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Peer Reviewer of *World Journal of Cardiology*, Tolga Aksu, MD, Associate Professor, Department of Cardiology, University of Health Sciences, Kocaeli Derince Training and Research Hospital, Kocaeli 41000, Türkiye. aksutolga@gmail.com

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EDITORIAL

Cardiovascular mechanisms of thyroid hormones and heart failure: Current knowledge and perspectives

Viktor Čulić

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Viktor Čulić, Department of Cardiology and Angiology, University Hospital Centre Split, University of Split School of Medicine, Split 21000, Croatia

Corresponding author: Viktor Čulić, MD, PhD, Full Professor, Senior Scientist, Department of Cardiology and Angiology, University Hospital Centre Split, University of Split School of Medicine, Šoltanska 2, Split 21000, Croatia. viktor.culic@st.t-com.hr

Abstract

A multiple hormonal imbalance that accompanies heart failure (HF) may have a significant impact on the clinical course in such patients. The non-thyroidal illness syndrome (NTIS), also referred to as euthyroid sick syndrome or low triiodothyronine syndrome, can be found in about 30% of patients with HF. NTIS represents a systemic adaptation to chronic illness that is associated with increased cardiac and overall mortality in patients with HF. While conclusions on thyroid-stimulating hormone, free triiodothyronine, total and free thyroxine are currently unresolved, serum total triiodothyronine levels and the ratio of free triiodothyronine to free thyroxine seem to provide the best correlates to the echocardiographic, laboratory and clinical parameters of disease severity. HF patients with either hyper- or hypothyroidism should be treated according to the appropriate guidelines, but the therapeutic approach to NTIS, with or without HF, is still a matter of debate. Possible treatment options include better individual titration of levothyroxine therapy, combined triiodothyronine plus thyroxine therapy and natural measures to increase triiodothyronine. Future research should further examine the cellular and tissue mechanisms of NTIS as well as new therapeutic avenues in patients with HF.

Key Words: Heart failure; Non-thyroidal illness syndrome; Low triiodothyronine syndrome; Therapy; Thyroxine; Triiodothyronine

Core Tip: The non-thyroidal illness syndrome, also referred to as euthyroid sick syndrome or low triiodothyronine syndrome, can be found in about 30% of patients with heart failure (HF). Serum total triiodothyronine levels and the ratio of free triiodothyronine to free thyroxine seem to correlate the best with the echocardiographic, laboratory and clinical parameters of the severity of HF. Future research should further explore cellular and tissue mechanisms of this syndrome as well as possible therapeutic options in patients with HF.

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INTRODUCTION

The cardinal symptoms of heart failure (HF) are fatigue and shortness of breath, which in more severe cases may be accompanied by signs such as peripheral edema, pulmonary crackles and elevated jugular venous pressure[1]. HF is caused by a structural and/or functional abnormality of the heart producing increased ventricular filling pressures and/or impaired cardiac output. According to the left ventricular ejection fraction (LVEF), HF is divided into the 3 subgroups: HF with preserved ejection fraction and LVEF ≥ 50%, HF with mildly reduced ejection fraction in those with LVEF between 41% and 49%, and HF with reduced ejection fraction and LVEF ≤ 40%[1]. In developed countries, primarily due to population ageing and significant advances in the management of cardiovascular diseases, the overall incidence of HF is continuously and substantially increasing[2,3].

HF: MULTIPLE HORMONAL IMBALANCE SYNDROME

A body of evidence suggests that HF is accompanied by a multiple hormonal imbalance which may affect the clinical course of such patients[4]. In older men with HF, a lower endogenous testosterone level contributes to the occurrence of HF[5] due to a lack of testosterone's favorable cardiac and peripheral effects[6], particularly on diastolic function[7]. Since estrogen's cardiovascular effects somewhat protect against HF, estrogen stimulation in postmenopausal women may be useful for improving cardiac functioning in this disease[8,9]. However, in men with HF, circulating levels of estradiol are also inversely associated with diastolic dysfunction independently of circulating testosterone levels and other clinical variables[10], whereas both low and high levels of estradiol are predictors of a poorer prognosis[11]. The multiple hormonal deficiency syndrome associated with HF also encompasses down-regulation of anabolic axes of growth hormone, its tissue effector insulin-like growth factor-1, and insulin signaling[4]. Finally, we now realize that alterations in the serum level, tissue concentration and metabolism of thyroid hormones (TH) are common hormone disturbances which accompany HF.

