

Risk Analysis of 2-year Mortality in Elderly Male Patients with Non-Thyroidal Illness Syndrome

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Abstract

Background Currently, the elderly population is rapidly increasing, and elderly patients with non-thyroidal illness syndrome (NTIS) in intensive care units (ICUs) have relatively severe symptoms and a poor prognosis. However, there are few studies on the correlation between NTIS and patient mortality among hospitalised elderly patients in the general ward.

Methods In the present study, 931 male inpatients ≥ 60 years of age who visited our hospital from January 2012 to December 2013 were selected and divided into the NTIS group and normal thyroid function (non-NTIS) group. Propensity score matching was used to match the two groups according to age and body mass index. Thyroid function, serum proteins, metabolic indicators, liver and kidney function and mortality were collected.

Results Serum total protein (TP), albumin (Alb), prealbumin (PA), haemoglobin (Hb), uric acid (UA), triglyceride (TG), and high-density lipoprotein cholesterol (HDL) levels were significantly lower in the NTIS group than in the non-NTIS group. The urea nitrogen (UN) and fasting blood glucose (FBG) levels were higher in the NTIS group than in the non-NTIS group. Total T_3 , TP, Alb, and PA levels were positively correlated with the Hb level and negatively correlated with FBG, UN, and creatinine (Cr) levels. The free T_3 level was positively correlated with TP, Alb, PA, Hb, and UA levels and negatively correlated with FBG, UN, and Cr levels. Multivariate Cox proportional hazards models indicated that a lower free T_3 level was associated with increased all-cause mortality after adjusting for covariates. The patients in the NTIS group had a lower survival rate at 2 years based on Kaplan–Meier survival curves. Receiver operating characteristic curve (ROC) analysis showed that a cut-off free T_3 level of 3.445 pmol/L yielded the highest sensitivity and specificity for predicting all-cause mortality at 2 years.

Conclusion Among elderly male inpatients, the survival rate was lower in the NTIS group than non-NTIS group. Serum protein levels and renal function decreased and the FBG level increased with decreasing total T_3 and free T_3 levels. A decreased free T_3 level in hospitalized elderly male patients was a predictor of poor prognosis.

Background

Many changes in thyroid hormones occur as a result of illness or nutritional deprivation. These changes consist of decreased levels of serum triiodothyronine (T_3) and/or thyroxine (T_4), without an increase in the thyroid-stimulating hormone (TSH) level, and usually accompanied by elevated reverse T_3 (rT_3) [1, 2]. The combination of these findings is termed non-thyroidal illness syndrome (NTIS), euthyroid sick syndrome, or low T_3 syndrome, indicating a systemic disease outside the thyroid that causes abnormal levels of thyroid hormones and is often considered a compensatory mechanism for the body. NTIS has been reported in patients with acute and chronic illnesses, including infectious diseases, cardiovascular and gastrointestinal diseases, cancer, and trauma [3], which are quite common in patients in intensive care units (ICUs) [4, 5]. In previous studies, NTIS showed a high sensitivity and specificity for predicting

patient mortality in ICU patients [6]. Serum T_3 levels further decrease as the severity of disease progresses. However, among hospitalised elderly patients in the general ward, data on the correlation between NTIS and patient mortality are lacking.

Elderly patients often have multiple chronic diseases and a poor nutritional status; thus, NTIS is quite common in these patients. Tognini [7] reported that among elderly patients (≥ 65 years of age) hospitalised for acute illness, the prevalence of NTIS was 31.9% and significantly associated with acute renal failure, New York Heart Association classification IV heart failure, and metastasised cancer disease. We identified elderly patients who were hospitalised in our hospital. Thyroid function measurements, the T_3 level, and serum levels of total protein (TP), albumin (Alb), prealbumin (PA), urea nitrogen (UN), creatinine (Cr), uric acid (UA), fasting blood glucose (FBG), blood lipids, alanine transaminase (ALT), aspartate transaminase (AST), and haemoglobin (Hb) were analysed, and the prediction of 2-year all-cause mortality based on free T_3 levels was assessed. In the present study, a reference basis for the prediction of disease outcome in hospitalised elderly male patients with NTIS was presented.

