

Cardiac and Inflammatory Biomarker Signatures in Hyperthyroidism Treated with 35 mg Carbimazole: Influence of Pre-Existing Heart Disease

Nawar fadhil Razooqi¹

¹Department of chemistry, college of science, Al-Nahrain university, Iraq

nawar.fadhil@nahrainuniv.edu.iq

Received: 2026, 04, Feb
Accepted: 2026, 10, Mar
Published: 2026, 27, Apr

Copyright © 2026 by author(s) and Bio Science Academic Publishing. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/40/>



Annotation: Background: Hyperthyroidism changes cardiovascular, inflammatory, and metabolic pathways. These changes may be aggravated by heart disease. Objective: Both to compare levels of thyroid hormones, proBNP, IL-6, lipid profile, renal function, glucose, and BMI among four groups and to determine whether or not proBNP and IL-6 can detect cardiac disease in hyperthyroid patients. Methods: It was an analytical cross-sectional study, which utilized a dataset of 140 participants (n = 50 healthy controls, n = 30 hyperthyroidism treated with 35 mg carbimazole, n = 30 heart disease, and n = 30 heart disease and hyperthyroidism). ELISA-based measurements were described as thyroid hormones, IL-6 and proBNP. Glucose, lipid profile, and renal functioning were characterized as Cobas c111 chemistry tests. Descriptive statistics, one-way ANOVA, Pearson correlation, Welch t test, and ROC analysis were performed. Results: There was no significant difference in age among groups (p = 0.159). FT4, FT3, TSH, IL-6, proBNP, BMI, triglycerides, glucose, creatinine and urea were found to have strong group effects (all p < .001). The highest level of IL-6 and proBNP was observed in the heart disease with hyperthyroidism. The largest differences were observed in the proBNP (116.00 vs. 847.22 pg/mL, p < .001, d = 4.29) and IL-6 (4.07 vs. 7.62 pg/mL, p < .001, d = 2.41) in the direct comparison between

hyperthyroidism with carbimazole proBNP correlated positively with IL-6 ($r = .70$, $p < .001$). TSH correlated inversely with FT4 ($r = -.79$, $p < .001$). ProBNP had an AUC of 1.000 and IL-6 had an AUC of 0.961 to discriminate heart disease among hyperthyroid patients. Conclusion: Heart disease patients who had hyperthyroidism had a different profile that was characterized by increased cardiac stress, increased inflammatory load, and poor metabolic and renal indices. ProBNP and IL-6 were the best predictors of cardiac involvement in this cohort.

Keywords: Hyperthyroidism; carbimazole; proBNP; IL-6; heart disease; ROC curve; thyroid hormones; biomarker.

Introduction

Hyperthyroidism is not an exclusive endocrine issue. It affects the whole circulation. It alters the heart rate, preload, afterload and myocardial oxygen demand. It is also capable of causing arrhythmia and heart failure. Excess thyroid hormone increases preload and contractility, decreases systemic vascular resistance, and increases cardiac output [1]. Thyrotoxicosis is thus characterized by cardiovascular symptoms. Well known manifestations include palpitations, dyspnea, edema, exercise intolerance, and congestive heart failure. Deaths among hyperthyroid patients are also increased and cardiac reasons constitute a significant percentage of the surplus risk [1]. The medical therapy of Graves hyperthyroidism still revolves around antithyroid drugs. First-line therapy is usually anti-thyroid drugs. Carbimazole is a member of the thionamide. Once it has been converted to methimazole, it blocks thyroid peroxidase and decreases the production of thyroid hormones. The dose titration is a common practice as it decreases cumulative exposure and can minimize dose-related side effects [2]. One hyperthyroid group in the current dataset was identified as taking 35 mg carbimazole, which is a clinically appropriate comparison group in assessing the incremental impact of heart disease. The possible role of inflammation in explaining why certain hyperthyroid patients acquire more cardiac phenotype is present. Interleukin-6 is a pleiotropic cytokine involved in acute phase signaling, hepatocyte responses, B-cell differentiation, T-cell biology and chronic inflammatory activation [3]. IL-6 is not just a passive marker. It indicates dynamic immunologic and tissue stress pathways. Higher levels of serum IL-6 have been observed in Graves disease, compared to healthy controls. Salvi et al. determined serum IL-6 using a high sensitivity solid phase ELISA and observed significantly greater levels in hyperthyroid Graves disease, compared to normal individuals [4]. This renders IL-6 a biologically viable predictor in research of cardiovascular burden in thyroid. The second layer is provided by cardiac stress biomarkers. BNP peptides occur in reaction to pressure overload and expansion of ventricular volumes. NT-proBNP is a more stable protein that has a longer biological half-life than BNP and can be used to diagnose and evaluate heart failure [5]. In a recent systematic review and meta-analysis, NT-proBNP was also found to be increased in overt hyperthyroidism, and could decrease after treatment with euthyroidism restored [5]. This is a clinically important point. An increase in natriuretic peptides in the state of hyperthyroidism can be regarded as a direct interaction of the thyroid and heart, however, significantly increased values can indicate the presence of a heart disease. Also worth noting is metabolic variables. There are various processes in lipoprotein

