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Original Article

Evaluation of B-Type Natriuretic Peptide (BNP) Levels in Patients with Hyperthyroidism

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Abstract

Background: *B-type natriuretic peptide (BNP) is a key biomarker for cardiac stress and heart failure, yet elevated BNP levels also occur in hyperthyroidism despite the absence of overt heart disease. Because thyroid hormone excess can independently increase heart rate, cardiac workload, and BNP secretion, understanding this relationship is essential to prevent misdiagnosis of heart failure in thyrotoxic patients.*

Objective: *This study aimed to evaluate plasma BNP levels in hyperthyroid patients compared to euthyroid individuals and to identify thyroid-related determinants of BNP elevation* ***Methods:*** *A cross-sectional study was conducted at the Department of Biochemistry, Bangladesh Medical University (BMU), including 90 adults aged 18–65 years: 45 with biochemically confirmed hyperthyroidism and 45 euthyroid controls. Individuals with cardiovascular, renal, or hepatic disease, pregnancy, or medications affecting thyroid or cardiac function were excluded. Plasma BNP, TSH, FT3, and FT4 were measured using microparticle enzyme immunoassay (MEIA). Statistical analysis involved group comparisons using t-tests and Mann–Whitney U tests, Spearman correlation, and multiple linear regressions to identify independent predictors of BNP levels.* ***Results:*** *Hyperthyroid patients had markedly higher BNP: median 215.50 pg/mL versus 34.25 pg/mL in controls ($p<0.001$). Both overt and subclinical hyperthyroid subgroups showed ~6-fold and ~5-fold higher BNP levels, respectively, than controls. Plasma BNP correlated positively with FT3 (free T3) and inversely with TSH. Multiple regression analysis identified FT3 as independent predictor of BNP levels.* ***Conclusion:*** *Elevated BNP in hyperthyroidism reflects subclinical cardiac stress from thyroid hormone excess rather than overt heart failure. Thyroid function assessment is essential when interpreting raised BNP to avoid misdiagnosis and guide appropriate management.*

Keywords: *Hyperthyroidism; B-type natriuretic peptide (BNP); cardiac biomarker; FT3.*

Introduction: B-type natriuretic peptide (BNP) is a cardiac neurohormone predominantly secreted by ventricular myocytes in response to increased wall stress and myocardial stretch. It serves as a sensitive and specific biomarker for diagnosing and prognosticating heart failure[1]. BNP reflects ventricular pressure overload and volume expansion, helping to differentiate cardiac from non-cardiac causes of dyspnea in clinical practice[2]. Produced initially as proBNP, this precursor is cleaved into the biologically active BNP and the inactive N-terminal pro-BNP (NT-proBNP) fragment. Their plasma levels correlate closely with the severity of left ventricular dysfunction and provide independent prognostic information in both acute and chronic heart failure[3].

However, BNP elevation is not confined to heart failure alone. Increased plasma BNP levels have also been reported in various non-cardiac conditions, including renal impairment, pulmonary hypertension, sepsis, and thyroid dysfunction[4–6]. Among endocrine disorders, hyperthyroidism has drawn particular interest for its influence on natriuretic peptide secretion. Hyperthyroidism augments cardiac output and myocardial oxygen demand through enhanced inotropy, chronotropy, and reduced systemic vascular resistance[7]. This hyperdynamic circulatory state can impose myocardial wall stress, potentially stimulating BNP release even in the absence of structural heart disease[8].

Several experimental and clinical studies suggest that thyroid hormones directly modulate BNP synthesis. Triiodothyronine (T3), the active thyroid hormone, exerts genomic effects on cardiomyocytes by binding

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to thyroid hormone receptors, thereby influencing transcription of genes regulating cardiac contractility and energy metabolism[9]. In vitro studies have demonstrated that T3 can upregulate the human BNP gene promoter, inducing BNP expression independent of ventricular wall stretch[10]. Moreover, free T3 (FT3) acts more potently than free thyroxine (FT4) in regulating cardiac gene transcription, possibly explaining the stronger clinical correlation between FT3 and BNP observed in thyrotoxic individuals[11].

