

Abnormal Thyroid Levels Increase Broken Heart Syndrome Risk

Team A: Dave Little, MD; Karen Wong, MD; Alex Piff

Team B: Kersten Bartelt, RN; Ted Stamp

Last updated 13 December 2023 • Check for updates at EpicResearch.org

Key Findings:

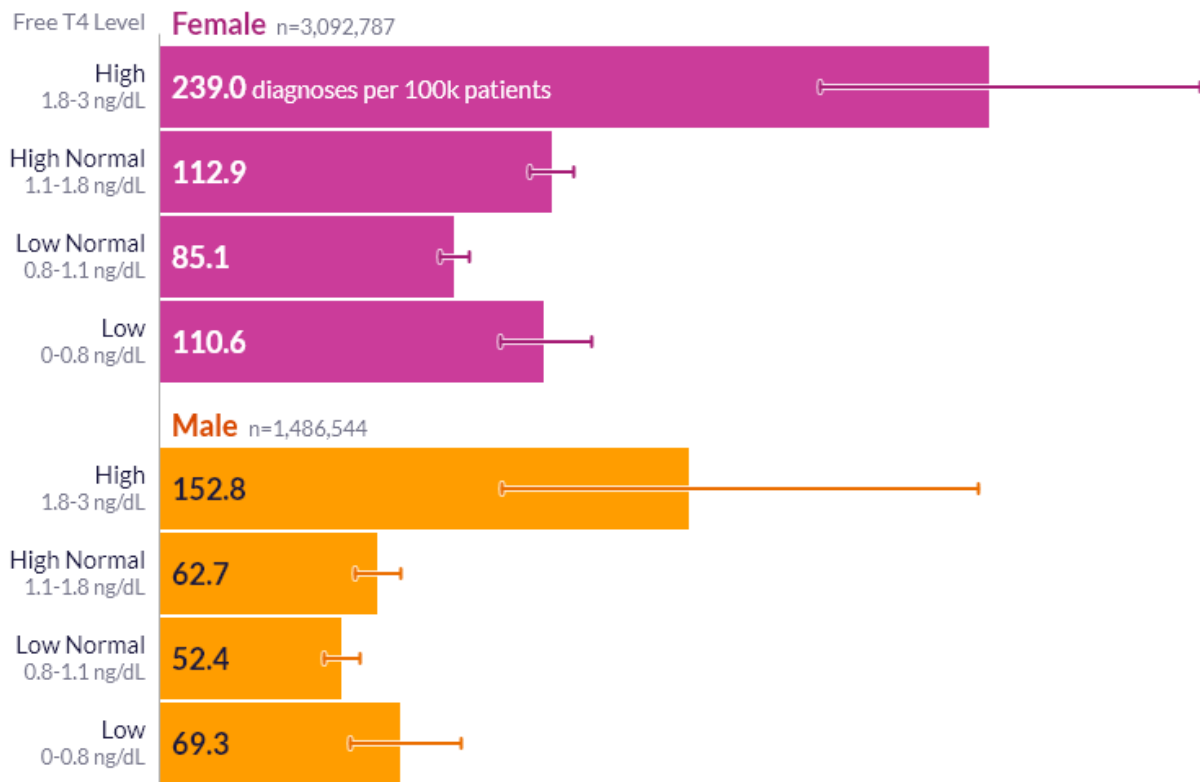
- Patients with a high free T4 level are more than twice as likely to be diagnosed with takotsubo cardiomyopathy than those with a T4 level on the low end of normal.

Takotsubo cardiomyopathy, also known as broken heart syndrome, is characterized by acute onset of chest pain, shortness of breath, and ECG changes, often following a physically or psychologically stressful event.¹ A previous study has suggested hyperthyroidism, or excess levels of thyroid hormone, may be associated with takotsubo cardiomyopathy, especially in cases where thyrotoxicosis was present.² We aimed to evaluate the risk of takotsubo cardiomyopathy based on a patient's free T4 level, which is a lab test used in diagnosing thyroid conditions.³

We studied 4,579,331 patients with a free T4 lab result between January 1, 2017, and October 4, 2023. We evaluated patients' risk of takotsubo cardiomyopathy by stratifying patients into four distinct categories based on the value of a randomly selected free T4 lab result that occurred during the study period: low, low normal, high normal, and high.

