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RESEARCH ARTICLE
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Characteristics Of Patients with Grave's Disease with ECG Sick Node Dysfunction (SND) With History of Thyroidectomy and PTU Treatment

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ABSTRACT

Background: Hyperthyroidism is an endocrine disorder with the second highest incidence after diabetes, and Graves' Disease is the most common cause of hyperthyroidism. About 60%-80% of hyperthyroidism cases are caused by Graves' disease where women in the age of 20-50 years are more dominant than men. Graves' disease is an autoimmune disorder, the presence of thyroid stimulating immunoglobulin (TSI), or can be called thyroid stimulating antibody (TSAb) secreted in the thyroid gland binds to thyroid stimulating hormone (TSH) receptors in the thyroid gland. Thus, stimulating the thyroid gland to work to produce thyroxine hormone based on stimulation from TSH receptors. Continuous stimulation of TSAb results in states of hyperthyroidism and thyroomegaly. Hyperthyroidism causes a weakened heart rate and ECG images that show sinus syndrome include sinus bradycardia (heart rate <40 bpm), sinus pause (sudden pause of sinus nodes shorter than 2-3 seconds), and sinus arrest (sudden pause of sinus nodes more than 2-3 seconds). PTU is one of the treatments carried out on grave's disease patients.

Objective: Know the characteristics of patients with Grave's Disease with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment.

Method: This research is a Systematic Review using the Preferred Reporting Items for Systematic Reviews and Meta-analyses method or commonly called PRISMA, this method is carried out systematically by following the correct research stages or protocols. Sources were taken from the PubMed site and Google Scholar site with journals published in 201 7-2022 and then screening results were obtained 15,486.

Results: Journal clustering was carried out and the number of journals indexed by Scopus Q1 was 2 journals, Q2 2 journals, indexed Sinta S1 1 journal, so that there were 5 journals extracted

Conclusion: The journal discusses age and lifestyle related to the characteristics of grave disease and grave disease risk factors determined based on age and sex and grave disease related to SND ECG images.

Keywords: *Graves Disease, SND, Thyroidectomy, PTU*

INTRODUCTION

Changes in thyroid function can cause changes in mood. Thyroid function disorders can be known from changes in thyroid levels and changes in Thyroid Stimulating Hormone (TSH) in the blood. Most of these disorders occur due to impaired synthesis of thyroid hormones. The thyroid gland produces thyroid hormones that function to control the speed of the body's metabolism. Hyperthyroidism indicates excessive activity of the thyroid gland in synthesizing thyroid hormones, thereby increasing metabolism in tissues. Subclinical hyperthyroidism is a condition in which low serum thyrotropin (TSH) levels (< 0.5 mU/L) are obtained while free thyroxine (fT4) and free triiodotorin (fT3) levels are within normal limits. Hyperthyroidism is a condition where there is a decrease and secretion of thyroid hormones, resulting in a decrease in the body's metabolic rate (Rago, 2018; Kotwal, 2018).

Thyroid hormones affect neurotransmitter function directly. Under normal circumstances, thyroid hormones affect tissue metabolism, tissue oxidation processes, growth processes, and protein synthesis. This thyroid hormone affects all cells in the body through the mechanism of transport of amino acids and electrolytes from extracellular fluid into cells, activation/synthesis of enzyme proteins in cells and improvement of intracellular processes

Changes in thyroid function will cause impaired cognitive function, behavior, and changes in feelings (mood) and anxiety. Two-thirds of thyroid disorder patients report that they have a psychiatric disorder. Some psychiatric disorders that often appear in people with thyroid disorders are anxiety, depression, phobias, obsessive-compulsive, and panic. The prevalence of anxiety disorders experienced by thyrotoxicosis sufferers is around 33-61%, while in hypothyroid patients the problems encountered include depressive disorders or bipolar disorder (Struja, 2017)

The thyroxine hormone produced by the thyroid gland has the function of maintaining the metabolic rate of tissues for the normal functioning of cells and the whole body, by stimulating the consumption of O2, protein synthesis and transcription of other genes in cells. The thyroxine hormone is said to be not essential for life, but the absence of this hormone will cause deterioration and slow physical and mental growth processes (Liu, 2017). An excess of this hormone will cause the body to metabolize quickly, tremors, nervousness to excessive heat production. Hyperthyroidism is an endocrine disorder with the second highest incidence after diabetes, and Graves' Disease is the most common cause of hyperthyroidism. About 60%-80% of hyperthyroidism cases are caused by Graves' disease where women at the age of 20-50 years are more dominant than men (Struja, 2017; Srikandi, 2020)

Graves' disease is an autoimmune disorder, the presence of thyroid stimulating immunoglobulin (TSI), or can be called thyroid stimulating antibody (TSAb) secreted in the thyroid gland binds to thyroid stimulating hormone (TSH) receptors in the thyroid gland. Thus, stimulating the thyroid gland to work to produce thyroxine hormone based on stimulation from TSH receptors. Continuous stimulation of TSAb results in states of hyperthyroidism and thyroomegaly. Almost all patients with Graves' disease have classic symptoms of hyperthyroidism. Symptoms of orbitopathy or demaopathy are also found, but do not stand alone without the classic symptoms of hyperthyroidism. Common symptoms that

appear in patients at a young age such as temperature intolerance, sweating, fatigue, weight loss, palpitations to tremors. In elderly patients' symptoms will be blurred and nonspecific, such as fatigue or weight loss. Accompanied by extrathyroidural symptoms such as ophthalmopathy, dermopathy and even oestheopathy (Liu, 2017; Pokhrel, 2022).

