Clinical and pathophysiologic insights of FT3/FT4 ratio in patients with Heart Failure with Preserved Ejection Fraction: data from the NETDiamond cohort

Ana Rita Leite (ana.leite7c@gmail.com)
Cardiovascular R&D Center - UniC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal https://orcid.org/0000-0002-4111-3787

João Sérgio Neves
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

António Angélico-Gonçalves
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Francisco Vasques-Nóvoa
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Francisca A. Saraiva
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Inês Beatriz Pinho
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Ana Cristina Oliveira
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Marta Borges-Canha
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Madalena von Hafe
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Catarina Vale
Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

André P. Lourenço

Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

José Paulo Araújo

Department of Internal Medicine, Centro Hospitalar Universitário São João, Porto, Portugal

Pedro von Hafe

Department of Internal Medicine, Centro Hospitalar Universitário de São João, Porto, Portugal

Jorge Almeida

Department of Internal Medicine, Centro Hospitalar Universitário de São João, Porto, Portugal

João Pedro Ferreira

Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal

Adelino Leite-Moreira

Cardiovascular R&D Center - UnIC@RISE, Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Portugal

---

Short Report

Keywords: thyroid hormones, FT3/FT4 ratio, heart failure with preserved ejection fraction, prognosis, biomarker

Posted Date: September 13th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2042487/v1

Abstract

Purpose

Thyroid dysfunction is common in patients with heart failure (HF). Impaired conversion of T4 into T3 is thought to decrease the availability of T3 and contribute to HF progression. In HF with preserved ejection fraction (HFpEF), it is not known whether changes in conversion of thyroid hormones (TH) are associated with clinical status and outcomes.

Methods

We evaluated 79 HFpEF participants of the NETDiamond cohort without known thyroid disease. We performed regression modelling to study the associations of TH and FT3/FT4 ratio with clinical and echocardiographic parameters, and survival analysis to evaluate associations with the composite of urgent HF visit, HF hospitalization or cardiovascular death, over a median follow-up of 2.8 years.

Results

The mean age was 73.5 years and 47% were men. The mean FT3/FT4 ratio was 2.63 (SD 0.43). Subjects with lower FT3/FT4 ratio were more likely to be obese and have atrial fibrillation. Lower FT3/FT4 ratio was associated with higher body fat (β=-5.60kg per FT3/FT4 unit, p = 0.034), higher pulmonary arterial systolic pressure (PASP) (β=-10.26mmHg, p = 0.002) and lower left ventricular ejection fraction (LVEF) (β = 3.60%, p = 0.008). Lower FT3/FT4 ratio was associated with higher risk for the composite HF outcome (HR = 2.50, 95%CI 1.04–5.88, per 1-unit decrease in FT3/FT4, p = 0.041).

Conclusions

In patients with HFpEF, lower FT3/FT4 ratio was associated with higher body fat, higher PASP and lower LVEF. Lower FT3/FT4 predicted a higher risk of urgent HF visit, HF hospitalization or cardiovascular death. These findings suggest that decreased FT4 to FT3 conversion may be associated with HFpEF progression.

Introduction

Thyroid hormones (TH) are crucial for the homeostasis of the cardiovascular system [1]. TH comprise thyroxine (T4) and triiodothyronine (T3), the latter being the most active form [2]. Peripheral conversion of T4 to T3 by type 1 and type 2 deiodinases are responsible for the majority of circulating T3 [3].

Up to 30% of heart failure (HF) patients have some form of thyroid dysfunction [4], which may contribute to the onset and progression of HF [4]. One of the mechanisms for thyroid dysfunction is an impaired

activity of deiodinases, decreasing the availability of T3 and leading to a state of functional hypothyroidism [5]. Persistent neuroendocrine activation, poor nutritional status, hypoxia, and inflammatory responses are thought to be hallmarks of this impairment [6, 7].

The ratio of free T3 (FT3) and free T4 (FT4) has been suggested as an indirect index of peripheral deiodinase activity and T4 to T3 conversion [8]. Previous studies performed in patients with coronary artery disease or dilated cardiomyopathy have demonstrated that low FT3/FT4 ratio levels, reflecting a lower conversion of T4 into T3, were independently associated with poor long-term prognosis [9, 10].

In patients with HF with preserved ejection fraction (HFpEF), the proinflammatory milieu may be involved in TH metabolism impairment [11]. However, the associations between FT3/FT4 ratio with clinical status and outcomes in HFpEF have not been well characterized.

