RESEARCH

C-reactive protein and thyroid-stimulating hormone levels as risk factors for hypothyroidism in patients with subacute thyroiditis

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Abstract

Objective: This study was designed to explore the relationships between the clinical characteristics and outcomes of patients with subacute thyroiditis (SAT).
Design: This is a single-center retrospective study.
Patients: Eighty-nine patients with SAT who were hospitalized in the Sir Run Run Shaw Hospital in Zhejiang, China, from October 2014 to September 2020 were included.
Methods: The Mann–Whitney *U*-test, chi-square test, and Cox regression analysis were conducted to identify the relationships between clinical characteristics and outcomes. Receiver operating characteristic (ROC) analysis was performed to determine the optimal cutoff levels of C-reactive protein (CRP) and thyroid-stimulating hormone (TSH).
Results: The hypothyroidism and recurrence rates were 15.7 and 16.9%, respectively. CRP (≥72.0 mg/L), TSH (<0.02 mIU/L), and free triiodothyronine (fT3) (≥4.10 pg/mL) were associated with hypothyroidism. The cutoff level was 97.80 mg/L for CRP (area under the curve (AUC), 0.717, $P = 0.014$; sensitivity, 57.1%; specificity, 84.0%) and 0.10 mIU/L for TSH (AUC, 0.752, $P = 0.004$; sensitivity, 100%; specificity, 46.0%) by ROC curve analysis for hypothyroidism. The factors under study were not associated with recurrence.
Conclusion: CRP and TSH were risk factors for hypothyroidism in SAT. Thyroid functions should be monitored closely for the early detection of hypothyroidism, especially in patients with CRP levels of more than 97.80 mg/L and TSH levels of less than 0.10 mIU/L.

Key Words
- subacute thyroiditis
- C-reactive protein
- thyroid-stimulating hormone
- hypothyroidism

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Introduction

Subacute thyroiditis (SAT), also known as De Quervain's thyroiditis, giant cell thyroiditis, or granulomatous thyroiditis, is an inflammatory thyroid disease, probably associated with viral infection (1). It is often characterized by neck pain, goiter, and systemic inflammation. Some scholars have proposed diagnostic criteria for SAT (2, 3). This disease is usually diagnosed according to systemic symptoms, such as acute fever, thyroid pain, and the phenomenon of significantly increased erythrocyte sedimentation rate (ESR), increased serum thyroid hormone levels, and decreased thyroid iodine uptake. However, more atypical cases, such as those without neck pain, have been reported (4, 5, 6). Recently, Stasiak *et al.* have proposed new and modified diagnostic criteria for SAT (7).

Although the disease is self-limited, patients still need treatment for pain and thyroid toxicity. However, no precise therapy has been established yet. For mild

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cases, nonsteroidal anti-inflammatory drugs (NSAIDs) are available clinically. However, for patients with severe pain, NSAIDs are ineffective; instead, glucocorticoid therapies are applied. Chinese guidelines recommend an initial dose of 30 mg/day for prednisone, but evidence-based researches were insufficient (3). Several studies have focused on the optimal doses of steroids (8, 9, 10). Some scholars have recommended an initial treatment with lower doses of prednisolone daily (8, 9). One study has shown that the treatment with an initial dose of 15 mg daily for steroids had similar efficacy and fewer adverse reactions (8). The initial dose should be maintained for approximately 1–2 weeks, and the dose should be reduced gradually when the patient's symptoms are relieved (8, 11).

The incidence of hypothyroidism after treatment is 5–27% (12, 13), and the incidence of recurrence ranges from 1.6–20% (14, 15). Many scholars have explored the risk factors for recurrence and hypothyroidism in patients with SAT. The risk of recurrence in patients with SAT was HLA-dependent, and the co-presence of HLA-B*18:01 and –B*35 was a determining factor (16). Some studies have shown that patients who received corticosteroid therapy tended to receive T4 therapy, whereas some studies have shown the opposite (13, 17).

This study was designed to describe the clinical characteristics of SAT and explore the relationships between those clinical characteristics and the outcomes in hospitalized patients with SAT.

