The 3rd Indonesia Symposium on Heart Failure and Cardiometabolic Disease 2023

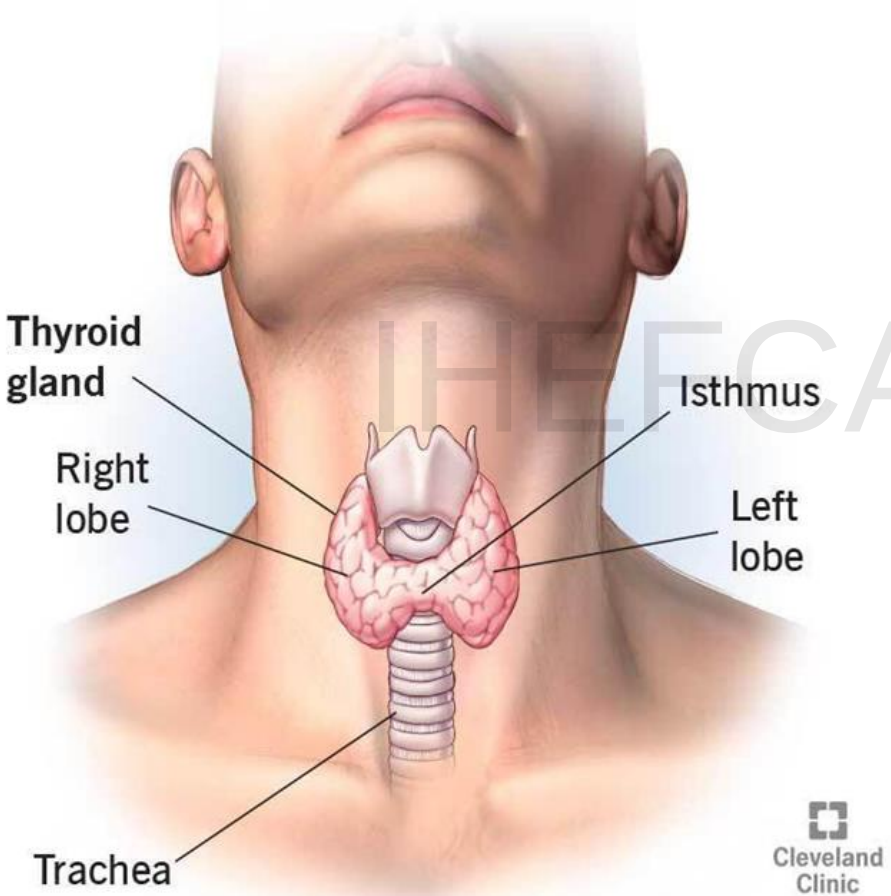
Understanding Thyroid Dysfunction in Heart Failure;

An Overlooked Feature

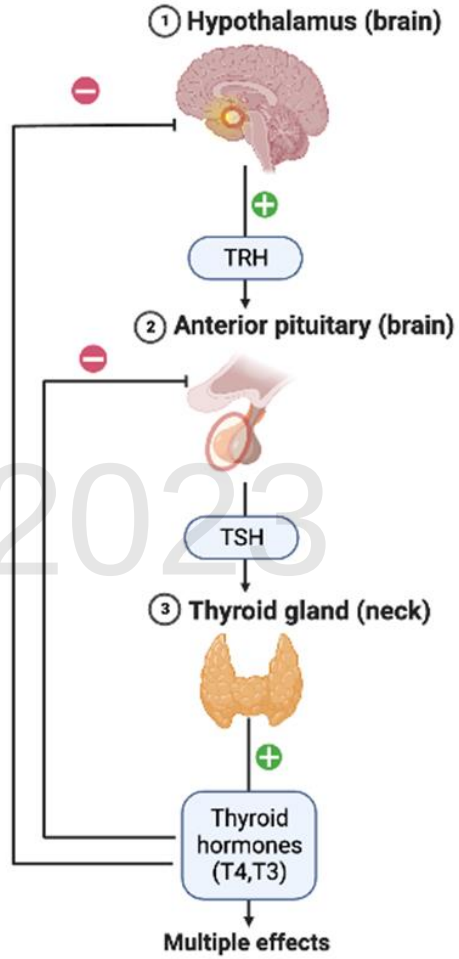
Leonardo Paskah Suciadi, MD.

Thyroid Physiology

Thyroid



Hypothalamic-pituitary-thyroid-axis



TRH - Thyrotropin-releasing hormone
TSH - Thyroid stimulating hormone
T4 - Thyroxine
T3 - Triiodothyronine
⊕ - Increase secretion ⊖ - Reduce secretion

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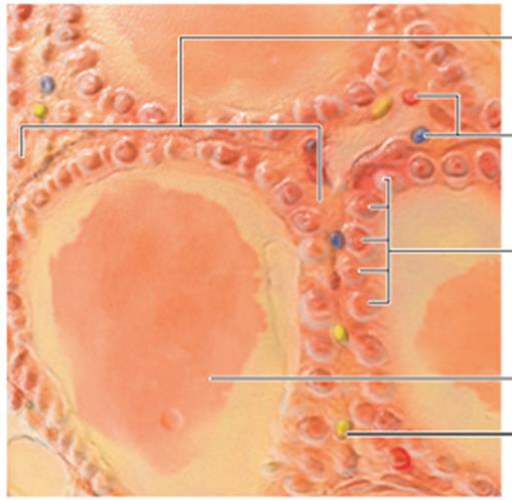
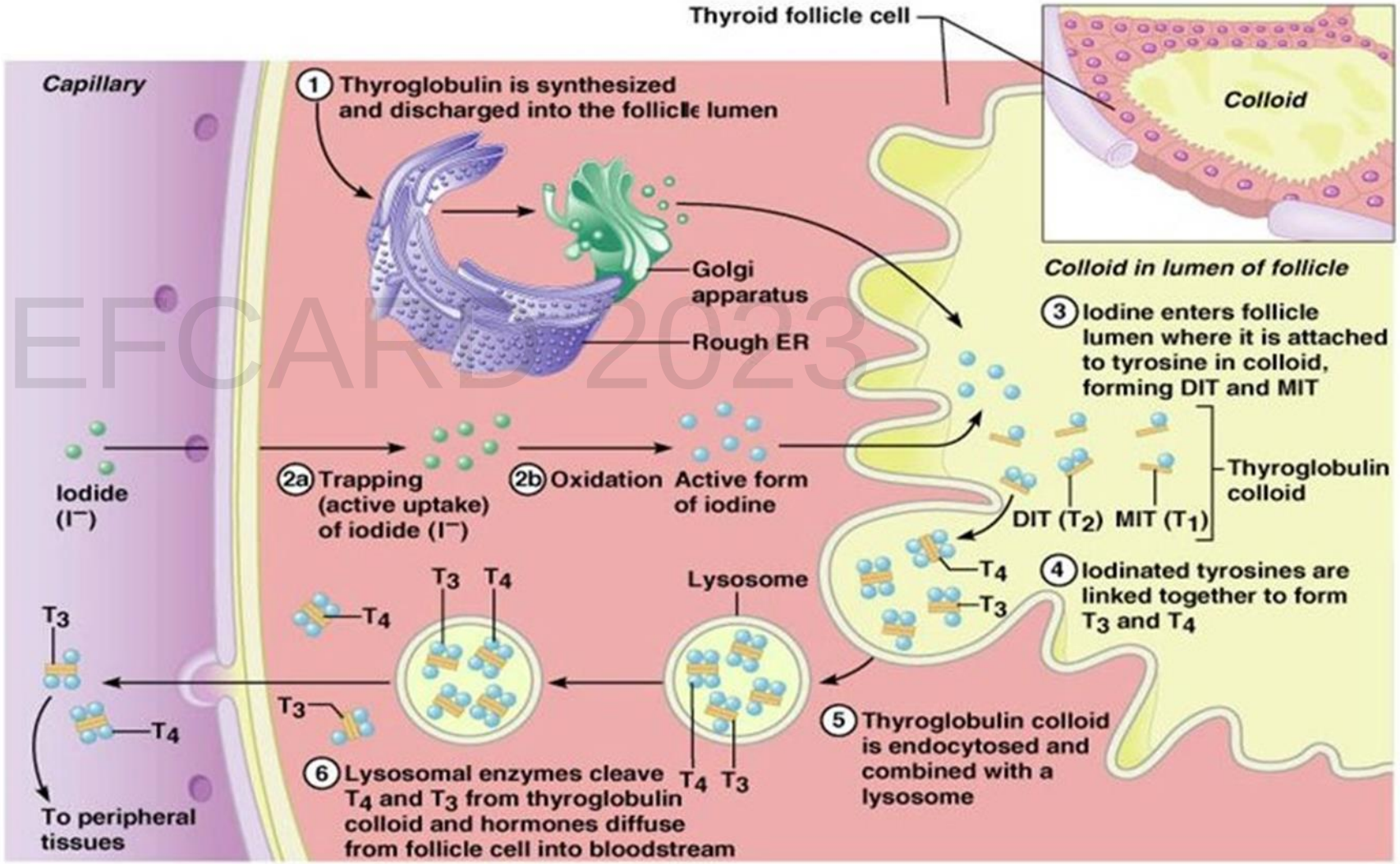
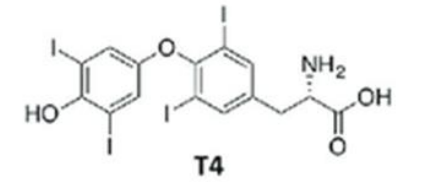
SYNTHESIS OF THYROID HORMONES