The test used to confirm Graves' disease is a calculation of TSAb. Elevated TSI and thyrotropin-binding inhibiting (TBI) immunoglobulins have sensitivity and specificity of 97% and 99% for diagnosis of Graves' disease. In addition, increasing iodine uptake in Radioactive Iodine Uptake Scan with I-123 or I-131 can also be the basis for establishing the diagnosis (Dakkak, 2022).

The initial laboratory examination for diagnosis is the TSH level test. If a low TSH is found, the next recommended examination is FT4 and FT3 if possible. If inspection is not possible, a total of T4 and T3 can be used. Total T4 and T3 levels accompanied by a decrease in TSH will confirm the diagnosis of hyperthyroidism. Graves's disease can be established with a history of disease, physical examination and simple laboratory examination. (8,9) The presence of orbitopathy, diffuse enlargement of the thyroid gland with or without bruits and pretibial myxedema can be the basis for a fairly strong diagnosis. But if signs and symptoms are not typical, a complete examination is still recommended (Aung, 2018; Alkaroshy 2021).

The main therapy for Graves' disease is decreased hormone secretion and rapid control of symptoms. There are three options for lowering thyroid hormone production; Thionamides, Radioactive Iodine (RAI), Thyroidectomy. Methimazole (MMI) and Propylthiouracil (PTU) are the most common drugs that are easy to get. This drug functions to inhibit Thyroid Peroxidase (TPO) in the thyroid gland, inhibiting the synthesis of T4 and T3. PTU also inhibits conversion from T4 to T3 in peripheral networks. With appropriate doses, 5-40mg daily for MMI and 150-450mg daily divided by three doses for PTU. When thyroid function has improved, this drug can be tappering-off until the condition of euthyroid. The maintenance dose of MMI is 5-10mg per day, and PTU 100-150mg a day is divided by 2 to 3 administrations (Eliana, 2017).

RAI therapy is given to patients aged 21 years and over, not pregnant or even planning to get pregnant for the next 1 years. MMI administration is recommended first until the condition is close to euthyroidism, then stopped 3-5 days before RAI administration. With a dose of I-131 10-25mCi fixed dose, monitored every 4 weeks until the condition of hypothyroid patients. Levothyroxine maintenance dose will be given and re-examined thyroid function in the next 6-12 months. Thyroidectomy is preferred for patients with large goiters (>80gr), anterior coli regional suppression, cancer, or nodules that are more than 4cm. Preparation for thyroidectomy is also the same as for RAI, euthyroid attempted condition, discontinuation of thyroid medications 7-10 days before removal. After surgery is completed, thionamides should be discharged, and replaced with levothyroxine with an initial dose of 1.6mcg/kgBB then adjusted to TSH levels every 6 weeks of examination (Mallick, 2018).

Beta-adrenergic should be given to patients with typical symptoms of Graves' disease, especially those with pulse frequency abnormalities of more than 90x/minute, cardiovascular disease, and old age. Propanolol 10mg40mg orally every 6-hour hours a day was shown to be good for control of T3 and T4 in peripheral tissues.

Dysfunction of the synarterial node (SA node, known as "*Sick Sinus Syndrome*", is one of the causes of heart rhythm disturbances, and can be caused by disturbances of either intrinsic factor or extrinsic factor of the SA node. The diagnosis of *Sick Sinus Syndrome* is established by the presence of heart rhythm disturbances with episodes of tachycardia-bradycardia, and accompanied by clinical symptoms such as; syncope, palpitations, or it can be without clinical symptoms (De regibus, 2017).

As we all know, severe cardiovascular complications of hypothyroidism include coronary heart disease, ventricular arrhythmias, atrioventricular block, myocardial systolic weakness, pericardial effusion, low cardiac output and hypertension. Rarely, hypothyroidism

can cause severe sick sinus syndrome that requires pacemaker treatment. Previous studies have also found that hypothyroidism can also cause mental disorders. It is reported that reported rare cases of hyperthyroidism accompanied by SND as a manifestation of cardiovascular and severe mental disorders, both of which are reversible and successfully treated with PTU (Huang, 2021).

Therefore, the role of ECG images of sick node dysfunction in predicting the prognosis of grave disease is questionable. To address this issue, we conducted a systematic review to comprehensively evaluate the predictive role of ECG sick sinus syndrome (SSS) images in Graves' disease prognosis.

Based on the background that has been described, the formulation of the problem "How is the characteristic of patients with Grave's Disease with ECG Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment" based on the literature? Knowing the characteristics of patients with Grave's Disease with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment. Knowing the concept of graves diseases with ECG sick node dysfunction (SND) Analyzing is the concept description of graves disease with ECG sick node dysfunction (SND) with thyroidectomy and PTU treatment history.

The results of this study can be used as an objective source of information about the characteristics of patients with Grave's Disease with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment. The results of this study can add insight into medical science in dealing with the characteristics of patients with Grave's Disease with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment. In addition, it is hoped that this research can be used as an object of research in medical education in Indonesia.

RESEARCH METHODS

This research is a Systematic Review using the Preferred Reporting Items for Systematic Reviews and Meta-analyses method or commonly called PRISMA, this method is carried out systematically by following the correct research stages or protocols. Systematic review is one method that uses review, review, structured evaluation, classification, and categorization of evidence based that has been produced previously. The steps in implementing systematic review are very planned and structured so that this method is very different from the method that is just for delivering literature studies. The procedure of this systematic review consists of several steps, namely 1) compiling Background and Purpose, 2) Research Question, 3) Searching for the literature 4) Selection Criteria 5) Practical Screen 6) Quality Checklist and Procedures 6) Dor Extraction Strategy, 7) Data Synthesis Strategy.