Materials and methods

Patients and data collection

This retrospective study included 95 Chinese patients who were diagnosed with SAT between October 2014 and September 2020 in the Department of Endocrinology and Metabolic Diseases, the Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University. Three patients were excluded due to incomplete data. Additionally, three patients were excluded because they had elevated thyroid antibodies and a long interval between SAT diagnosis and outcomes. The study complies with the Declaration of Helsinki and was approved by the Ethics Committee of Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University.

As in previous studies (2, 5, 8), the inclusion criteria for the diagnosis of SAT in this study were as follows: (1) painful, tender, hard goiter often accompanied by symptoms and signs resembling an upper respiratory infection; (2) increased ESR or C-reactive protein (CRP); (3) depressed thyroid radionuclide uptake; (4) transient hyperthyroidism; and (5) hypoechoic areas with blurred margins on thyroid ultrasonography. For patients who did not meet the aforementioned criteria but were suspected of SAT, fine-needle aspiration and cytology of the thyroid were performed. Patients were considered to have SAT if histological findings were compatible with SAT. Those who had SAT with GD were excluded. Hypothyroidism was defined as free thyroxine (fT4) levels below the normal reference range and thyroid-stimulating hormone (TSH) levels above the normal reference range. Recurrence was defined based on the relapse of clinical symptoms, such as neck pain, usually accompanied by an increase in CRP or ESR.

All laboratory tests, ultrasonographic examinations, and thyroid uptake scans were performed before the patients received treatment. White blood cell (WBC) count, neutrophil (Neu) count, mean platelet volume (MPV), platelets (PLT), and lymphocytes were measured using an automatic blood analysis line (CAL-8000; Mindray Medical International Limited, Shenzhen, China). CRP was determined using immunoturbidimetry. Triiodothyronine (T3), free triiodothyronine (fT3), thyroxine (T4), fT4, TSH, thyroid peroxidase antibody (aTPO), thyroglobulin antibody (aTG), and thyrotropin receptor antibody (TRAb) were measured using the Elecsys electrochemiluminescence immunoassay (Roche Holding AG). The thyroid volume of each lobe was calculated using the formula proposed by Brunn *et al.:* thyroid volume (mL) = 0.479 × length (cm) × thickness (cm) × width (cm) (18). The total volume was the sum of both lobes, excluding the isthmus. The reference ranges were as follows: WBC (3.5–9.5 × 109/L), Neu (1.8–6.3 × 109/L), MPV (6.5–13.0 fL), PLT (1.10–3.20 × 109/L), ESR (1–15 mm/h), CRP (0–6 mg/L), TSH (0.35–4.94 mIU/L), T4 (4.87–11.72 ug/dL), fT4 (0.70–1.48 ng/dL), T3 (0.64–1.52 ng/mL), fT3 (1.71–3.71 pg/mL), aTG (0–4.11 IU/mL), aTPO (0–5.61 IU/mL), and TRAb (0–1.22 IU/L).

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (version 24.0; IBM Corp.). Results were presented as median (range) for variables. Additionally, each quantitative variable was converted to a classified variable based on its median or medical reference range. For comparisons between groups, the Mann–Whitney *U*-test was used. Categorical variables were reported as frequencies, and relationships among them were examined using the chi-square test. Cox regression

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analysis was employed to evaluate the relationship between hypothyroidism or recurrence and variables. Receiver operating characteristic (ROC) analysis was performed to determine the optimal cutoff levels of variables by yielding the maximum sums of sensitivity and specificity from the curve. *P*-values of less than 0.05 were used to denote statistical significance.

Results

The characteristics of the patients

Eighty-nine patients with SAT, including 61 females and 28 males, were enrolled in this study. The clinical characteristics of the patients are shown in Table 1. The median age was 50 years. The disease started in summer in 36.0% (32/89) of the patients and in autumn in 28.1% (25/89) of the patients. Moreover, 82.0% (73/89) of the patients had a fever in the process. Then, 91.0% (81/89) of the patients had neck pain. Among all patients, 23 females and 5 males experienced 'crawling neck pain' – neck pain from one side to the other, which was more frequent in summer and autumn than in winter and spring (64.2% vs 35.8%). Four (50%) of eight patients who did not have pain had SAT in spring. Hypertension was found in 19 (21.3%) patients, diabetes mellitus was found in 18 (20.2%) patients, and 2 patients had Hashimoto thyroiditis.