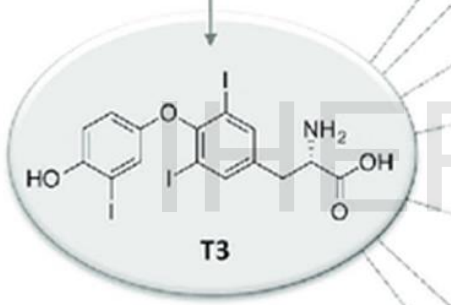


Thyroid gland cells



Thyroid and body metabolism





BRAIN
Development and function
Myelinization

PITUITARY
TSH production
Growth hormone

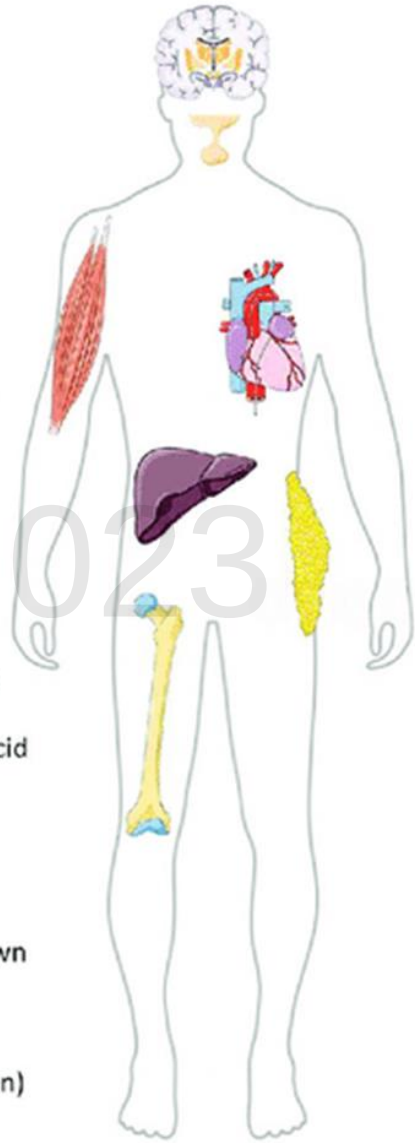
HEART
Cardiac output
Heart rate
Hypertrophy

MUSCLE
Protein catabolism
Energy expenditure

LIVER
Mitosis
Gluconeogenesis
Fatty acid β-oxidation/synthesis
Cholesterol synthesis/uptake
Cholesterol conversion to bile acid
Apolipoprotein A1
HDL receptor (SR-B1)

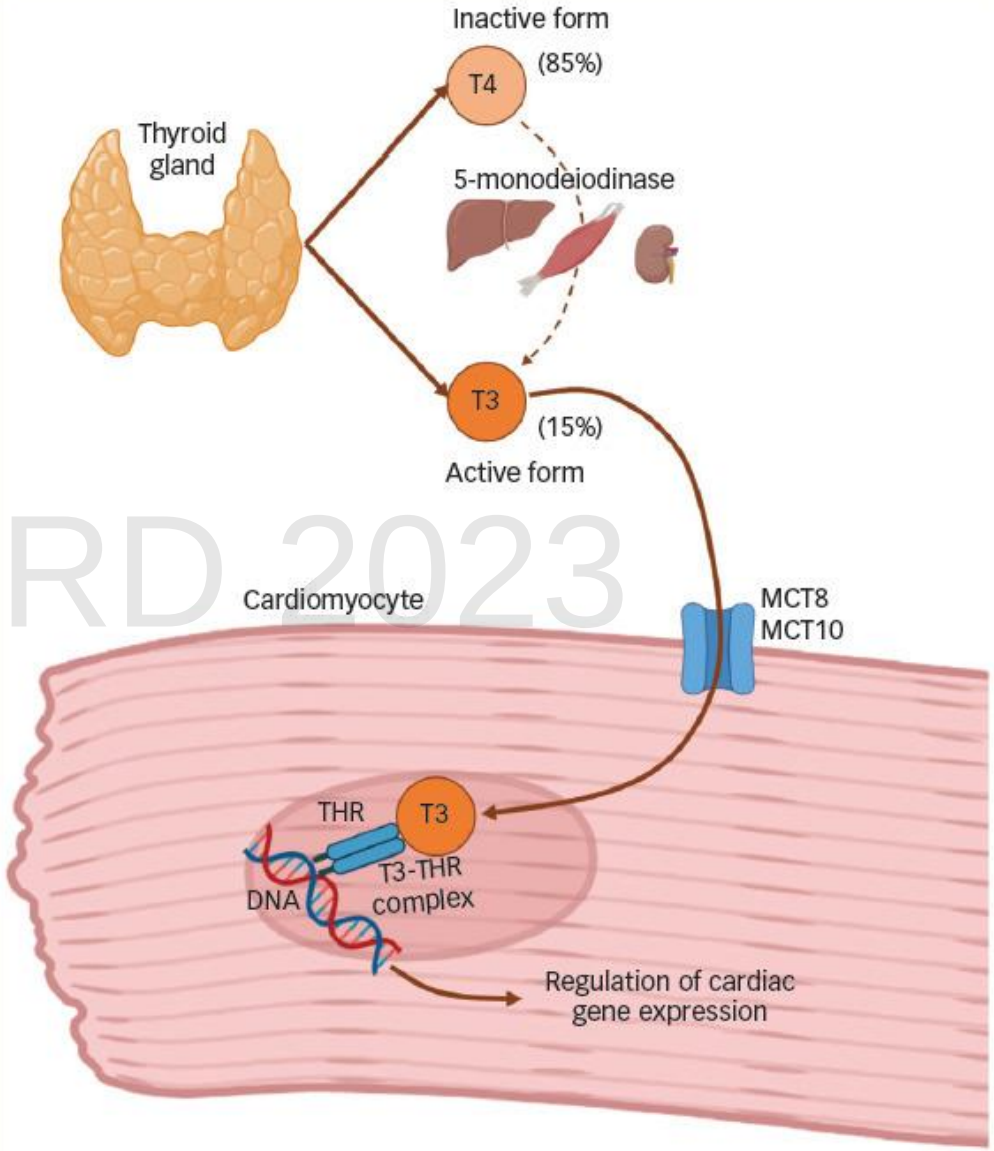
ADIPOSE TISSUE
Lipolysis
Adaptive thermogenesis in brown adipose tissues

SKELETAL SYSTEM
Growth and maturation (children)
Bone resorption (adult)



Saponaro F, et al. Frontiers in Medicine. 2020: 7; 331

Thyroid hormone production and regulation of cardiac gene expression

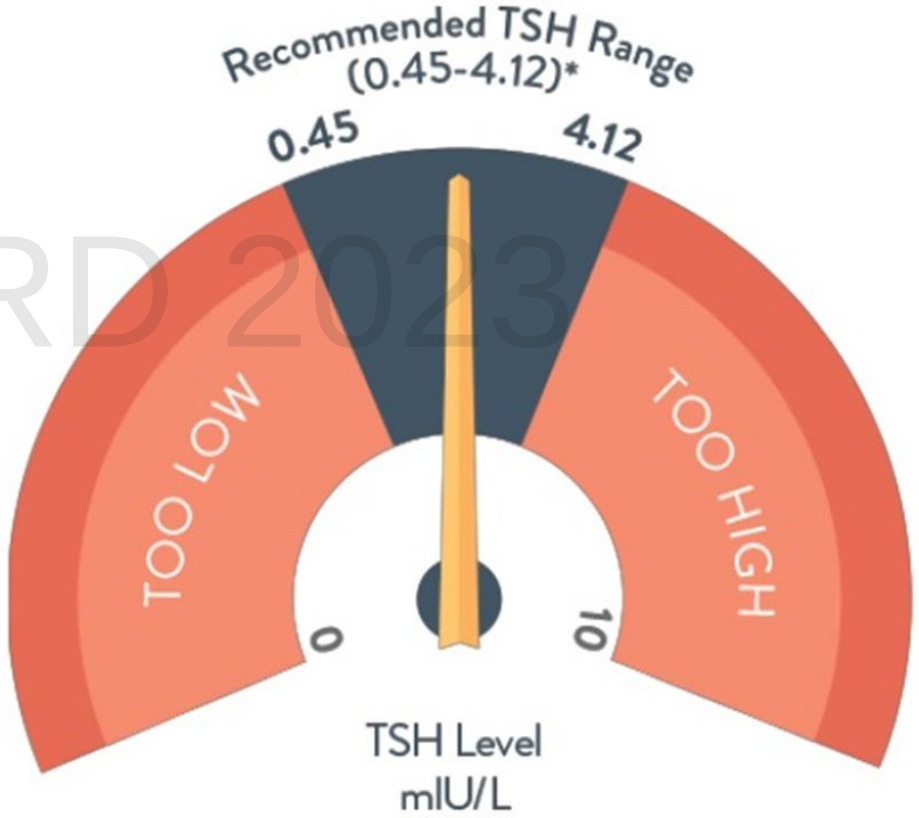


Quiros-Aldave JE, et al. touchREV Endocrinol. 2023; 19(1): 78–84.

MCT8/10 = monocarboxylate transporter 8/10; T3 = triiodothyronine; T4 = tetraiodothyronine (thyroxine); THR = thyroid hormone receptor.

TSH Function

- Controls the synthesis of **Triiodothronine (T3)** and **Thyroxin (T4),** which regulates body's metabolic activities
- **T3** increases ability to consume Oxygen for production of energy, increases Metabolic Rate, and stimulates rate of protein synthesis in the Body
- **T4** increases heart rate, BMR, & improves brain development.