We found that for female patients, those with a high free T4 level were more than twice as likely (181% more likely) to be diagnosed with takotsubo cardiomyopathy within the year following their lab test compared with those with levels in the low normal range, as seen in Figure 1. Female patients with a low free T4 saw a risk 33% greater than those with a free T4 in the low normal range. For male patients, their risk was also more than twice as likely (192% more likely) if their free T4 was high compared to male patients with a free T4 in the low normal range. For male patients with a low free T4, the risk was 32% greater than for those with a free T4 in the low normal range.

One-Year Takotsubo Cardiomyopathy Risk by Free T4 Level



"One-Year Takotsubo Cardiomyopathy Risk by Free T4 Level," 2023. EpicResearch.org

Figure 1. The rate of being diagnosed with takotsubo cardiomyopathy within a year of a random free T4 level. Low is defined as 0-0.8 ng/dL, low normal is defined as 0.8-1.1 ng/dL, high normal is defined as 1.1-1.8 ng/dL, and high is defined as 1.8-3 ng/dL.

While the risk of takotsubo cardiomyopathy is increased in patients with low free T4 levels, the difference is not statistically significant compared to patients with normal free T4 levels. Our findings suggest that hyperthyroidism, as defined by high levels of free T4, is associated with an increased risk of takotsubo cardiomyopathy.

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 220 million patients from 222 Epic organizations including 1,276 hospitals and more than 27,200 clinics, serving patients in all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Singh, T., Khan, H., Gamble, D. T., Scally, C., Newby, D. E., & Dawson, D. (2022). Takotsubo syndrome: Pathophysiology, emerging concepts, and clinical implications. *Circulation*, 145(13), 1002-1019. <https://doi.org/10.1161/circulationaha.121.055854>
2. Omar, S., Ali, E., Mazek, H., Mahmood, T., Soontrapa, S., & Suarez, J. (2015). Takotsubo cardiomyopathy associated with hyperthyroidism treated with thyroidectomy. *Proceedings (Baylor University Medical Center)*, 28(2), 194-195. <https://doi.org/10.1080/08998280.2015.11929227>
3. Thyroxine (T4) test. (2022, June 7). Medlineplus.gov. <https://medlineplus.gov/lab-tests/thyroxine-t4-test/>

Data Definitions

Term	Definition
Study period	1/1/2017 - 10/4/2023
Study population	Patients 18 or older who had a T4 lab result with no history of takotsubo cardiomyopathy or order for levothyroxine before free T4 lab test.
Levothyroxine	Order for "levothyroxine sodium."
Takotsubo cardiomyopathy	An encounter or billing diagnosis with ICD-10-CM code I51.81.
Free T4 lab	A randomly selected lab with one of the following LOINC codes: 3024-7, 3122-2, or 6892-4.
Free T4 lab categories	Low: 0-0.8 ng/dL Low normal: 0.8-1.1 ng/dL High normal: 1.1-1.8 ng/dL High: 1.8-3 ng/dL

Table 1: One-Year Takotsubo Cardiomyopathy Risk by Free T4 Level

Sex	T4 Category	Patients	Rate per 100,000	95% CI Lower	95% CI Upper
All	1 - Low	347,686	98.1	88.2	109.0
All	2 - Low Normal	2,476,622	74.8	71.5	78.3
All	3 - High Normal	1,710,975	95.6	91.0	100.3
All	4 - High	44,048	213.4	174.4	261.1
Female	1 - Low	242,418	110.6	98.1	124.6
Female	2 - Low Normal	1,700,029	85.1	80.8	89.6
Female	3 - High Normal	1,119,380	112.9	106.9	119.3
Female	4 - High	30,960	239.0	190.5	299.9
Male	1 - Low	105,268	69.3	55.2	87.2
Male	2 - Low Normal	776,593	52.4	47.6	57.8
Male	3 - High Normal	591,595	62.7	56.6	69.4
Male	4 - High	13,088	152.8	98.9	235.9