Moreover, WBC, maximum body temperature, CRP, and TSH were available for 89 patients; MPV, PLT, ESR, and T4 were available for 88 patients; Neu, lymphocyte and T3 were available for 87 patients; fT3, aTG, and aTPO were available for 85 patients; fT4 was available for 84 patients; TRAb was available for 62 patients. Thyroid ultrasonography was performed on every patient, whereas thyroid volume results were available for 66 patients. All patients were examined for thyroid uptake scan, and those results were found to be reduced. WBC, Neu, PLT, and ESR levels were above the normal range in 31.5% (28/89), 40.2% (35/87), 30.3% (27/89), and 100% (88/88) of the patients, respectively. Furthermore, CRP levels were within the normal range in 4.5% (4/89) of the patients, all of whom were female, with a medical history longer than 2 months. On the first visit to our clinic, 83.1% (74/89) of the patients had hyperthyroidism, and 16.8% (15/89) of them were euthyroid. Moreover, 19.1% (17/89) of the patients showed an increase in both aTG and aTPO levels, whereas an increase in aTG or aTPO levels was observed in 64.0% (57/89) and 22.5% (20/89) of the patients, respectively. Among the patients, 22.6% (14/62) had elevated TRAb levels. In this study, male patients had higher Neu, CRP, and TRAb levels ($P = 0.046$, 0.008, and 0.014, respectively). Furthermore, patients with fever had higher Neu, PLT, CRP, TSH, T3, fT3, T4, and fT4 evels ($P < 0.05$).

Therapies of the patients

Among the 89 patients, 24.7% (22/89) were treated with NSAIDs alone, 16.9% (15/89) were treated with steroids alone, and 58.4% (52/89) were treated with both NSAIDs and steroids. Diclofenac sodium and celecoxib were the most frequently used NSAIDs, accounting for 70.3% (52/74) and 33.8% (25/74) of the patients, respectively. Among patients treated with steroids, 77.6% (52/67) received oral dosage forms, and 46.3% (31/67) received injections.

Patient outcomes

The total hypothyroidism rate in the study was 15.7%. Twelve (85.7%) of the 14 cases who had hypothyroidism occurred within 2 months of treatment, and the latest was after 166 days. Age, BMI, disease course, WBC, Neu, lymphocyte, PLT, MPV, ESR, aTG, aTPO, TRAb, thyroid volumes, the rate of fever, neck pain, and therapies were similar in the normal and hypothyroidism groups ($P > 0.05$). Significant differences in CRP, TSH, T3, fT3, T4, and fT4 levels were observed between the two groups ($P = 0.014$, 0.004, 0.029, 0.024, 0.016, and 0.030, respectively).

In the univariate regression analysis, CRP (≥72.0 mg/L), TSH (<0.02 mIU/L), and fT3 (≥4.10 pg/mL) were significantly associated with a higher incidence of hypothyroidism (Table 2). The cutoff level was 97.80 mg/L for CRP (area under the curve (AUC), 0.717; $P = 0.014$; sensitivity, 57.1%; specificity, 84.0%) and 0.10 mIU/L for TSH (AUC, 0.752; $p = 0.004$; sensitivity, 100%; specificity, 46.0%), determined by ROC curve analysis (Fig. 1). However, in the multivariate analysis, none of the following factors had significant associations with hypothyroidism: ESR (hazard ratio (HR) = 1.273; 95% CI = 0.371–4.371; $P = 0.702$), CRP (HR = 3.608; 95% CI = 0.706–18.432; $P = 0.123$), TSH (HR = 0.222; 95% CI = 0.043–1.142; $P = 0.072$), fT3 (HR = 1.181; 95% CI = 0.274–5.093; $P = 0.824$).

The total recurrence rate in the study was 16.9%. Half of the cases occurred within 2 weeks after the drugs were stopped, and the latest recurrence happened in 219 days. No significant differences in basic data, inflammatory biomarkers, thyroid volume, thyroid function tests, and treatment were found between the recurrence and non-recurrence groups ($P > 0.05$) (Table 1). However, none of the

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Table 1 The clinical characteristics and therapies of SAT patients with different outcomes.