The data used to search the literature is through selection based on grave disease criteria, which concern medical research and social health. Next, apply a review of the literature related to anxiety disorders and Graves' disease. Articles are searched using PubMed and Google Scholar as databases. The search for research articles relevant to this research topic was carried out using keywords: graves disease, sick node dysfunction (SND), and graves disease with thyroidectomy and PTU treatment.

Publication time

The journals taken are journals published in 201 7-2022

Inclusion and exclusion criteria

Inclusion criteria

- Research articles published in 201 7-2022
- The dependent variable in the research article was followed by graves disease with ECG sick sinus syndrome (SSS) images.
- The independent variable in the research article was anxiety disorders
- Articles indexed by Scopus 1.2 and Sinta 1.2

Exclusion criteria

- Research articles with incomplete text
- Literature review/systematic review based articles
- Does not discuss dependent variables / unrelated articles

- Articles with incomplete content

Publication Search Strategy

Publication searches on Pubmed and Google Scholar use the selected keywords, namely cervical cancer, characteristics of cervical cancer, and iron deficiency anemia.

RESULTS AND DISCUSSION

Research Results

In this chapter, we will describe the resultsand analysis using 34 journals related to the characteristics of patients with Grave's Disease with ECG Sick Node Dysfunction (SND) images with a history of thyroidectomy and PTU treatment with 5 journals that have been fully accessed. Journals obtained are screened and extracted into a table to make it easier to explain the contents of the journal. Based on the results of journal clustering, it was found that the number of journals indexed by Scopus Q1 amounted to 2 journals, Q2 2 journals, indexed Sinta S1 1 journal, so that there were 34 journals extracted and used as a reference for our systematic review work.

Analystis Data

Data information about cervical cancer as an independent variable analyzed is presented in the form of a table containing the title of the journal, year of publication, author of the purpose in the journal, samples and criteria, research instruments, between data or research methods and research results in the journal.

TABLE 1: Journal Analysis

No	Journal Title and Researcher Name	Purpose	Population/ Sample	Instruments	Analystis Data / Research Methods	Result	Journal Clustering
1	Hypothyroidism and Complicated Sick Sinus Syndrome and Acute Severe Psychiatric Disorder: A Case Report Rui Huang, Li Yan, Yuhua Lei Yuanhong Li (2021)	Rare cases of severe hypothyroidism patients accompanied by sick sinus syndrome (SSS) as a cardiovascular manifestation requiring heavy heart and mental racing annoyance	A 42-year-old woman with hyperthyriodism and sick sinus syndrome with mental disorder	Manganalyze case report	Analyze rare case reports	This is the first reported case of hypothyroidism with sick sinus syndrome requires pacemakers and psychiatric disorders, and symptoms can be corrected and reversed after thyroxine supplementation. This case highlights the importance of screening for hypothyroidism when facing unexplained psychosis or sick sinus syndrome, in particular if combined.	Q1
2	Hyperthyroidim and Sick Sinus Syndrome, a Rare but Challenging Association: A Study of Three Cases	The study looked at case reports of 48-year-olds, 63-year-olds, and 66-year-olds	A female patient aged 48, 63, and 66 was brought in to the emergency department by him family.	Analyze case reports on three cases	Hyperthyroidism is usually associated with sinus tachycardia or supraventricular tachyarrhythmias, but rarely with sinus node dysfunction or other conduction annoyance	Hyperthyroidism and SSS are rare associations, identified mostly in patients with Graves' disease, even In the subclinical stage, raises therapeutic problems in the presence of concomitant	Q2

	M Tudoran, C Tudoran (2017)					tachyarrhythmias. Evolution well in most cases, after normalization of the thyroid hormones, rarely requiring implantation of a pacemaker	
3	Sick sinus syndrome and hyperthyroidism: A rare phenomenon Nitesh Kumar, Diwakar Verma, Kapil Gupta, Madhu Kiran, Prakarti Yadav, Shatrughan Pareek (2021)	This study is to look at case reports that are 70 years old	A 70-year-old female patient was taken to the emergency department by him family. He has a history of those feelings dizziness and lightheadedness. He is a known case of diabetes mellitus, hyperthyroidism, hypertension, and atria fibrillation with controlled ventricular rate.	Analyze case reports	Analyze rare case reports	Hyperthyroidism and SSS are rare phenomena; This happens especially among patients with Graves' disease. SSS/ SA/AV node blocks can be corrected by treating hyperthyroidism to euthyrodism, which can negate requires a pacemaker. This case highlights the presence of SSS in hyperthyroidism followed by installation of a pacemaker. With control of hyperthyroidism, normal rhythm and pacemaker can finally be eliminated.	Q2
4	An Adolescent Patient with Sick Sinus Syndrome Complicated by Hypothyroidism Carrying an SCN5A Variant A Case Report Hiroaki Yamane,MD, Mitsuru Seki, MD, Takahiro Ikeda, MD, Ayumi Matsumoto,MD, Sadahiro Furui, MD, Tomoyuki Sato, MD, Kazuhiro Muramatsu, MD, Toshihiro Tajima, MD and Takanori Yamagata, MD (2022)	This study was to look at case reports of 13-year-olds	A 13-year-old girl was referred to our hospital for bradycardia, as revealed by the school's electrocardiographic (ECG) screening. No ECG abnormalities has been observed during school screening conducted 3 the previous year. She doesn't have any syncopal episodes She reported noticing facial and lower leg edema as well as quickly tired over the past 2 years. An analysis His growth curve also revealed that he experienced a slowdown in growth during this 2-year period. No family history of arrhythmia, sudden death, or congenital heart disease..	Analyze case reports.	Analyze case reports .	In this report, we have presented case 13- a one-year-old girl with SSS who has the SCN5A variant and has also developed hypothyroidism. Current case highlights the importance of genetic analysis, including for the SCN5A variant, in patients with hypothyroidism with complications of SSS or cardiac conduction disorders.	Q2