Factors that Affect Thyroid Function

Negative Factors

Factors that reduce the production of thyroid hormones

- Stress, trauma
- Infections: flu, Lyme disease, ear infections, etc
- Radiation
- Certain medications
- Autoimmune disease
- Fluoride: interferes with iodine
- Toxic load: pesticides, mercury, calcium, lead

Factors that increase conversion of T4 to rT3

- Stress, trauma
- Infections
- Low-calorie diet
- Inflammation
- Toxic load
- Liver/kidney dysfunction
- Certain medications

90% 10%

T4

rT3 T3

Y

Positive Factors

Factors necessary for proper production of thyroid hormones

- Minerals: iron, iodine, zinc, selenium, copper, magnesium
- Vitamins: A, D, C, E, B2, B3, B4, B6, B12
- Amino acids: Tyrosine

Factors that increase conversion of T4 to T3

- Selenium
- Zinc
- Proper gut and liver function

Factors that improve cellular sensitivity to thyroid hormones

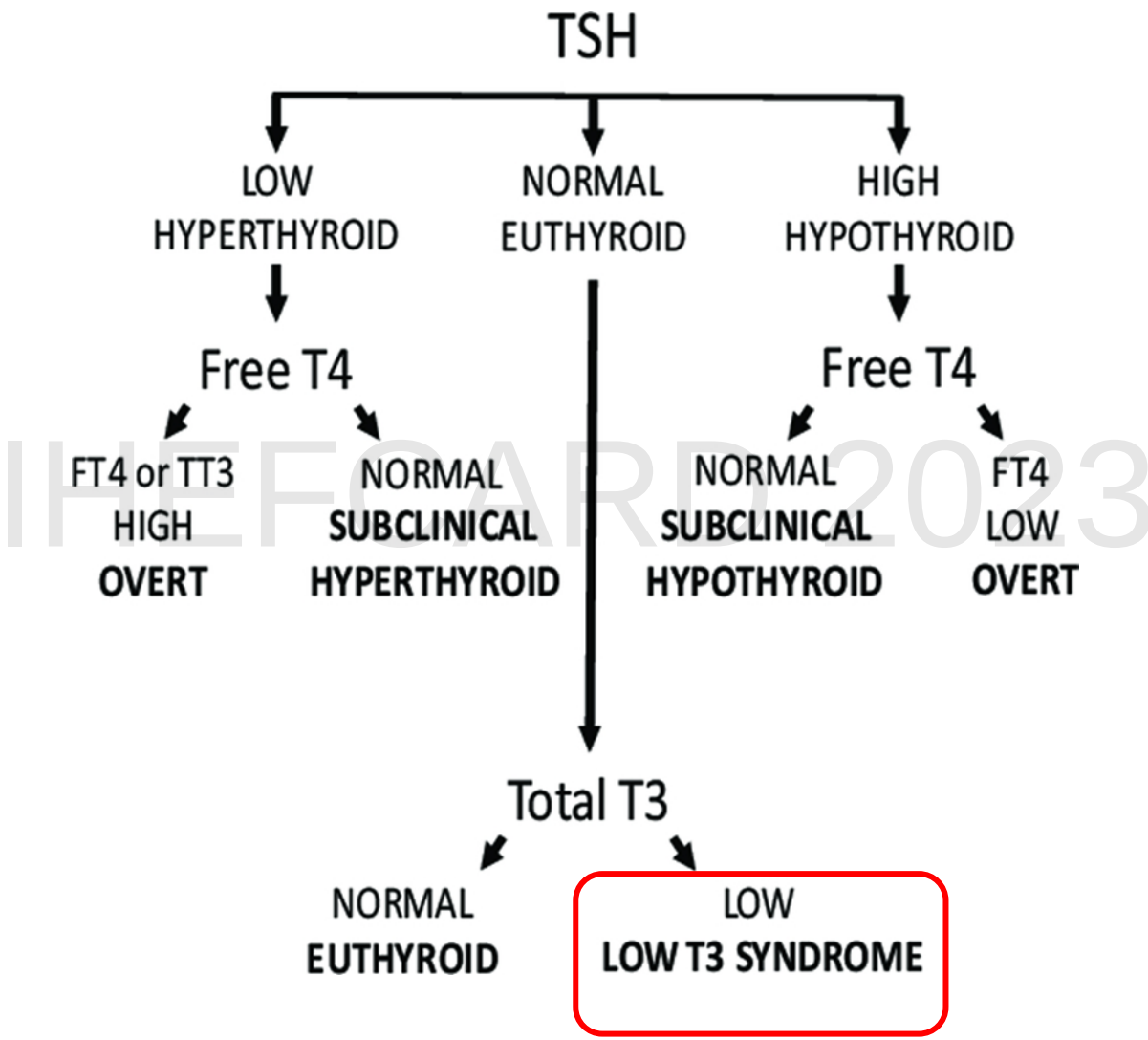
- Vitamin A
- Zinc
- Exercise

Cell

rT3 (inactive) competes with T3 (active) for the receptors (binding sites) on cells, reducing their ability to 'see' T3

www.nourzibdeh.com/ThyroidHealth

Thyroid Dysfunction



Kannan L. Circ Heart Fail. 2018 Dec;11(12):e005266.

Hyperthyroid and Heart Failure

- Upregulate ß -1 receptor
- Hypermetabolism + hyperadrenaline
- Commonly as **high-output HF**

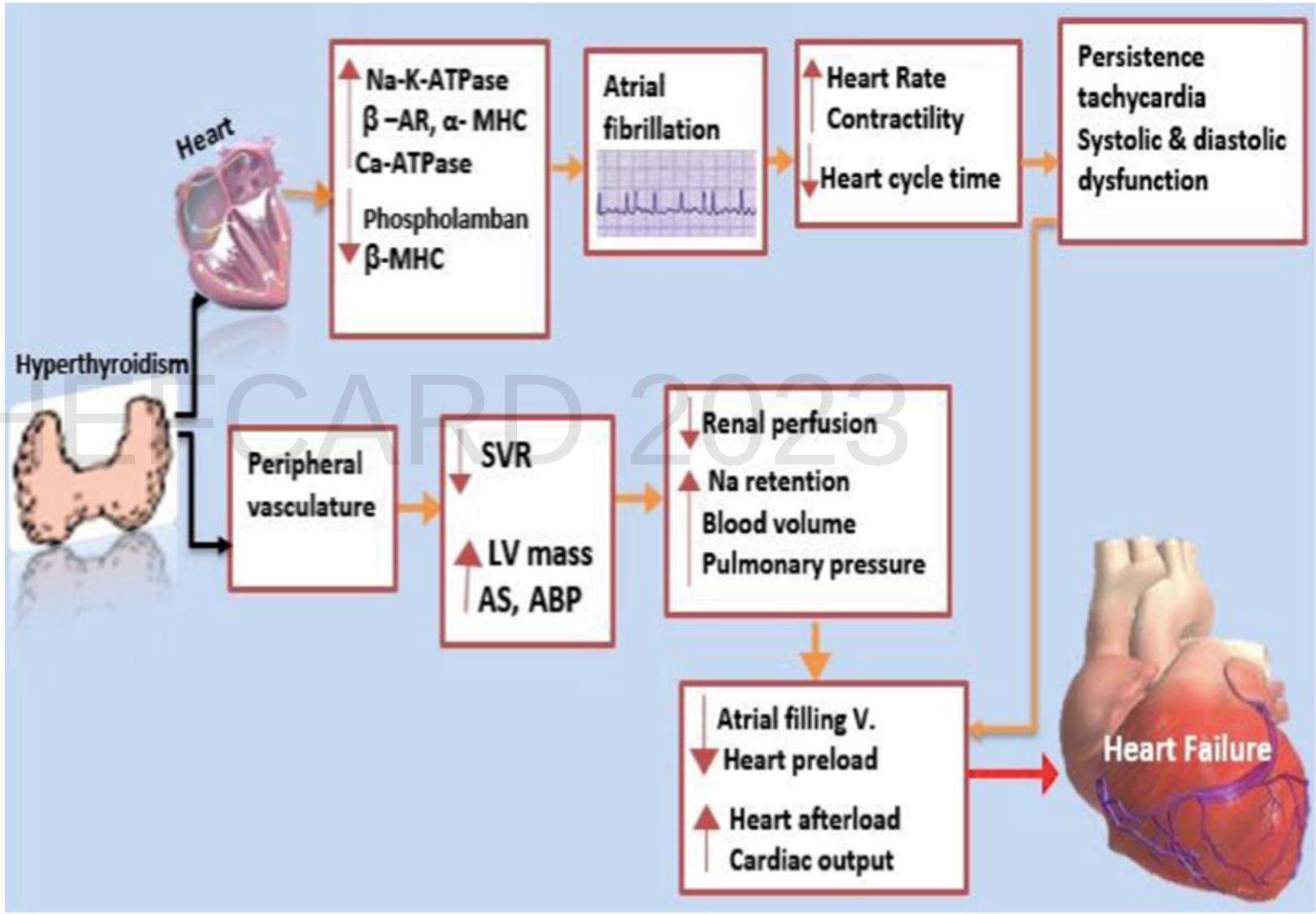
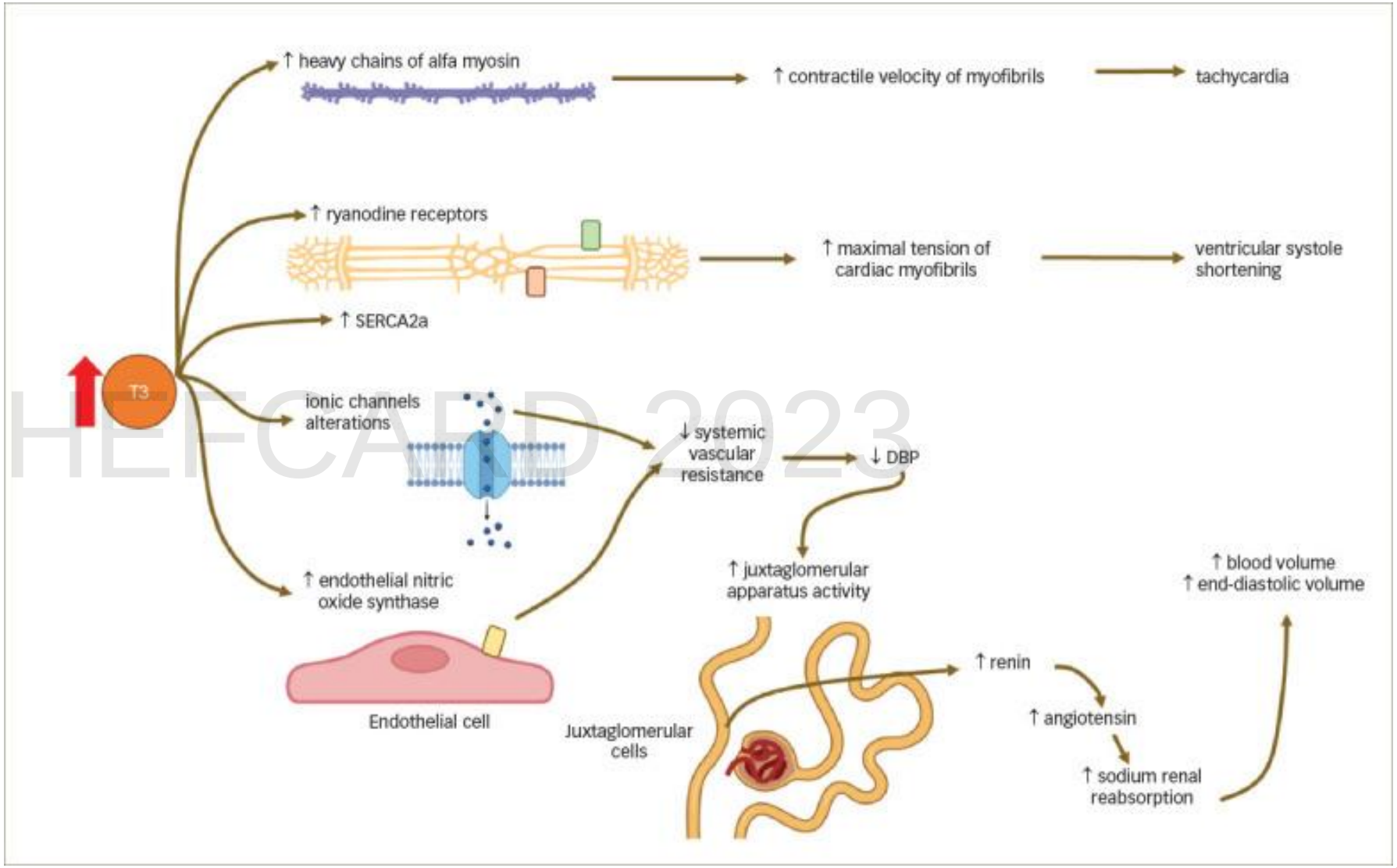