	All patients (n = 89)	Patients without hypothyroidism or recurrence (n = 50)	Patients with hypothyroidism (n = 14)	*P*-value	Patients with recurrence (n = 15)	*P*-value
Gender (male/female, cases)	28/61	15/35	6/8	0.520	6/9	0.535
Age (years, M (range))	50 (23–78)	49 (23–69)	53 (28–77)	0.162	46 (32–78)	0.607
BMI (kg/m^2, M (range))	21.3 (15.1–30.9)	21.1 (15.2–30.9)	21.9 (17.0–25.5)	0.974	21.8 (18.8–25.8)	0.279
Course (days, M (range))	30 (8–730)	30 (10–330)	30 (15–150)	0.876	40 (8–730)	0.463
WBC (×109/L, M (range))	8.2 (4.7–20.9)	8.2 (4.7–20.9)	8.6 (5.5–13.5)	0.721	8.6 (6.3–16.1)	0.533
Neu (×109/L, M (range))	5.9 (2.4–17.4)	5.9 (2.4–17.4)	6.3 (2.7–10.6)	0.741	5.92 (3.3–12.98)	0.869
Lymphocyte (×109/L, M (range))	1.6 (0.3–3.3)	1.6 (0.7–3.3)	1.5 (0.3–2.4)	0.535	1.67 (0.6–2.6)	0.710
PLT (×109/L, M (range))	299 (48–596)	293 (119–529)	344 (48–596)	0.186	314.5 (59–456)	0.801
MPV (fL, M (range))	8.0 (0.4–12.8)	8.2 (6.5–12.8)	7.8 (0.4–11.3)	0.371	7.8 (6.7–12.3)	0.678
ESR (mm/h, M (range))	87 (18–140)	85.0 (18–140)	98 (27–117)	0.160	85 (20–105)	0.623
CRP (mg/L, M (range))	70.3 (0.2–242.5)	68.4 (1.0–170.7)	101.2 (15.2–173.6)	0.014[a]	43.6 (0.2–127)	0.418
TSH (mIU/L, M (range))	0.02 (0–2.62)	0.06 (0–1.59)	0.01 (0–0.08)	0.004[a]	0.04 (0–2.62)	0.385
T3 (ng/mL, M (range))	1.39 (0.77–4.45)	1.29 (0.83–4.45)	1.65 (1.13–2.42)	0.029[a]	1.41 (0.77–3.64)	0.765
fT3 (pg/mL, M (range))	4.10 (2.46–18.08)	3.90 (2.62–13.58)	4.83 (3.26–11.81)	0.024[a]	4.12 (2.46–10.5)	0.945
T4 (ug/dL, M (range))	11.70 (5.17–239.00)	12.0 (5.27–239.00)	17.16 (6.70–24.00)	0.016[a]	10.54 (5.17–24)	0.437
fT4 (ng/dL, M (range))	1.61 (0.84–40.90)	1.60 (0.9–40.90)	2.78 (1.24–40.72)	0.030[a]	1.34 (0.84–35.7)	0.241
aTG (IU/mL, M (range))	6.41 (0.77–1000)	8.32 (0.77–467.4)	20.86 (1.25–84.49)	0.337	6.41 (1.94–1000)	0.930
aTPO (IU/mL, M (range))	1.08 (0.01–1589.49)	1.61 (0.01–1589.49)	2.97 (0.3–157.09)	0.341	0.64 (0.12–1000)	0.151
TRAb (IU/L, M (range))	0.69 (0.03–18.15)	0.73 (0.3–4.78)	0.77 (0.3–17.09)	0.753	0.66 (0.03–18.15)	0.979
Thyroid volume (cm^3, M (range))	17.2 (5.6–40.0)	17.1 (5.9–32.1)	15.7 (5.6–40.0)	0.748	19.3 (9.9–28.4)	0.990
Season (cases (%))				0.358		0.637
Spring	17 (19.1)	8 (16.0)	4 (28.6)		3 (20.0)	
Summer	32 (36.0)	16 (32.0)	5 (35.7)		6 (40.0)	
Autumn	25 (28.1)	19 (38.0)	2 (14.3)		3 (20.0)	
Winter	15 (16.9)	7 (14.0)	3 (21.4)		3 (20.0)	
Pain (cases (%))				0.381		0.854
One side	24 (27.0)	16 (32.0)	2 (14.2)		4 (26.7)	
Both side	29 (32.6)	16 (32.0)	5 (35.7)		4 (26.7)	
Crawling	28 (31.5)	14 (28.0)	4 (28.6)		6 (40.0)	
No	8 (9.0)	4 (8.0)	3 (21.4)		1 (6.6)	
Fever (cases (%))				0.437		0.282
Yes	73 (82.0)	41 (82.0)	13 (92.9)		10 (66.7))	
No	16 (18.0)	9 (18.0)	1 (7.1)		5 (33.3)	
Therapy						
NSAIDS (cases (%))				0.160		0.721
Yes	74 (83.1)	40 (80.0)	14 (100)		11 (73.3)	
No	15 (16.9)	10 (20.0)	0 (0)		4 (26.7)	
Steroids (cases (%))				0.170		0.715
Yes	67 (75.3)	39 (78.0)	8 (57.1)		13 (86.7)	
No	22 (24.7)	11 (22.0)	6 (42.9)		2 (13.3)	
Complications (cases (%))						
Hypertension	19 (21.3)	12 (24.0)	4 (28.6)	0.736	1 (6.7)	0.268
Diabetes mellitus	18 (20.2)	11 (22.0)	4 (28.6)	0.723	3 (20.0)	1.000
Hashimoto thyroiditis	2 (2.2)	0	1 (5.9)		1 (6.7)	