TH METABOLISM, NON-THYROIDAL ILLNESS SYNDROME AND HF

By stimulating TH receptors present in the heart and vascular endothelial tissue, TH directly regulate the dynamics of the cardiovascular system and may modulate cardiovascular risk factors, primarily arterial hypertension, hyperlipidemia and thrombogenesis. Fluctuation of the TH concentration in both peripheral tissues and circulation substantially affect cardiovascular function, whereas both hyperthyroidism and hypothyroidism may induce HF. Untreated hyperthyroidism may lead to a hyperdynamic state with increased cardiac output caused by increased myocardial contractility and heart rate coupled with increased cardiac preload due to reduced systemic vascular resistance[12]. The long-term consequences of hyperthyroidism include cardiac hypertrophy, chronically increased preload and development of cardiac arrhythmias, all of which may lead to HF[13]. In contrast, hypothyroidism is associated with reduced myocardial contractility, heart rate and cardiac output, and increased peripheral vascular resistance[14]. Both overt[15] and subclinical[16,17] hypothyroidism may be associated with systolic dysfunction of the left ventricle (LV).

Besides hyper- or hypothyroidism, the non-thyroidal illness syndrome (NTIS), also referred to as euthyroid sick syndrome or low triiodothyronine (T_3) syndrome, can be found in about 30% of patients with HF[18,19]. NTIS is not an isolated pathophysiological condition; it is rather a systemic adaptation to chronic illness. NTIS affects the pathophysiology of TH at the level of the hypothalamic-pituitary-thyroid axis, including organ and tissue levels[20]. This syndrome is characterized by a decrease in serum T_3 levels, an increase in reverse T_3 and a reduction in serum thyroxine (T_4). Absent is the expected rise in the serum levels of thyroid-stimulating hormone (TSH)[20]. Changes in serum TH levels have been suggested as an independent predictor of cardiac and overall mortality associated with NTIS[18,21,22]. This is not surprising since TH have important cardioprotective effects against HF at the level of the myocytes, the interstitium and the vasculature, with a strong antiapoptotic effect on myocytes, and reduction of interstitial fibrosis[19]. At the same time, increased reverse T_3, the inactive TH metabolite, is an important predictor of both acute- and long-term

Table 1 The chief areas of future research of non-thyroidal illness syndrome in heart failure

Area of research	Clinical parameters
Best correlations of TH with clinical, echocardiographic and laboratory parameters of HF	Total serum T_3 (LVEF, LVDD, NT-proBNP)
	Free T_3/free T_4 ratio (cardiac chamber diameters, LVEF, NYHA class)
	Reverse T_3 (predictor of mortality)
Possible treatment options	Better individual titration of levothyroxine therapy
	Combined T_3 + T_4 therapy
	Natural measures to increase T_3
Parameters of clinical status/improvement monitoring	LVEF
	LVDD
	NT-proBNP
	HF cardinal symptom attenuation/alleviation
	HF signs attenuation/alleviation

HF: Heart failure; TH: Thyroid hormones; LVEF: Left ventricular ejection fraction; LVDD: Left ventricular diastolic dysfunction; NT-proBNP: N-terminal pro-B-type natriuretic peptide; T_3: Triiodothyronine; T_4: Thyroxine.

mortality[19].

CURRENT KNOWLEDGE AND UNANSWERED QUESTIONS

Given the body of evidence linking NTIS with poor prognosis in HF, three clinically relevant questions remain unanswered: (1) Which TH are most associated with the cardiovascular parameters and should be measured to identify those who should be treated; (2) when and how such patients should be treated; and (3) what parameters should be monitored to assess the efficacy of the therapy (Table 1).

