·临床研究·

游离三碘甲状腺原氨酸降低对感染诱发的老年多器官功能障碍综合征的早期预测价值

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【摘 要】 目的 探讨游离三碘甲状腺原氨酸(FT3)降低对感染诱发的老年多器官功能障碍综合征(i-MODSE)是否具有早期预测作用。**方法** 回顾性分析2017年1月至2021年12月于空军军医大学第一附属医院老年病科出院的755例老年(≥65岁)感染患者的临床资料,根据住院期间是否发生多器官功能障碍综合征(MODS)将患者分为MODS组(n=80)和对照组(n=675),分析人口学特征和包括FT3在内的实验室检查结果对i-MODSE的影响。采用SPSS 26.0统计软件进行数据分析。根据数据类型,分别采用t检验、Mann-Whitney U检验或χ^2检验进行组间比较。采用二元logistic回归分析i-MODSE发生的影响因素。**结果** 755例患者中,MODS发生率为10.60%(80/755)。与对照组相比,MODS组FT3显著降低[(2.67±0.87)和(3.40±0.79) pmol/L;P<0.001]。logistic回归分析结果显示,FT3降低是老年感染患者MODS发生的独立危险因素(OR=4.748,95%CI 2.387~9.443;P<0.001)。**结论** FT3降低是老年感染患者MODS发生的独立危险因素,可以应用于早期预测i-MODSE。

【关键词】 老年人;游离三碘甲状腺原氨酸;感染;多器官功能障碍综合征

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Early predictive value of decrease in free triiodothyronine for infection-induced multiple organ dysfunction syndrome in the elderly

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【Abstract】 Objective To explore whether the decrease of free triiodothyronine (FT3) has early predictive value in infection-induced multiple organ dysfunction syndrome in the elderly (i-MODSE). **Methods** The clinical data of 755 elderly infected patients (≥65 years old) who were discharged from the Department of Geriatrics, First Affiliated Hospital of Air Force Military Medical University from January 2017 to December 2021 were retrospectively analyzed. According to the occurrence of multiple organ dysfunction syndrome (MODS) during hospitalization, the patients were divided into MODS group (n=80) and control group (n=675). The effects of demographic characteristics and laboratory tests, including FT3, on i-MODSE were analyzed. The data were analyzed by SPSS statistics 26.0. Data comparison between two groups was performed using student's t test, Mann-Whitney U test or Chi-square test depending on different data types. Binary logistic regression was used to analyze the influencing factors of i-MODSE. **Results** Among the 755 patients, the incidence of MODS was 10.60% (80/755). FT3 level was significantly lower in the MODS group than the control group [(2.67±0.87) vs (3.40±0.79) pmol/L; P<0.001]. Logistic regression analysis showed that FT3 decline was an independent risk factor for the occurrence of MODS in elderly infected patients (OR=4.748, 95%CI 2.387-9.443; P<0.001). **Conclusion** FT3 decline is an independent risk factor for the occurrence of MODS in elderly patients with infection, and can be used to predict i-MODSE in the early stage.

【Key words】 aged; free triiodothyronine; infection; multiple organ dysfunction syndrome

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感染诱发的老年多器官功能障碍综合征(infection-induced multiple organ dysfunction syndrome in the elderly, i-MODSE)是指老年人(≥65 岁)在器官老化和患有多种慢性疾病的基础上,由感染激发、短时间内序贯或同时发生 2 个或 2 个以上器官功能障碍或衰竭的综合征[1]。感染是老年人发生多器官功能障碍综合征(multiple organ dysfunction syndrome, MODS)的首位诱因,约占全部诱因的 80.9%[2]。i-MODSE 患者往往患有多种慢性病,整体修复能力减退,且存在多种治疗矛盾,导致其病死率极高,可达 75%~100%[3,4]。在我国人口老年化趋势日益明显的情况下,加强对老年感染患者的临床研究,预防或减少 i-MODSE 的发生、降低患者病死率尤为重要。