Hyperthyroidism profoundly impacts cardiovascular physiology by increasing heart rate, pulse pressure, and cardiac output while lowering systemic vascular resistance[12],[13]. These hemodynamic changes can mimic features of heart failure—such as tachycardia, palpitations, exertional dyspnea, and peripheral edema—leading to potential diagnostic confusion[14]. Elevated BNP in hyperthyroid patients may therefore be misinterpreted as a marker of heart failure rather than a consequence of thyrotoxicosis-induced cardiac hyperactivity. Clinicians unaware of this relationship risk unnecessary cardiac investigations or misdiagnosis of heart failure in patients whose cardiac function is essentially preserved.

Beyond functional alterations, overt hyperthyroidism may cause subtle structural changes in the myocardium, including increased left ventricular mass and wall thickness[15]. Studies in both overt and subclinical hyperthyroidism have demonstrated elevated BNP or NT-proBNP levels, which tend to normalize after achieving a euthyroid state[16],[17]. A recent meta-analysis confirmed that antithyroid treatment leading to normalization of thyroid hormone levels significantly reduces circulating natriuretic peptides, reinforcing the causal role of thyroid hormones in BNP elevation[18].

Despite these observations, previous reports have yielded inconsistent associations between thyroid hormone levels and BNP. Variability in study design, disease severity, assay method, and presence of comorbidities may contribute to these discrepancies[19]-[21]. Some investigations found a strong positive association of FT3 with BNP, while others indicated weak or non-significant correlations, particularly in subclinical disease[22]. Furthermore, studies show that FT3 levels correlate with cardiac structure and function even within the euthyroid range, linking higher FT3 concentrations with increased ventricular wall thickness and resting heart rate[23]. Thyroid hormones may continuously influence myocardial BNP secretion, making it essential to distinguish thyrotoxic cardiac stress from true heart failure when interpreting elevated BNP levels, especially in emergency settings[24].

The present study aims to compare plasma BNP concentrations between hyperthyroid and euthyroid individuals and to identify the principal hormonal predictors of BNP elevation. Because thyroid hormone excess can elevate BNP independently of underlying cardiac disease, distinguishing this effect is clinically important. Clarifying this relationship will improve BNP interpretation in hyperthyroid patients and reduce the risk of heart failure misdiagnosis, thereby minimizing unnecessary investigations and inappropriate treatment.

Materials and Methods

This cross-sectional analytical study was conducted in the Department of Biochemistry, Bangladesh Medical University, in collaboration with the Department of Endocrinology, between July 2014 and June 2015 to evaluate the relationship between thyroid hormones and plasma B-type natriuretic peptide (BNP) levels in hyperthyroid patients. A total of 90 adults aged 18–65 years were enrolled, comprising 45 newly diagnosed hyperthyroid patients and 45 age- and sex-matched euthyroid controls. Hyperthyroidism was defined by suppressed thyroid-stimulating hormone (TSH <0.4 mIU/L) with elevated free triiodothyronine (FT3) and/or free thyroxine (FT4), while controls had all thyroid parameters within reference ranges. Individuals with cardiovascular disease, renal or hepatic impairment, pregnancy, diabetes, or use of medications affecting thyroid or cardiac function were excluded.

Clinical evaluations included heart rate, blood pressure, and body mass index (BMI). Venous blood samples were collected for biochemical analysis. Serum TSH, FT3, and FT4 were measured using microparticle enzyme immunoassay (MEIA; Abbott Laboratories), and plasma BNP was quantified using the Abbott AxSYM MEIA assay (detection range: 0–5000 pg/mL), with BNP >100 pg/mL considered elevated.

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Data analysis was performed using SPSS version 22. Continuous variables were presented as mean ± SD or median with interquartile range. Group comparisons used independent-samples t-tests or Mann–Whitney U tests. Spearman correlation assessed associations between variables, and multiple linear regression was applied to identify independent predictors of BNP levels. Statistical significance was defined as $p < 0.05$. Ethical approval was granted by the Institutional Review Board of Bangladesh Medical University, and written informed consent was obtained from all participants.