Clinical research has provided some insight into the correlation of particular TH with the clinical parameters of HF. In general, the findings regarding TSH[23-25], free T_3 (fT_3)[25,26], total T_4 and free T_4 (fT_4)[25,27] are, at best, inconclusive. On the other hand, findings on two other TH indicators, although also relatively scarce, seem less contradictory. It has been suggested that total T_3 is closely associated with LVEF[25], LV diastolic dysfunction (LVDD)[25,27] and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels[25,28]. The role of T_3 as the most important TH in HF was strongly supported by a 2008 study by Pingitore *et al*[26]. This study showed that intravenous T_3 administered to patients with chronic HF due to dilated cardiomyopathy produced a significantly improved neuroendocrine profile and ventricular performance expressed through LV end-diastolic volume. Moreover, the stroke volume was increased without change in external and intra-cardiac workload, and was probably mediated through inodilating properties, *i.e.*, positive inotropic effect and a favorable effect of T_3 on diastolic dysfunction and vascular resistance[26]. Additionally, it has been suggested that fT_3/fT_4 ratio is associated with cardiac chamber sizes, LVEF and NYHA class[23,29]. Therefore, it seems that total T_3 and fT_3/fT_4 ratio may serve as the best correlates to cardiac function, clinical status and progression of HF.

TREATMENT POSSIBILITIES

HF patients with either hyper- or hypo-thyroidism should be treated according to the appropriate guidelines. However, the therapeutic approach to NTIS, with or without HF, is still a matter of debate. In the case of persistent symptoms despite previous substitutional levothyroxine therapy and serum TSH values within the reference range, the T_4 plus T_3 combination has been suggested as a treatment option by the European Thyroid Association[30] regardless of reported contradictory findings[31,32]. Perhaps natural measures to raise T_3, such as lowering stress levels, having a healthy diet, along with emphasis on regular exercise[33] and selenium intake[34], may achieve clinically relevant improvement through changes in TH levels in HF patients.

Obviously, it is difficult to distinguish persistent hypothyroid symptoms despite achieved normal TSH from the typical HF symptoms. In this light, the whole concept of NTIS, more commonly called low T_3 syndrome when associated with HF, should be additionally explored in better-designed randomized clinical trials with rigorous selection criteria. The effect of any explored therapeutic option could be assessed by a change in LVEF, LVDD and NT-proBNP levels or through HF symptom alleviation, and correlated with TH improvement. Still, although these suggested therapeutic interventions appear useful and logical, we must be prepared for disappointment, as demonstrated by testosterone supplementation in HF within the physiologic range[35] after several decades of seemingly promising results[36].

CONCLUSION

TH are among the chief regulators of the cardiovascular system. At present, it seems that serum total T_3 levels and a fT_3/fT_4 ratio show the best correlation to echocardiographic, laboratory and clinical parameters of the severity of HF. Future research should further explore the role of hormonal changes in HF, particularly cellular and tissue mechanisms of NTIS as well as possible therapeutic options.

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Country of origin: Croatia

ORCID number: Viktor Čulić 0000-0002-4026-0195.

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REFERENCES

1 **McDonagh TA**, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021; **42**: 3599-3726 [PMID: 34447992 DOI: 10.1093/eurheartj/ehab368]

2 **Tsao CW**, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, Baker-Smith CM, Beaton AZ, Boehme AK, Buxton AE, Commodore-Mensah Y, Elkind MSV, Evenson KR, Eze-Nliam C, Fugar S, Generoso G, Heard DG, Hiremath S, Ho JE, Kalani R, Kazi DS, Ko D, Levine DA, Liu J, Ma J, Magnani JW, Michos ED, Mussolino ME, Navaneethan SD, Parikh NI, Poudel R, Rezk-Hanna M, Roth GA, Shah NS, St-Onge MP, Thacker EL, Virani SS, Voeks JH, Wang NY, Wong ND, Wong SS, Yaffe K, Martin SS; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. *Circulation* 2023; **147**: e93-e621 [PMID: 36695182 DOI: 10.1161/CIR.0000000000001123]