5	Graves' disease and mental disorders Atsushi Fukaoa, Junta Takamatsub, Takeshi Arishimac, Mika Tanakad, Toshio Kawaie, Yasuki Okamotof, Akira Miyauchic ,Akihisa Imagawa (20 20)	The study looked at whether Graves' disease and mental disorder were related	Conducted literature review of articles from 1985-2014	Analyzing journals on pubmed, and elsevier	Systemic review studies	Mental disorders, depression and anxiety often converge with GD. Psychosocial factors include stress and awareness of the disease as well as Biological factors including the effects of thyroid hormones can influence the course of the disease. Psychosomatic approaches include antipsychotic drugs and psychotherapy based on bio-psycho-social medical models are considered useful in GD patients with mental Symptoms concomitant with hyperthyroidism.	Q2
6.	Digital Interventions for GeneralizedAnxiety Disorder (GAD): SystematicReview and Network Meta-Analysis Pedro Saramago (2021)	Generalized anxiety disorder is the most common mental health condition based on weekly prevalence. Digital interventions have been used as alternatives or as a supplement to conventional therapies to improve access, patient choice, and clinical results. Little is known about their comparative effectiveness to generalize anxiety disorders.	We included 21 randomized controlled trials with a total of 2,350 participants from the generalized anxiety disorder population	We conducted a systematic review and meta-analysis of randomized networks controlled trials comparing digital interventions with treatment, non-digital interventions, non-therapeutic control, and no intervention.	Combined results using analysis Covariance and rank based on surface under cumulative rating curve shows that antidepressant drugs and group therapy have a higher probability than Digital interventions are the "best" interventions. Supported digital interventions are: Not necessarily "better" than unsupported (pure self-help).	Due to the very wide confidence interval, the results of the network meta-analysis It is inconclusive whether digital intervention is better than no intervention and non-therapeutic active controls, or whether they provide additional benefits to the standard therapy. Future research will need to compare digital interventions with one-on-one therapies and with a non-digital self-help manual and to include antidepressant medication as a treatment comparators and effect modifiers.	Q2
7.	Thyroid ultrasonography reporting: consensus of Italian ThyroidAssociation (AIT), Italian Society of Endocrinology (SIE), Italian Society of	Thyroid ultrasound (USA) is the gold standard for thyroid imaging and its widespread use is due to its spatially optimal resolution to superficial anatomical structure, low cost and lack of health risks	Thyroid US is an important tool for diagnosis and follow-up of autoimmune thyroid disease, to assess nodule size and echo structure and determine risk malignancy in thyroid nodules.	Literature review	Analysis of literature review	A pattern of AS autoimmune thyroid disease is defined. Signs of AS malignancy in thyroid nodules are classified and scored in each nodule. We also propose simplified nodule risk stratification, based on the predictive value of	Q3

	Ultrasonography in Medicine and Biology (SIUMB) and UltrasoundChapter of Italian Society of Medical Radiology (SIRM) T. Rago (2018)					each AS mark, classified and scored according to the strength of the relationship with malignancy, but also the approximate reproducibility between different operators.	
8.	Graves Disease with Heart Rhythm Disorders M Agung Yudistira Permana (2020)	Hyperthyroidism is an endocrine disorder with the second highest incidence after diabetes, the most common cause of hyperthyroidism (60%-80% of cases) is Graves' disease. Graves' disease is an autoimmune disorder, the presence of thyroid stimulating immunoglobulin (TSI), or can be called thyroid stimulating antibody (TSAb) secreted in the thyroid gland binds to thyroid stimulating hormone (TSH) receptors in the thyroid gland stimulates the thyroid gland to work to produce hormones	Pthere was this case obtained Ms. FF 47th came with chest palpitations since one week before entering the hospital, accompanied by excessive sweating and trembling hands. There is an enlargement of the thyroid gland that is the color of the skin, painless with a limit of not having the heart	Case report analysis	Case report analysis	Graves' disease is a metabolic disease that is not uncommon, especially in women aged 20-50 years. Establishing the diagnosis can be done by examining the history of the disease, physical examination and laboratory. Even with long treatment and continuous follow-up, the drugs that can now be obtained are proven to produce good outcomes for patients.	S3
9.	Experience with outpatient thyroidectomy for Graves' disease in a high-volumetertiary care center Reema Mallick (2018)	Outpatient thyroidectomy is increasingly being performed. Thyroidectomy for Graves' disease, However, it has a greater risk of periprocedural complications, limiting same-day use Procedure. We strive to show that these patients can be managed by outpatient surgery.	Experience of an endocrine surgeon with thyroidectomy for Graves examined from January 2016-November 2017. Forty-one patients met the criteria.	Case Report	Case report analysis	Although these patients can pose greater technical and physiological challenges, in optimally selected patients and in the setting of experienced surgeons with additional trained staff, ambulatory thyroidectomy can be safely used for patients with Graves' disease	Q2
10.	Antithyro id Drug Therapy	Graves' disease (GD) is the most	Hypothyroidism, and	Literature review	Literature review analysis	Relapses in GD patients on OAT	Q3