Methods

Subjects

The data were acquired from the First Medical Center and the Second Medical Center of Chinese PLA General Hospital. The inclusion criteria for the study were as follows: 1) ≥ 60 years of age, 2) male, 3) hospitalised between January 2012 and December 2013, and 4) complete data on thyroid function. The exclusion criteria were as follows: 1) diagnosed with thyroid disease such as hyperthyroidism, hypothyroidism, subclinical hyperthyroidism, subclinical hypothyroidism, or Hashimoto's thyroiditis, 2) taking amiodarone, euthyroid, glucocorticoid, dopamine, or interferon, and 3) history of thyroid surgery. Because there were fewer female patients in our hospital, only male patients were selected as research subjects to reduce the influence of sex bias on the results. A total of 931 subjects were enrolled in the present study. The subjects were divided based on the presence of NTIS into the NTIS group and normal thyroid function (non-NTIS) group. Because the baseline age and body mass index (BMI) in the two groups differed significantly, the groups were matched by age and weight using the propensity score matching (PSM). After the matching, the total number of study subjects was 852: 192 NTIS patients and 660 normal thyroid function subjects. At the end of the 2-year follow-up, 157 people died, and 45 were lost to follow-up (5.28%). The time and cause of death were recorded for all deceased patients.

Study protocol

Venous blood was drawn from all patients 8–10 hours after an overnight fast, and total T_4 , total T_3 , free T_3 , free T_4 , TSH, TP, Alb, PA, UN, Cr, UA, ALT, AST, and Hb levels were measured. Radioimmunoassay was used to measure the serum levels of total T_3 , free T_3 , total T_4 , free T_4 , and TSH. The Sysmex Xt-1800 Automated Hematology Analyzer (SYSMEX Corporation, Japan) was used for routine blood tests. Biochemistry measurements were performed using i-CHROMA Reader (Boditech Med Inc. Korea). Normal

thyroid hormone levels are as follows: total T₄ (55.34–160.88 nmol/L), total T₃ (1.01–2.95 nmol/L), free T₃ (2.76–6.3 pmol/L), free T₄ (10.42–24.32 pmol/L), and TSH (0.35–5.5 uIU/mL). Intra-batch and batch-to-batch variations were < 3.35% and < 5.04%, respectively.

Diagnostic criteria for NTIS

Decreased serum total T₃ and/or free T₃, normal or mildly reduced total T₄ or free T₄, and normal TSH levels were the diagnostic criteria for NTIS [8].

Statistical analysis

PSM (1:4) was used to account for demographic differences in the selected participants. SPSS 22.0 was used for the statistical analysis. Normally distributed data are expressed as means ± standard deviation ($\bar{x} \pm SD$) and non-normally distributed data as quartiles. Normally distributed data were compared between the two groups using *t*-test or *t'*-test. The rank sum test was used to compare the data distribution between the two groups. All data were evaluated using two-sided tests. Correlations were determined using Pearson correlation analysis for normally distributed data and Spearman's test for non-normally distributed data. The ROC curve was used to calculate the relationship between free T₃ level and all-cause mortality. Overall survival at 24 months was estimated using the Kaplan–Meier method. Bivariate and multivariate Cox proportional hazards models were used to evaluate the risk factors associated with patient mortality. Statistical significance was set at $P < 0.05$.

Results

Comparison of baseline data between the NTIS and non-NTIS groups

To minimize research bias, PSM was used to match the two groups according to two major factors that influence metabolic indicators and mortality: age and BMI. After matching, statistically significant differences in age and BMI were not observed (Table 1).