3 **GBD 2017 Disease and Injury Incidence and Prevalence Collaborators**. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018; **392**: 1789-1858 [PMID: 30496104 DOI: 10.1016/S0140-6736(18)32279-7]

4 **Saccà L**. Heart failure as a multiple hormonal deficiency syndrome. *Circ Heart Fail* 2009; **2**: 151-156 [PMID: 19808331 DOI: 10.1161/CIRCHEARTFAILURE.108.821892]

5 **Njoroge JN**, Tressel W, Biggs ML, Matsumoto AM, Smith NL, Rosenberg E, Hirsch CH, Gottdiener JS, Mukamal KJ, Kizer JR. Circulating Androgen Concentrations and Risk of Incident Heart Failure in Older Men: The Cardiovascular Health Study. *J Am Heart Assoc* 2022; **11**: e026953 [PMID: 36285783 DOI: 10.1161/JAHA.122.026953]

6 **Bušić Ž**, Čulić V. Central and peripheral testosterone effects in men with heart failure: An approach for cardiovascular research. *World J Cardiol* 2015; **7**: 504-510 [PMID: 26413227 DOI: 10.4330/wjc.v7.i9.504]

7 **Čulić V**, Bušić Ž. Testosterone levels and heart failure in obese and non-obese men. *Int J Cardiol* 2014; **176**: 1163-1166 [PMID: 25129302 DOI: 10.1016/j.ijcard.2014.07.253]

8 **Iorga A**, Cunningham CM, Moazeni S, Ruffenach G, Umar S, Eghbali M. The protective role of estrogen and estrogen receptors in cardiovascular disease and the controversial use of estrogen therapy. *Biol Sex Differ* 2017; **8**: 33 [PMID: 29065927 DOI: 10.1186/s13293-017-0152-8]

9 **Iorga A**, Li J, Sharma S, Umar S, Bopassa JC, Nadadur RD, Centala A, Ren S, Saito T, Toro L, Wang Y, Stefani E, Eghbali M. Rescue of Pressure Overload-Induced Heart Failure by Estrogen Therapy. *J Am Heart Assoc* 2016; **5** [PMID: 26802104 DOI: 10.1161/JAHA.115.002482]

10 **Čulić V**, Bušić Ž, Bušić M. Circulating sex hormones, alcohol consumption and echocardiographic parameters of cardiac function in men with