游离三碘甲状腺原氨酸(free triiodothyronine, FT3)是甲状腺功能指标中的一项。在老年住院患者[5]和脓毒症患者[6]中,甲状腺激素的改变非常常见,其中就包括 FT3 的降低。FT3 降低被认为与某些危重疾病的预后相关,如新型冠状病毒肺炎[7]、脓毒症休克[8]、心肌梗死[9]等。也有研究发现 FT3 降低可以预测非危重症患者的死亡率[10]。还有研究发现 FT3 降低与多种器官衰竭的预后相关[11-13],但它们与器官衰竭甚至 MODS 的发生是否相关尚不清楚。本研究旨在探讨 FT3 降低是否可以早期预测 i-MODSE 的发生。

1 对象与方法

1.1 研究对象

回顾性分析空军军医大学第一附属医院老年病科 2017 年 1 月至 2021 年 12 月出院的 755 例老年感染患者的临床和实验室检查资料,根据患者在住院期间是否发生 MODS 将患者分为多器官功能障碍综合征组(MODS 组,$n=80$)和对照组($n=675$)。纳入标准:(1)年龄≥65 岁;(2)存在肺部或泌尿系感染。肺部感染诊断标准:肺部影像学检查出现新的浸润影,同时存在以下指标中的最少一项:咳嗽和咳痰、呼吸困难、呼吸急促、体温>38℃或<36℃、白细胞计数>10×10^9/L 或<4×10^9/L。泌尿系感染诊断标准:尿培养阳性(细菌和/或真菌≥10^5cfu/ml),同时存在以下指标中的最少一项:膀胱刺激征阳性(尿频、尿急、尿痛)、腰痛、发热。序贯器官衰竭评估评分增加 2 分或 2 分以上被用来确定单个器官功能障碍[14,15],MODS 定义为 2 个或 2 个以上器官功能障碍。排除标准:(1)恶性肿瘤;(2)器官移植;(3)入院前 3 个月内有任何重大手术;(4)急性失血性休克;(5)住院时间<3 d;(6)病历资料不全。

此外,还根据 FT3 水平将患者分为低 FT3 组与非低 FT3 组,比较 2 组患者 i-MODSE 发生率的差异。本研究经西京医院伦理委员会批准。

1.2 方法

记录患者年龄、性别等信息,收集患者确诊感染后 24 h 内 FT3、游离甲状腺素(free thyroxine, FT4)、促甲状腺激素(thyroid stimulating hormone, TSH)等指标结果,分析这些变量对 i-MODSE 发生的影响。本医疗机构 FT3 的正常参考值范围为:3.1~6.8 pmol/L。

1.3 统计学处理

采用 SPSS 26.0 统计软件进行数据分析。符合正态分布的连续性变量用均数±标准差($\bar{x}\pm s$)表示,组间比较采用 t 检验;非正态分布的连续性变量用中位数(四分位数间距)表示,组间比较采用 Mann-Whitney U 检验进行分析。分类变量以例数(百分率)表示,组间比较采用 χ^2 检验。采用二元 logistic 回归分析 i-MODSE 发生的影响因素。绘制受试者工作特征(receiver operator characteristic, ROC)曲线,确定相关指标识别 i-MODSE 的截断值,并计算曲线下面积(area under the curve, AUC),评价变量的鉴别能力。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 MODS 组与对照组基线资料比较

共 755 例老年感染患者纳入本研究,年龄 65~100 岁,平均(84.42±7.73)岁;男性 477 例(63.18%);80 例(10.60%)患者在住院期间发生 MODS。与对照组相比,MODS 组患者年龄更大,男性占比更高,FT3 更低,差异均有统计学意义($P<0.05$);而 FT4 和 TSH 比较,差异无统计学意义($P>0.05$;表 1)。

2.2 低 FT3 组与非低 FT3 组 i-MODSE 发生率比较

将 FT3 值低于正常参考值范围下限(3.1 pmol/L)的患者($n=302$)纳入低 FT3 组,其余患者纳入非低 FT3 组($n=453$),比较 2 组患者 i-MODSE 的发生率。结果显示,低 FT3 组患者年龄更大,i-MODSE 的发生率更高,差异均有统计学意义($P<0.05$;表 2)。