	for Graves' Disea se andImplicatio ns for Recurrence Jia Liu, (2017)	common cause of hyperthyroidism worldwide. Current therapy options for GD include antithyroid drugs (ATD), radioactive iodine, and thyroidectomy.	Corrects immune disorders while avoiding radiation exposure and invasive procedures. But relatively high Recurrence rates are a major concern for the treatment of OAT, which is attributed to several such influencing factors as clinical characteristics, treatment strategies, and genetic and environmental factors.			treatment are associated with several influential factors such as clinical characteristics, treatment strategies, and genetic and environmental factor. Of these influencing factors, some can be modified But some cannot be modified. Risk of recurrence may occur reduced by adjusting modifiable factors as much as possible. If the evaluation of recurrence based on non-modifiable factors strongly indicates a high risk of recurrence, Definitive treatment such as radioactive iodine or thyroidectomy is considered an appropriate therapeutic approach	
11.	Sick sinus syndrome and hyperthyroidism : A rare phenomenon Nitesh Kumar, (2021)	Cardiovascular complications play a very important role in hyperthyroidism and increased mortality and morbidity risk. In addition to tachyarrhythmias, impaired function of the systolic and diastolic ventricles Dysfunction can cause thyrotoxic cardiomyopathy in a small percentage of patients, as in others high complication of mortality. Bradycardia in hyperthyroidism is a rare phenomenon associated with with sinus node dysfunction, atrioventricular node dysfunction, and conduction disorders, or	The 70-year-old female patient was taken to Emergency Department with a history of dizziness, dizziness, and bradycardia. When Waiting in an emergency, she had an episode of syncope, followed by regaining consciousness afterwards 20 minutes. The patient is transferred for the installation of a pacemaker.	Case report	Case report analysis	Hyperthyroidism and SSS are rare phenomena; it occurs mainly among patients with Graves' disease. SSS/ SA/AV node block can be corrected by treating hyperthyroidism to euthyrodism, which can negate requires a pacemaker. This case highlights the presence of SSS in hyperthyroidism followed by the installation of a pacemaker. With control of hyperthyroidism, The rhythm returns to normal and the pacemaker can finally be removed	Q2

		due to the effect of the drug, namely beta blockers					
12.	Thyrotropin Receptor Antibodies—An Overview Kotwal (2018)	Thyroid autoimmunity affects about 5% of the population, and its research relies heavily on use autoantibodies. Thyroid-stimulating hormone receptors (TSHR) Autoantibodies (TRAb) play a central role in evaluation Graves' disease (GD), Graves' ophthalmopathy (GO) and pretibial myxedema (PTM). However, there is still controversy regarding diagnostic accuracy of overall TRAb assays and them prognostic utility.	We review and analyze literature reporting TRAb test and its clinical usefulness.	Literature review	Literature review analysis	The evidence accumulated over the years conclusively suggests that TRAb is a pathogenic element for GD, GO, and PTM. We have improved our testing capabilities year, and the current generation of TBII and TSI tests is Able to provide physicians with diagnostic and prognostic information for these patients. For some entities, the information may turn out to be a more appropriate therapeutic option (GD), while for other entities the information is being collected (GO and maybe PTM).	Q3
13.	Evaluation of the Use of Antithyroid Drugs in Hyperthyroid Patients at Dr. M. Djamil Padang Hospital, Indonesia Juwita, (2018)	This study aims to determine the pattern of use of antiioid drugs and evaluate the accuracy of the use of antiioid drugs in hyperthyoid patients covering the right indications, right drugs, right patients and right doses.	period January-December 2015 at the Special Polyclinic of RSUP Dr. M. Djamil Padang. The number of patients who met the inclusion criteria was 175 patients	Retrospective study	This research is a descriptive research with retrospective data collection using patient medical records during the period January-December 2015 at the Special Polyclinic of Dr. M. Djamil Padang Hospital. The number of patients who met the inclusion criteria was 175 patients.	Theantiioid drugs used in hyperthyoid patients were PTU (82.75%) and thyrozol (17.25%). The results showed that the inaccuracy of indications and inaccuracies of the drug were not found, while there were 13 patients (7.43%) not the right dose, and 1 patient (0.57%) not the right patient.	S3
14.	Hypothyroidism and Complicated Sick Sinus Syndrome and Acute Severe Psychiatric Disorder: A Case Report Rui Huang, Li Yan, Yuhua Lei	Rare cases of severe hypothyroidism patients accompanied by sick sinus syndrome (SSS) as a cardiovascular manifestation requiring heavy heart and mental racing annoyance	A 42-year-old woman with hyperthyriodism and sick sinus syndrome with mental disorder	Manganalyze case report	Analyze rare case reports	This is the first reported case of hypothyroidism with sick sinus syndrome requires pacemakers and psychiatric disorders, and symptoms can be corrected and reversed after thyroxine supplementation. This case highlights the	Q1