Image source : https://link.springer.com/article/10.1007/s42000-020-00208-8

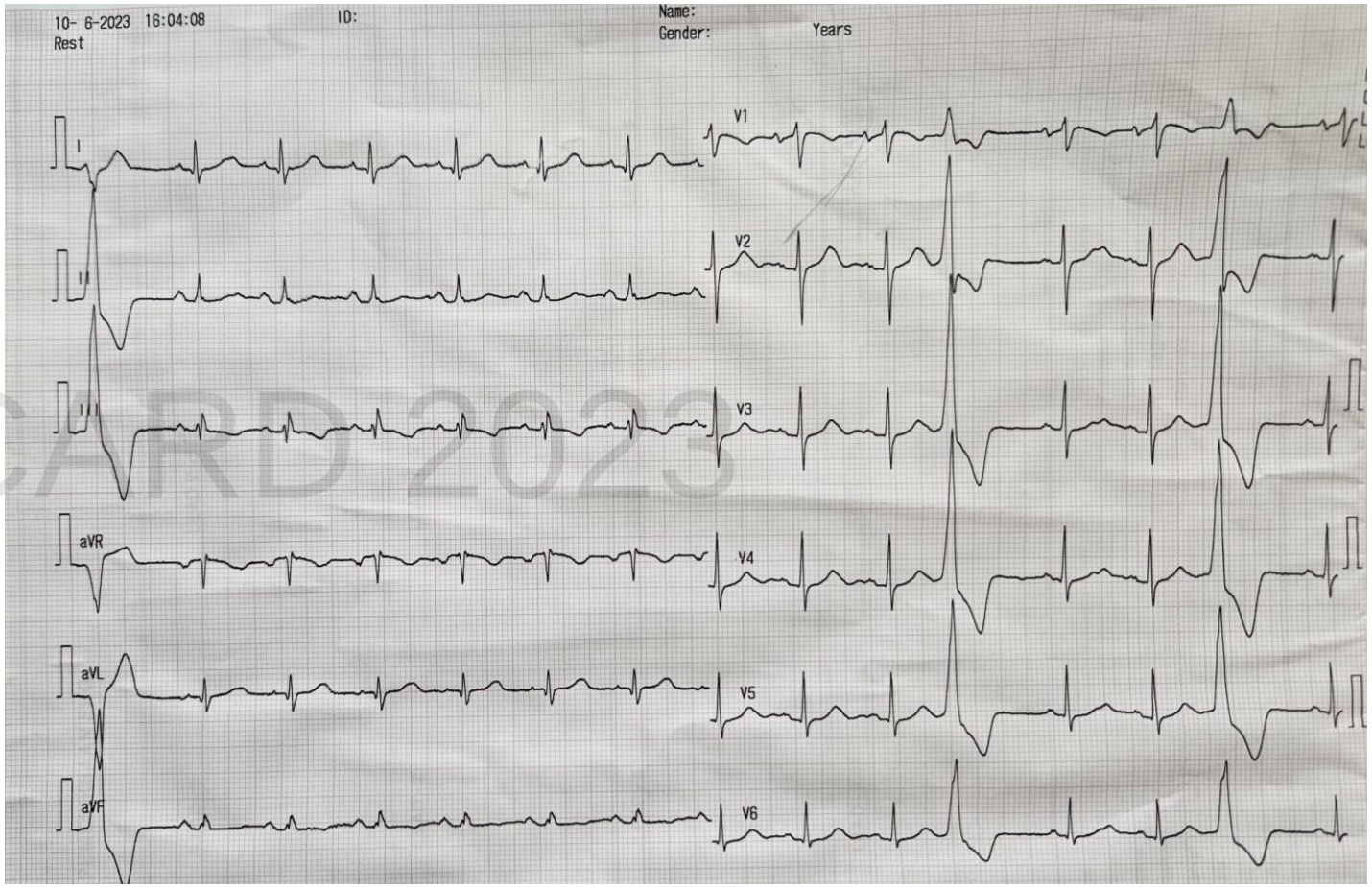
Genomic and non-genomic effects of excess thyroid hormones on the cardiovascular system



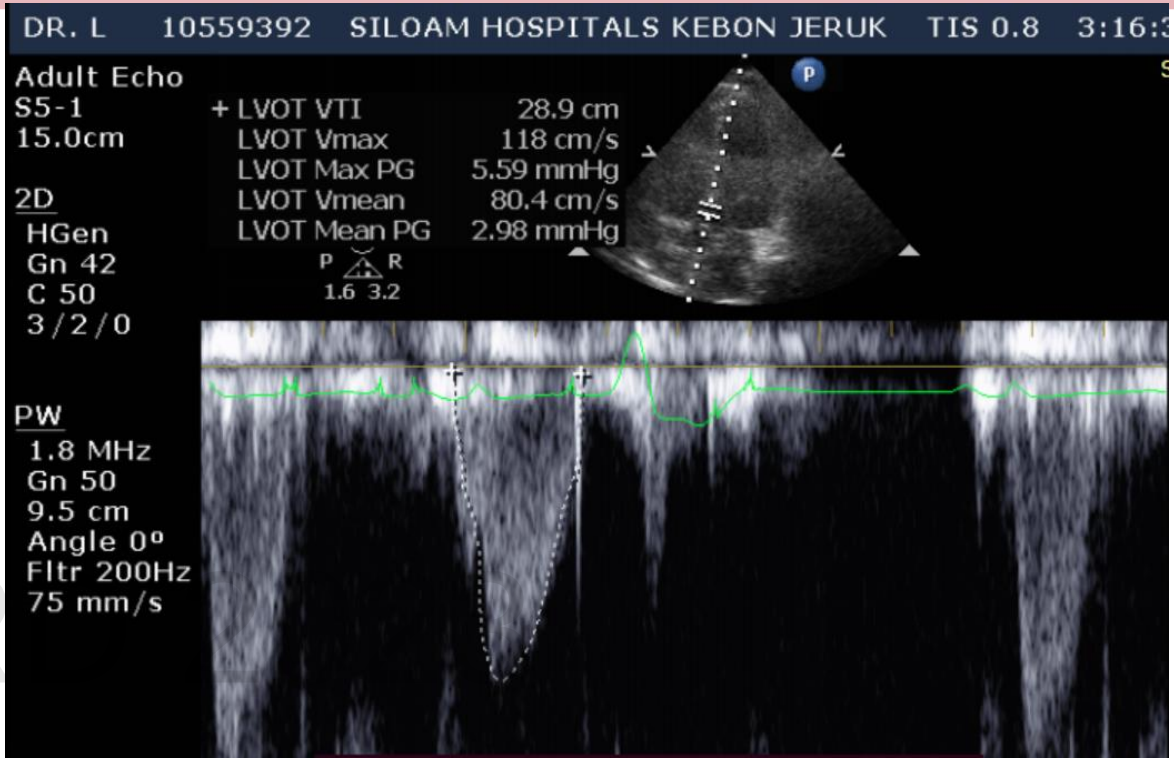
Quiros-Aldave JE, et al. touchREV Endocrinol. 2023; 19(1): 78–84.

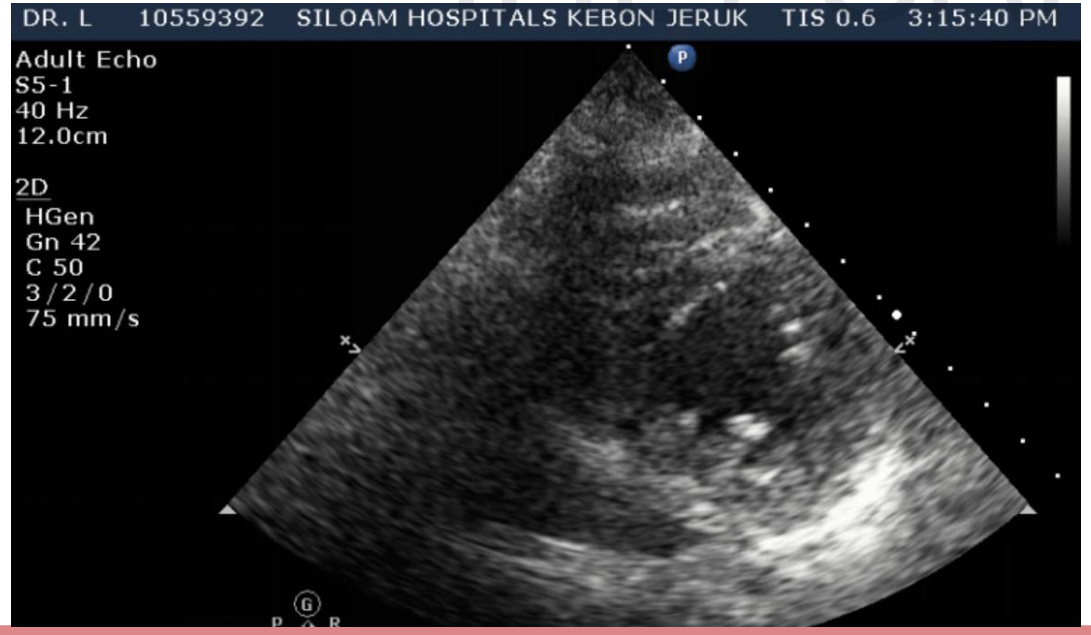
Mrs. S, 65 yo.