表1 MODS组与对照组患者基线资料比较

Table 1 Comparison of baseline data between MODS group and control group

Item	MODS group(n=80)	Control group(n=675)	P value
Age[years, $M(Q_1, Q_3)$]	92.00(86.00,94.00)	85.00(79.00,90.00)	<0.001
Gender[n(%)]			0.005
Male	62(77.50)	415(61.48)	
Female	18(22.50)	260(38.52)	
FT3(pmol/L, $\bar{x}\pm s$)	2.67±0.87	3.40±0.79	<0.001
FT4(pmol/L, $\bar{x}\pm s$)	15.81±3.59	16.22±3.14	0.284
TSH[μIU/ml, $M(Q_1, Q_3)$]	1.69(0.76,3.04)	2.12(1.15,3.58)	0.081
MAP(mmHg, $\bar{x}\pm s$)	84.18±11.83	91.15±11.41	<0.001
WBC[$\times10^9$/L, $M(Q_1, Q_3)$]	6.21(4.88,11.06)	6.91(5.38,9.26)	0.026
HGB(g/dl, $\bar{x}\pm s$)	10.52±2.11	12.12±2.07	<0.001
PLT[$\times10^9$/L, $M(Q_1, Q_3)$]	140.00(87.00,227.00)	172.00(139.00,222.00)	<0.001
TBIL[μmol/L, $M(Q_1, Q_3)$]	16.30(8.90,22.80)	12.10(9.00,16.10)	0.255
CRE[μmol/L, $M(Q_1, Q_3)$]	84.00(68.00,135.00)	96.00(79.00,116.00)	0.615
TC(mmol/L, $\bar{x}\pm s$)	3.25±1.12	3.66±0.95	0.004
TG[mmol/L, $M(Q_1, Q_3)$]	0.81(0.58,1.43)	0.98(0.71,1.34)	0.099
APTT[s, $M(Q_1, Q_3)$]	33.70(28.60,40.80)	28.80(25.50,32.80)	<0.001
NT-proBNP[pg/L, $M(Q_1, Q_3)$]	3.62(1.64,6.28)	0.55(0.24,1.56)	<0.001

MODS: multiple organ dysfunction syndrome; FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid stimulating hormone; MAP: mean arterial pressure; WBC: white blood cell; HGB: hemoglobin; PLT: platelet; TBIL: total bilirubin; CRE: serum creatinine; TC: total cholesterol; TG: triglycerides; APTT: activated partial thromboplastin time; NT-proBNP: N-terminal pro-brain natriuretic peptide. 1 mmHg=0.133 kPa.

表2 低FT3组与非低FT3组患者i-MODSE发生情况比较

Table 2 Comparison of occurrence of i-MODSE between low FT3 group and non-low FT3 group

Item	Low FT3 group(n=302)	Non-low FT3 group(n=453)	P value
Age[years, $M(Q_1, Q_3)$]	87.00(83.00,92.00)	84.00(77.00,89.00)	<0.001
Gender[n(%)]			0.622
Male	194(64.24)	283(62.47)	
Female	108(35.76)	170(37.53)	
Occurrence rate of i-MODSE[n(%)]			<0.001
i-MODSE	61(20.20)	19(4.19)	
Non-i-MODSE	241(79.80)	434(95.81)	

FT3: free triiodothyronine; i-MODSE: infection-induced multiple organ dysfunction syndrome in the elderly.

2.3 i-MODSE的危险因素分析

对各研究变量进行二元logistic回归单因素分析,再将其中P<0.05的变量纳入多因素分析,结果显示FT3降低是i-MODSE发生的独立危险因素(OR=4.748, 95% CI 2.387~9.443; P<0.001)。i-MODSE的其他危险因素还包括年龄增长、总胆红素升高和活化部分凝血活酶时间延长(表3)。

2.4 危险因素对i-MODSE的预测效能分析

分别绘制FT3降低等危险因素预测i-MODSE的ROC曲线,结果显示FT3降低的AUC为0.747(95%CI 0.688~0.806; P<0.001),其预测i-MODSE的效能较高。当FT3取最佳截断值3.29 pmol/L时,灵敏度和特异度分别为56.7%和86.3%(表4,图1)。

3 讨 论

本研究结果显示,与对照组相比,MODS组患者的FT3更低;多因素logistic回归分析证实了FT3降低是i-MODSE发生的独立危险因素,且具有较高的预测效能。

MODS是住院患者的严重并发症,极大地增加了住院患者的死亡风险。FT3降低已被证实与多种疾病的预后相关,但其是否与MODS之间存在关联还未见报道。该单中心回顾性病例对照研究首次探讨了FT3与MODS之间的关系,结果显示FT3降低与i-MODSE的发生独立相关。