	Yuanhong Li (2021)					importance of screening for hypothyroidism when facing unexplained psychosis or sick sinus syndrome, in particular if combined.	
15.	2018 European Thyroid AssociationGuideline for the Management ofGraves' Hyperthyroidism George J. Kahaly (2018)	Graves' disease (GD) is a systemic autoimmune disorder characterized by antigen-specific infiltration of T. thyroid cells into tissues that express thyroid-stimulating hormone receptors (TSH-R). Stimulating autoantibodies (Ab) in GD activate TSH-R leading to thyroid hyperplasia and unregulated production and secretion of thyroid hormones	Patients with Graves' newly diagnosed hyperthyroidism is usually treated medically for 12-18 months with methimazole (MMI) as Preferred drug. In children with GD, 24 to 36 months MMI courses are recommended.	Case report	Case report analysis	Ongoing preclinical and clinical trials assess the effectiveness of new drugs and/or substances that can modify the natural history of GD by modulating it Pathogenesis. These therapeutic agents include TSH-R monoclonal Abs [164], peptide TSH-R immunomodulators, and small molecule TSH-R ligands [165] that can blocks the thyroid-stimulating effects of TSH-R-Ab acts as an antagonist of TSH-R-Ab	Q1
16.	Graves' disease and mental disorders Atsushi Fukao (2020)	Mental disorders are very much integrated with thyroid disease. Because of its regulatory effects on serotonin and noradrenaline, T3 has been closely linked to depression and anxiety	Study of literature review data from 1998-2017	Literature review	Analysis of literature review	Mental disorders, depression and anxiety often converge with GD. Psychosocial factors include stress and awareness of the disease as well as Biological factors including the effects of thyroid hormones can influence the course of the disease. Psychosomatic approaches include antipsychotic drugs and psychotherapy based on bio-psycho-social medical models are considered useful in GD patients with mental concomitant symptoms with hyperthyroidism	Q2
17.	The Role of Cytotoxic T-lymphocyte-associated Protein4 (CTLA-4) Gene, Thyroid	Graves' disease or Graves' disease (GD) is a common condition found in denserotoxicosis. Management of GD begins with the	Comparing 72relapsed subjects and 72 non-relapsing subjects at 12 months after discontinuation of antithyroid treatment	Case control studies	Genetic polymorphism examination is performed using PCR-RFLP. The number of regulatory T cells	The genetic polymorphism of the CTLA-4 gene in nucleotide 49 in codon 17 in exon 1, the TSHR SNP gene rs2268458 in intron 1, the number of	S1

	Stimulating Hormone Receptor(TSHR) Gene and Regulatory T-cells as Risk Factors for Relapse in Patients with Graves Disease Fatimah, Eliana (2017)	administration of antithyroid drugs, although patients need a long time to achieve recovery or remission.			was calculated using flow cytometry analysis (flw cytometry) and ELISA examination to measure TRAb. Logistic regression is performed because the dependent variable is a categorical variable	regulatory T cells and TRAb levels act as risk factors for relapse in Graves' disease patients	
18.	Long-Term Antithyroid Drug Treatment: A Systematic Review and Meta-Analysis Azizi (2017)	Some studies have reported inconsistent findings about the advantages and disadvantages of long-term treatment with antithyroid drugs (ATD). A systematic review and meta-analysis were conducted to clarify various aspects of long-term treatment with ATD	Medlines and the Cochrane Library for trials published between 1950 and May 2016 were systematically searched.	Literature review	Studies containing data for long-term treatment of OAT (>24 months) were included. Summary Estimates of combined prevalence, odds ratio, and weighted mean difference are calculated by random effect type.	Of the 587 related articles found, six met the inclusion criteria. Long-term OAT treatment induces a remission rate of 57% [confidence interval (CI) 45–68%], a higher rate in adults than non-adults (61% vs. 53%). The complication rate was 19.1% [CI 9.6–30.9%], of which only 1.5% was the primary complication. The annual remission rate for each year of treatment is 16% [CI 10–27%], which is higher in adults than non-adults (19% vs. 14%). However, it should be noted that this is not an actual linear correlation, but a positive relationship can be suggested between time and remission rate. Meta-regression revealed that smoking had a significant decreasing effect on remission rates. Conclusions: Long-term treatment of OAT is effective and safe, especially in adults, suggesting that it should be considered an alternative treatment for Graves' disease	Q2
19.	Predicting outcomes and complications	Radioiodine (RAI) is an effective treatment for Graves'	655 episodes of RAI in Graves' thyrotoxicosis patients (2006–2015)	Retrospective cohort studies	Retrospective Analysis of cohort studies	Treatment failure after RAI occurs in the predictable group and	Q3

	following radioiodine therapy in Graves' thyrotoxicosis Thuzar Aung (2018)	thyrotoxicosis but is related with a failure rate of 15% and can be a risk factor for thyroid eye disease (TED) and weight gain. We sought to examine predictors of RAI failure, weight gain, TED and patient satisfaction				this should be reflected in the information provided to the patient. Weight gain is common and may not be fully explained by a Return to the pre-thyrotoxic baseline. We were unable to detect any significant post-RAI impacts dysthryoidism in weight gain, TED or thyroid symptoms in this large group.	
20.	Sex-Dependent Phenotypic Variability of an SCN5A Mutation: BrugadaSyndrome and Sick Sinus Syndrome Yoshiyasu Aizawa, MD, PhD; Taishi Fujisawa, MD; Yoshinori Katsumata, MD; Shun Kohsaka, MD; Akira Kunitomi, MD;Seiko Ohno, MD; Keiko Sonoda, MD; Hidemori Hayashi, MD; Rintaro Hojo, MD; Seiji Fukamizu, MD; Satoshi Nagase, MD; Shogo Ito, MD; (2018)	Brugada syndrome (BS) is known to be 9 times more common in men than women. However, little is known about development of sick sinus syndrome in female members with familial BS	A total of 7 families, including 25 BS Patients (12 females and 13 males), were admitted. Seven are probands and 18 are members of my family. Ten out of 12 women patients and none of the 13 male patients developed sick sinus syndrome. Sudden death or spontaneous ventricular fibrillation Occurs in 7 of 13 male patients and 2 of 12 female patients	Clinical Case	Clinical Case Analysis	Familial BS exists where female patients develop sick sinus syndrome but male patients do not. Some female patients with sick sinus syndrome have unrecognized BS. Information should be collected not only about the family a history of sudden death or BS, but also whether a pacemaker was implanted in a woman's limb	Q2
21.	Hyperthyroidim and Sick Sinus Syndrome, a Rare but Challenging Association: A Study of Three Cases M Tudoran, C Tudoran (2017)	The study looked at case reports of 48-year-olds, 63-year-olds, and 66-year-olds	A female patient aged 48, 63, and 66 was brought in to the emergency department by him family.	Analyze case reports on three cases	Hyperthyroidism is usually associated with sinus tachycardia or supraventricular tachyarrhythmias, but rarely with sinus node dysfunction or other conduction annoyance	Hyperthyroidism and SSS are rare associations, identified mostly in patients with Graves' disease, even In the subclinical stage, raises therapeutic problems in the presence of concomitant tachyarrhythmias. Evolution	Q2