Our aim was to explore the association of FT3/FT4 ratio and TH with clinical, anthropometric and echocardiographic parameters, as well as their prognostic impact in a cohort of stable HFpEF individuals.

Methods

The NETDiamond (NEw Targets in DIAstolic heart failure: from coMOrbidities to persoNalizeD medicine) study is an ongoing single-center, prospective cohort study dedicated to multiomics-driven discovery of novel pathophysiological mechanisms and therapeutic targets in HFpEF. Participants were recruited from the HF Outpatient Clinic at Centro Hospitalar Universitário São João (CHUSJ) in Porto, Portugal. Eligibility criteria for NETDiamond study included: 1) diagnosis of HFpEF made by a group of HF specialists according to the European Society of Cardiology recommendations [12]; and 2) stable patients defined as those whose symptoms and signs have remained generally unchanged for at least 3 months. The exclusion criteria included one or more of the following: 1) moderate-to-severe cardiac valvular dysfunction; 2) end-stage kidney failure; 3) high level of dependency (ECOG $\geq$ 3). At enrolment, a comprehensive collection of clinical/imaging data and biological samples was performed. This study complies with the Declaration of Helsinki. The CHUSJ Ethical Committee approved the protocol and all subjects gave written, informed consent.

In our analysis, patients with history of thyroid disease or taking medications that could interfere with thyroid function were excluded. Seventy-nine participants were included.

Thyroid hormones [thyroid-stimulation hormone (TSH), FT3, and FT4] were measured using an Abbott Architect i2000 analyzer (Abbott Diagnostics, Lisbon, Portugal). The FT3/FT4 ratio was calculated dividing plasma concentrations of FT3 by FT4 levels. Glomerular filtration rate (GFR) was estimated using Chronic Kidney Disease Epidemiology Collaboration formula.

Continuous variables are presented as mean (standard deviation, SD), if normally distributed, or as median (25th to 75th percentiles), if non-normally distributed. Variables with skewed distribution were transformed to their natural logarithm. Categorical variables are presented absolute and relative

frequencies. Baseline characteristics of the population were categorized according to TH and FT3/FT4 ratio tertiles.

A cross-sectional analysis using linear and ordered logistic regression models was performed to analyze the associations of TH and FT3/FT4 ratio (independent variables) with clinical, anthropometric and echocardiographic measurements (dependent variables). Regression models were adjusted for age, sex, body mass index (BMI), estimated GFR and brain natriuretic peptide (BNP) levels.

The prognosis outcome was defined as time-to-first event in a composite of urgent HF visits with diuretic intensification, HF hospitalization or cardiovascular death. Cox proportional hazards models were used to evaluate the association between TH and FT3/FT4 ratio at study entry and the composite outcome, unadjusted and adjusted for age, sex and BNP. Schoenfeld residuals were assessed to check the proportional hazard assumption. Survival according to TH and FT3/FT4 tertiles was evaluated by Kaplan-Meier curves.

The statistical analyses were performed using Stata® software, version 17. Two-sided P values < 0.05 were considered significant.

Results

Study population

The mean age of the 79 subjects included was 73.5 (SD 8.2) years and 47% were men. The mean FT3/FT4 ratio was 2.63 (SD 0.43). Subjects with lower FT3/FT4 ratio were more likely to be older, and to have higher BMI, orthopnea, obesity, type 2 diabetes, atrial fibrillation and hs-TnI levels (Table S1). Tables S2-S4 present the baseline characteristics according to TSH, FT4 and FT3 tertiles.

Associations of thyroid function with clinical and echocardiographic parameters

The results from the cross-sectional analysis are presented in Table 1 for FT3/FT4 ratio and Table S5 for TH.