Table 1
Baseline patient characteristics before and after PSM

Variable	Before PSM				After PSM			
	NTIS (n = 193)	Non-NTIS (n = 738)	t	P	NTIS (n = 192)	Non-NTIS (n = 660)	t	P
Age	87.90 ± 5.99	85.97 ± 8.57	3.36	< 0.01	87.84 ± 5.96	87.56 ± 6.16	0.56	0.57
BMI	23.68 ± 3.62	23.97 ± 3.12	-1.11	0.27	23.72 ± 3.56	23.88 ± 3.13	-0.57	0.57
<i>PSM</i> propensity score matching, <i>NTIS</i> non-thyroidal illness syndrome, <i>BMI</i> body mass index								
After matching by age and BMI, the total T ₃ , free T ₃ , total T ₄ (all P < 0.001), and TSH levels (P = 0.001) were significantly lower in the NTIS group than in the non-NTIS group. In comparisons of baseline biochemical indicators, TP, Alb, PA, Hb, UA, TG, and HDLC levels were significantly lower, whereas UN and FBG levels were higher, in the NTIS group than in the non-NTIS group (Table 2).								

Table 2
Comparison of baseline data between the NTIS and non-NTIS groups ($\bar{x} \pm SD$)

	Total (n = 852)	NTIS group (n = 192)	Non-NTIS group (n = 660)	t/Z	P
Total T ₃ ($\mu\text{mol/L}$)	1.27 \pm 0.31	0.90 \pm 0.16	1.38 \pm 0.25	-25.21	< 0.001
Free T ₃ (pmol/L)	3.63 \pm 0.83	2.63 \pm 0.54	3.92 \pm 0.66	-24.78	< 0.001
Total T ₄ ($\mu\text{mol/L}$)	86.34 \pm 16.31	75.10 \pm 16.38	89.60 \pm 14.78	-11.67	< 0.001
Free T ₄ (pmol/L)	15.99 \pm 2.73	15.62 \pm 2.99	16.10 \pm 2.63	-2.17	0.31
TSH (uIU/mL)	1.88 (1.30, 2.88)	1.68(1.04, 2.74)	1.95(1.36, 2.93)	-3.37	0.001
TP (g/L)	66.37 \pm 6.34	64.48 \pm 6.67	66.92 \pm 6.14	-4.78	< 0.001
Alb (g/L)	38.06 \pm 4.57	34.82 \pm 4.43	39.01 \pm 4.17	-12.08	< 0.001
PA (mg/dL)	23.19 \pm 7.52	21.86 \pm 9.18	23.58 \pm 6.93	-2.79	0.005
Hb (g/L)	119.10 \pm 18.99	111.46 \pm 18.30	121.32 \pm 18.63	-6.48	< 0.001
UA ($\mu\text{mol/L}$)	335.25 \pm 100.74	320.34 \pm 120.80	339.58 \pm 93.78	-2.34	0.02
FBG (mmol/L)	5.88 \pm 1.88	6.68 \pm 2.28	5.65 \pm 1.68	6.83	< 0.001

T₃ triiodothyronine, T₄ thyroxine, TSH thyroid-stimulating hormone, TP total protein, Alb albumin, PA prealbumin, Hb haemoglobin, UA uric acid, FBG fasting blood glucose, TC total cholesterol, TG triglyceride, HDLC high-density lipoprotein cholesterol, LDLC low-density lipoprotein cholesterol, ALT alanine transaminase, AST aspartate transaminase, UN urea nitrogen, Cr creatinine

	Total (n = 852)	NTIS group (n = 192)	Non-NTIS group (n = 660)	t/Z	P
TC (mmol/L)	3.99 ± 0.88	4.07 ± 1.06	3.97 ± 0.82	1.48	0.14
TG (mmol/L)	1.20(0.87, 1.65)	1.05(0.79, 1.65)	1.21(0.90, 1.65)	-2.09	0.04
HDLC (mmol/L)	1.19 ± 0.37	1.13 ± 0.42	1.20 ± 0.35	-2.37	0.02
LDLC (mmol/L)	2.30 ± 0.75	2.34 ± 0.91	2.28 ± 0.69	0.94	0.35
ALT (U/L)	13.00(10.00, 20.00)	13.00(9.00, 22.00)	13.00(10.00, 20.00)	-0.54	0.59
AST (U/L)	15.00(18.00, 23.00)	19.00(14.00, 26.83)	18.00(15.00, 22.00)	-0.90	0.37
UN (mmol/L)	6.40(5.20, 8.90)	7.80(5.90, 11.30)	6.20(5.10, 8.30)	-5.95	< 0.001
Cr (µmol/L)	82.00(69.00, 99.00)	82.00(66.25, 121.75)	82.00(70.25, 97.00)	-1.07	0.285
<p><i>T₃</i> triiodothyronine, <i>T₄</i> thyroxine, <i>TSH</i> thyroid-stimulating hormone, <i>TP</i> total protein, <i>Alb</i> albumin, <i>PA</i> prealbumin, <i>Hb</i> haemoglobin, <i>UA</i> uric acid, <i>FBG</i> fasting blood glucose, <i>TC</i> total cholesterol, <i>TG</i> triglyceride, <i>HDLC</i> high-density lipoprotein cholesterol, <i>LDLC</i> low-density lipoprotein cholesterol, <i>ALT</i> alanine transaminase, <i>AST</i> aspartate transaminase, <i>UN</i> urea nitrogen, <i>Cr</i> creatinine</p>					