						well in most cases, after normalization of the thyroid hormones, rarely requiring implantation of a pacemaker	
22.	Sick sinus syndrome and hyperthyroidism : A rare phenomenon Nitesh Kumar, Diwakar Verma, Kapil Gupta, Madhu Kiran, Prakarti Yadav, Shatrughan Pareek (2021)	This study is to look at case reports that are 70 years old	A 70-year-old female patient was taken to the emergency department by him family. He has a history of those feelings dizziness and lightheadedness. He is a known case of diabetes mellitus, hyperthyroidism, hypertension, and atria fibrillation with controlled ventricular rate.	Analyze case reports	Analyze rare case reports	Hyperthyroidism and SSS are rare phenomena; This happens especially among patients with Graves' disease. SSS/ SA/AV node blocks can be corrected by treating hyperthyroidism to euthyrodism, which can negate requires a pacemaker. This case highlights the presence of SSS in hyperthyroidism followed by installation of a pacemaker. With control of hyperthyroidism, normal rhythm and pacemaker can finally be eliminated.	Q2
23.	An Adolescent Patient with Sick Sinus Syndrome Complicated by Hypothyroidism Carrying an SCN5A Variant A Case Report Hiroaki Yamane,MD, Mitsuru Seki, MD, Takahiro Ikeda, MD, Ayumi Matsumoto,MD, Sadahiro Furui, MD, Tomoyuki Sato, MD, Kazuhiro Muramatsu, MD, Toshihiro Tajima, MD and Takanori Yamagata, MD (2022)	This study was to look at case reports of 13-year-olds	A 13-year-old girl was referred to our hospital for bradycardia, as revealed by the school's electrocardiographic (ECG) screening. No ECG abnormalities has been observed during school screening conducted 3 the previous year. She doesn't have any syncopal episodes She reported noticing facial and lower leg edema as well as quickly tired over the past 2 years. An analysis His growth curve also revealed that he experienced a slowdown in growth during this 2-year period. No family history of arrhythmia, sudden death, or congenital heart disease.	Analyze case reports.	Analyze case reports .	In this report, we have presented case 13- a one-year-old girl with SSS who has the SCN5A variant and has also developed hypothyroidism. Current case highlights the importance of genetic analysis, including for the SCN5A variant, in patients with hypothyroidism with complications of SSS or cardiac conduction disorders.	Q2

24.	Graves' disease and mental disorders Atsushi Fukaoa, Junta Takamatsub, Takeshi Arishimac, Mika Tanakad, Toshio Kawaie, Yasuki Okamotof, Akira Miyauchic, Akihisa Imagawa (20 20)	The study looked at whether Graves' disease and mental disorder were related	Conducted literature review of articles from 1985-2014	Analyzing journals on pubmed, and elsevier	Systemic review studies	Mental disorders, depression and anxiety often converge with GD. Psychosocial factors include stress and awareness of the disease as well as Biological factors including the effects of thyroid hormones can influence the course of the disease. Psychosomatic approaches include antipsychotic drugs and psychotherapy based on bio-psycho-social medical models are considered useful in GD patients with mental Symptoms concomitant with hyperthyroidism.	Q2
25.	A homozygous SCN5A mutation associated with atrial standstill and suddendeath Reina Bianca Tan, MD (2018)	The purpose of the study was to determine the clinical and biophysical consequences of novel SCN5A mutations identified in families with progressive and sudden atrial congestion death.	Families of sporadic cases of congenital cardiac arrest are genetically genetic Filtering. Human Embryonic Kidney 293 cells transfected by wild type (WT) or cDNA SCN5A mutant.	Clinical Case	Biophysical properties are studied using whole-cell using patch clamps method.	A new homozygous SCN5A mutation, p.V1340L, was identified in the proband and he sister. The proband has a complete atrial cessation while the sister experiences a partial atrial termination. Heterozygous mutations are identified in mothers, fathers, and brothers. All three are normal sinus rhythm and no symptoms. The mutant Nav1.5 (V1340L) reduces the current density of Nav1.5 and exhibits a shift in depolarization in voltage-dependent steady-state activation (WT: −35.3 ± 1.62 mV; V1340L: −22.4 ± 2.59 mV; P = 0.001). Conclusion: SCN5A mutations losing homozygous function most likely cause the atria to stall and sudden death due to suppression of action potential initiation.	Q2

DISCUSSION

Characteristics of patients with Grave's Disease with ECG description of Sick Node Dysfunction (SND) with History of Thyroidectomy and Treatment of PTU Based on Age

In study subjects with hyperthyroidism, the most common picture of heart rhythm disorders was rapid response atrial fibrillation of 6 people, sinus tachycardia 4 people, normal response atrial fibrillation and RBBB of 3 people each, benign VES 2 people, and atrial flutter, SVES, and sinus tachycardia with RBBB of 1 person each.