metabolism that are controlled by thyroid hormones. Thyroid activity has an influence on the total cholesterol, LDL cholesterol, triglycerides and HDL cholesterol. Rizos et al. summarized findings that an increase in TSH is related to an increase in total cholesterol, LDL cholesterol, and triglycerides and a decrease in HDL cholesterol even in the normal range [6]. Mechanistic links were also outlined using HMG-CoA reductase, LDL receptors, cholesteryl ester transfer protein, lipoprotein lipase and hepatic lipase [6]. This same review observed that TSH and BMI have a positive relationship [6]. BMI is the most popular index of anthropometric measurements and it is estimated as the weight of the body divided by height squared in meters [7]. Although this is the case, there are limited integrated datasets that make comparisons between healthy controls, medically treated hyperthyroidism, isolated heart disease, and combined heart disease and hyperthyroidism. This gap matters. Two patients can share the same level of thyroid hormone but with a very different risk of cardiovascular disease. ProBNP or IL-6 may thus be additive to FT3, FT4 and TSH alone. The current paper was planned to characterize the biochemical profile of these four groups, examine the relationship between thyroid, inflammatory, cardiac, metabolic, and renal markers, compare hyperthyroid patients who were on carbimazole treatment with hyperthyroid patients who also had heart disease, as well as assess the diagnostic value of the chosen biomarkers through ROC analysis.

Materials and Methods

This study was conducted in Baghdad, Iraq, Al-Kindi Teaching Hospital from 1st November 2024 to 30th April 2025 vide letter No. 4545/QM/Approval/SJKDH379 dated 9th March 2024. This study was prepared as an analytical cross-sectional study. The recruitments included 140 participants allocated to four predefined groups: healthy control (n = 50), hyperthyroidism treated with 35 mg *carbimazole* (n = 30), heart disease without hyperthyroidism (n = 30), and heart disease with hyperthyroidism (n = 30). Recruitments biochemical results included age, sex, BMI, glucose, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, FT3, FT4, TSH, IL-6, proBNP, creatinine, and urea. Anthropometry. BMI was calculated using the standard Quetelet equation: $BMI = \text{weight (kg)} / \text{height (m)}^2$ [7]. Laboratory methods. Thyroid hormones (FT3, FT4, and TSH), IL-6, and proBNP were described in the protocol as ELISA-based measurements. Glucose, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, creatinine, and urea were described as chemistry analytes measured on a Cobas c111 automated analyzer, Roche Diagnostics, Mannheim, Germany. However, Statistical analysis. Continuous variables were summarized as mean and standard deviation. Sex was summarized as counts. One-way analysis of variance (ANOVA) was used for four-group comparison. Pearson correlation was used to evaluate linear associations among selected biomarkers. A focused Welch two-sample t test compared the hyperthyroidism + carbimazole group with the heart disease + hyperthyroidism group. Receiver operating characteristic (ROC) analysis evaluated the ability of selected biomarkers to discriminate heart disease within the two hyperthyroid groups. Statistical significance was set at $p < .05$.

Results

A total of 140 participants were analyzed. Age did not differ significantly among the four groups (ANOVA, $p = 0.159$). Sex distribution was balanced across the dataset. Healthy controls included 24 females and 26 males. The hyperthyroidism + carbimazole group included 17 females and 13 males. The heart disease group included 17 females and 13 males. The heart disease + hyperthyroidism group included 11 females and 19 males.