Correlations of total T₃ and free T₃ levels with important biochemical indicators

Correlation analysis showed that total T₃ was positively correlated with the levels of TP (r = 0.15, P < 0.001), Alb (r = 0.40, P < 0.001), PA (r = 0.08, P = 0.01), and Hb (r = 0.37, P < 0.001). Total T₃ was negatively correlated with the levels of FBG (r = - 0.28, P < 0.001), UN (r = - 0.26, P < 0.001), and Cr (r = - 0.12, P < 0.001).

Free T₃ was positively correlated with the levels of TP (r = 0.14, P < 0.001), Alb (r = 0.50, P < 0.001), PA (r = 0.19, P < 0.001), Hb (r = 0.40, P < 0.001), and UA (r = 0.11, P = 0.001). Free T₃ was negatively correlated

with the levels of FBG ($r = -0.26, P < 0.001$), UN ($r = -0.20, P < 0.001$), and Cr ($r = -0.05, P < 0.001$; Table 3).

Table 3
Factors associated with total T₃ and free T₃

	Total T ₃		Free T ₃	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
TP	0.15	< 0.001	0.14	< 0.001
Alb	0.40	< 0.001	0.50	< 0.001
PA	0.08	0.01	0.19	< 0.001
Hb	0.37	< 0.001	0.40	< 0.001
UA	0.06	0.07	0.11	0.001
FBG	-0.28	< 0.001	-0.26	< 0.001
TC	-0.07	0.05	0.01	0.70
TG	0.03	0.46	0.06	0.09
HDLC	0.06	0.08	0.07	0.06
LDLC	0.00	0.93	0.06	0.11
ALT	0.04	0.25	0.04	0.21
AST	-0.06	0.08	-0.06	0.07
UN	-0.26	< 0.001	-0.20	< 0.001
Cr	-0.12	< 0.001	-0.05	< 0.001

TP total protein, *Alb* albumin, *PA* prealbumin, *Hb* haemoglobin, *UA* uric acid, *FBG* fasting blood glucose, *TC* total cholesterol, *TG* triglyceride, *HDLC* high-density lipoprotein cholesterol, *LDLC* low-density lipoprotein cholesterol, *ALT* alanine transaminase, *AST* aspartate transaminase, *UN* urea nitrogen, *Cr* creatinine

Effects of the free T₃ level on mortality according to Cox proportional hazards models

Univariate Cox proportional hazards models showed that the free T₃ level was associated with reduced patient mortality. Among the other biochemical indicators, Alb and Hb levels were negatively, whereas FBG, total cholesterol (TC), and ALT levels were positively, correlated with patient mortality. Multivariate models adjusted for other confounding factors showed that a lower free T₃ level in elderly male patients is associated with all-cause mortality. Other indicators including Alb and Hb levels were negatively correlated and the ALT level positively correlated with patient mortality. Patients with respiratory diseases

(RD), chronic kidney disease (CKD), and tumours had a higher mortality rate (Table 4). Furthermore, according to ROC analysis of the free T₃ level and 2-year mortality rate, a cut-off free T₃ level of 3.45 pmol/L yielded the highest Youden index (0.327), with a sensitivity of 0.675 and specificity of 0.642 (Fig. 1).

