Patient Preference and Adherence

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REVIEW

A Systematic Review of Patient Preferences, Expectations, and Values for the Management and Treatment of Graves Disease

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Objective: To systematically synthesize evidence on treatment preferences, values, and expectations among patients with Graves' disease (GD), in order to understand the disease's impact on quality of life and inform clinical decision-making..

Methods: PubMed, Embase, Web of Science, and Cochrane Library were searched for articles about GD, patient preferences, and expectations from database inception to December 2024. Studies included in the review must report raw data on patient-reported outcomes, preferences or experiences relating to GD, and must undergo quality assessment according to the Agency for Healthcare Research and Quality (AHRQ).

Results: Twenty-one studies involving patients with GD were included. Although preferences varied, several trends emerged: 1) Most patients reported that GD significantly disrupted their quality of life and social functioning, with 60% experiencing severe discomfort. 2) Antithyroid drugs (ATD) was the most preferred initial treatment (64%), followed by surgery (25%) and radioactive iodine therapy (RAI) (11%), with concerns about radioactivity and surgical complications influencing decisions. 3) Key factors affecting treatment choices included remission rates, recovery time, impact on daily life, and physician recommendations. 4) Graves' ophthalmopathy (GO) patients faced additional challenges, including social withdrawal and appearance-related distress, with female patients expressing greater concern about disfigurement.

Conclusion: This systematic review indicates that GD, particularly GO, significantly impairs patients' self-confidence, quality of life, and social functioning. Treatment choices are influenced by expected outcomes, personal circumstances, psychological concerns, and economic factors. ATD remains the preferred first-line treatment, though individual preferences vary significantly, emphasizing the importance of personalized approaches and decision aids.

Keywords: graves disease, patient preferences, shared decision-making, treatment expectations, graves ophthalmopathy, systematic review

Introduction

Graves Disease (GD) is a complex immune-mediated disease caused by autoantibodies. Autoantibodies activate thyroid-stimulating hormone receptors, stimulating the synthesis and secretion of thyroid hormone and thyroid growth.[1] GD induces a hyperthyroid state marked by thyrotoxicosis, triggering multisystem manifestations. Neuromuscular disturbances (tremors, irritability, insomnia), metabolic dysregulation (unintentional weight loss, heat intolerance), and cardiopulmonary sequelae (tachycardia, dyspnea, atrial fibrillation) are pathognomonic, often accompanied by goitrous thyroid enlargement.[2] A cohort study of 500,000 people showed that the incidence of atrial fibrillation in patients with thyrotoxicosis over the age of 65 was approximately 13%.[3] In addition, Graves Ophthalmopathy (GO) is also a common complication of GD, with an incidence of 25%-50%, causing great damage to the patient's vision and even the risk of vision loss.[4,5]

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The current treatments for GD mainly include antithyroid drugs (ATD), radioactive iodine therapy (RAI), and thyroidectomy.[6] Because the treatment methods are controversial, treatment selection is challenging for both patients and doctors.[7] In addition, as a chronic disease, long-term management of the disease is also a continuous physical and mental burden for patients. Current clinical decision-making focuses on achieving biochemical targets for thyroid function and controlling complications, but pays insufficient attention to patients' subjective treatment experience, quality of life needs, and value trade-offs.[8] The purpose of this study is to systematically summarize evidence on treatment options and clinical outcome determinants for Graves' disease (GD). The study also aims to resolve controversies between various therapies and identify unmet needs of GD patients, with the ultimate goal of optimizing personalized treatment choices.

Methods

Selection Criteria

This systematic review was registered in PROSPERO (CRD42024614238) and employed a structured literature search focusing on three core aspects: adult populations with GD, research exploring patient-centred outcomes (such as preferences, expectations and values in disease management), factors influencing treatment decision-making. Exclusions included topics unrelated to GD, publications in languages other than English, and non-primary research formats (eg reviews, letters, posters).

Data Sources and Search Strategy

Four electronic databases (PubMed, Embase, Web of Science and Cochrane Library) were systematically queried from their respective inception dates until December 2024. In order to comprehensively retrieve relevant literature, a strategy combining MeSH terms and keyword searching was employed, with PubMed being used as a case. The initial literature search on GD was conducted using MeSH terms, followed by keyword searches in the title or abstract using terms such as "Graves" disease', "hyperthyroidism", and so forth. These searches were subsequently merged. The same approach was applied to the literature search, with a focus on "patient preference", "patient compliance" or "patient values". The results of the disease and patient preference components were then combined. Table 1 shows the PubMed search strategy. Equivalent syntax adaptations were applied to other platforms based on their respective indexing systems.