Table 1
Associations of FT3/FT4 ratio with clinical, anthropometric and echocardiographic parameters

	OR (95% CI) per FT3/FT4 unit	**P value**
Clinical parameters		
NYHA class[1]	0.94 (0.28–3.19)	0.924
Peripheral edema	0.44 (0.07–2.88)	0.393
Orthopnea	0.53 (0.11–2.48)	0.417
PND	0.65 (0.11–3.77)	0.635
	β (95% CI) per FT3/FT4 unit	**P value**
Anthropometric parameters[2]		
Body Fat, kg	**-5.60 (-10.77 to -0.42)**	**0.034**
Soft Lean mass, kg	-4.45 (-9.07 to 0.18)	0.059
Skeletal Muscle Mass, kg	-2.52 (-5.38 to 0.34)	0.083
Percent Body Fat, %	-2.72 (-6.94 to 1.51)	0.204
ECW/TBW ratio, %	-0.46 (-1.11 to 0.19)	0.161
Echocardiographic parameters		
LAVI, mL/m^2	-4.47 (-11.01 to 2.07)	0.177
Septum thickness, mm	0.14 (-0.97 to 1.25)	0.805
Ejection fraction, %	**3.60 (0.96 to 6.24)**	**0.008**
PASP, mmHg	**-10.26 (-16.68 to -3.84)**	**0.002**
Deceleration time, ms	-32.44 (-79.53 to 14.64)	0.171
E/E' ratio	0.35 (-1.91 to 2.61)	0.756

The values shown are odds ratios or linear regression coefficients and 95% confidence intervals, with FT3/FT4 ratio as independent variable, and clinical, anthropometric and echocardiographic parameters as dependent variables. Results were adjusted for age, sex, BMI, eGFR and BNP levels. TSH and BNP were log-transformed.

[1] The odds ratio for NYHA functional class are estimated per one class increase.

[2] Linear regression models for anthropometric parameters are adjusted for all variables stated, except for BMI.

Abbreviations: TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine; CI, confidence interval; NYHA, New York Heart Association; ECW/TBW, extracellular water to total body water; LAVI, left atrial volume index; PASP, pulmonary arterial systolic pressure.
Regarding anthropometric parameters, FT3/FT4 ratio and FT3 were negatively associated with body fat (β=-5.60kg, 95%CI -10.77 to -0.42 kg, per FT3/FT4 unit, p = 0.034; and β=-6.70kg, 95%CI -13.01 to -0.39 kg, per 1 pg/mL of FT3, p = 0.038, respectively).

Concerning echocardiographic measurements, FT3/FT4 ratio was positively associated with left ventricular ejection fraction (LVEF) (β = 3.60%, 95%CI 0.96 to 6.24%, per FT3/FT4 unit, p = 0.008) and negatively associated with pulmonary arterial systolic pressure (PASP) (β=-10.26mmHg, 95%CI -16.68 to -3.84 mmHg, per FT3/FT4 unit, p = 0.002). FT3 was positively associated with LVEF (β = 4.17%, 95%CI 0.89 to 7.44%, per 1 pg/mL of FT3, p = 0.013) and negatively associated with deceleration time (β=-70.31ms, 95%CI -125.08 to -15.53 ms, per 1 pg/mL of FT3, p = 0.013). FT4 was positively associated with PASP (β = 16.35mmHg, 95%CI 7.44 to 25.26 mmHg, per 0.5 ng/dL of FT4, p = 0.001).

No associations were found between FT3/FT4 or TH and other clinical parameters of HF severity.

Association of thyroid function with the risk for clinical events

Over a median of 2.8 years of follow-up, there were 32 first events of the composite HF endpoint. Participants in lower FT3/FT4 ratio tertiles had higher risk for the composite endpoint (HR = 1.59, 95%CI 1.01–2.50 per FT3/FT4 tertile decrease; p for trend = 0.047) (Fig. 1). In the fully adjusted model, lower levels of FT3/FT4 ratio were associated with higher risk for the composite outcome (HR = 2.50, 95%CI 1.04–5.88, per 1-unit decrease in FT3/FT4, p = 0.041; Table S6). No significant associations were found between TSH, FT4 or FT3 and the risk for the combined outcome (Table S6; Figure S1).

Discussion

In this cohort of patients with chronic HFpEF, we showed that subjects with lower FT3/FT4 ratio were more likely to have a higher clinical severity of HF and higher prevalence of obesity, diabetes and atrial fibrillation. Furthermore, lower levels FT3/FT4 ratio were associated with higher body fat, lower LVEF and higher PASP. Lastly, a lower FT3/FT4 ratio was associated with a higher risk of urgent HF visit, HF hospitalization or cardiovascular mortality.

As previously stated, the ratio of FT3/FT4 has been suggested as an indirect index of peripheral conversion of T4 into T3 [8]. Deiodinases' activity appears to be disturbed in several acute and chronic illnesses, including HF [4]. Although this decrease in T3 levels is seen as an adaptative response to reduce energy expenditure, questions have been raised regarding the role of this mechanism in HF [6, 11].