Thyroid hormone measurements showed a clear four-group pattern. FT3 and FT4 were markedly higher in the two hyperthyroid groups, while TSH was markedly lower. ANOVA showed highly significant differences for FT4, FT3, and TSH (all $p < .001$). Tukey post hoc testing indicated that the two hyperthyroid groups were both significantly different from healthy controls and from the

isolated heart disease group. However, FT3, FT4, and TSH did not differ significantly between the two hyperthyroid groups. This means that the added cardiac phenotype was not explained by substantially greater biochemical thyroid excess alone.

Inflammatory and cardiac stress markers showed the strongest separation. IL-6 was highest in the heart disease + hyperthyroidism group. proBNP was also highest in that group. ANOVA confirmed strong group effects for IL-6 and proBNP (both $p < .001$). Tukey comparisons showed that IL-6 was significantly different across all pairwise group contrasts. The combined phenotype therefore appeared to represent both greater inflammatory activity and greater myocardial stress.

Metabolic and renal markers also showed meaningful deterioration in the combined group. BMI, glucose, triglycerides, total cholesterol, LDL cholesterol, creatinine, and urea were all significantly different across the four groups. The heart disease + hyperthyroidism group showed the most adverse mean values for most of these variables, while the healthy control group showed the lowest overall burden.

When the two hyperthyroid groups were compared directly using Welch t testing, proBNP showed the largest difference. Mean proBNP was 116.00 pg/mL in the hyperthyroidism + carbimazole group and 847.22 pg/mL in the heart disease + hyperthyroidism group ($p < .001$, Cohen's $d = 4.29$). Mean IL-6 was 4.07 pg/mL and 7.62 pg/mL, respectively ($p < .001$, $d = 2.41$). BMI, triglycerides, glucose, LDL cholesterol, total cholesterol, creatinine, and urea were also significantly higher in the combined group. In contrast, FT3, FT4, and TSH did not differ significantly between the two hyperthyroid groups.

Table 1. Descriptive statistics by study group.

Variable	Healthy control (n = 50)	Hyperthyroidis m + 35 mg carbimazole (n = 30)	Heart disease (n = 30)	Heart disease + hyperthyroidism (n = 30)	p
Age (years)	55.3 +/- 15.8	59.5 +/- 14.8	51.6 +/- 15.3	51.7 +/- 15.4	0.159
BMI (kg/m ²)	24.61 +/- 3.18	22.85 +/- 2.88	30.10 +/- 3.48	28.15 +/- 3.69	< .001
FT3 (pg/mL)	3.12 +/- 0.38	5.67 +/- 0.72	3.03 +/- 0.44	5.77 +/- 0.92	< .001
FT4 (ng/dL)	1.23 +/- 0.14	2.23 +/- 0.23	1.16 +/- 0.17	2.36 +/- 0.38	< .001
TSH (mIU/L)	2.083 +/- 0.664	0.111 +/- 0.056	2.173 +/- 1.066	0.087 +/- 0.044	< .001
IL-6 (pg/mL)	1.92 +/- 0.77	4.07 +/- 1.07	6.32 +/- 1.55	7.62 +/- 1.78	< .001
proBNP (pg/mL)	59.91 +/- 28.28	116.00 +/- 39.27	919.45 +/- 310.63	847.22 +/- 237.75	< .001
Glucose (mg/dL)	95.64 +/- 10.01	101.03 +/- 12.11	120.76 +/- 16.01	119.60 +/- 14.19	< .001
Total cholesterol (mg/dL)	175.82 +/- 21.07	172.92 +/- 25.73	222.08 +/- 32.32	204.52 +/- 27.99	< .001

Triglycerides (mg/dL)	129.60 +/- 22.71	117.09 +/- 25.27	186.70 +/- 39.33	164.69 +/- 33.47	< .001
HDL (mg/dL)	51.24 +/- 6.88	51.46 +/- 7.07	42.88 +/- 5.96	48.76 +/- 7.94	< .001
LDL (mg/dL)	108.06 +/- 17.83	104.02 +/- 20.64	141.62 +/- 34.78	130.99 +/- 19.29	< .001
Creatinine (mg/dL)	0.91 +/- 0.16	1.01 +/- 0.18	1.47 +/- 0.40	1.31 +/- 0.31	< .001
Urea (mg/dL)	28.19 +/- 5.15	33.59 +/- 5.71	48.58 +/- 10.87	45.11 +/- 9.66	< .001

Values are mean +/- SD.

Table 2. Welch t test comparing the two hyperthyroid groups.