[a]$P < 0.05$ was considered statistically significant.

aTG, thyroglobulin antibody; aTPO, thyroid peroxidase antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; fT3, free triiodothyronine; fT4, free thyroxine; MPV, mean platelet volume; Neu, neutrophil; PLT, platelets; T3, triiodothyronine; T4, thyroxine; TRAb, thyrotropin receptor antibody; TSH, thyroid-stimulating hormone; WBC, white blood count.

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factors under study had a significant difference regarding recurrence in the Cox regression analysis (Table 3).

For the group receiving NSAIDs alone and the group receiving steroids alone, hypothyroidism developed in 18.2% (4/22) and 0% (0/15) of the patients, respectively, and recurrence developed in 9.1% (2/22) and 26.7% (4/15) of the patients, respectively. The 2 patients who were treated with celecoxib alone did not develop hypothyroidism or recurrence, whereas, among the 12 patients treated with diclofenac alone, 4 had hypothyroidism, and recurrence was observed in 1 patient.

Discussion

SAT is self-limited inflammatory thyroid disease, and some patients feel mild and transient discomfort, which received little attention. Unfortunately, some patients must undergo treatment because they experience severe neck pain, insomnia, and even anxiety. They may be concerned about drug efficacy, side effects, and therapeutic prognosis. In this study, we described the clinical characteristics of the hospitalized patients diagnosed with SAT, and the prognosis (hypothyroidism and recurrence) is not correlated with certain treatments. Simultaneously, we found that CRP and TSH were associated with hypothyroidism, and the cutoff levels for the two parameters were calculated.

Several studies have shown that a higher proportion of patients who had SAT were females (12, 13, 19). In this study, the female-to-male ratio was 2.18:1, and 62.9% of them were in the 40–60 age range, which confirms the findings of previous studies. The increased frequency of certain types of HLA was reported in patients with SAT, and in 2020, Stasiak *et al.* found an association between HLA and SAT (7, 20). Besides, viral infection has been considered a triggering factor for SAT, such as coxsackieviruses, echoviruses, and adenoviruses (7, 21). Similar to the results of previous studies (13, 22, 23), most patients had the disease in summer and autumn, which conforms to the peak of enterovirus disease incidence. In this study, male patients were more likely to have higher Neu, CRP, and TRAb levels. Neu and CRP were considered indicators of inflammation. Additionally, a similar phenomenon was found in patients with severe acute respiratory syndrome coronavirus 2 (COVID-19) infection (24). No further studies have explained this phenomenon; it might be because males have a stronger response to inflammation.

Table 2 Univariate and stepwise multivariate Cox hazard analysis of variables associated with hypothyroidism in SAT patients.