Table 4

Effects of thyroid hormone levels, biochemical indicators, and systemic diseases on mortality according to Cox proportional hazards models

Parameters	Univariate adjusted				Multivariate adjusted			
	β	HR	95% CI	P	β	HR	95% CI	P
Free T ₃ (pmol/L)	-1.30	0.27	(0.19, 0.38)	< 0.001	-0.66	0.52	(0.35, 0.77)	0.001
Alb (g/L)	-1.55	0.21	(0.15, 0.29)	< 0.001	-0.94	0.39	(0.27, 0.56)	< 0.001
Hb (g/L)	-1.54	0.21	(0.16, 0.29)	< 0.001	-0.84	0.43	(0.30, 0.62)	< 0.001
UA (μ mol/L)	-0.19	0.82	(0.53, 1.29)	0.40	-0.06	0.95	(0.58, 1.53)	0.82
FBG (mmol/L)	0.62	1.86	(1.30, 2.66)	0.001	-0.01	0.99	(0.67, 1.48)	0.96
TC (mmol/L)	0.99	2.69	(1.63, 4.75)	0.001	0.23	1.26	(0.68, 2.36)	0.46
ALT (U/L)	1.12	3.07	(1.99, 4.75)	< 0.001	1.18	3.26	(2.03, 5.22)	< 0.001
RD	1.16	3.20	(2.33, 4.39)	< 0.001	0.42	1.52	(1.06, 2.17)	0.02
NSD	-0.02	0.99	(0.58, 1.68)	0.96	0.16	1.18	(0.68, 2.04)	0.56
CVD	0.42	1.52	(0.85, 2.75)	0.16	-0.04	0.96	(0.53, 1.75)	0.89
CKD	1.08	2.95	(2.07, 4.20)	< 0.001	1.00	2.72	(1.91, 3.89)	< 0.001
Tumour	1.04	2.82	(2.05, 3.88)	< 0.001	0.97	2.63	(0.83, 3.77)	< 0.001

T₃ triiodothyronine, *Alb* albumin, *Hb* haemoglobin, *UA* uric acid, *FBG* fasting blood glucose, *TC* total cholesterol, *ALT* alanine transaminase, *RD* respiratory diseases, *NSD* nervous system disease, *CVD* cardiovascular disease, *CKD* chronic kidney disease

Comparison of survival rate between the NTIS and non-NTIS groups

A total of 157 patients died during the 2-year follow-up period, including 68 deaths in the NTIS group, with a mortality rate of 35.42%, and 89 deaths in the non-NTIS group, with a mortality rate of 13.48%. Kaplan–

Meier survival analyses showed that the survival rate in both groups decreased with time. At 24 months, the survival rate in the NTIS group was 64.58%, which was significantly lower than that in the non-NTIS group (86.52%), as shown in Fig. 2 (log-rank $\chi^2 = 70.56$, $P < 0.001$).

Discussion

In the elderly population, thyroid hormone levels can help monitor health status, predict short-term and long-term clinical prognoses, predict disease severity, and assess quality of life and survival status. In previous studies, the frequency of thyroid dysfunction increased with advancing age in the hospitalised elderly patients. The prevalence of NTIS in hospitalised severely or debilitated elderly patients can be as high as 32%-62% [7, 9, 10]. In the present study, among the 931 elderly male patients hospitalised for various reasons, there were 193 NTIS patients (20.73% prevalence rate). After matching by age and BMI, the Alb levels were significantly lower, and the renal function indices and FBG levels higher, in the NTIS group than in the non-NTIS group. In addition, the 2-year survival rate was significantly lower in the NTIS group than in the non-NTIS group. A reduced free T_3 level was strongly associated with all-cause mortality in NTIS patients, a similar finding of previous studies [11, 12].