Variable	Hyperthyroidism + 35 mg carbimazole mean	Heart disease + hyperthyroidism mean	p value	Cohen's d
proBNP (pg/mL)	116.00	847.22	< .001	4.29
IL-6 (pg/mL)	4.07	7.62	< .001	2.41
BMI (kg/m²)	22.85	28.15	< .001	1.60
Triglycerides (mg/dL)	117.09	164.69	< .001	1.61
Glucose (mg/dL)	101.03	119.60	< .001	1.41
LDL (mg/dL)	104.02	130.99	< .001	1.35
Total cholesterol (mg/dL)	172.92	204.52	< .001	1.18
Creatinine (mg/dL)	1.01	1.31	< .001	1.17
FT4 (ng/dL)	2.23	2.36	0.109	0.42
TSH (mIU/L)	0.11	0.09	0.073	-0.47

The largest effect sizes were observed for proBNP and IL-6.

Figure 1. Group differences in thyroid, inflammatory, and cardiac biomarkers

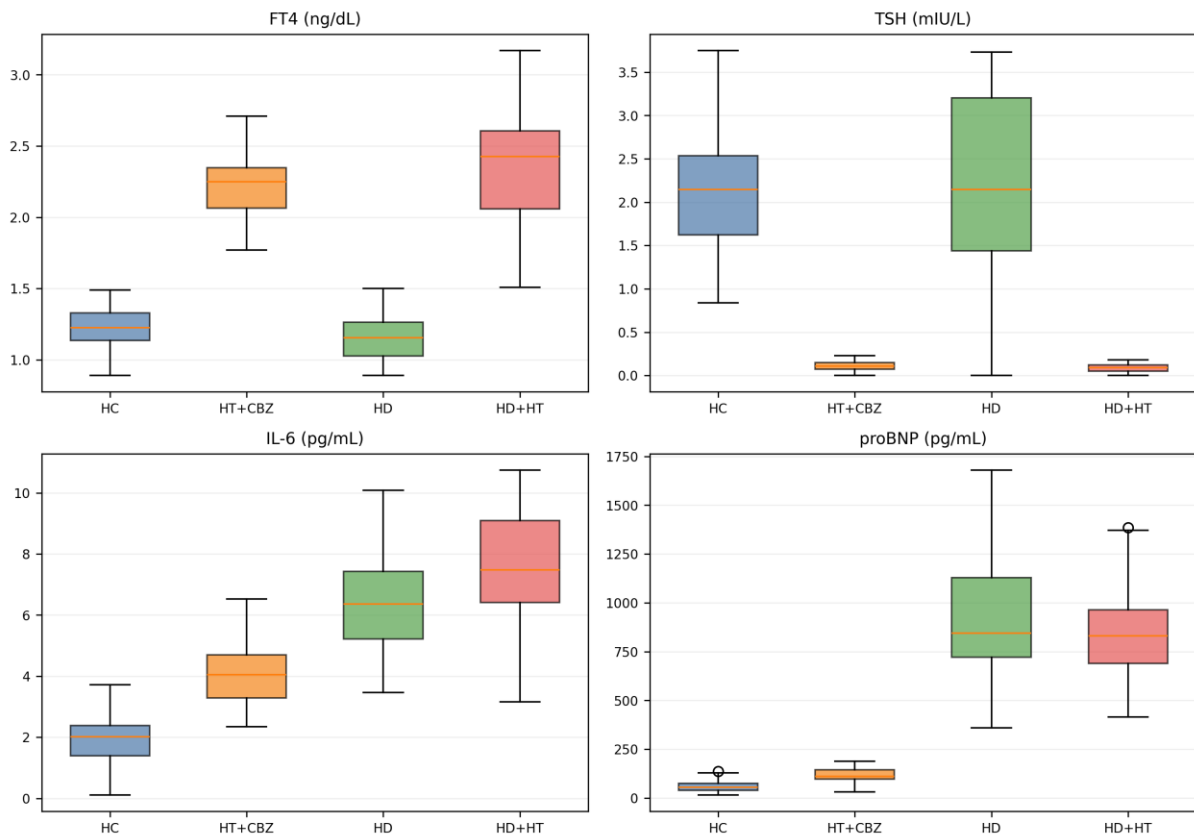


Figure 1. Boxplots of FT4, TSH, IL-6, and proBNP across the four study groups.