Persistently low T3 levels negatively influence myocardial function and structure, impairing cardiac remodeling in a similar way as in HF progression [6, 13]. In HFpEF, lower T3 levels were previously associated with increased symptom burden, higher BNP levels and worse diastolic function [14].

Patients with lower FT3/FT4 ratio had a higher prevalence of metabolic and cardiac comorbidities. In fact, these comorbidities may further impair deiodinase activity. On the other hand, lower levels of active TH can also worsen or predispose to these comorbidities. Hypothyroidism contributes to weight gain, due to a decrease in resting energy expenditure [15], and may increase the vulnerability to arrhythmias such as atrial fibrillation [16].

Lower FT3/FT4 ratio and FT3 levels were associated with lower LVEF and higher deceleration time, which suggests worsening of both systolic and diastolic functions with lower levels of active TH. On the other hand, PASP was found to be higher with higher FT4 and lower FT3/FT4 ratio levels. Even though hyperthyroidism is associated with pulmonary hypertension [1], we did not find association between FT3 and PASP. Pulmonary hypertension is common and a marker of dismal prognosis in patients with HFpEF [17]. It is then plausible that patients with higher levels of PASP have further impairment in deiodinase activity, hence, lower levels of active TH.

Several studies have shown that both lower T3 and higher T4 levels were independent predictors of poor outcomes in HF [18, 19]. In a recent retrospective study, FT3/FT4 ratio was shown to predict cardiovascular and all-cause mortality in HF patients, with a greater predictive value in HFpEF [20]. These studies increase the robustness of our analysis and underline the potential use of FT3/FT4 ratio as a prognostic metric in this subtype of HF.

Some limitations of our analysis are noteworthy. This is an observational study, which limits our ability to comment on causality and generalize our results. Our study had limited statistical power to detect associations of TH and FT3/FT4 ratio with clinical parameters and outcomes; a larger sample size might have shown more consistent associations. Despite our effort to adjust for relevant confounding factors, we cannot exclude that residual confounding may have influenced our results. We only evaluated thyroid hormones in a single moment, not taking into account potential variations of these parameters.

In conclusion, in patients with HFpEF, a lower FT3/FT4 ratio was associated with a worse clinical status, cardiac function and long-term prognosis. A decreased conversion of FT4 to FT3 might be a mechanism associated with HFpEF progression and decompensation. More studies addressing the thyroid-heart interaction in HFpEF are needed.

Declarations

Funding

This study was funded by national funds through FCT – Portuguese Foundation for Science and Technology, under the scope of the Cardiovascular R&D Centre – UnIC (POCI-01-0145-FEDER-016385,

UIDB/00051/2020 and UIDP/00051/2020)

Competing Interests

JPF is a consultant for Boehringer Ingelheim and AstraZeneca. He has received research support from Novartis, Boehringer Ingelheim, AstraZeneca and Bayer through his institution. JSN has received consulting or speaker fees from AstraZeneca, BIAL, Boehringer Ingelheim, Lilly, Merck, and Novo Nordisk. MBC has received speaker fees from AstraZeneca.

Author Contributions

AAG, FVN, FAS, IBP, ACO, APL, JPA, PvH, JA and ALM designed the NETDiamond cohort, recruited participants and collected clinical data. ARL, JSN, FVN, JPF and MBC conceived and designed the study. JSN, JPF, AAG, FVN and MBC provided methodological and statistical advice. ARL and JSN drafted the first version of the manuscript. All authors provided clinical feedback in interpreting the results, contributed critically to subsequent revisions and approved the final version of the manuscript.

Ethics approval

This study complies with the Declaration of Helsinki. The CHUSJ Ethical Committee approved the protocol.

Consent to participate

All subjects gave written, informed consent to participate in this study.

Consent to publish

Not applicable.