Data Extraction and Quality Assessment

The process of literature review entailed independent screening of studies by two authors based on established inclusion and exclusion criteria. The initial screening process was conducted on the basis of a title and abstract review. Disagreements

Table 1 Search Strategy for PubMed

Query	Search Term
1	"Hyperthyroidism"[MeSH Terms] OR "Graves Disease"[MeSH Terms]
2	"Graves Disease"[Title/Abstract] OR "Graves Disease"[Title/Abstract] OR "GD"[Title/Abstract] OR "disease graves"[Title/Abstract] OR "disease graves"[Title/Abstract] OR "hyperthyroidism autoimmune"[Title/Abstract] OR "postpartum thyroiditis"[Title/Abstract] OR "subacute thyroiditis"[Title/Abstract] OR "painless thyroiditis"[Title/Abstract] OR "hyperthyroidism*"[Title/Abstract] OR "Thyrotoxicosis"[Title/Abstract]
3	1 OR 2
4	"patient preference"[MeSH Terms]
5	"patient* preference*"[Title/Abstract] OR "patient* expectation*"[Title/Abstract] OR "patient* value*"[Title/Abstract] OR "patient* view*"[Title/Abstract] OR "patient* perspective*"[Title/Abstract] OR "patient* perception*"[Title/Abstract] OR "patient* decision*"[Title/Abstract]
6	4 OR 5
7	3 AND 6

were addressed through discussion or correspondence with the corresponding authors. Data extraction for study type, study design, sample size, etc. was conducted independently by two reviewers, with guidance provided by the Agency for Healthcare Research and Quality (AHRQ).[9] This scale, a standard tool for evaluating observational studies, employs an 11-point checklist with "Yes" (1 point), "No" (0 points), and "Uncertain" (0 points) as potential responses. The evaluation of studies was conducted using a structured grading system, categorizing them as low (0–3), moderate (4–7), or high (8–11) quality based on their scores. As illustrated in Figure 1, the flow diagram delineates the systematic review process.

Result

Characteristics of Included Studies

A total of 2413 articles were included in the four databases. After deduplication and browsing the title and abstracts, 116 articles were found. After reading the full text, 21 articles met the inclusion criteria. Studies on patients' cognition and preferences for hyperthyroidism were mainly distributed in the United Kingdom (n=6), the United States (n=6), New Zealand (n=4), Sweden (n=1), Italy (n=1), Denmark (n=1), Czech Republic (n=1) and Australia (n=1). The time span of the included literature was from 1998 to 2024. The time span of the included literature was from 1998 to 2024. Despite the age of some of the literature, its systematic reporting of patients' views of GD, the factors influencing their choice of treatment plan, and the results of their final choice renders it relevant for inclusion. Table 2 provides a summary of the 21 studies, including sample size, study type, study description and the most important research results.

Quality of Life and Social Functioning Impairment in Patients with GD

Patients with GD frequently experience significant disruption to their quality of life and social functioning. Ljunggren et al reported that 60% of GD patients experienced severe discomfort, with 66% acknowledging that the disease impaired their social interactions.[10] In a similar vein, Palestini et al found that 66% of GD patients perceived the disease as detrimental to their normal daily activities, although 89% did not consider medication treatment and regular examinations burdensome.[13] Nexø et al highlighted a common challenge where patients struggled to distinguish whether their symptoms were disease-related, leading to delayed diagnosis; additionally, most participants expressed a desire for greater recognition of their disease status from others.[19] Regarding information-seeking behaviors, Purdy et al observed