Figure 2. Distribution of IL-6 and proBNP by study group

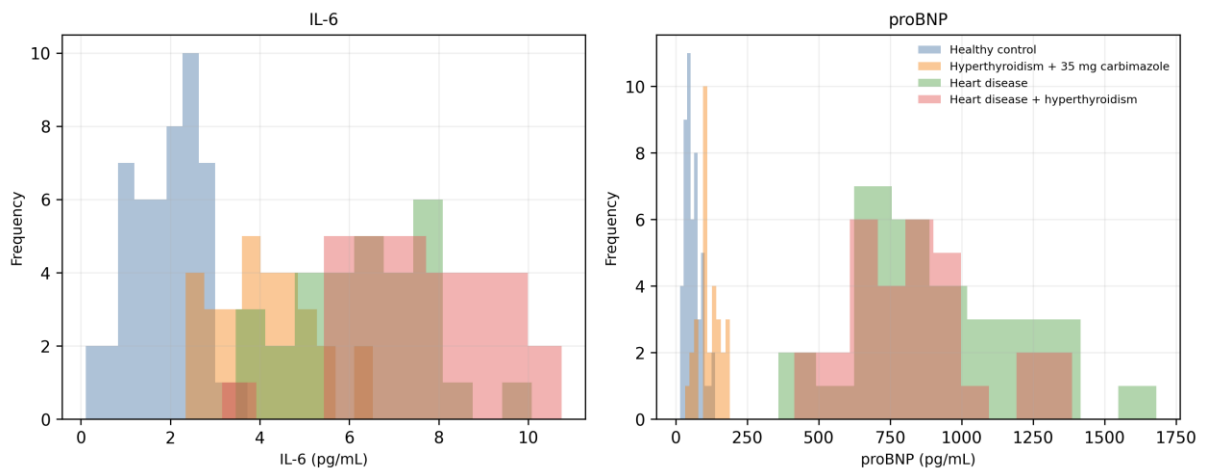


Figure 2. Histograms of IL-6 and proBNP by study group.

Correlation analysis demonstrated a strong positive relationship between proBNP and IL-6 ($r = 0.70, p < .001$). BMI correlated positively with IL-6 ($r = 0.46, p < .001$). TSH showed a strong inverse correlation with FT4 ($r = -0.79, p < .001$). These findings suggest that myocardial stress and inflammation moved together in this cohort, whereas thyroid axis suppression followed the expected biochemical pattern of thyrotoxicosis.

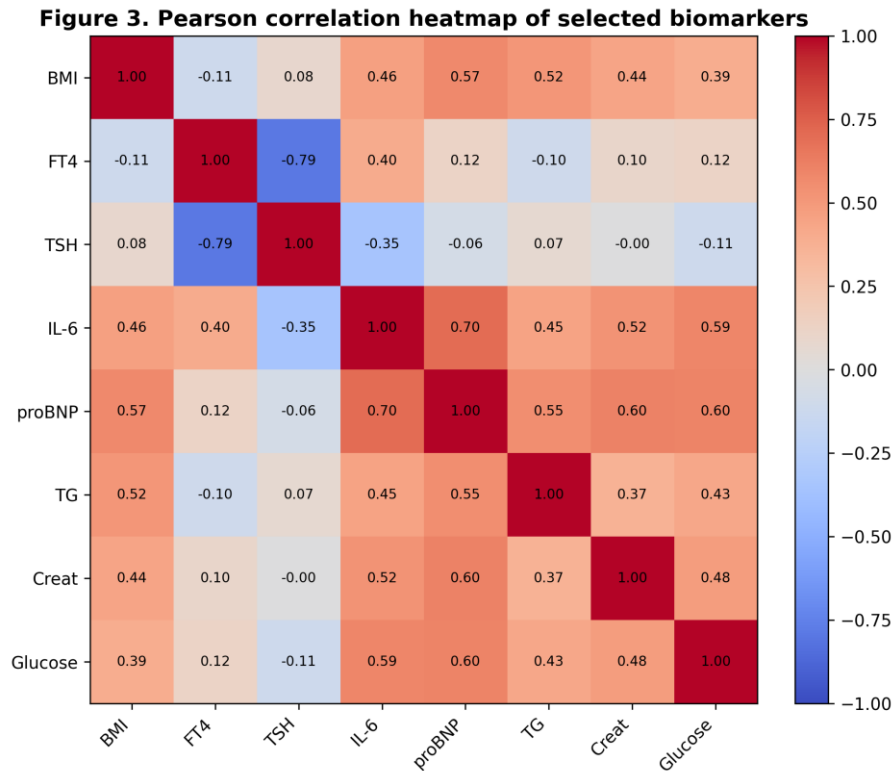


Figure 3. Pearson correlation heatmap among selected biomarkers.