Results:

Table I: Baseline characteristics of study subjects (n=90)

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Parameter		Hyperthyroid (n=45)	Euthyroid (n=45)	p-value
Age (years)	Mean ± SD	36.27 ± 12.25	35.4 ± 11.7	*0.739
	Range (min-max)	18 - 62	18 – 65	
Sex (numbe	Male	16 (36%)	20 (44%)	**0.389
	Female	29 (64%)	25 (56%)	
Height (cm)	Mean ± SD	159.13 ± 8.28	159.62 ± 9.23	*0.792
Weight (kg)	Mean ± SD	53.84 ± 6.70	59.68 ± 8.79	*0.001
BMI (kg/m^2)	Mean ± SD	21.24 ± 1.70	23.27 ± 1.93	*0.000

* p-value Obtained from unpaired t-test ** p-value Obtained from Chi-Square test
Figures in the parenthesis denote corresponding percentage

Table I shows comparable mean ages and identical age ranges (18–65 years) across groups, with no significant differences in age or sex distribution. BMI was significantly lower in hyperthyroid patients (21.24 ± 1.70 kg/m²) than in euthyroid controls (23.27 ± 1.93 kg/m²; $p < 0.001$).

Table II: Distribution of cardiovascular parameters between two groups (n=90)

Parameter	Group		p-value
	Hyperthyroid (n=45) mean ± SD	Euthyroid (n=45) mean ± SD	
Pulse (beat/min)	94.76 ± 9.11	78.58 ± 5.98	0.0000
SBP (mmHg)	121.67 ± 10.06	118.00 ± 7.40	0.0679
DBP (mmHg)	81.00 ± 6.27	78.58 ± 5.98	0 .0952

p-values have been obtained from unpaired t-test
Table II shows that hyperthyroid patients had a significantly higher pulse rate than controls (94.76 ± 9.11 vs. 78.58 ± 5.98 beats/min; $p<0.0001$). Differences in systolic and diastolic blood pressure were minimal and not statistically significant ($p=0.0679$ and $p=0.0952$, respectively).

Table III: Distribution of BNP levels among study subjects (n=90):

Parameter	Group		p-value
	Hyperthyroid (n=45) Median	Euthyroid (n=45) Median	
BNP (pg/ml)	215.50	34.25	0.0000

p-value obtained from Mann-Whitney test
Table III shows the distribution of B-type natriuretic peptide (BNP) among the study subjects. Median BNP was markedly higher in the hyperthyroid group (215.50 pg/mL) compared with the euthyroid group (34.25 pg/mL), and this difference was statistically significant ($p<0.001$).

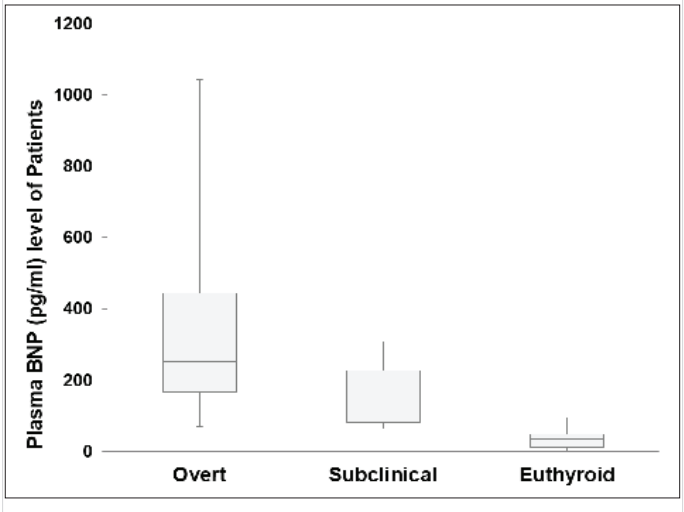

Figure 1: BNP Levels in subgroups of hyperthyroidism (overt and subclinical)

The boxplot illustrates plasma BNP concentrations across three groups: overt hyperthyroidism, subclinical hyperthyroidism, and euthyroid controls. Overt hyperthyroid patients show the highest BNP levels, with a wide distribution and several values extending above 1000 pg/mL. Subclinical hyperthyroid patients exhibit moderately elevated BNP levels with a narrower range.