References

1. Cappola, A.R., Desai, A.S., Medici, M., Cooper, L.S., Egan, D., Sopko, G., Fishman, G.I., Goldman, S., Cooper, D.S., Mora, S., Kudenchuk, P.J., Hollenberg, A.N., McDonald, C.L., Ladenson, P.W.: Thyroid and Cardiovascular Disease: Research Agenda for Enhancing Knowledge, Prevention, and Treatment. Thyroid. 29, 760–777 (2019). https://doi.org/10.1089/thy.2018.0416
2. Samuels, H.H., Tsai, J.S., Casanova, J., Stanley, F.: Thyroid hormone action: in vitro characterization of solubilized nuclear receptors from rat liver and cultured GH1 cells. J. Clin. Invest. 54, 853–865 (1974). https://doi.org/10.1172/JCI107825
3. Bianco, A.C., Kim, B.W.: Deiodinases: implications of the local control of thyroid hormone action. J. Clin. Invest. 116, 2571 (2006). https://doi.org/10.1172/JCI29812
4. Vale, C., Neves, J.S., von Hafe, M., Borges-Canha, M., Leite-Moreira, A.: The Role of Thyroid Hormones in Heart Failure. Cardiovasc. Drugs Ther. 33, 179–188 (2019). https://doi.org/10.1007/s10557-019-

06870-4

5. Razvi, S.: Novel uses of thyroid hormones in cardiovascular conditions. Endocrine. 66, 115–123 (2019). https://doi.org/10.1007/s12020-019-02050-4
6. Biondi, B.: The Management of Thyroid Abnormalities in Chronic Heart Failure. Hear. Fail Clin. 15, 393–398 (2019). https://doi.org/10.1016/j.hfc.2019.02.008
7. Wajner, S.M., Goemann, I.M., Bueno, A.L., Larsen, P.R., Maia, A.L.: IL-6 promotes nonthyroidal illness syndrome by blocking thyroxine activation while promoting thyroid hormone inactivation in human cells. J. Clin. Invest. 121, 1834–1845 (2011). https://doi.org/10.1172/JCI44678
8. Maia, A.L., Goemann, I.M., Meyer, E.L., Wajner, S.M.: Deiodinases: the balance of thyroid hormone: type 1 iodothyronine deiodinase in human physiology and disease. J Endocrinol. 209, 283–297 (2011). https://doi.org/10.1530/JOE-10-0481
9. Yuan, D., Zhang, C., Jia, S., Liu, Y., Jiang, L., Xu, L., Zhang, Y., Xu, J., Xu, B., Hui, R., Gao, R., Gao, Z., Song, L., Yuan, J.: Predictive value of free triiodothyronine (FT3) to free thyroxine (FT4) ratio in long-term outcomes of euthyroid patients with three-vessel coronary artery disease. Nutr. Metab. Cardiovasc. Dis. 31, 579–586 (2021). https://doi.org/10.1016/j.numecd.2020.10.011
10. 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. 7, 113–118 (2005). https://doi.org/10.1016/j.ejheart.2004.04.016
11. Neves, J.S., Vale, C., von Hafe, M., Borges-Canha, M., Leite, A.R., Almeida-Coelho, J., Lourenço, A., Falcão-Pires, I., Carvalho, D., Leite-Moreira, A.: Thyroid hormones and modulation of diastolic function: a promising target for heart failure with preserved ejection fraction, http://journals.sagepub.com/doi/10.1177/2042018820958331, (2020)
12. McDonagh, T.A., Metra, M., Adamo, M., Gardner, R.S., Baumbach, A., Böhm, M., Burri, H., Butler, J., Celutkiene, J., Chioncel, O., Cleland, J.G.F., Coats, A.J.S., Crespo-Leiro, M.G., Farmakis, D., Gilard, M., Heymans, S.: 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, https://academic.oup.com/eurheartj/article/42/36/3599/6358045, (2021)
13. Cokkinos, D. V., Chryssanthopoulos, S.: Thyroid hormones and cardiac remodeling. Heart Fail. Rev. 21, 365–372 (2016). https://doi.org/10.1007/S10741-016-9554-7/FIGURES/2
14. Selvaraj, S., Klein, I., Danzi, S., Akhter, N., Bonow, R.O., Shah, S.J.: 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. 110, 234–239 (2012). https://doi.org/10.1016/j.amjcard.2012.02.068
15. Mcaninch, E.A., Bianco, A.C.: Thyroid hormone signaling in energy homeostasis and energy metabolism. Ann. N. Y. Acad. Sci. 1311, 77–87 (2014). https://doi.org/10.1111/NYAS.12374
16. Zhang, Y., Dedkov, E.I., Teplitsky, D., Weltman, N.Y., Pol, C.J., Rajagopalan, V., Lee, B., Martin Gerdes, A.: Both hypothyroidism and hyperthyroidism increase atrial fibrillation inducibility in rats. Circ. Arrhythmia Electrophysiol. 6, 952–959 (2013). https://doi.org/10.1161/CIRCEP.113.000502