NTIS is often associated with nutritional deficiencies or acute and chronic diseases. Protein and UA levels are indicators of nutritional status. Proteins also play an important role in the synthesis and transport of thyroid hormones. In several studies, the serum Alb level was reduced, and the free T_3 level was positively correlated with the Alb level, in patients with NITS [13, 14]. In the present study, the Alb levels were also significantly reduced in the NTIS group compared with the non-NTIS group. Correlation analysis showed that TP, Alb, and PA levels decreased as the total T_3 and free T_3 levels decreased. Hypothetically, decreased Alb levels leads to a decrease in the conversion of T_4 to T_3 , resulting in a decrease in T_3 levels or a decrease in T_4 binding to the protein, which accelerates the removal of thyroid hormones [15, 16]. In the present study, the free T_3 level was also positively correlated with the UA and Hb levels, further confirming that fasting and hunger can cause NTIS [5].

The T_4 level is strongly associated with CKD. NTIS is a common thyroid dysfunction in CKD patients [13, 17], and its mechanism is associated with the kidney's involvement in the synthesis, secretion, and metabolism of thyroid hormones. In kidney disease, chronic metabolic acidosis and inflammatory factors lead to the inhibition of deiodinase activity, and the conversion of T_4 to T_3 in peripheral tissues is reduced [18]. Hypothalamic–pituitary–thyroid axis dysfunction [19] combined with loss of T_4 in the urine causes total T_3 and total T_4 levels to decrease. A decrease in the glomerular filtration rate (GFR) reduces iodine excretion, resulting in an iodine-blocking effect (Wolff–Chaikoff effect) [19]. Song et al. [20] retrospectively analysed 2,284 subjects with normal TSH levels and found that as the estimated GFR (eGFR) decreased in CKD patients, the prevalence of low T_3 syndrome gradually increased; the eGFR was positively correlated with the serum T_3 level and was independent of age and serum protein levels. In another study, reduced free T_3 levels predicted an increased risk of cardiovascular events in CKD patients with proteinuria [21]. In patients with chronic haemodialysis, reduced free T_3 levels were a strong

predictor of all-cause mortality [22]. In the present study, among hospitalised elderly male patients, the UN and Cr levels in the NTIS group were higher than in the non-NTIS group. Correlation analysis showed total T_3 and free T_3 levels were negatively correlated with UN and Cr levels. After adjusting for confounding factors, all-cause mortality was significantly increased in CKD patients.

Compared with young, short-term diabetic patients, the elderly are more likely to develop NTIS. Some studies have compared the thyroid function status of diabetic patients according to age, disease course, and blood glucose control status and found lower free T_3 levels in diabetic patients than in normal controls [23, 24]; furthermore, the incidence of cardiovascular events in patients with type 2 diabetes and NTIS was significantly increased [25]. Aging, long diabetes duration, poor blood sugar control, and several complications can increase the prevalence of NTIS, especially in patients with diabetic nephropathy and ketoacidosis [26, 27]. In the present study, total T_3 and free T_3 levels were also negatively correlated with the FBG level.

In this study, at the end of the 2-year follow-up, a total of 157 patients had died (18.43% mortality rate). Kaplan–Meier survival analyses showed that the survival rate was significantly lower in the NTIS group (64.58%) than in the non-NTIS group (86.52%). Cox proportional hazards models showed that after removing confounding factors, reduced free T_3 levels increased the risk of all-cause death. The ROC analysis showed that when using a free T_3 cut-off level of 3.45 pmol/L, the Youden index was highest, with a sensitivity of 0.675 and specificity of 0.642, indicating that when free T_3 levels are less than 3.45 pmol/L, the risk of death increases. In a recent study of 1,190 patients with acute heart failure, the survival rates were significantly lower in patients with low free T_3 compared with normal levels, and a multivariate Cox proportional hazards model showed that a low free T_3 level was an independent predictor of mortality [28]. Studies on ICU patients and hospitalised chronic patients reported the free T_3 level to be an independent predictor of all-cause mortality [11, 29]. Similar to previous studies, a lower free T_3 level in the present study was associated with a worse prognosis in elderly male patients with chronic diseases.