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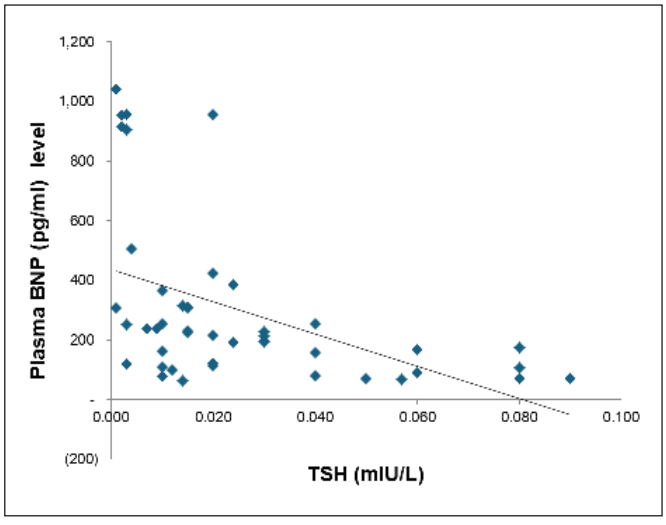

Figure 2: Correlation between BNP and TSH among the hyperthyroid group (n=45)

The scatterplot (Figure 2) demonstrates a clear negative correlation between TSH and plasma BNP, with BNP levels rising as TSH decreases, as reflected by the downward-sloping regression line. This relationship was statistically significant in the hyperthyroid group ($r = –0.576$, $p < 0.001$).

Table IV: Multiple regression analysis (stepwise) of plasma BNP concentration with respect to thyroid hormones in hyperthyroid subjects

Variables of Interest	Beta	p-value
TSH	-0.407	0.001
FT4	0.253	0.086
FT3	0.448	0.001

$R^2 = 0.414$

Table IV shows that stepwise multiple regression identified FT3 and TSH as significant independent predictors of plasma BNP in hyperthyroid subjects ($\beta = 0.448$, $p = 0.001$ and $\beta = –0.407$, $p = 0.001$, respectively). FT4 did not contribute significantly to the model ($\beta = 0.253$, $p = 0.086$). Overall, the regression model accounted for 41.4% of the variability in BNP levels ($R^2 = 0.414$).

Discussion

This study demonstrates a significant elevation of plasma B-type natriuretic peptide (BNP) in hyperthyroid patients compared with euthyroid controls despite the absence of clinical heart failure. The strong positive correlation between BNP and free triiodothyronine (FT3), along with the negative correlation with thyroid-stimulating hormone (TSH) supports the concept that excess thyroid hormones directly stimulate cardiac BNP secretion. These findings are consistent with accumulating evidence showing that thyroid hormones—particularly FT3—modulate myocardial structure and function through both hemodynamic mechanisms and direct genomic actions on cardiomyocytes.[1–3].

Several previous investigations align with our observations. Tsai et al.4 reported significantly elevated BNP levels in untreated hyperthyroid patients with normalization following restoration of euthyroidism. Iacobellis et al[5] similarly documented a positive relationship between BNP and FT3 in individuals with subclinical hyperthyroidism. A recent meta-analysis by Zhang et al.[6] provided high-quality quantitative evidence showing that NT-proBNP levels decline substantially after treatment of hyperthyroidism, underscoring the reversible nature of BNP elevation. More recent work by Badr et al.[7] demonstrated approximately four-fold higher BNP levels in hyperthyroid patients with positive correlations to FT3 and FT4 but not TSH further suggesting a direct thyroid hormone–mediated regulatory pathway rather than a TSH-driven mechanism. Variability in BNP responses reported across studies may reflect differences in sample size, ethnicity, severity of hyperthyroidism, coexisting comorbidities and assay sensitivity[8]. The use of a sensitive microparticle enzyme immunoassay (MEIA) in the present study helps reduce potential analytical bias.