表 3 i-MODSE 危险因素的单因素和多因素 logistic 回归分析

Table 3 Univariate and multivariate logistic regression analysis of risk factors for i-MODSE

Factor	Univariate analysis		Multivariate analysis	
	OR (95%*CI*)	*P* value	*OR*(95%*CI*)	*P* value
Age	1.140(1.093-1.189)	<0.001	1.123(1.048-1.204)	0.001
Male	2.158(1.249-3.730)	0.006	0.843(0.320-2.223)	0.731
FT3(decrease)	3.045(2.228-4.162)	<0.001	4.748(2.387-9.443)	<0.001
FT4	0.960(0.891-1.034)	0.283		
TSH	0.928(0.832-1.035)	0.182		
MAP	0.948(0.928-0.968)	<0.001	0.971(0.939-1.004)	0.079
WBC	1.087(1.022-1.157)	0.008	0.896(0.793-1.013)	0.079
HGB	0.698(0.623-0.783)	<0.001	0.890(0.704-1.124)	0.328
PLT	0.992(0.989-0.996)	<0.001	1.002(0.996-1.008)	0.580
TBIL	1.026(1.007-1.045)	0.007	1.064(1.022-1.108)	0.002
CRE	1.004(0.998-1.009)	0.183		
TC	0.620(0.447-0.860)	0.004	1.192(0.757-1.878)	0.448
TG	1.029(0.666-1.590)	0.897		
APTT	1.119(1.084-1.155)	<0.001	1.086(1.024-1.152)	0.006
NT-proBNP	1.182(1.122-1.246)	<0.001	1.087(0.999-1.183)	0.052

i-MODSE: infection-induced multiple organ dysfunction syndrome in the elderly; FT3: free triiodothyronine; FT4: free thyroxine; TSH: thyroid stimulating hormone; MAP: mean arterial pressure; WBC: white blood cell count; HGB: hemoglobin; PLT: platelet count; TBIL: total bilirubin; CRE: serum creatinine; TC: total cholesterol; TG: triglycerides; APTT: activated partial thromboplastin time; NT-proBNP: N-terminal pro-brain natriuretic peptide.

表 4 危险因素对 i-MODSE 的预测效能

Table 4 Predictive efficacy of risk factors for i-MODSE

Factor	AUC	95%*CI*	*P* value	Cut-off value	Sensitivity	Specificity	Youden index
FT3(decrease)	0.747	0.688-0.806	<0.001	3.29	0.567	0.863	0.430
Age	0.732	0.676-0.787	<0.001	90.00	0.588	0.752	0.340
APTT	0.729	0.669-0.790	<0.001	31.85	0.622	0.714	0.336
TBIL	0.539	0.462-0.616	0.255	14.15	0.532	0.636	0.168

i-MODSE: infection-induced multiple organ dysfunction syndrome in the elderly; FT3: free triiodothyronine; APTT: activated partial thromboplastin time; TBIL: total bilirubin; AUC: area under the curve.

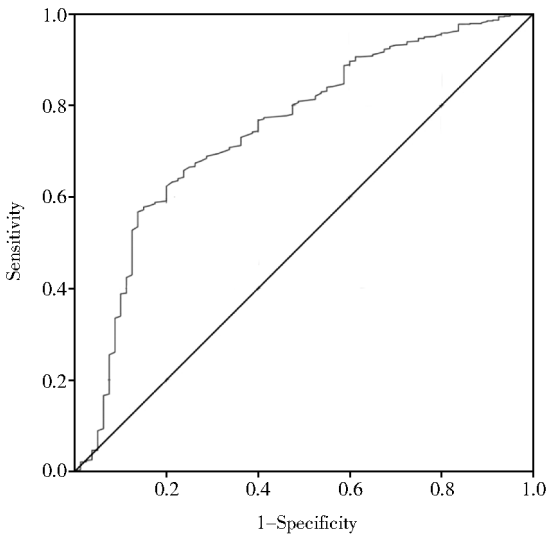

图 1 FT3 预测 i-MODSE 的 ROC 曲线

Figure 1 ROC curve of FT3 for predicting i-MODSE

FT3: free triiodothyronine; i-MODSE: infection-induced multiple organ dysfunction syndrome in the elderly; ROC: receiver operating characteristic.