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Gender (male vs female)	1.718 (0.596–4.953)	0.316		
Age (≥50 years vs <50 years)	1.631 (0.546–4.869)	0.380		
BMI (≥21.26 kg/m^2 vs <21.26 kg/m^2)	1.373 (0.476–3.957)	0.557		
Course (≥30 days vs <30 days)	0.749 (0.260–2.159)	0.592		
WBC (≥8.2 × 109/L vs <8.2 × 109/L)	0.973 (0.341–2.775)	0.960		
Neu (≥5.9 × 109/L vs <5.9 × 109/L)	1.313 (0.456–3.786)	0.614		
Lymphocyte (≥1.6 × 109/L vs <1.6 × 109/L)	0.859 (0.301–2.450)	0.777		
PLT (≥299.0 × 109/L vs <299.0 × 109/L)	1.327 (0.460–3.824)	0.601		
MPV (≥8.1 fL vs <8.1 fL)	0.640 (0.222–1.846)	0.409		
ESR (≥89 mm/h vs <89 mm/h)	2.870 (0.899–9.162)	0.075[b]	1.273 (0.371–4.371)	0.702
CRP (≥72.0 mg/L vs <72.0 mg/L)	4.376 (1.220–15.700)	0.024[ab]	3.608 (0.706–18.432)	0.123
TSH (≥0.02 mIU/L vs <0.02 mIU/L)	0.198 (0.055–0.711)	0.013[ab]	0.222 (0.043–1.142)	0.072
T3 (≥1.36 ng/mL vs <1.36 ng/mL)	1.915 (0.642–5.716)	0.244		
fT3 (≥4.10 pg/mL vs <4.10 pg/mL)	3.898 (1.072–14.177)	0.039[ab]	1.181 (0.274–5.093)	0.824
T4 (≥12.35 ug/dL vs <12.35 ug/dL)	1.891 (0.634–5.645)	0.253		
fT4 (≥1.80 ng/dL vs <1.80 ng/dL)	2.542 (0.782–8.263)	0.121		
aTG (≥4.12 IU/mL vs <4.12 IU/mL)	1.377 (0.384–4.935)	0.624		
aTPO (≥5.62 IU/mL vs <5.62 IU/mL)	1.100 (0.345–3.507)	0.872		
TRAb (≥1.23 IU/L vs <1.23 IU/L)	1.949 (0.487–7.801)	0.346		
Thyroid volume (≥16.81 mm^3 vs <16.81 mm^3)	0.535 (0.157–1.829)	0.319		
Steroids (yes vs no)	0.438 (0.152–1.263)	0.126		

[a]$P < 0.05$ was considered statistically significant. [b]Variables were included in the multivariate Cox hazard analysis if they had an univariate *P*-value ≤ 0.1 for hypothyroidism.

aTG, thyroglobulin antibody; aTPO, thyroid peroxidase antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; fT3, free triiodothyronine; fT4, free thyroxine; HR, hazard ratio; MPV, mean platelet volume; Neu, neutrophil; PLT, platelets; T3, triiodothyronine; T4, thyroxine; TRAb, thyrotropin receptor antibody; TSH, thyroid-stimulating hormone; WBC, white blood count.