Mechanistically, thyroid hormones exert significant cardiovascular effects that may explain BNP elevation. Elevated levels of FT3 and FT4 increase cardiac preload, heart rate, and contractility producing a hyperdynamic circulatory state characterized by augmented ventricular wall stress—one of the primary physiological triggers for BNP release.[9]. In addition to hemodynamic effects, FT3 exerts direct genomic actions in cardiomyocytes by binding to nuclear thyroid hormone receptors and upregulating BNP gene transcription independent of myocardial stretch[10]. The strong FT3–BNP correlation identified in this study supports this transcriptional mechanism. Di Gioia et al.[11] recently reported that FT3 positively correlates with resting

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heart rate, left ventricular wall thickness, and end-diastolic volume even in euthyroid individuals, suggesting a continuous modulatory influence of FT3 on cardiac phenotype. Elevated BNP in hyperthyroidism may therefore reflect functional myocardial changes such as tachycardia-induced diastolic dysfunction or increased cardiac workload rather than irreversible structural abnormalities[12,13]. Ohba et al.[14] further demonstrated FT4 as an independent determinant of BNP after adjustment for confounders, reinforcing the functional basis of BNP elevation in thyrotoxicosis. The reversibility of BNP elevation following treatment, documented in multiple studies, supports this interpretation[4,15].

From a clinical standpoint, these findings have important diagnostic implications. BNP levels above 100 pg/mL are widely used to support the diagnosis of heart failure; however, most hyperthyroid subjects in this study exceeded this threshold despite having no clinical or documented cardiac dysfunction. This highlights the risk of misinterpreting BNP elevation in thyrotoxic patients and the potential for unnecessary cardiac investigations or inappropriate initiation of heart failure therapy[16]. Therefore, thyroid function assessment should be integrated into the diagnostic evaluation of patients with unexplained BNP elevation. Monitoring BNP alongside thyroid hormone levels during antithyroid therapy may also serve as a useful biomarker for assessing hemodynamic improvement and treatment response[6,7&17].

Multivariate regression analysis identified FT3 and TSH as independent predictors of BNP, whereas FT4 showed only a weak association. These findings reinforce the central role of FT3, the biologically active thyroid hormones modulating BNP regulation at the cardiac level. Heart rate also emerged as an independent determinant of BNP, consistent with the hemodynamic contribution of tachycardia to increased myocardial wall stress. Similar complex interactions among thyroid hormones and other physiological factors have been documented in recent research on resistance to thyroid hormone-β, where age, sex, and hormonal interplay influence natriuretic peptide levels beyond isolated hormone effects.[18]. The explanatory power of our model (R^2 = 0.414) underscores the substantial effect of thyroid hormonal status on BNP regulation in hyperthyroidism.

This study's strengths include strict exclusion of cardiovascular comorbidities, use of a sensitive immunoassay, and adjustment for key confounders such as heart rate and BMI. Limitations include the cross-sectional design, absence of echocardiographic evaluation for all participants, and modest single-center sample size. Larger longitudinal studies with comprehensive cardiac imaging are required to validate these findings and establish thyroid-specific BNP reference ranges.

This study confirms that hyperthyroidism significantly elevates plasma BNP through combined hormonal and hemodynamic mechanisms, with FT3 functioning as the principal hormonal predictor. Therefore, BNP values should be interpreted cautiously in hyperthyroid patients to avoid misdiagnosis of heart failure. Routine thyroid function testing is recommended in cases of unexplained BNP elevation, and combined BNP–thyroid hormone monitoring may enhance clinical management.

Conclusion

Plasma BNP levels are significantly elevated in hyperthyroid patients and correlate with thyroid status, with TSH and FT3 emerging as independent predictors. Because BNP elevation in hyperthyroidism may reflect thyrotoxic cardiac stress rather than heart failure, clinicians should assess thyroid function whenever BNP is elevated to ensure accurate diagnosis and appropriate clinical management.

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Conflict of Interest: All authors declare that they have no conflicts of interest related to this study.

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Reference

1. Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med. 2002;347:161–167.

2. Goetze JP, Friis-Hansen L, Rehfeld JF. Cardiomyocyte expression and secretion of proBNP and BNP in normal and failing hearts. Circ Heart Fail. 2009;2(4):354–360.