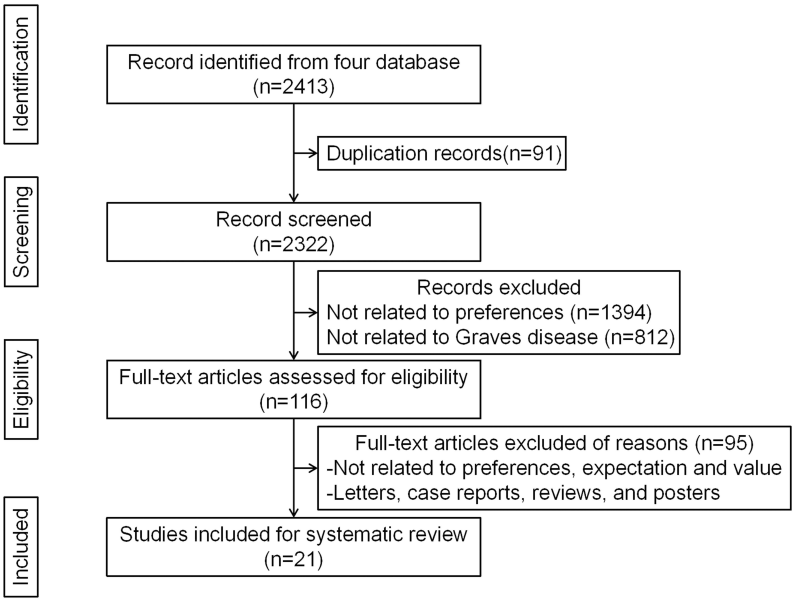

Figure 1 Flow diagram of the systematic literature review process. From an initial 2413 records identified from four databases, 91 duplicates were removed. The remaining 2322 records were screened, leading to the exclusion of 2206 records (1394 not related to preferences and 812 not related to Graves' disease). The remaining 116 full-text articles were assessed for eligibility, of which 95 were excluded for various reasons (not related to preferences, expectations, and values; or being letters, case reports, reviews, or posters). This resulted in a final selection of 21 studies included for the systematic review.

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Table 2 Characteristics of Included Studies and Summary of Results

No.	Author	Country	Date	Study design	Sample Size	Study Description	Preferences, Expectations, and Values	Score
1	Ljunggren et al[10]	Sweden	1998	Randomized Controlled Trial	174	Evaluated GD patients' perspectives on different treatment methods through questionnaires	Over 50% of patients were not concerned about adverse reactions associated with treatment	9
2	Terwee et al[11]	New Zealand	2003	Cross-sectional	237	Both physicians and patients assessed the degree of facial disfigurement in GO patients before and after different treatment methods via questionnaires	Key determinants of disfigurement were eyelid retraction, severe eyelid swelling, and proptosis	7
3	Grodski et al[12]	Australia	2007	Retrospective cohort study	63	Assessed perspectives and satisfaction of GD patients who underwent thyroidectomy through questionnaires	88% of patients who underwent thyroidectomy expressed high satisfaction with the surgery	10
4	Palestini et al[13]	Italy	2007	Retrospective cohort study	108	Investigated GD patients' perspectives on surgical treatment through questionnaires	89% of patients were satisfied with post-surgical outcomes	8
5	Estcourt et al[14]	United Kingdom	2008	Semi-structured interviews	25	Explored thyroid eye disease patients' perspectives on their condition through face-to-face interviews	Changes in appearance and capabilities caused by the disease altered patients' social identity	7
6	Jin et al[15]	United States	2012	Cross-sectional	634	Compared differences between medical and surgical treatment for GD patients based on a cross-sectional study	44% of patients who received surgical treatment selected this option based on personal preference	9
7	Karhanová et al[16]	Czech	2013	Cross-sectional	25	Evaluated patients' preferences for diplopia treatment options in GO through a cross-sectional study	The vast majority of patients preferred semi-transparent occlusion therapy during the active phase of GO	7
8	Brito et al[17]	United States	2015	Cross-sectional	68	Assessed GD patients' perspectives on an "encounter decision tool (GD Choice)" through questionnaires	The "encounter decision tool (GD Choice)" significantly improved patients' understanding of GD and their comfort level when selecting treatment strategies	9
9	Stathopoulos et al[18]	United Kingdom	2015	Retrospective study	59	Analyzed patient preferences through reviewing clinical data of GD patients	Patients' personal preferences dominated the decision-making process between surgical treatment and radioactive iodine therapy	7
10	Nexø et al[19]	Denmark	2015	Cross-sectional	16	Explored thyroid disease patients' perspectives through one-on-one qualitative interviews	Physical and mental hyperactivity leading to insufficient rest was the greatest challenge for hyperthyroidism patients	8
11	Purdy AC et al[20]	United States	2017	Retrospective Study	13	Evaluated website information readability and accuracy through a scoring system	Patients preferred accessing information on easily readable websites, despite the information not always being the most accurate	7