The present study had several limitations including failure to evaluate many factors that affect the patient prognosis. Although age and BMI were matched between the two groups, the treatment plan, treatment timing, severity of the patient's condition, and response to the treatment plan could have affected the patient's condition. Due to the small sample size, many influencing factors were difficult to quantify. The patients were not stratified according to the above-mentioned factors. In addition, only elderly male inpatients were analysed in the study. Whether the above study results can be generalised to the general population requires further research.

Conclusion

In summary, among elderly male patients hospitalised for multiple causes, the 2-year survival rate was lower in the NTIS group than non-NTIS group. As the total T_3 and free T_3 levels decreased, the protein

levels and renal function worsened, and the FBG level increased. A lower free T₃ level was associated with an increased risk of all-cause mortality.

Abbreviations

NTIS
non-thyroidal illness syndrome; ROC:Receiver operating characteristic curves; T₃:triiodothyronine; T₄:thyroxine; TSH thyroid-stimulating hormone; TP:total protein; Alb:albumin; PA:prealbumin; Hb:haemoglobin, UA:uric acid, TG:triglyceride; HDLC:high-density lipoprotein cholesterol; UN:urea nitrogen; FBG:fasting blood glucose; Cr:creatinine; ICU:intensive care units; ALT:alanine transaminase; AST:aspartate transaminase; BMI:body mass index; PSM:propensity score matching; TC:total cholesterol; RD:respiratory diseases; CKD:chronic kidney disease; NSD:nervous system disease; CVD:cardiovascular disease.

Declarations

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Authors' contributions

ST Y conceived, designed and developed the project. M W, XM G, L L and ZY G assisted in data collection. HZ L, XY M and ZH L conducted data analysis. XY M and HZ L developed the initial drafts of the manuscript. CL L and ZH L helped in revising subsequent drafts. All authors read and approved the final manuscript.

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Availability of date and materials

The datasets used in the analyses described in this study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Chinese PLA General Hospital. The permission to access the raw data was granted by the Ethics Committee of Chinese PLA General

Hospital. Due to the retrospective design of the study and accordingly national guidelines, the local ethic committee confirmed, that informed consent was not necessary from participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

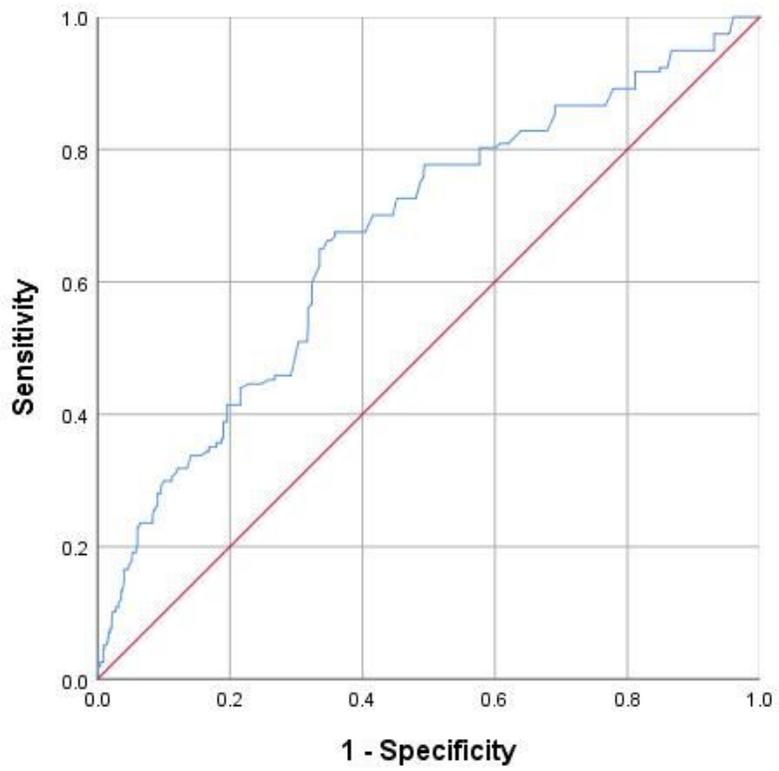


Figure 1

Receiver operating characteristic curve assessing the ability of the free triiodothyronine (T3) level to predict all-cause mortality (free T3 cut-off level, 3.445; sensitivity, 67.5%; specificity, 64.2%).

