1.8, 10.7)	7.7 (1.7, 11.9)	0.54
Colloid solution, ml/kg	7.7(6.5, 8.6)	7.7(6.6, 8.6)	7.7(6.0, 8.6)	0.23
Red blood cells	12 (0.8 %)	10 (0.8 %)	2 (0.9 %)	0.93
Sodium bicarbonate	199 (13.3 %)	160 (12.7 %)	39 (16.7 %)	0.10

*$P < 0.05$.

3.4. Multivariate logistic regression

Confounding effects of preoperative factors on SIRS were adjusted by using stepwise multivariate logistic regression model (detailed in Table 5). Compared with non-smoker, the current smokers suffered a higher risk of postoperative SIRS (OR 1.58, 95 % CI 1.09–2.29, $P = 0.016$) and yet former smoker did not have a statistically higher risk (OR 1.12, 95 %CI 0.59–2.13, $P = 0.723$). Decreased HCT (defined as HCT < 40 % for male and < 37 % for female), neutropenia (< 1.5 × 10^9/L) and abnormal NEUT% (< 0.5 or > 0.7) were associated with a higher risk of SIRS (OR 1.51, 95 %CI 1.11–2.04; OR 1.74, 95 %CI 1.14–2.65; OR 1.36, 95 %CI 1.01–1.83, respectively). The patients with PT > 16.3s has 1.42 times higher risk of postoperative SIRS than those with lower PT (95 %CI 1.57–3.74, $P < 0.001$).

Table 5
Multivariate logistic regression analysis of SIRS after thermal ablation of HCC.

	Adjusted OR (95 %CI)	*P* value
Smoking history (vs. Never)		
Current	1.58 (1.09–2.29)	0.016*
Former	1.12 (0.59–2.13)	0.723
Decreased HCT†	1.51 (1.11–2.04)	0.008*
NEUT $< 1.5 \times 10^9$/L	1.74 (1.14–2.65)	0.010*
NEUT% < 0.5 or > 0.7	1.36 (1.01–1.83)	0.040*
PT > 16.3s	2.42 (1.57–3.74)	<0.001*

*$P < 0.05$; † Decreased HCT was defined as a hematocrit concentration of less than 37.0 % for women and less than 40.0 % for men; HCT, red blood cell volume; HGB, hemoglobin; NEUT, neutrophils; ALT, alanine aminotransferase; PT, prothrombin time.

4. Discussion

With the advantages of less trauma, faster recovery and lower hospitalization cost than conventional hepatectomy, thermal ablation has been a promising strategy for HCC. In our study of 1491 ablation sessions performed over six years, 15.7 % patients developed postoperative SIRS after thermal ablation of HCC, which is similar to the previous studies [10,19]. Previously our team demonstrated that thermal ablation is safe in terms of major complications related to this procedure [10]. This study also showed that thermal ablation is a safe therapeutic strategy with no mortality and rare more severe complications related to SIRS.

SIRS is intrinsically an unbalanced inflammatory response involving endothelial cell activation, inflammatory mediator release, and immune cell activation [6]. It could be triggered by thermal ablation, which could cause heat injury in tissues surrounding the tumor, produce tissue coagulation and necrosis, and release neoantigen to blood circulation, eventually induce a systemic reaction [20], manifesting as significant increased secretion of chemokines and proinflammatory cytokines [21,22]. Postoperative SIRS is preliminary stage of sepsis or multiple organ dysfunction [23] and this study focused on the more severe complications related to SIRS (0.1–2.7 %). The most frequent major complication was pneumonia (2.7 %, 41/1491), which attracted less attention in previous studies. However, the incidence of pneumonia was higher than that of other postoperative pulmonary complications (such as pleural effusion and acute lung injury) reported previously [24–26].

Our study suggested that current smoking, decreased HCT, NEUT $< 1.5 \times 10^9$/L, NEUT% < 0.5 or > 0.7 and PT > 16.3s were the predictive factors for postoperative SIRS. The results showed that current smoking was associated with higher risk of SIRS, which is consistent with the published literatures [27]. Smoking could induce an excess production of inflammatory mediators and lead to systemic immune dysfunction [28]. HCT is one of the critical biomarkers for the diagnosis of anemia and also a critical biomarker in several inflammatory diseases such as sepsis and malignant tumors [29]. Consistent with earlier researches [30], abnormal neutrophil percentage increase the risk for postoperative SIRS. Priming of neutrophils is involved in secretion of cytokines. Neutrophilia may lead to overproduction of ROS and proinflammatory cytokines that trigger SIRS [31]. Neutropenia would increase risk for infection, septic shock, and death [32,33].

This study indicates that PT is associated with risk of postoperative SIRS. In accordance with the result, researchers found that PT in SIRS group was significantly higher than that in control group [34]. Inflammation induces activation of coagulation, and coagulation also considerably affects inflammatory activity [35]. Prolonged PT may also be associated with preoperative cirrhosis, which occurred in over 80 % cases in the cohort. The new balance of coagulation function established among patients with cirrhosis is fragile and coagulation failure is related to evolution of SIRS and sepsis [36].

Many studies reveal that albumin and bilirubin levels reflect severity of liver disease and SIRS occurs in patients with advanced cirrhosis [12,13]. Similarly, the univariate analysis showed that albumin and bilirubin levels were associated with SIRS. Nevertheless, there was no significance after adjusting the confounding factors using stepwise logistic regression. Notably, ALBI scores (calculated by bilirubin and albumin), which is currently accepted as a better indicator of underlying liver disease status [37,38], were not significantly different between the SIRS and non-SIRS group. The reason for this might selection bias of patients. Our study enrolled a majority of patients with early-stage HCC (95.6 % of patients with ALBI grade I, 91.3 % with Child-Pugh A and 75.5 % with BCLC stage 0 or A), while other studies had previously reported mostly the advanced cases.

In addition, we found that postoperative SIRS significantly increased the risk of more severe complications (such as pneumonia, ARDS, acute left cardiac insufficiency and cardiac arrest), increased costs as well as prolonged hospital stay. Therefore, early recognition and supervision of SIRS are essential to implement preventive measures so as to benefit the patients physically and economically.

There are also some limitations in our study. Firstly, this study is a single-center retrospective study, for which possible residual confounding may occur. Secondly, there is a lack of detailed follow-up data and long-term outcomes (such as response to thermal ablations and survival) could not be further clarified. Therefore, a prospective multiple-center study will be needed for generalization and validation.

In conclusion, current smoking, decreased HCT, NEUT $< 1.5 \times 10^9$/L, NEUT% < 0.5 or > 0.7 and PT > 16.3s are risk factors for postoperative SIRS after thermal ablation for HCC. Postoperative SIRS is associated with poor short-term prognosis. The study will help early identify high-risk populations of SIRS.

Ethics statement

This study was approved by the Ethnic Committee of the Third Affiliated Hospital of Sun Yat-sen University ([2021]02-379-01), with waiver of informed consent.

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Data availability

The datasets analyzed during the study are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Xiaorong Peng: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis. **Jibin Xing:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Hao Zou:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis. **Mengya Pang:** Methodology, Investigation, Data curation. **Qiannan Huang:** Writing – review & editing. **Shaoli Zhou:** Resources, Data curation. **Kai Li:** Supervision, Resources, Project administration, Conceptualization. **Mian Ge:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e25443.

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