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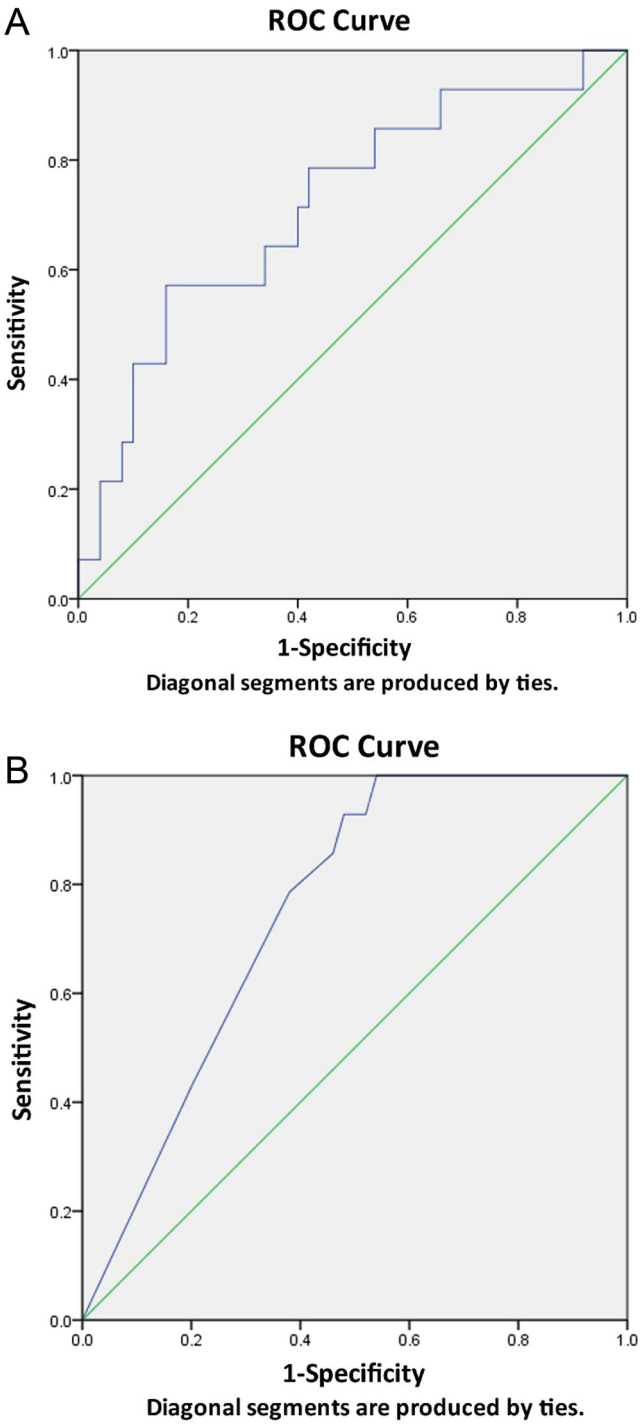

Figure 1
ROC curve analysis of CRP and TSH levels to identify a cutoff level for hypothyroidism. (A) The cutoff level for CRP was found to be 97.80 mg/L (AUC: 0.717, *P*: 0.014; sensitivity: 57.1%; specificity: 84.0%) and (B) the cutoff level for TSH was found to be 0.10 mIU/L (AUC: 0.752, *P*: 0.004; sensitivity: 100%; specificity: 46.0%).

Neck pain was considered the main symptom of SAT for a long time. However, recently, several painless SAT cases were reported in the literature (5, 25, 26, 27). In this study, 9.0% (8/89) of the patients were painless. This situation may be attributed to the development of diagnostic techniques.

Studies have reported that the incidence of hypothyroidism was 5–27% (12, 13). In this study, the total hypothyroidism rate was 15.7%. Patients who developed hypothyroidism had higher T3, fT3, T4, fT4, and CRP levels than the normal group, while therapies were similar in both groups. A study in the 1990s has reported that TSH receptor antibodies became positive in many patients with SAT, probably resulting in thyroid dysfunction (28). While other studies have reported female and thyroid antibody positivity as risk factors for hypothyroidism (12, 17, 29), no statistical results could confirm the aforementioned factors in this study. Instead, CRP and TSH were found to be risk factors for hypothyroidism, especially CRP levels of more than 97.80 mg/L and TSH levels of less than 0.10 mIU/L. Although fT3 (≥4.10 pg/mL) was associated with a higher incidence of hypothyroidism, we did not consider it due to its specific correlation with TSH. CRP is considered an inflammatory biomarker, and TSH indicates the functional status of the thyroid gland. The sensitivity of the TSH cutoff value calculated in this study was 100%, possibly because these patients have severe inflammation damage and a strong inhibitory effect on thyroid function. The laboratory data we collected were all during admission when patients were at the stage of suffering from severe symptoms. Severe inflammation may significantly affect the thyroid gland, leading to hypothyroidism, which occurred in patients with SAT with high CRP and TSH levels.

Despite receiving appropriate treatments, 1.6–20% of the patients had SAT recurrence (5, 14, 15, 17). The total recurrence rate in this study was 16.9%. Some studies have reported that the risk of recurrence of SAT was HLA-dependent (16). Additionally, Sencar *et al.* have reported that recurrences were observed more frequently in patients receiving steroid therapy only than those treated with NSAIDs only (17). This trend was also found in this study, in which 4 of 15 patients treated with steroids alone had a recurrence, whereas 2 of 22 patients treated with NSAIDs alone had a recurrence. A study has reported that recurrence in patients with SAT may be due to the harmful effects of steroids on viral replication and clearance (17).