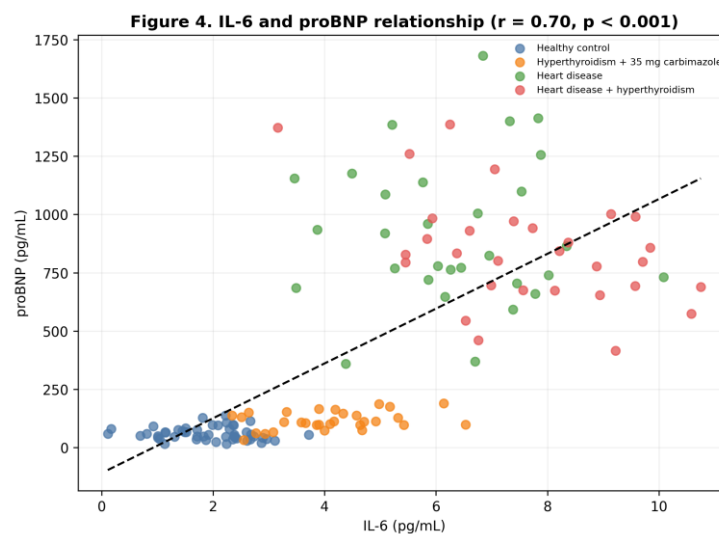


Figure 4. Scatter plot showing the positive association between IL-6 and proBNP.

ROC analysis focused on discrimination of heart disease within hyperthyroid patients. proBNP achieved an AUC of 1.000. IL-6 achieved an AUC of 0.961. BMI and creatinine showed more modest but still informative discrimination. The optimal threshold for proBNP in this dataset was approximately 415.07 pg/mL, with 100.0% sensitivity and 100.0% specificity. The optimal IL-6 threshold was approximately 5.45 pg/mL, with sensitivity of 96.7% and specificity of 93.3%. These ROC results should be interpreted cautiously because they were developed in a single cohort without external validation.

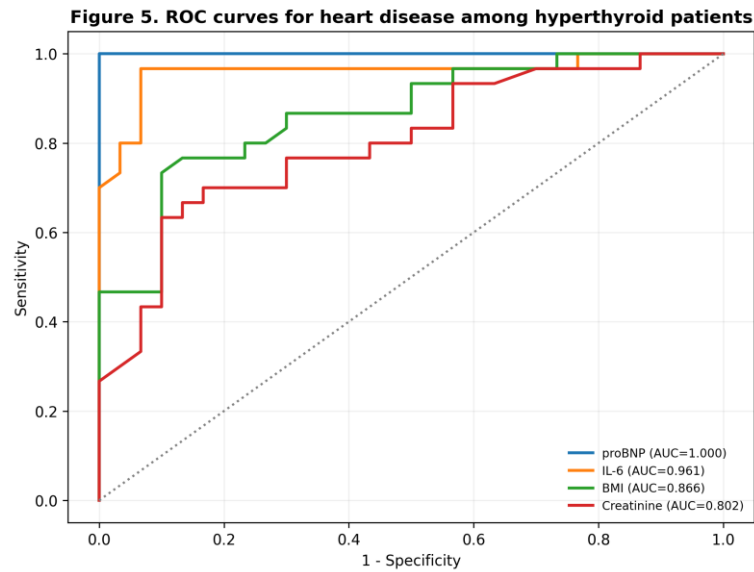


Figure 5. ROC curves for discrimination of heart disease among hyperthyroid patients.

Table 3. Selected Pearson correlations.

Pair	Pearson r	Interpretation
proBNP vs IL-6	0.70	strong positive
TSH vs FT4	-0.79	strong negative
BMI vs IL-6	0.46	moderate positive
Glucose vs triglycerides	0.43	moderate positive
Creatinine vs urea	0.50	moderate positive
Total cholesterol vs LDL	0.34	moderate positive

Positive coupling between IL-6 and proBNP was one of the strongest signals in the dataset.

Table 4. ROC performance for detecting heart disease among hyperthyroid patients.