- Palpitation and DOE
  Prior CVD-NH, DM
- CM, BP 156/58 mmHg, HR 98 bpm,
  RR 20 x/min, Afebris
- Regularly irregular heart rhythm,
  No murmur
  Minimal rales at bibasilar lung
  No LL oedema



Holter 1x24: average HR 98, VE beats 26%, No AF





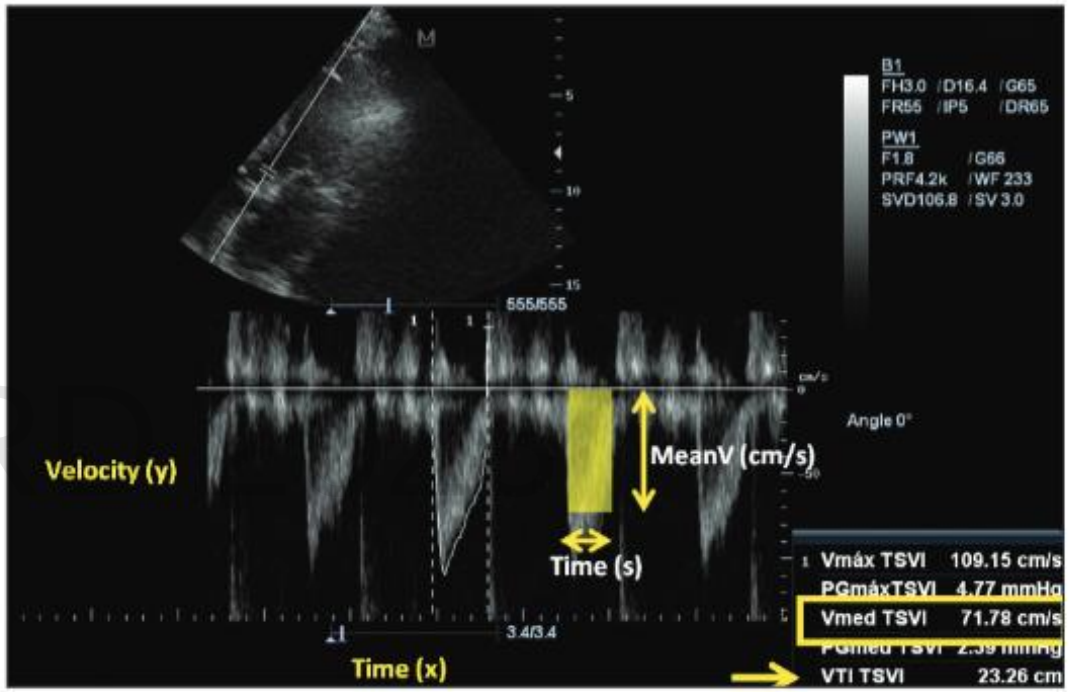
TSH: **0.298**	(0.35 – 4.94)
FT4: 1.71	(2.0 – 4.4)
FT3: 1.37	(0.7 – 1.48)

High output state on echocardiography

$A = \pi . r^2$

$A = D^2 \times 0.785$

$SV(cm^3) = A\ (cm^2) \times VTI\ (cm)$



In a patient with HR > 95 bpm, the corresponding VTI should be **<22 cm**; otherwise, high cardiac output will be assumed.

Rapid Ultrasound in Shock (RUSH) Velocity-Time Integral A Proposal to Expand the RUSH Protocol. Journal of Ultrasound in Medicine. 2015

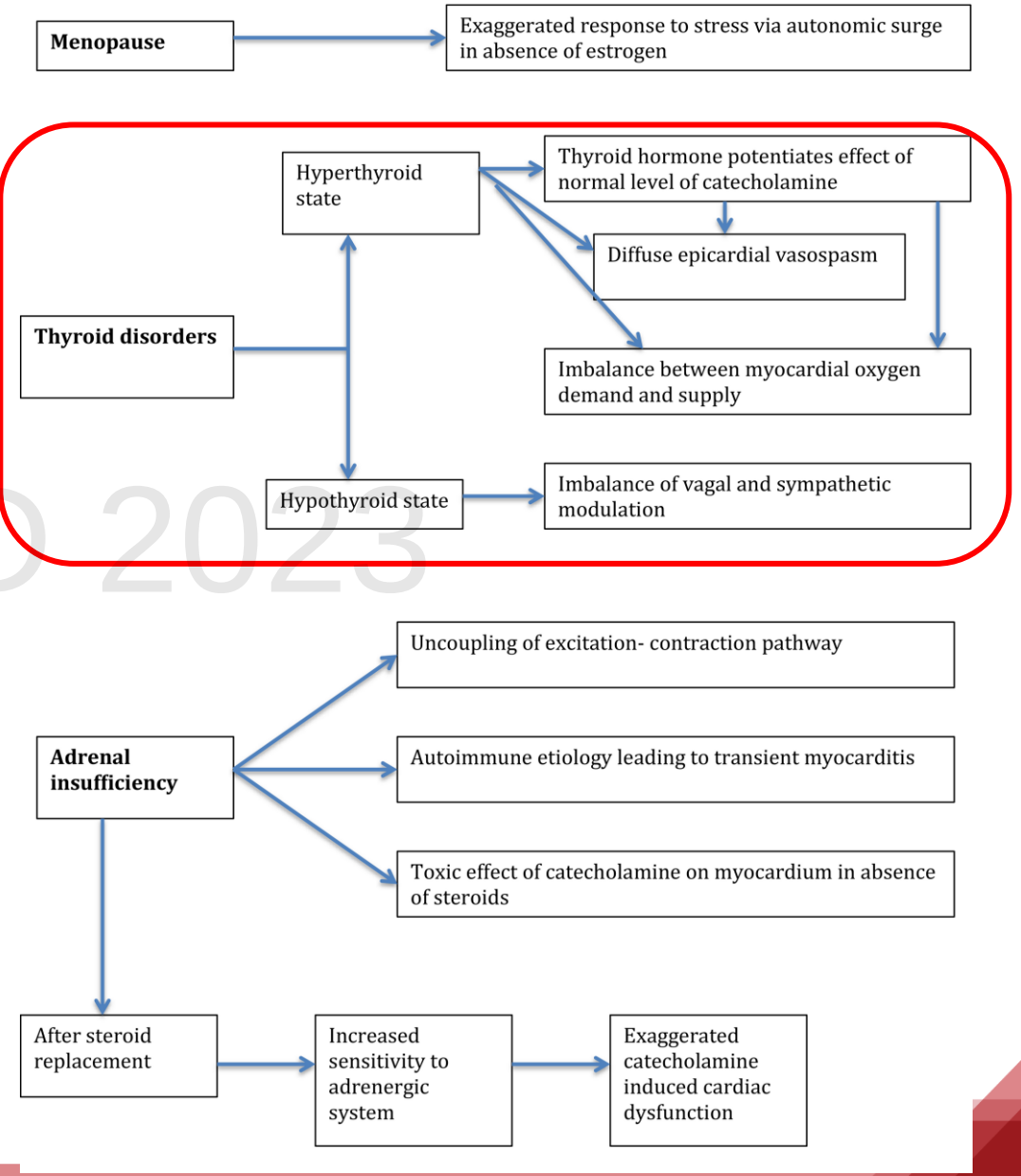
Thyrotoxic Cardiomyopathy

- Approximately **1%** of patients with thyrotoxicosis
- Potentially lethal form of dilated cardiomyopathy that causes **severe impairment of left ventricular function** and might lead to cardiogenic shock.
- Early diagnosis is crucial as the patient is critically ill and needs urgent supportive therapy
- **Graves' disease** is the most common cause of underlying hyperthyroidism. But, uncontrolled hyperthyroidism can also trigger this cardiomyopathy.
- Likely **reversible** after achieving a euthyroid state.

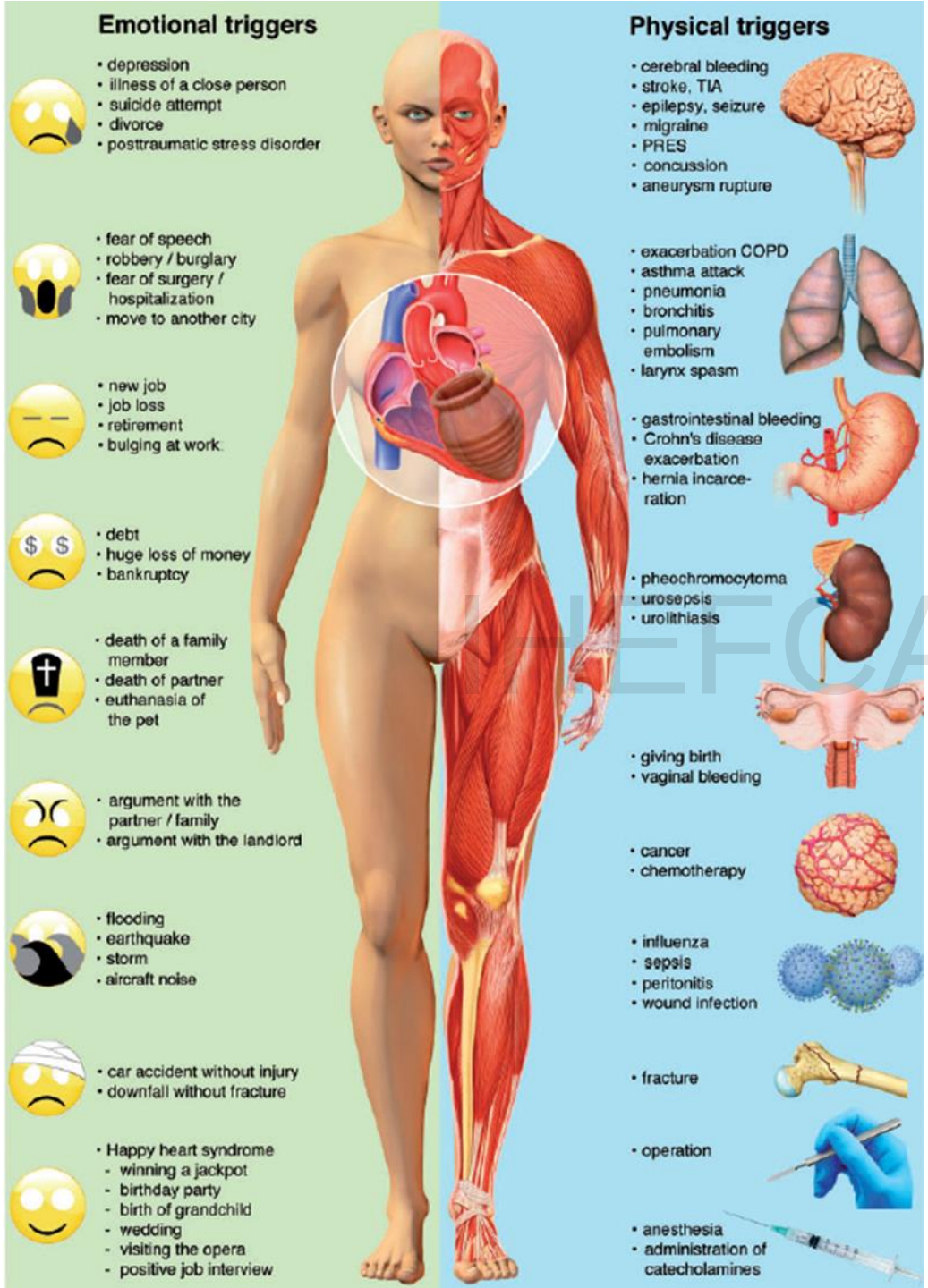
Quiros-Aldave JE, et al. touchREV Endocrinol. 2023; 19(1): 78–84.