heart failure. *Int J Cardiol* 2016; **224**: 245-251 [PMID: 27661414 DOI: 10.1016/j.ijcard.2016.09.050]
11 **Jankowska EA**, Rozentryt P, Ponikowska B, Hartmann O, Kustrzycka-Kratochwil D, Reczuch K, Nowak J, Borodulin-Nadzieja L, Polonski L, Banasiak W, Poole-Wilson PA, Anker SD, Ponikowski P. Circulating estradiol and mortality in men with systolic chronic heart failure. *JAMA* 2009; **301**: 1892-1901 [PMID: 19436016 DOI: 10.1001/jama.2009.639]
12 **Cooper DS**, Biondi B. Subclinical thyroid disease. *Lancet* 2012; **379**: 1142-1154 [PMID: 22273398 DOI: 10.1016/S0140-6736(11)60276-6]
13 **Biondi B**, Cappola AR. Subclinical hypothyroidism in older individuals. *Lancet Diabetes Endocrinol* 2022; **10**: 129-141 [PMID: 34953533 DOI: 10.1016/S2213-8587(21)00285-0]
14 **Klein I**, Danzi S. Thyroid disease and the heart. *Circulation* 2007; **116**: 1725-1735 [PMID: 17923583 DOI: 10.1161/CIRCULATIONAHA.106.678326]
15 **Kisso B**, Patel A, Redetzke R, Gerdes AM. Effect of low thyroid function on cardiac structure and function in spontaneously hypertensive heart failure rats. *J Card Fail* 2008; **14**: 167-171 [PMID: 18325465 DOI: 10.1016/j.cardfail.2007.10.018]
16 **Biondi B**, Fazio S, Palmieri EA, Carella C, Panza N, Cittadini A, Bonè F, Lombardi G, Saccà L. Left ventricular diastolic dysfunction in patients with subclinical hypothyroidism. *J Clin Endocrinol Metab* 1999; **84**: 2064-2067 [PMID: 10372711 DOI: 10.1210/jcem.84.6.5733]
17 **Monzani F**, Di Bello V, Caraccio N, Bertini A, Giorgi D, Giusti C, Ferrannini E. Effect of levothyroxine on cardiac function and structure in subclinical hypothyroidism: a double blind, placebo-controlled study. *J Clin Endocrinol Metab* 2001; **86**: 1110-1115 [PMID: 11238494 DOI: 10.1210/jcem.86.3.7291]
18 **Wang B**, Liu S, Li L, Yao Q, Song R, Shao X, Li Q, Shi X, Zhang JA. Non-thyroidal illness syndrome in patients with cardiovascular diseases: A systematic review and meta-analysis. *Int J Cardiol* 2017; **226**: 1-10 [PMID: 27776249 DOI: 10.1016/j.ijcard.2016.10.039]
19 **Razvi S**, Jabbar A, Pingitore A, Danzi S, Biondi B, Klein I, Peeters R, Zaman A, Iervasi G. Thyroid Hormones and Cardiovascular Function and Diseases. *J Am Coll Cardiol* 2018; **71**: 1781-1796 [PMID: 29673469 DOI: 10.1016/j.jacc.2018.02.045]
20 **Fliers E**, Boelen A. An update on non-thyroidal illness syndrome. *J Endocrinol Invest* 2021; **44**: 1597-1607 [PMID: 33320308 DOI: 10.1007/s40618-020-01482-4]
21 **Iervasi G**, Pingitore A, Landi P, Raciti M, Ripoli A, Scarlattini M, L'Abbate A, Donato L. Low-T3 syndrome: a strong prognostic predictor of death in patients with heart disease. *Circulation* 2003; **107**: 708-713 [PMID: 12578873 DOI: 10.1161/01.cir.0000048124.64204.3f]
22 **Kannan L**, Shaw PA, Morley MP, Brandimarto J, Fang JC, Sweitzer NK, Cappola TP, Cappola AR. Thyroid Dysfunction in Heart Failure and Cardiovascular Outcomes. *Circ Heart Fail* 2018; **11**: e005266 [PMID: 30562095 DOI: 10.1161/CIRCHEARTFAILURE.118.005266]
23 **Kozdag G**, Ural D, Vural A, Agacdiken A, Kahraman G, Sahin T, Ural E, Komsuoglu B. Relation between free triiodothyronine/free thyroxine ratio, echocardiographic parameters and mortality in dilated cardiomyopathy. *Eur J Heart Fail* 2005; **7**: 113-118 [PMID: 15642542 DOI: 10.1016/j.ejheart.2004.04.016]