Our findings showed that patients with higher CRP and lower TSH levels were more likely to develop hypothyroidism. Closer monitoring of thyroid function

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Table 3 Univariate Cox hazard analysis of variables associated with recurrence in SAT patients.

Variable	HR (95% CI)	*P*-value*
Gender (male vs female)	1.541 (0.548–4.330)	0.412
Age (≥49 years vs <49 years)	0.811 (0.294–2.238)	0.686
BMI (≥21.48 kg/m^2 vs <21.48 kg/m^2)	2.056 (0.702–6.020)	0.188
Course (≥30 days vs <30 days)	1.019 (0.348–2.981)	0.973
WBC (≥8.2 × 109/L vs <8.2 × 109/L)	1.136 (0.412–3.136)	0.805
Neu (≥5.9 × 109/L vs <5.9 × 109/L)	1.711 (0.573–5.107)	0.336
Lymphocyte (≥1.6 × 109/L vs <1.6 × 109/L)	1.148 (0.398–3.311)	0.798
PLT (≥294.0 × 109/L vs <294.0 × 109/L)	1.330 (0.462–3.835)	0.597
MPV (≥8.2 fL vs <8.2 fL)	0.748 (0.259–2.157)	0.591
ESR (≥85 mm/h vs <85 mm/h)	1.076 (0.390–2.967)	0.888
CRP (≥66.6 mg/L vs <66.6 mg/L)	0.669 (0.238–1.880)	0.446
TSH (≥0.04 mIU/L vs <0.04 mIU/L)	0.931 (0.337–2.567)	0.890
T3 (≥1.30 ng/mL vs <1.30 ng/mL)	1.164 (0.442–3.211)	0.769
fT3 (≥3.94 pg/mL vs <3.94 pg/mL)	1.210 (0.407–3.603)	0.732
T4 (≥11.24 ug/dL vs <11.24 ug/dL)	0.677 (0.241–1.905)	0.460
fT4 (≥1.58 ng/dL vs <1.58 ng/dL)	0.621 (0.203–1.899)	0.404
aTG (≥4.12 IU/mL vs <4.12 IU/mL)	0.954 (0.293–3.098)	0.937
aTPO (≥5.62 IU/mL vs <5.62 IU/mL)	0.520 (0.115–2.349)	0.395
TRAb (≥1.23 IU/L vs <1.23 IU/L)	2.087 (0.610–7.142)	0.241
Thyroid volume (≥17.2 cm^3 vs <17.2 cm^3)	1.326 (0.404–4.348)	0.642
Steroids	1.712 (0.386–7.590)	0.479

*P < 0.05 was considered statistically significant (variables were included in the multivariate analysis if they had an univariate P-value ≤ 0.1 for hypothyroidism).
aTG, thyroglobulin antibody; aTPO, thyroid peroxidase antibody; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; fT3, free triiodothyronine; fT4, free thyroxine; HR, hazard ratio; MPV, mean platelet volume; Neu, neutrophil; PLT, platelets; T3, triiodothyronine; T4, thyroxine; TRAb, thyrotropin receptor antibody; TSH, thyroid-stimulating hormone; WBC, white blood count.

should be applied to take hormone replacement therapy in time. Besides, some patients with SAT still relapsed after receiving treatments. Although no statistical difference was found, recurrence seemed more likely to occur in patients treated with steroid therapy only.

This study has several limitations. First, it was a retrospective study. Data including the symptoms, laboratory results, and therapies in the medical records might be incomplete. Secondly, all data collected in this study were from inpatients. Most patients in the study had high inflammatory indicators or strong symptoms of discomfort at the beginning of the disease. Thus, the proportion of increased indicators, such as ESR, CRP, and Neu, was higher than that reported in other studies, which may deviate the conclusion.

Conclusion

In conclusion, this study showed that the total hypothyroidism rate was 15.7%, and the total recurrence rate was 16.9%. CRP and TSH were risk factors for hypothyroidism. Thyroid functions should be monitored more closely to detect hypothyroidism early, especially in patients with CRP levels of more than 97.80 mg/L and TSH levels of less than 0.10 mIU/L.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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