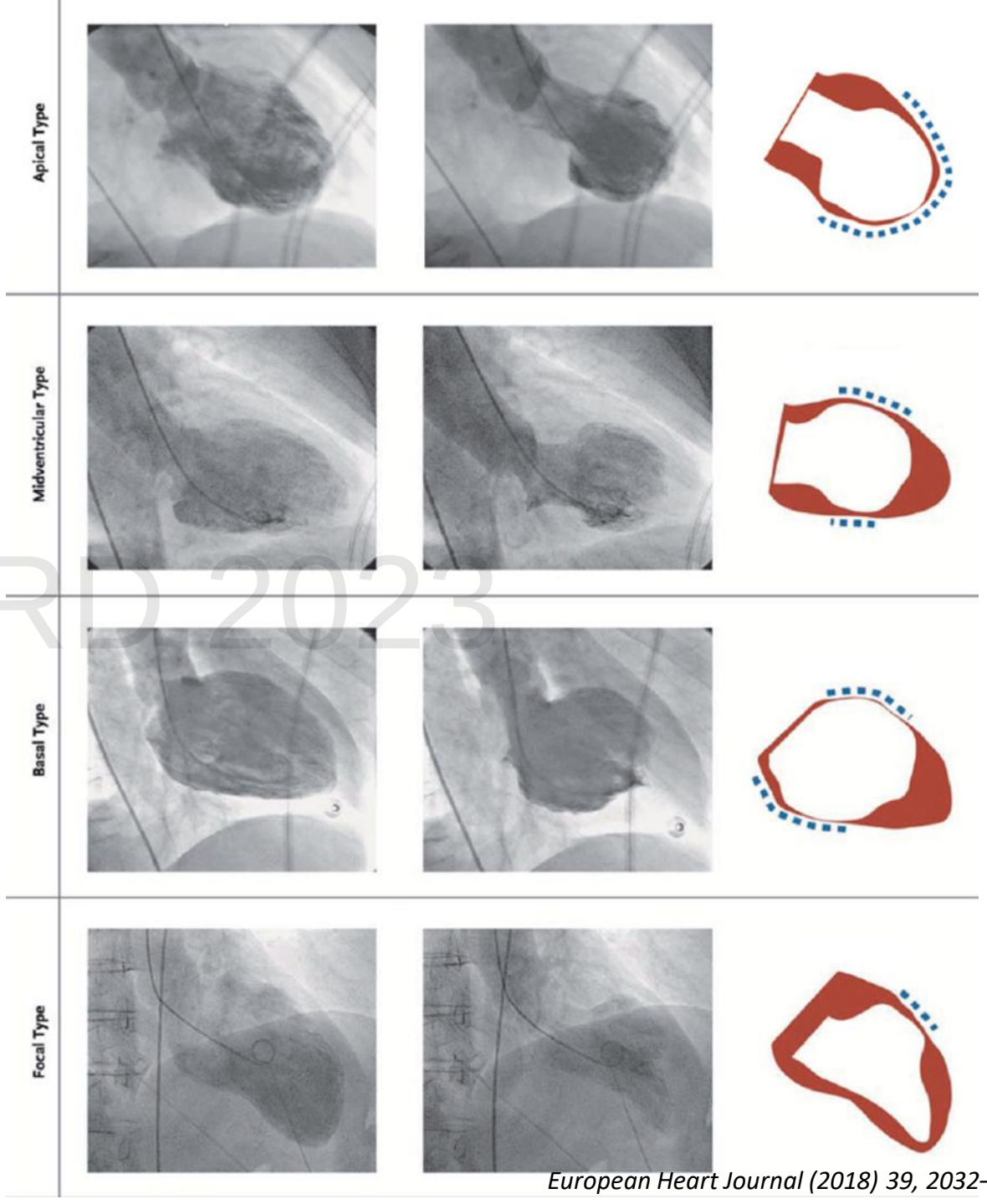
Takotsubo Syndrome in endocrine conditions

It has been reported to occur in patients with Graves disease, Hashimoto thyroiditis, toxic multinodular goiter, apathetic hyperthyroidism, thyroid storm, iatrogenic hyperthyroidism, subclinical hyperthyroidism, transient hyperthyroid states, following radioactive iodine treatment, following thyroidectomy, and even in hypothyroid or euthyroid states