FT3 降低与 i-MODSE 发生之间的具体机制尚不清楚,其潜在机制可能包括以下几个方面。(1)甲状腺激素在免疫平衡中发挥重要作用,尤其是先天性免疫反应。FT3 水平降低可影响中性粒细胞和其他免疫细胞的功能和活性,从而导致免疫系统功能障碍[16]。(2)有研究报告,三碘甲状腺原氨酸补充剂可通过增加抗凝血酶Ⅲ水平来保护脓毒症患者免于并发弥散性血管内凝血。因此推断,FT3 降低可能会引起或者加重脓毒症患者的凝血系统功能障碍[17]。(3)FT3 降低可能会引起心功能障碍。这是由于甲状腺激素在生理和病理条件下的心血管稳态中具有重要作用,对心脏收缩力、舒张功能、心率和全身血管阻力均具有重要影响,对心脏具有保护作用[18]。(4)FT3 水平升高可增加肺表面活性物质的合成,降低肺泡表面张力,增加肺顺应性,从而改善肺功能,说明 FT3 降低可能与呼吸功能障碍相关[19]。

本研究存在以下局限性：(1)属于回顾性研究，有待前瞻性研究加以证实；(2)单中心研究，缺乏外部验证，需要多中心、更大样本量的研究进行验证。综上所述，本研究结果显示 FT3 降低是 i-MODSE 发生的独立危险因素，临床上可考虑用以早期预测 i-MODSE 的发生。

【参考文献】

[1] 国家老年疾病临床医学研究中心(解放军总医院)《感染诱发的老年多器官功能障碍综合征诊治中国专家共识》撰写组. 感染诱发的老年多器官功能障碍综合征诊治中国专家共识[J]. 中华老年多器官疾病杂志, 2018, 17(1): 3-15. DOI: 10.11915/j.issn.1671-5403.2018.01.002.
Writing Group of Chinese Experts' Consensus on the Diagnosis and Treatment of Infection Induced Multiple Organ Dysfunction Syndrome in the Elderly, National Clinical Research Center for Geriatric Diseases (Chinese PLA General Hospital). Chinese experts' consensus on diagnosis and treatment of infection induced multiple organ dysfunction syndrome in the elderly[J]. Chin J Mult Organ Dis Elderly, 2018, 17(1): 3-15. DOI: 10.11915/j.issn.1671-5403.2018.01.002.

[2] 钱小顺, 韩亚玲, 侯允天, 等. 1605例老年多器官功能衰竭的临床分析[J]. 中华老年多器官疾病杂志, 2002, 1(1): 7-10. DOI: 10.3969/j.issn.1671-5403.2002.01.003.
Qian XS, Han YL, Hou YT, *et al*. Clinical features of multiple organ failure in the elderly: a report of 1605 cases[J]. Chin J Mult Organ Dis Elderly, 2002, 1(1): 7-10. DOI: 10.3969/j.issn.1671-5403.2002.01.003.

[3] 徐海, 范玲, 黄芪, 等. 老年重症肺炎合并多器官功能衰竭的临床分析[J]. 中华医院感染学杂志, 2017, 27(7): 1518-1520. DOI: 10.11816/cn.ni.2017-163246.
Xu H, Fan L, Huang Q, *et al*. Clinical analysis of severe pneumonia complicated with multiple organ failure in the elderly[J]. Chin J Nosocomiol, 2017, 27(7): 1518-1520. DOI: 10.11816/cn.ni.2017-163246.

[4] 中国老年医学学会, 国家老年疾病临床医学研究中心(解放军总医院), 解放军老年医学专业委员会. 感染诱发的老年多器官功能障碍综合征诊断与治疗中国指南2019[J]. 中华老年多器官疾病杂志, 2019, 18(11): 801-838. DOI: 10.11915/j.issn.1671-5403.2019.11.174.
Chinese Geriatrics Society, National Clinical Research Center for Geriatric Diseases (Chinese PLA General Hospital), PLA Geriatrics Professional Committee. 2019 China guideline for diagnosis and treatment of infection-induced multiple organ dysfunction syndrome in the elderly[J]. Chin J Mult Organ Dis Elderly, 2019, 18(11): 801-838. DOI: 10.11915/j.issn.1671-5403.2019.11.174.