12	Hookham J et al[21]	United Kingdom	2017	Cross-sectional	214	Collected data on patients' concerns and reasons for choosing surgery or radioactive iodine for GD treatment using survey questionnaires	Patient satisfaction was higher with surgical treatment compared to radioactive iodine ablation	9
13	Mitchell AL et al[22]	United Kingdom	2017	Prospective study	160	Gathered patients' perspectives on alert cards distributed to GD patients	The majority of patients who provided feedback appreciated the initiative of distributing early warning cards	8
14	Wickwar S et al[23]	United Kingdom	2018	Semi-structured interviews	14	Explored GO patients' expectations regarding GO orbital decompression surgery through face-to-face interviews	Most participants considered the surgery worthwhile	7
15	Conaglen HM et al[8]	New Zealand	2018	Prospective study	123	Investigated reasons for treatment choices and satisfaction levels through survey questionnaires	The primary factors influencing treatment choices were impact on daily life and physician recommendations	9
16	Sukpanich R et al[24]	United States	2020	Prospective study	109	Developed and administered a questionnaire to identify key factors driving patients' preferences for thyroidectomy methods	Risk of recurrent laryngeal and mental nerve injury, hospital distance, and treatment cost were the most influential factors	9
17	Hamilton LOW et al[25]	United Kingdom	2020	Prospective Cohort study	54	Used the GBI scale to determine GD patients' opinions on total thyroidectomy	Most patients reported improved quality of life following total thyroidectomy	9
18	Asban A et al[26]	United States	2020	Retrospective Study	237	Collected information on reasons for hyperthyroidism patients undergoing total thyroidectomy	The primary reason for patients choosing surgical treatment was intolerance to antithyroid medications	7
19	Van Kinschot CMJ et al[27]	New Zealand	2021	Discrete choice experiment	286	Collected GD patients' treatment preferences through questionnaires	Remission rate was the factor of greatest concern to patients when making treatment choices	7
20	Hidalgo J et al[28]	United States	2022	Retrospective Study	55	Collected clinical information before and after GD patients received clinical decision support tools	Remission rate was the most important factor in GD treatment decision-making	7
21	Jansen HI et al[29]	New Zealand	2024	Cross-sectional	532	Collected data on GD patients' needs regarding the 'Graves recurrent event after therapy+' (GREAT+) score through online questionnaires	Most patients perceived Graves' disease as very serious	8

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that patients preferred accessing private websites with lower readability barriers, despite these sources having lower accuracy rates compared to academic, governmental, and nonprofit websites which offered more accurate information but presented higher barriers to comprehension.[20]

Patterns and Drivers of Treatment Preferences: Multidimensional Concerns and Heterogeneity in Patient Choices

Treatment preferences among GD patients vary considerably and are influenced by multiple factors. Ljunggren et al noted that over 92% of patients expressed satisfaction with their chosen treatment, although dissatisfaction events were more frequent in the surgical group compared to the medication group; notably, patients' primary concern regarding RAI treatment stemmed from fear of radioactive isotopes.[10] Grodski et al reported that one-third of patients opted for surgery as their definitive treatment despite the absence of specific indications,[12] while Jin et al identified economic factors as crucial determinants in patients' decisions between surgical versus medical treatment.[15] Decision-making tools such as "GD Choice" were found by Brito et al to effectively enhance patients' understanding and decision-making regarding GD treatment options.[17] According to Stathopoulos et al, patients typically preferred surgical intervention over RAI therapy after failed medical treatment, primarily due to radiophobia.[18]

Patient concerns regarding specific treatment modalities have been well-documented in the literature. Hookham et al discovered that common reasons for refusing surgery included concerns about general anesthesia, scarring, and voice changes, while RAI was often rejected due to risks of close contact restrictions and disease exacerbation; significantly, 92% of patients found physician discussions beneficial for decision-making.[21] Conaglen et al reported treatment distribution as: 64% receiving ATD, 11% RAI, and 25% surgery, with recovery time and impact on daily life being patients' primary concerns when making treatment decisions.[8] Age-related preferences were noted by Sukpanich et al, with patients ≤60 years more accepting of "TransOral Endoscopic Thyroidectomy - Vestibular Approach (TOETVA)", while those >60 years preferred traditional incisions.[24] Hamilton et al found that most patients could tolerate only minor post-surgical side effects such as weight gain and mood changes.[25]