Thyroid hormones, particularly T3 are important regulators in cardiac gene expression. Some of these genes are positively regulated and negatively regulated. An increase in the amount of T3 binding to TRs will induce positively regulated genes and will suppress negatively regulated genes. These regulated genes include:

Alpha myosin heavy chainwhich can increase myocardial contractility. Ion channels Na+-K + ATPase and voltage-gated potassium ATPase, which regulate the electrochemical response of the myocardium. Changes in the electrochemical function of the myocardium can result in increased systolic depolarization and diastolic repolarization resulting in a decrease in the duration of the action potential duration. This can lead to an increase in Left Ventricular Mass (LVM)

Research on patients with hypothyroidism, hyperthyroidism, and groups of people who have normal TSH shows that patients with primary hyperthyroidism have the most severe levels of anxiety compared to other groups. Another study stated that patients with subclinic hyperthyroidism and subclinic hypothyroidism had higher anxiety scores compared to euthyroid subjects. This opinion is different from the results of other studies that state that there is no relationship between thyroid disorders and mental disorders, both depression and anxiety.

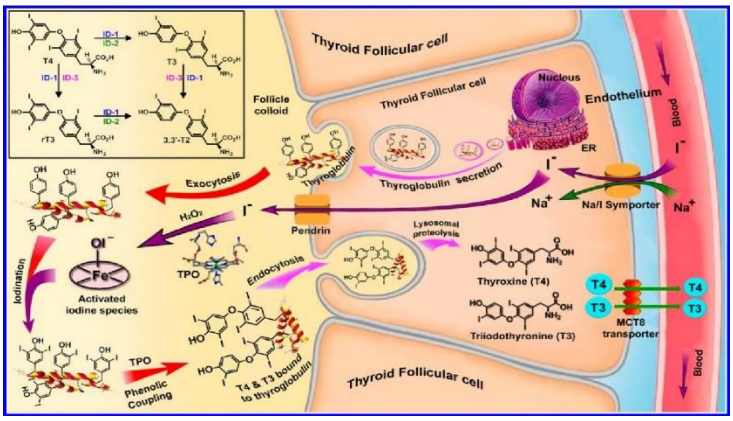

FIGURE 1: PTU Treatment Cycle and Effect on SND ECG (Gonen, 2021)

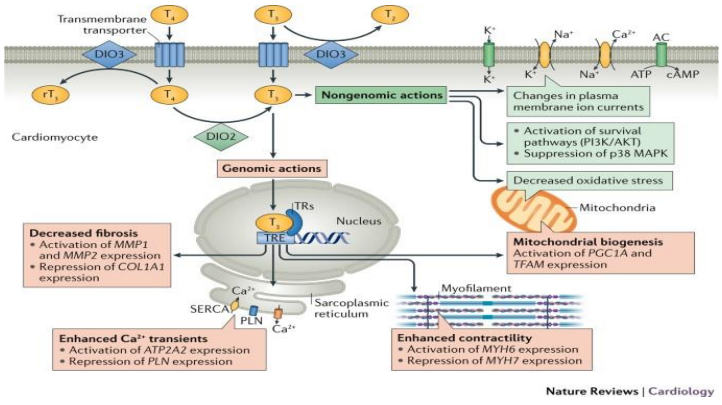

FIGURE 2: Thyroidectomy effect and Hyperthyroid effect on cardiovascular disease (Calgary, 2021)

J Popul Ther Clin Pharmacol Vol 30(13):e80–e97; 18 May 2023.

The results of Gonen's study, in hyperthyroid patients also showed a 30% SND ECG picture and was obtained in patients who were treated with PTU increased the incidence due to the influence of Na+ and MCT8 receptors so that this happened. Thyroidectomy action causes SND events to occur riskier due to the influence of the thyroid hormone production process that has been modified from the previous normal TSH.

Research limitations &; medical implications

In this study there are research limitations experienced by researchers. Researchers identified limitations including:

1. There are some journals that cannot be accessed in full / Full Text so that the author takes a long time to find journals.
2. The author needs time to collect journals related to the problem to be used as a reference source that is appropriate to the problem.
3. The author needs more timeto analyze and understand the contents of the journal and collect journals or books related to the problem to be used as appropriate reference sources.
4. Limited number of journals related to research variables on the characteristics of patients with Grave's Disease with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment.
5. At least researchers found a journal that lists detailed results about the characteristics of Grave's Disease sufferers with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment.
6. The results of the study showed that grave disease conditions were associated with ECG images of Sick Node Dysfunction (SND). Based on the results of this study, medical personnel are expected to gain insight into the characteristics of patients with Grave's Disease with ECG images of Sick Node Dysfunction (SND) with a History of Thyroidectomy and PTU Treatment.

CONCLUSION

After a series of processes passed, based on the results of research in Scopus and Sinta indexed journals regarding systematic review of the characteristics of anxiety disorder sufferers in Graves disease who have ECG Sick Sinus Syndrome (SSS) images, it can be concluded that the majority of journals discuss age, gender related to risk factors Graves disease. From the sub-chapters obtained, it can be concluded that the risk factors for Graves disease are determined based on age, sex, lifestyle. As well as graves disease related ECG picture of Sick Node Dysfunction.

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