17. Lam, C.S.P., Roger, V.L., Rodeheffer, R.J., Borlaug, B.A., Enders, F.T., Redfield, M.M.: Pulmonary hypertension in heart failure with preserved ejection fraction: a community-based study. J. Am. Coll. Cardiol. 53, 1119–1126 (2009). https://doi.org/10.1016/J.JACC.2008.11.051
18. Kannan, L., Shaw, P.A., Morley, M.P., Brandimarto, J., Fang, J.C., Sweitzer, N.K., Cappola, T.P., Cappola, A.R.: Thyroid Dysfunction in Heart Failure and Cardiovascular Outcomes. Circ. Hear. Fail. 11, e005266 (2018). https://doi.org/10.1161/CIRCHEARTFAILURE.118.005266
19. Hamilton, M.A., Stevenson, L.W., Luu, M., Walden, J.A.: Altered thyroid hormone metabolism in advanced heart failure. J. Am. Coll. Cardiol. 16, 91–95 (1990). https://doi.org/https://doi.org/10.1016/0735-1097(90)90462-X
20. Wang, C., Han, S., Li, Y., Tong, F., Li, Z., Sun, Z.: Value of FT3/FT4 Ratio in Prognosis of Patients With Heart Failure: A Propensity-Matched Study. Front. Cardiovasc. Med. 9, 888 (2022). https://doi.org/10.3389/fcvm.2022.859608

Figures

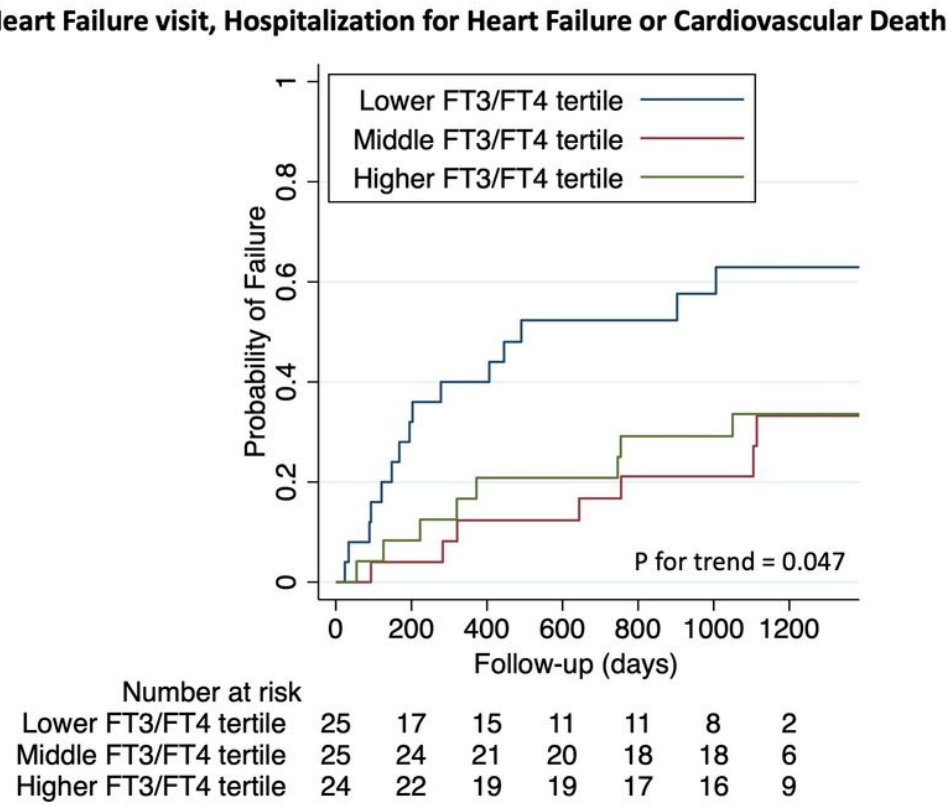

Figure 1

Kaplan-Meier curves for the composite outcome of urgent HF visits with diuretic intensification, HF hospitalization and cardiovascular death, by FT3/FT4 ratio tertiles.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ElectronicSupplementarymaterial.docx