Treatment selection patterns and long-term considerations also emerged as important themes. Asban et al observed that most patients initially preferred ATD treatment, considering surgery only after developing drug intolerance, resistance, or obstructive symptoms.[26] Van Kinschot et al determined that ATD remained patients' most preferred treatment option, with generally negative attitudes toward RAI compared to surgery.[27] Hidalgo et al noted patients' unwillingness to commit to long-term ATD therapy.[28] Finally, Jansen et al reported that the "Graves recurrent event after therapy+ (GREAT+)" score effectively predicted individual recurrence probability after ATD discontinuation, with 55% of patients choosing RAI or thyroidectomy when facing higher recurrence probabilities.[29]

Psychosocial Burden, Social Dysfunction and Multidimensional Interventions in Patients with GO

GO presents unique challenges that influence patient management approaches and outcomes. Estcourt et al suggested that non-face-to-face communication methods, such as internet and telephone consultations, might be more suitable for GO patients.[14] Terwee et al discovered that GD patients typically overestimated the severity of disfigurement caused by GO, with female patients expressing greater concern about appearance-related changes.[11] The psychosocial impact was highlighted by Estcourt et al, who noted that GO led to significant changes in patients' daily lives, resulting in social withdrawal.[14] Regarding management strategies, Karhanová et al recommended semi-transparent occlusion for patients during the active phase of GO and while awaiting surgery.[16] Mitchell et al found that distributing GO warning cards helped improve patients' understanding of the condition and increased GO diagnosis rates.[22] Post-surgical perspectives were examined by Wickwar et al, who reported that patients generally experienced improvements in appearance and health status following orbital decompression surgery, though dissatisfaction commonly stemmed from issues related to surgical care and rehabilitation processes.[23]

Discussion

GD is the most common cause of thyrotoxicosis, affecting approximately 3% of women and 0.5% of men over their lifetime.[30] Conventional treatment options of ATD, RAI, or thyroidectomy have remained largely unchanged for many years, although most patients relapse after a course of ATD or require lifelong thyroid hormone replacement therapy after RAI or surgery.[31] Each treatment approach has its limitations. ATDs are non-invasive and do not require surgery or radiation, but their disadvantages may be the need for long-term medication and possible side effects such as liver damage and neutropenia.[32] RAI has the advantage of being a one-time treatment, but its disadvantages are permanent hypothyroidism and the possibility of relapse after treatment.[33] Thyroidectomy can quickly and more completely relieve the disease, but there are risks such as lifelong hypothyroidism and nerve damage.[34] Understanding the preferences and treatment expectations of GD patients can help patients and clinicians make more personalized decisions and improve patient well-being and compliance.

This study included 21 articles, summarizing GD patients' views on the disease, their expectations for treatment, and their views and treatment preferences for GO. The results showed that most GD patients believed that the disease affected their normal lives, especially those with GO, and they were eager to get help. However, there are currently limited channels for obtaining popular science knowledge about graves, and there are problems such as high barriers to access and insufficient accuracy. Therefore, more accessible and understandable channels must be established through official outlets for the prevention and treatment of Graves' disease. These channels could include regular community education, science popularization websites, and early warning cards. Clinicians should also help patients cope with the psychological stress caused by the disease.

This study showed that most patients prefer ATD treatment due to fear of radioactive substances and surgery as well as economic factors. Although current studies have shown that ATD treatment is effective and safe, the adverse reactions and compliance issues of the drug are still not suitable for some Graves patients.[35] Therefore, clinicians can use predictive tools to improve risk assessment, identify patient preferences, strengthen communication with patients to clarify their core demands, and develop individualized treatment for each Graves patient.

Limitations

This study was a qualitative retrospective analysis, and some of the included literature was not precise enough about the preferences and expectations of GD patients. In addition, there was no precise and standardized information to quantify patients' preferences, expectations, and values. The methods used to review the literature and summarize the research results were somewhat empirical and subjective, which may lead to biased results.

Conclusion

This systematic review demonstrates that the disease significantly impairs quality of life and social functioning of GD patients, especially GO patients. Treatment choices are influenced by expected outcomes, personal circumstances, psychological concerns, and economic factors. ATD remains the preferred first-line treatment. However, individual preferences vary significantly, which emphasizes the importance of personalized approaches and decision aids. Additionally, establishing effective communication channels is crucial to helping GD patients better understand the indications and prognosis of RAI, and thyroidectomy, as well as for making shared decisions.

Disclosure

The authors report no conflicts of interest in this work.

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