[5] Iglesias P, Muñoz A, Prado F, *et al*. Alterations in thyroid function tests in aged hospitalized patients: prevalence, aetiology and clinical outcome[J]. Clin Endocrinol (Oxf), 2009, 70(6): 961-967. DOI: 10.1111/j.1365-2265.2008.03421.x.

[6] Angelousi AG, Karageorgopoulos DE, Kapaskelis AM, *et al*. Association between thyroid function tests at baseline and the outcome of patients with sepsis or septic shock: a systematic review[J]. Eur J Endocrinol, 2011, 164(2): 147-155. DOI: 10.1530/EJE-10-0695.

[7] Beltrão FEL, Beltrão DCA, Carvalhal G, *et al*. Thyroid hormone levels during hospital admission inform disease severity and mortality in COVID-19 patients[J]. Thyroid, 2021, 31(11): 1639-1649. DOI: 10.1089/thy.2021.0225.

[8] Liu YC, Jiang TY, Chen ZS, *et al*. Thyroid hormone disorders: a predictor of mortality in patients with septic shock defined by Sepsis-3?[J]. Intern Emerg Med, 2021, 16(4): 967-973. DOI: 10.1007/s11739-020-02546-2.

[9] Abdu FA, Mohammed AQ, Liu L, *et al*. Low free triiodothyronine as a predictor of poor prognosis in patients with myocardial infarction with non-obstructive coronary arteries[J]. Front Endocrinol (Lausanne), 2021, 12: 681978. DOI: 10.3389/fendo.2021.681978.

[10] Biegelmeyer E, Scanagata I, Alves L, *et al*. T3 as predictor of mortality in any cause non-critically ill patients[J]. Endocr Connect, 2021, 10(8): 852-860. DOI: 10.1530/EC-21-0080.

[11] Cappola AR, Desai AS, Medici M, *et al*. Thyroid and cardiovascular disease research agenda for enhancing knowledge, prevention, and treatment[J]. Circulation, 2019, 139(25): 2892-2909. DOI: 10.1161/CIRCULATIONAHA.118.036859.

[12] Yamazaki Y, Shoji T, Miyashima M, *et al*. Low free triiodothyronine level as a predictor of cardiovascular events and all-cause mortality in patients undergoing hemodialysis: the DREAM cohort[J]. J Atheroscler Thromb, 2021, 28(10): 1071-1082. DOI: 10.5551/jat.60624.

[13] Feng HL, Li Q, Cao WK, *et al*. Changes in thyroid function in patients with liver failure and their clinical significance: a clinical study of non-thyroidal illness syndrome in patients with liver failure[J]. Hepatob Pancreat Dis Int, 2020, 19(6): 561-566. DOI: 10.1016/j.hbpd.2020.05.001.

[14] Singer M, Deutschman CS, Seymour CW, *et al*. The third international consensus definitions for sepsis and septic shock (sepsis-3)[J]. JAMA, 2016, 315(8): 801-810. DOI: 10.1001/jama.2016.0287.

[15] Xu YY, Li NY, Gao JM, *et al*. Elevated serum tenascin-C predicts mortality in critically ill patients with multiple organ dysfunction[J]. Front Med (Lausanne), 2021, 8: 759273. DOI: 10.3389/fmed.2021.759273.

[16] Montesinos MDM, Pellizas CG. Thyroid hormone action on innate immunity[J]. Front Endocrinol (Lausanne), 2019, 10: 350. DOI: 10.3389/fendo.2019.00350.

[17] Luo B, Yu Z, Li YP, *et al*. Thyroid hormone disorders and sepsis[J]. Biomed Mater Eng, 2017, 28(s1): S237-S241. DOI: 10.3233/BME-171646.

[18] Mastorci F, Sabatino L, Vassalle C, *et al*. Cardioprotection and thyroid hormones in the clinical setting of heart failure[J]. Front Endocrinol (Lausanne), 2019, 10: 927. DOI: 10.3389/fendo.2019.00927.

[19] Dulchavsky SA, Ksenzenko SM, Saba AA, *et al*. Triiodothyronine (T3) supplementation maintains surfactant biochemical integrity during sepsis[J]. J Trauma, 1995, 39(1): 53-57. DOI: 10.1097/00005373-199507000-00007.

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