Gupta S, et al. Journal of the AHA. 2018

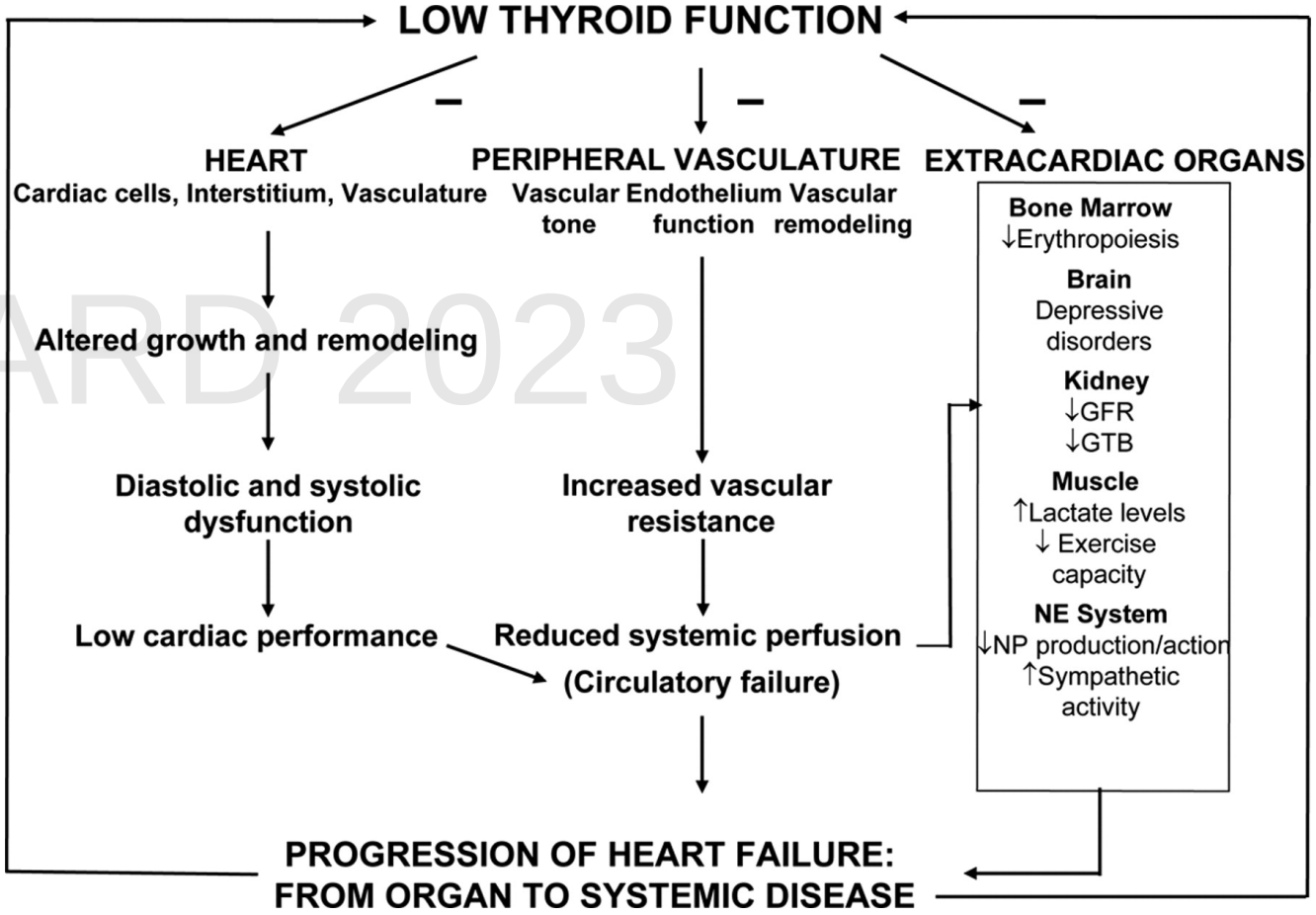




European Heart Journal (2018) 39, 2032–2046

Hypothyroid and Cardiovascular System

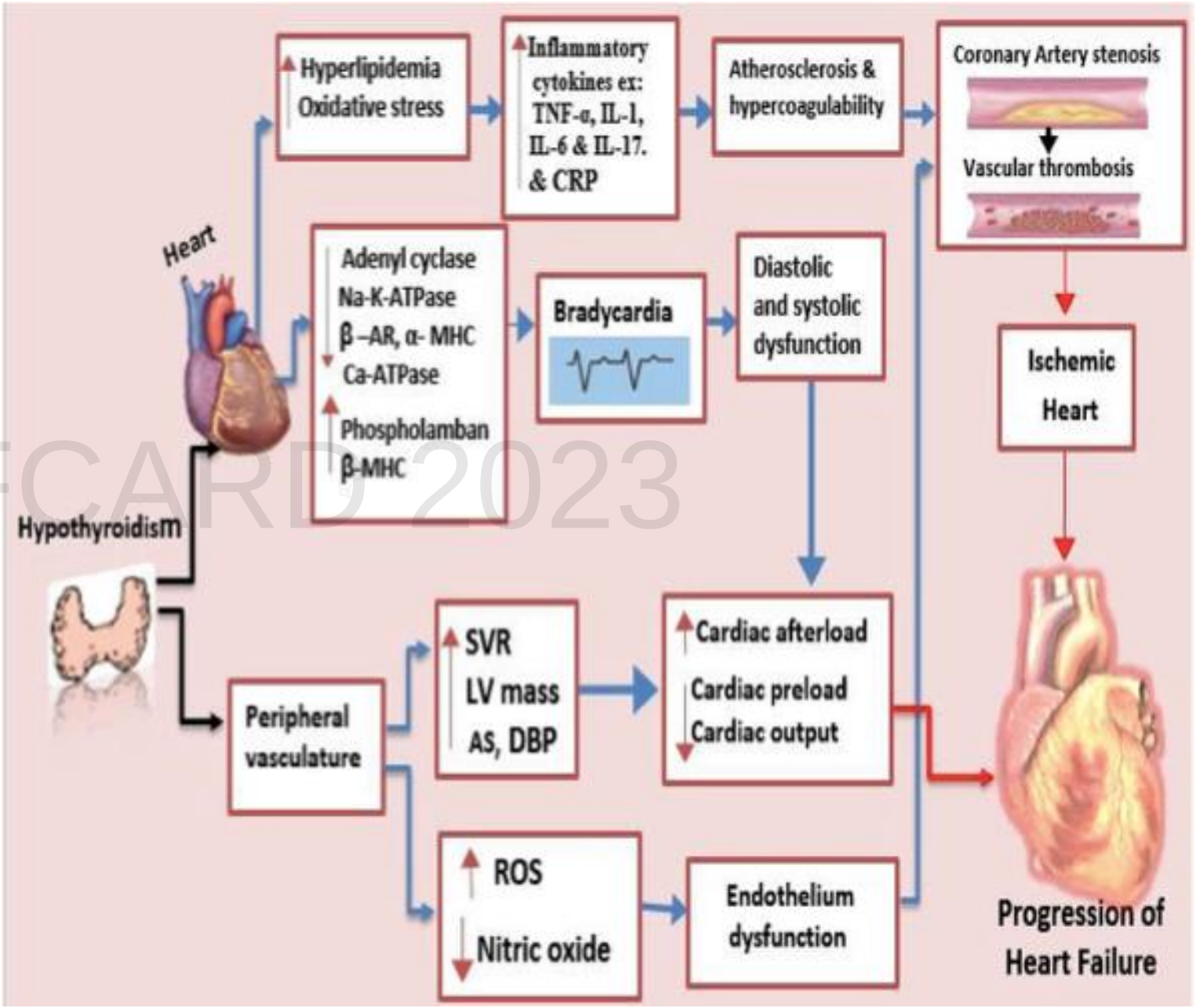
- Effects:
  - (Diastolic) hypertension
  - Dyslipidemia
  - Microvascular dysfunction
  - Reduced production of nitrite oxide
  - Carotid intima – media thickening
  - Atherosclerosis
  - LV diastolic dysfunction



https://www.ahajournals.org/doi/10.1161/circulationaha.109.917922

Hypothyroid and Heart Failure

- Hypothyroidism suppresses myosin heavy chain 6 protein expression and enhances myosin heavy chain 7 protein expression and induces **cardiac atrophy** as a result.



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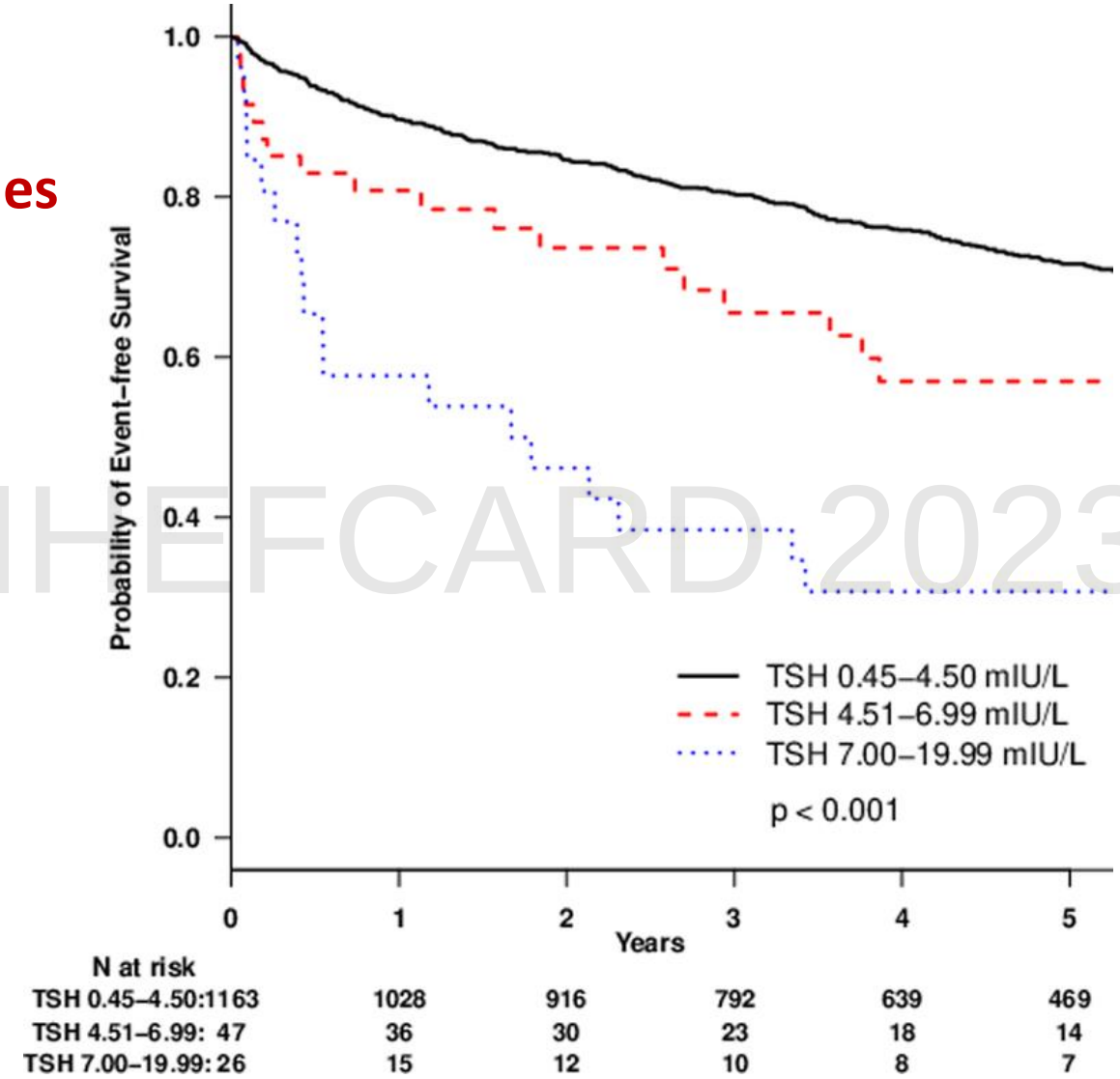
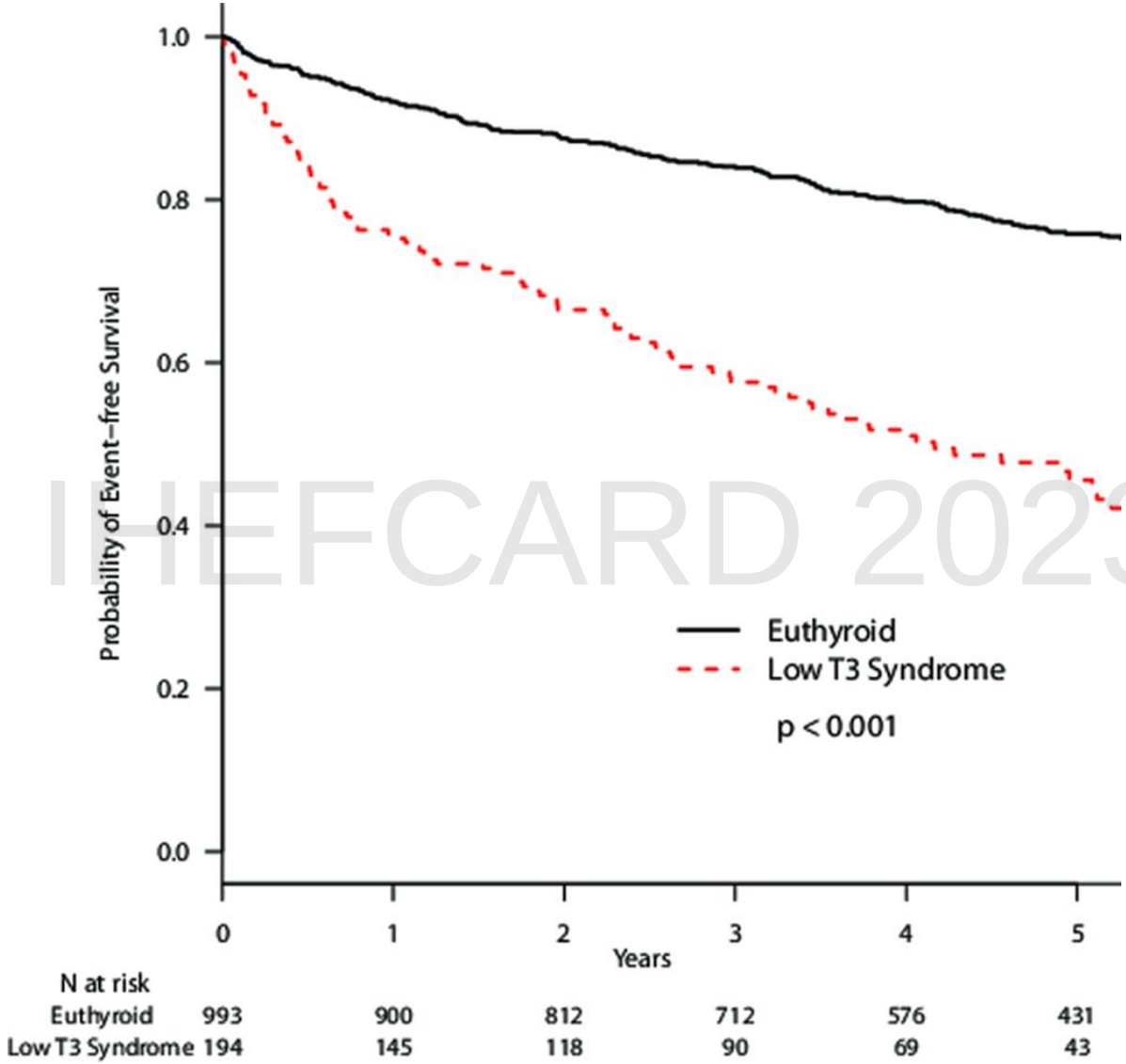
TSH levels and outcomes in HF patients



Kannan L. Circ Heart Fail. 2018 Dec;11(12):e005266.