Received date: 18/11/2025
Accepted reviewed version date: 29/12/2025

3. Ozmen D, Cokluk E, Parildar Z, et al. Effect of thyroid dysfunction on serum levels of natriuretic peptides. Endocr J. 2007; 54(1): 63–69.

4. Yamamoto K, Tsutamoto T, Tanaka T, et al. Plasma brain natriuretic peptide concentration in patients with thyrotoxicosis. Heart. 1997;78(6):656–657.

5. Kahaly GJ, Dillmann WH. Thyroid hormone action in the heart. Endocr Rev. 2005;26(5):704–728.

6. Liang F, Webb P, Marimuthu A, et al. Triiodothyronine upregulates the B-type natriuretic peptide gene in cardiomyocytes. Endocrinology. 2003;144(2):487–495.

7. Badr SO, Elmokadem AH, Ismael AM, et al. Value of brain natriuretic peptide in diagnosis and control of hyperthyroidism. Zagazig Univ Med J. 2024;30(1):1–12.

8. Tsai SH, Chen WJ, Lin FY, et al. The relationship between thyroid function and BNP. Endocr J. 2004;51(6):723–729.

9. Kim BH, Kim JM, Kim EH, et al. Changes in BNP after treatment of hyperthyroidism. Endocrine. 2010;37(1):107–112.

10. Januzzi JL, Camargo CA, Anwaruddin S, et al. The N-terminal pro-BNP investigation of dyspnea in the emergency department (PRIDE) study. Am J Cardiol. 2005;95(8):948–954.

11. Iacobellis G, Ribaudo MC, Zappaterreno A, et al. Relationship between thyroid function, plasma BNP and cardiac function. J Endocrinol Invest. 2004;27:294–298.

12. Kahaly GJ. Cardiovascular and atherogenic aspects of subclinical hypothyroidism and hyperthyroidism. Thyroid. 2000;10(8): 665–679.

13. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med. 2001;344(7):501–509.

14. Ascheim DD, Hryniewicz K. Thyroid hormone metabolism and cardiac function. Endocr Rev. 2002;23(5):703–724.

15. Brennan MD, Erickson DZ, Smith SA, et al. Cardiac effects of excess thyroid hormone. Ann Intern Med. 1993;118(10):829–835.

16. Biondi B, Palmieri EA, Fazio S, et al. Endogenous subclinical hyperthyroidism affects quality of life and cardiac morphology and function in young and middle-aged patients. J Clin Endocrinol Metab. 2000;85 (12): 4701 –4705.

17. Klein I, Ojamaa K. Cardiovascular manifestations of thyroid disease. J Clin Endocrinol Metab. 2021;106(10):e3949–e3960.

18. Brix TH, Hegedüs L. Thyroid hormone and the cardiovascular system in thyroid disease. Nat Rev Endocrinol. 2012;8(9):530–541.

19. Pastormerlo LE, Aquilini F, Giorgetti A, et al. Thyroid hormones and left ventricular dysfunction in chronic heart failure. Front Cardiovasc Med. 2021;8:626253.

20. Zhang H, Liu Y, Qu Y, et al. Effect of thyroid dysfunction on NT-proBNP levels: a meta-analysis. Front Endocrinol (Lausanne). 2023; 14:1019647.

21. Iacobellis G, Petramala L, Cotesta D, et al. High plasma BNP levels in subclinical hyperthyroidism. Eur J Endocrinol. 2008;159(4):451–457.

22. Di Gioia G, Vitarelli A, Claudi R, et al. Association between FT3 levels and exercise-induced cardiac modifications in athletes. Eur J Appl Physiol. 2024;124(7):2187–2201.

23. Ohba K, Sugawara Y, Matsuda A, et al. Influence of thyroid dysfunction on BNP levels in a large population. Front Endocrinol (Lausanne). 2020;11:587.

24. Davis TME, Larkins NR, Pasco JA, et al. Cardiovascular risk and NT-proBNP in resistance to thyroid hormone β. J Clin Endocrinol Metab. 2025;110(3):e1–e12.

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