Biomarker	AUC	95% CI	Cutoff	Sensitivity	Specificity
proBNP	1.000	1.000-1.000	415.07	100.0%	100.0%
IL-6	0.961	0.897-1.000	5.45	96.7%	93.3%
BMI	0.866	0.765-0.949	26.31	76.7%	86.7%
Creatinine	0.802	0.690-0.904	1.21	63.3%	90.0%

ROC results were calculated only within the two hyperthyroid groups and require external validation.

Discussion

This analysis exhibited a trend. The overall biochemical profile of hyperthyroid patients with heart disease was the worst. They had the highest proBNP values. Their values of IL-6 were also the highest. Besides that, they had elevated BMI, triglycerides, glucose, creatinine and urea compared to hyperthyroid patients receiving carbimazole in isolation. The composite phenotype thus seems to indicate more than excess of thyroid hormone. It indicates cardiac stress, inflammation, and overall metabolic load. The outcomes of the thyroid hormone tests were internally consistent. The two hyperthyroid groups had the anticipated trend of increased FT3 and FT4 and low TSH. Nevertheless, the levels of FT3, FT4 and TSH were not significantly different between

hyperthyroid patients on carbimazole and hyperthyroid patients who had another heart disease [8][9][10]. This is a significant point. A significantly worse biochemical thyrotoxic state did not contribute to the difference between the two groups. The most separating variables were proBNP and IL-6. This adds to the concept that myocardial strain and inflammatory activation of cardiac activity in hyperthyroidism might be more closely associated with cardiac involvement than with thyroid hormone levels per se. The proBNP finding is biologically plausible. NT-proBNP is an instrument released under the influence of stress on the ventricular wall and is a known predictor of the severity of heart failure and prognosis [5]. It was also demonstrated by Zhang et al. that the levels of natriuretic peptides can be elevated in overt hyperthyroidism and can decrease with euthyroidism, which is achieved after treatment [5]. Our discoveries go farther than that reasoning. The proBNP was significantly greater in this cohort in the presence of hyperthyroidism and heart disease than it was in the presence of hyperthyroidism and carbimazole alone [11][12][13][14][15]. The ROC was a bold analysis. proBNP had an AUC of 1.000 in this data. It is a good indicator, but must not be hyped. In a single cohort, perfect discrimination is possible in circumstances whereby the sample is small or the sample groups are distinct. External validation is critical. IL-6 also worked quite well. Tanaka et al. referred to IL-6 as a central signal of acute phase, immune activation, and chronic inflammatory disease biology [3]. Salvi et al. have found that the serum IL-6 is increased in hyperthyroid Graves disease and have compared the difference using high-sensitivity ELISA [4]. In the current analysis, the highest IL-6 was found in the group of heart disease + hyperthyroidism and AUC was 0.961. The positive correlation between IL-6 and proBNP is strong, which indicates that there is a movement of inflammatory activation and myocardial stress. Such a trend is possible in hyperthyroid heart disease, where immune, vascular, and hemodynamic mechanisms may be mutually reinforcing. The lipid and metabolic results are also consistent with the past studies. Lipoprotein metabolism is regulated by thyroid functioning by acting on HMG-CoA reductase, LDL receptors, cholesteryl ester transfer protein, and lipases [6]. In the current data, the combined heart disease and hyperthyroid group had a worse triglycerides, total cholesterol and LDL cholesterol. There was also an increased glucose and BMI. A positive correlation between TSH and BMI was also found to be reviewed by Rizos et al. [6]. Despite the fact that the current study does not support a mechanism, the metabolic profile would indicate that thyroid malfunction and heart disease may have a cardiometabolic amplification loop in selected patients. Renal markers were also shifted towards the negative. The levels of creatinine and urea were much higher in the heart disease + hyperthyroidism group. These alterations can be indicative of reduced renal perfusion or cardiorenal interaction or increased chronic disease burden. Their ROC analysis also demonstrated some discriminative value but they were obviously weaker than proBNP and IL-6. This, clinically, implies that renal chemistry cannot be seen as a second-order issue in such patients. The data consistently demonstrates that hyperthyroid patients develop heart disease, which is linked to the elevated level of cardiac biomarker release, inflammatory activity, and poor metabolism and renal indices. In practice, it seems that proBNP is the most informative single marker within this cohort. IL-6 provides valuable information as well. Combined, they can be useful in determining hyperthyroid patients that require more cardiovascular evaluation.