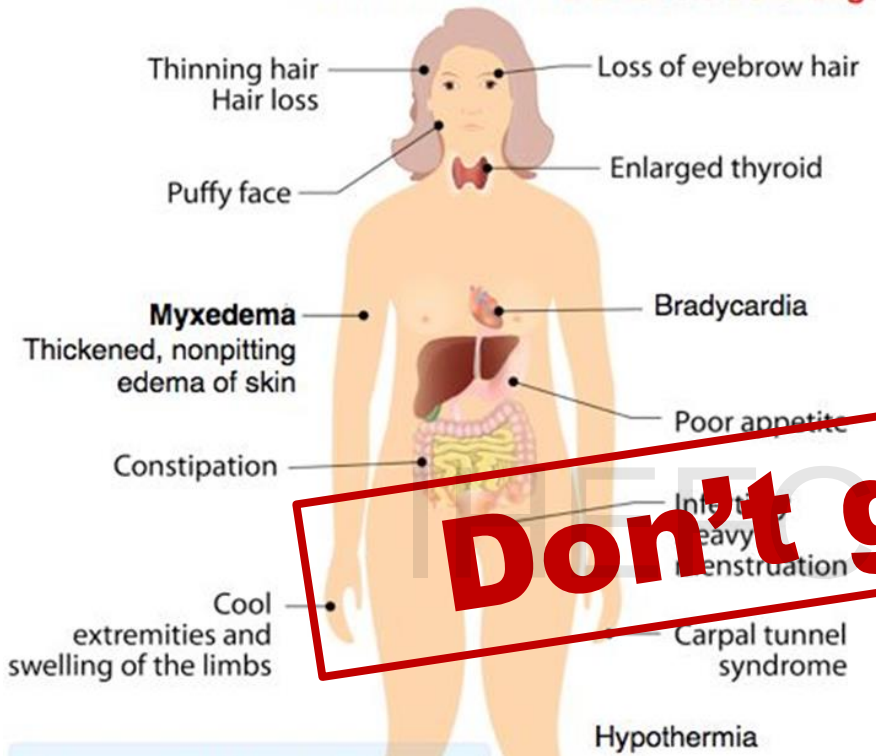
Low T3 syndrome in HF patients



Kannan L. Circ Heart Fail. 2018 Dec;11(12):e005266.

Myxedema Coma

Severe **hypothyroidism** resulting in a decompensated metabolic state and **mental status change**



Precipitating factors
- Infection
- Cold exposure
- Stroke
- Meds (amiodarone, lithium)

- **Laboratory findings**
- Hypoglycemia, Hyponatremia
- Hypoxemia, hypercapnea
- Prolonged QT, low voltage
- Pericardial effusion

Management
- Supportive (airway, rewarming)
- Hydrocortisone
- Levothyroxine (T4)
- +/- T3 supplementation

Don't get fooled!

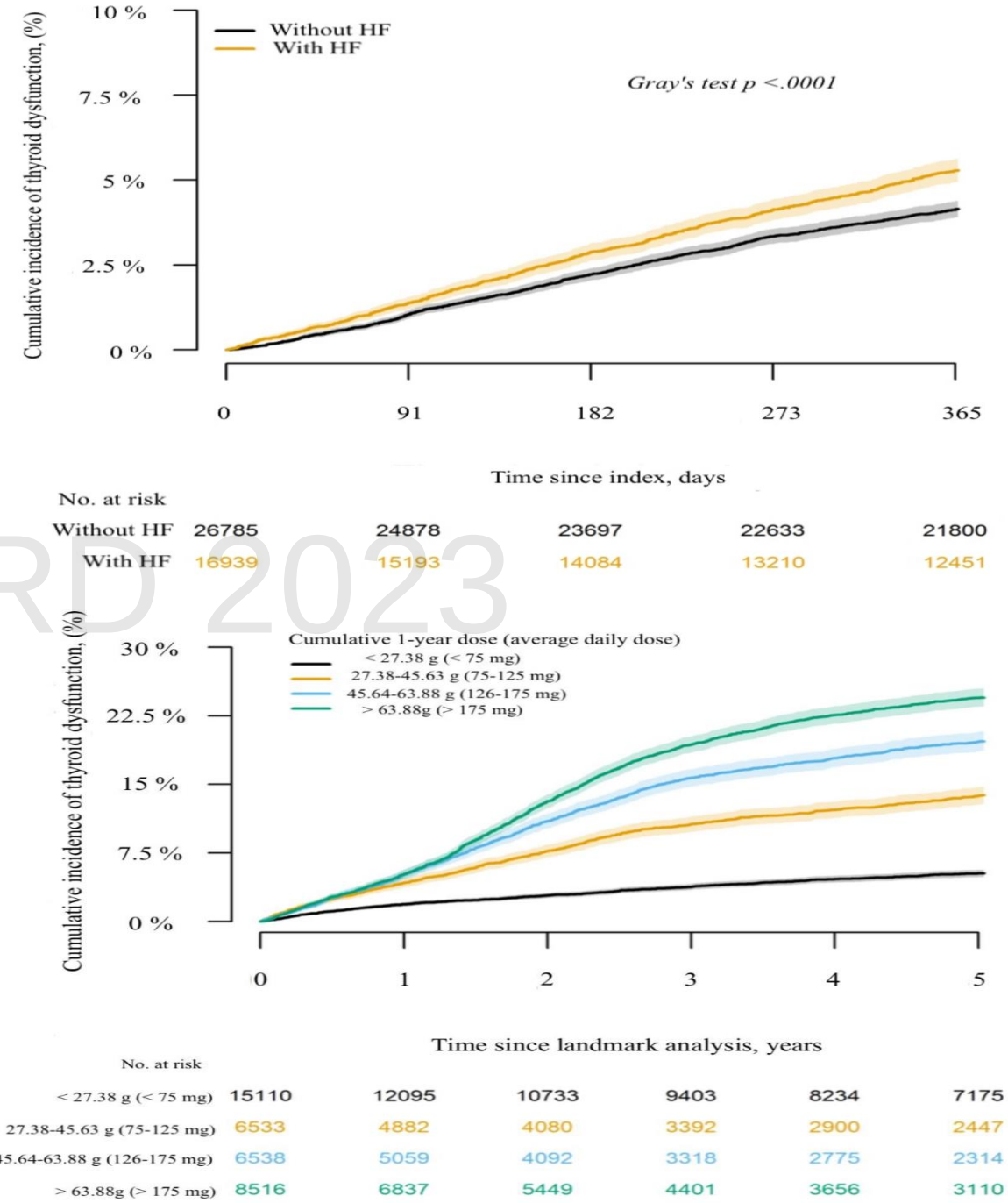
Amiodarone and thyroid

- Contains approximately **37% iodine** by weight
- The effects of amiodarone on the thyroid are attributed to its high iodine content, direct toxic effects on the thyroid, and effects on thyroid hormone metabolism
- **Hypothyroidism** presents more commonly than hyperthyroidism
- Strict **monitoring of thyroid function** is recommended while administering Amiodarone therapy

Bhattad PB, et al. Cureus. 2023 Apr; 15(4): e37659.

Incidence of thyroid dysfunction following initiation of amiodarone treatment in patients with and without heart failure: a nationwide cohort study (Danish)

- All Danish residents who initiated amiodarone treatment between **2000–2018** without a history of thyroid dysfunction
- Total of 43,724 patients; of whom 16,939 (38%) had a history of HF



Ali SAA, et al. European Heart Journal (2022) 43 (Supplement), 431

Management

Thyroid-specific therapy

- Aimed to restore **euthyroid**
- **Hypothyroid;**
  - Hormone replacement
- **Hyperthyroid;**
  - Anti Thyroid Drugs : Thionamides (Propylthiouracil [PTU], Carbimazole [CBZ], Methimazole [MMI])
  - Radioactive Iodine (RAI) Therapy
  - Thyroidectomy
- Remission and relapse

Management of HF

- HFrEF/HFmrEF vs HFpEF
- High output states → fluid redistribution → BB (1st line)
- AFRVR
  - Rate control: BB, DHP-CCB (if preserved EF)
  - Digoxin: less effective
  - Amiodarone can be safely used in acute setting, along with anti-thyroid drug.
- Treat HTN: SBP vs DBP
- Thyroid storm, keep in eye Takotsubo syndrome
- Hypothyroid, think about:
  - Chronic coronary syndrome
  - Myxedema!

Conclusion

- **Assessment of thyroid functions** is recommended in all patients with HF as both hyper- or hypothyroid could **cause or precipitate HF** (reversible)

- HF could lead into **subclinical hypothyroid** or **low T3 syndrome**, which is associated with poorer outcomes

- Some endocrine abnormalities, including thyroid dysfunction, might potentially lead to **Takotsubo Syndrome**

Thank you