24 **Ripoli A**, Pingitore A, Favilli B, Bottoni A, Turchi S, Osman NF, De Marchi D, Lombardi M, L'Abbate A, Iervasi G. Does subclinical hypothyroidism affect cardiac pump performance? Evidence from a magnetic resonance imaging study. *J Am Coll Cardiol* 2005; **45**: 439-445 [PMID: 15680725 DOI: 10.1016/j.jacc.2004.10.044]
25 **Turić I**, Velat I, Bušić Ž, Čulić V. Circulating thyroid hormones and clinical parameters of heart failure in men. *Sci Rep* 2023; **13**: 20319 [PMID: 37985786 DOI: 10.1038/s41598-023-47391-3]
26 **Pingitore A**, Galli E, Barison A, Iervasi A, Scarlattini M, Nucci D, L'abbate A, Mariotti R, Iervasi G. Acute effects of triiodothyronine (T3) replacement therapy in patients with chronic heart failure and low-T3 syndrome: a randomized, placebo-controlled study. *J Clin Endocrinol Metab* 2008; **93**: 1351-1358 [PMID: 18171701 DOI: 10.1210/jc.2007-2210]
27 **Selvaraj S**, Klein I, Danzi S, Akhter N, Bonow RO, Shah SJ. Association of serum triiodothyronine with B-type natriuretic peptide and severe left ventricular diastolic dysfunction in heart failure with preserved ejection fraction. *Am J Cardiol* 2012; **110**: 234-239 [PMID: 22502900 DOI: 10.1016/j.amjcard.2012.02.068]
28 **Wang K**, Ojamaa K, Samuels A, Gilani N, Zhang K, An S, Zhang Y, Tang YD, Askari B, Gerdes AM. BNP as a New Biomarker of Cardiac Thyroid Hormone Function. *Front Physiol* 2020; **11**: 729 [PMID: 32733267 DOI: 10.3389/fphys.2020.00729]
29 **Nägele MP**, Barthelmes J, Kreysing L, Haider T, Nebunu D, Ruschitzka F, Sudano I, Flammer AJ. Endocrine hormone imbalance in heart failure with reduced ejection fraction: A cross-sectional study. *Health Sci Rep* 2022; **5**: e880 [PMID: 36320653 DOI: 10.1002/hsr2.880]
30 **Wiersinga WM**, Duntas L, Fadeyev V, Nygaard B, Vanderpump MP. 2012 ETA Guidelines: The Use of L-T4 + L-T3 in the Treatment of Hypothyroidism. *Eur Thyroid J* 2012; **1**: 55-71 [PMID: 24782999 DOI: 10.1159/000339444]
31 **Grozinsky-Glasberg S**, Fraser A, Nahshoni E, Weizman A, Leibovici L. Thyroxine-triiodothyronine combination therapy *vs* thyroxine monotherapy for clinical hypothyroidism: meta-analysis of randomized controlled trials. *J Clin Endocrinol Metab* 2006; **91**: 2592-2599 [PMID: 16670166 DOI: 10.1210/jc.2006-0448]
32 **Wiersinga WM**. T4+T3 Combination Therapy: An Unsolved Problem of Increasing Magnitude and Complexity. *Endocrinol Metab (Seoul)* 2021; **36**: 938-951 [PMID: 34587734 DOI: 10.3803/EnM.2021.501]
33 **Altaye KZ**, Mondal S, Legesse K, Abdulkedir M. Effects of aerobic exercise on thyroid hormonal change responses among adolescents with intellectual disabilities. *BMJ Open Sport Exerc Med* 2019; **5**: e000524 [PMID: 31423321 DOI: 10.1136/bmjsem-2019-000524]
34 **Barcza Stockler-Pinto M**, Carrero JJ, De Carvalho Cardoso Weide L, Franciscato Cozzolino SM, Mafra D. Effect of selenium supplementation *via* brazil nut (bertholletia excelsa, hbk) on thyroid hormones levels in hemodialysis patients: a pilot study. *Nutr Hosp* 2015; **32**: 1808-1812 [PMID: 26545554 DOI: 10.3305/nh.2015.32.4.9384]
35 **Tao J**, Liu X, Bai W. Testosterone Supplementation in Patients With Chronic Heart Failure: A Meta-Analysis of Randomized Controlled Trials. *Front Endocrinol (Lausanne)* 2020; **11**: 110 [PMID: 32231640 DOI: 10.3389/fendo.2020.00110]
36 **Toma M**, McAlister FA, Coglianese EE, Vidi V, Vasaiwala S, Bakal JA, Armstrong PW, Ezekowitz JA. Testosterone supplementation in heart failure: a meta-analysis. *Circ Heart Fail* 2012; **5**: 315-321 [PMID: 22511747 DOI: 10.1161/CIRCHEARTFAILURE.111.965632]

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