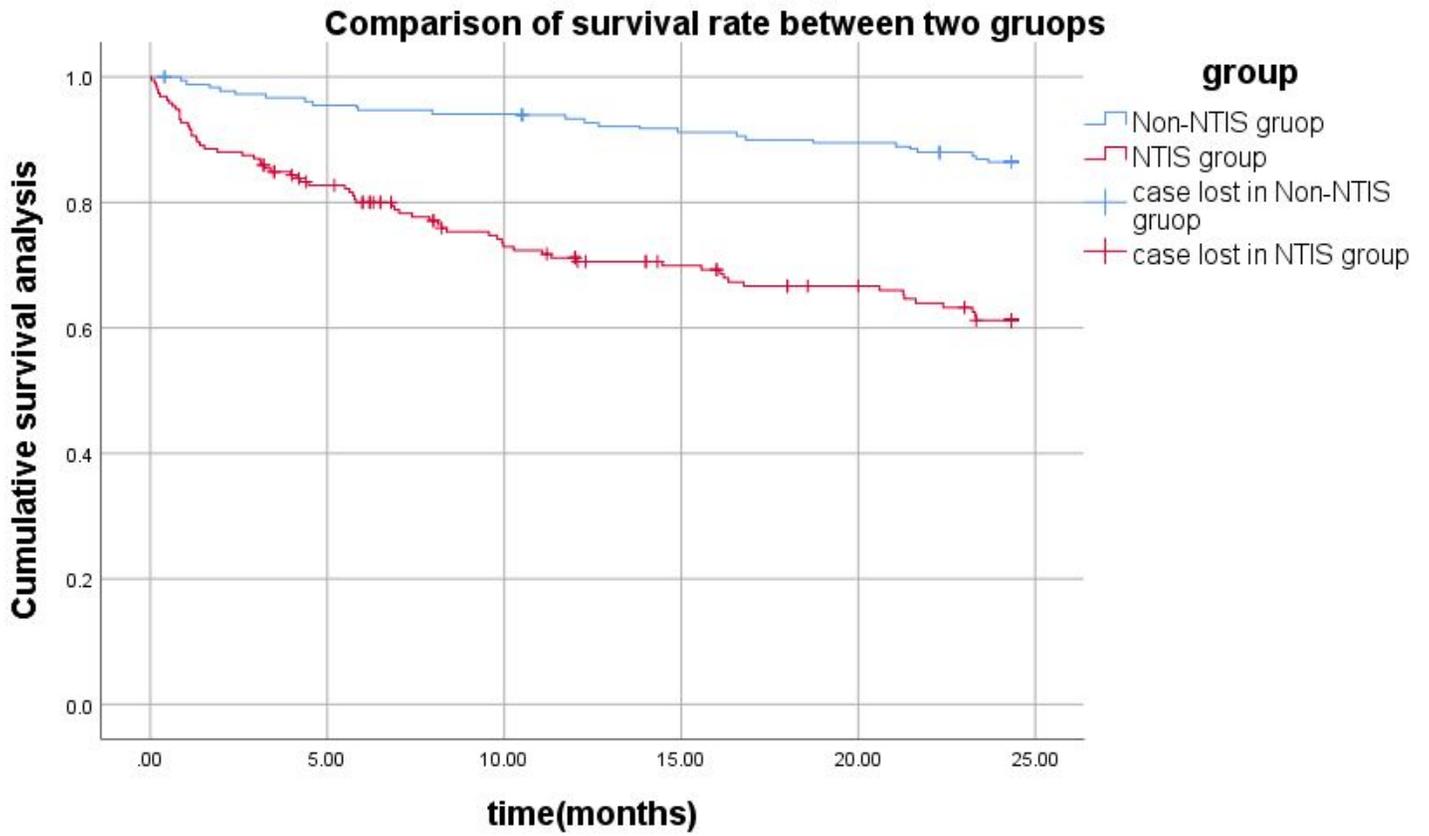


Figure 2

Kaplan–Meier survival curves of the NTIS and non-NTIS groups over 24 months.