Conclusion

A different biochemical pattern was observed in patients with hyperthyroidism and co-morbid heart disease in this dataset. Their proBNP and IL-6 were significantly higher as compared to hyperthyroid patients receiving 35mg carbimazole alone. They also possessed poorer BMI, triglycerides, glucose, creatinine, and urea. This difference could not be attributed to the levels of thyroid hormone alone. The best discriminator of cardiac involvement was proBNP. IL-6 was the second strongest. These indicators should be confirmed in larger prospective cohorts.

References

- [1] S. Ertek and A. F. Cicero, "Hyperthyroidism and cardiovascular complications: A narrative review on the basis of pathophysiology," *Archives of Medical Science*, vol. 9, no. 5, pp. 944–952, 2013, doi: 10.5114/aoms.2013.38685.
- [2] A. Abbara *et al.*, "Pharmacodynamic response to anti-thyroid drugs in Graves' hyperthyroidism," *Frontiers in Endocrinology*, vol. 11, Art. no. 286, 2020, doi: 10.3389/fendo.2020.00286.
- [3] T. Tanaka, M. Narazaki, and T. Kishimoto, "IL-6 in inflammation, immunity, and disease," *Cold Spring Harbor Perspectives in Biology*, vol. 6, no. 10, Art. no. a016295, 2014, doi: 10.1101/cshperspect.a016295.
- [4] M. Salvi *et al.*, "Increased serum concentrations of interleukin-6 (IL-6) and soluble IL-6 receptor in patients with Graves' disease," *The Journal of Clinical Endocrinology & Metabolism*, vol. 81, no. 8, pp. 2976–2979, 1996, doi: 10.1210/jcem.81.8.8768861.
- [5] H. Zhang *et al.*, "Effect of thyroid dysfunction on N-terminal pro-B-type natriuretic peptide levels: A systematic review and meta-analysis," *Frontiers in Endocrinology*, vol. 14, Art. no. 1083171, 2023, doi: 10.3389/fendo.2023.1083171.
- [6] C. V. Rizos, M. S. Elisaf, and E. N. Liberopoulos, "Effects of thyroid dysfunction on lipid profile," *The Open Cardiovascular Medicine Journal*, vol. 5, pp. 76–84, 2011, doi: 10.2174/1874192401105010076.
- [7] F. Q. Nuttall, "Body mass index: Obesity, BMI, and health: A critical review," *Nutrition Today*, vol. 50, no. 3, pp. 117–128, 2015, doi: 10.1097/NT.0000000000000092.
- [8] D. S. Ross *et al.*, "2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis," *Thyroid*, vol. 26, no. 10, pp. 1343–1421, 2016, doi: 10.1089/thy.2016.0229.
- [9] B. Biondi and D. S. Cooper, "The clinical significance of subclinical thyroid dysfunction," *Endocrine Reviews*, vol. 29, no. 1, pp. 76–131, 2008, doi: 10.1210/er.2006-0043.
- [10] B. Biondi and D. S. Cooper, "Thyroid hormone excess and the heart," *Circulation*, vol. 116, no. 15, pp. 1725–1735, 2007, doi: 10.1161/CIRCULATIONAHA.106.678326.
- [11] G. J. Kahaly and L. Bartalena, "Graves' disease," *New England Journal of Medicine*, vol. 376, no. 19, pp. 1842–1853, 2017, doi: 10.1056/NEJMra1510030.
- [12] M. Klein and K. Ojamaa, "Thyroid hormone and the cardiovascular system," *New England Journal of Medicine*, vol. 344, no. 7, pp. 501–509, 2001, doi: 10.1056/NEJM200102153440707.
- [13] M. Antonelli, P. Fallahi, S. M. Ferrari, A. Ragusa, A. Ruffilli, and A. Antonelli, "Cytokines (interleukin-6 and tumor necrosis factor- α) in autoimmune thyroid diseases," *Autoimmunity Reviews*, vol. 14, no. 10, pp. 922–930, 2015, doi: 10.1016/j.autrev.2015.06.014.
- [14] A. Jabbar, M. Pingitore, A. Pearce, B. Zaman, S. Iervasi, and M. Razvi, "Thyroid hormones and cardiovascular disease," *Nature Reviews Cardiology*, vol. 14, no. 1, pp. 39–55, 2017, doi: 10.1038/nrcardio.2016.174.
- [15] G. Brent, "Mechanisms of thyroid hormone action," *Journal of Clinical Investigation*, vol. 122, no. 9, pp. 3035–3043, 2012, doi: 10.1172/JCI60047.