Dietary Pattern Intervention in Autoimmune Thyroiditis: A Review and Individualized Treatment Strategies Postprint

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Abstract

Background Autoimmune thyroiditis (AIT) is the leading cause of thyroid dysfunction, severely impacting patients' quality of life. In recent years, dietary patterns have attracted considerable attention as a potential approach to modulate immunity and metabolism; however, systematic summaries of their clinical effectiveness and individualized application strategies are lacking.

Objective This study employs a scoping review methodology to systematically evaluate the effects of different dietary patterns on AIT and propose individualized treatment strategies, providing evidence-based support for clinical practice.

Methods Literature from databases including CNKI, PubMed, and Web of Science was searched from inception to March 1, 2025. Based on inclusion and exclusion criteria, 23 studies (including 12 randomized controlled trials) were included, covering nine dietary patterns such as gluten-free diet (GFD), Mediterranean diet (MD), and low-carbohydrate diet. Two researchers independently screened literature and extracted data, with graded recommendations formulated based on evidence quality and clinical applicability.

Results GFD and MD represent the two intervention modalities with the highest level of evidence support, applicable respectively to AIT patients with comorbid celiac disease and metabolic abnormalities (Grade B recommendation). Low-carbohydrate diet, anti-inflammatory diet, autoimmune protocol diet, among others, demonstrate potential benefits in specific populations, but the overall evidence grade is Level C or D. Individualized treatment strategies must integrate patients' immune status, metabolic characteristics, and dietary adherence to construct a dynamic individualized management pathway.

Conclusion Dietary intervention serves as an important adjunctive component in the comprehensive management of AIT. Due to their robust evidence

support, GFD and MD are recommended as preferred foundational intervention strategies, with precise application based on individual patient characteristics in clinical practice. Other dietary patterns may hold value in specific populations but lack high-quality research support. In practical application, comprehensive assessment of patients' immune status and metabolic characteristics is necessary to formulate individualized management strategies, thereby enhancing therapeutic efficacy and adherence.

Full Text

Application of Dietary Pattern Intervention in Autoimmune Thyroiditis: A Review and Individualized Treatment Strategies

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Abstract

Background: Autoimmune thyroiditis (AIT) is the leading cause of thyroid dysfunction, significantly affecting patients' quality of life. In recent years, dietary patterns have attracted considerable attention as potential pathways to regulate immunity and metabolism, but there is a lack of systematic summaries regarding their clinical effectiveness and individualized application strategies. **Objective:** This study employed a scoping review approach to systematically assess the impact of different dietary patterns on AIT and propose individualized treatment strategies, providing evidence-based guidance for clinical practice. **Methods:** Databases including CNKI, PubMed, and Web of Science were searched for relevant literature from their inception to March 2025. A total of 23 studies (including 12 randomized controlled trials) were included, covering nine dietary patterns such as gluten-free diet (GFD), Mediterranean diet (MD), and low-carbohydrate diet. Two researchers independently screened the literature and extracted data, and recommendations were made based on the quality of evidence and clinical applicability. **Results:** The GFD and the MD are the two interventions with the highest evidence support for AIT patients with coeliac

disease and metabolic abnormalities, respectively (Grade B recommendation). Low-carb diets, anti-inflammatory diets, and autoimmune protocol diets have shown potential benefits in specific populations, but the overall evidence grade is C or D. An individualized treatment strategy should consider the patient's immune status, metabolic characteristics, and dietary adherence, establishing a dynamic individualized management pathway. **Conclusion:** Dietary intervention plays an important complementary role in the comprehensive treatment of AIT. Given the robust evidence, GFD and MD are recommended as the primary basic intervention strategies, which should be precisely applied according to the individual characteristics of patients in clinical practice. Other dietary patterns may have value in specific populations but lack high-quality evidence support. In practical applications, it is essential to comprehensively evaluate the patient's immune status and metabolic characteristics to develop individualized management strategies, thereby enhancing therapeutic efficacy and adherence.

Key words: Thyroiditis, autoimmune; Caloric restriction; Diet; Dietary patterns; Scoping review; Therapeutic strategy

Introduction

Autoimmune thyroiditis (AIT) represents a category of thyroid autoimmune diseases mediated by abnormal immune system responses, primarily including Hashimoto's thyroiditis (HT) and Graves' disease (GD) subtypes[1]. Epidemiological data indicate that approximately 7.5% of the global population suffers from AIT[2], with Chinese adult thyroid autoantibody positivity rates reaching 14.19% overall, including anti-thyroid peroxidase antibody (TPOAb) positivity at 10.19% and anti-thyroid globulin antibody (TGAb) positivity at 9.7%[3]. AIT has become the leading cause of thyroid dysfunction. Current clinical treatments for AIT primarily focus on correcting thyroid function abnormalities[4]. Although levothyroxine (LT4) replacement therapy effectively normalizes biochemical thyroid function indicators, some patients continue to experience fatigue, cognitive dysfunction, and metabolic disorders even after biochemical normalization. This phenomenon suggests that hormone replacement alone cannot comprehensively block disease progression. Both the "Hashimoto's Thyroiditis Disease-Evidence-Based Diagnosis and Treatment Guidelines (2024)"[4] and the "Beijing Expert Consensus on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Hashimoto's Thyroiditis (2021, Beijing)"[5] explicitly identify dietary intervention as an important strategy in comprehensive AIT management, emphasizing the need to dynamically adjust intake of iodine, selenium, vitamin D, and other nutrients based on thyroid function status and individual metabolic characteristics, while avoiding allergens to delay disease progression and improve clinical outcomes. In recent years, dietary intervention as a non-pharmacological approach has garnered significant attention, with research suggesting it may influence AIT progression through immune modulation and metabolic pathways, though specific effects and applicability remain inconsistent. Taking gluten-free diet (GFD) as an example,

some studies demonstrate it can improve antibody levels and thyroid function, but efficacy is often influenced by factors such as comorbid celiac disease (CD), individual immune status, and vitamin D levels. Some research even indicates that long-term GFD implementation in non-celiac AIT populations may pose risks of micronutrient imbalance and gut microecological disruption. Therefore, this study employs a scoping review methodology[6] to systematically integrate the effects of different dietary patterns on AIT patients and propose individualized stratified recommendation strategies, addressing the current gap in detailed nutritional intervention guidelines and providing evidence-based support for clinical decision-making.

Methods

1.1 Research Question Formulation

Through literature review, the following questions were identified: (1) How do different dietary patterns affect thyroid function, antibody levels, and metabolic health in AIT patients? (2) Which dietary pattern is more suitable for different patient characteristics? (3) What are the limitations of existing studies, and how should future research be improved?

1.2 Search Strategy

A systematic search was conducted in Chinese databases (CNKI, Wanfang Data, Chinese Biomedical Literature) and international databases (Web of Science, PubMed, EMbase). The search strategy combined MeSH terms and free text with Boolean operators. Chinese search strategy: ("dietary intervention" OR "nutritional intervention" OR "gluten-free diet" OR "low-carbohydrate diet" OR "anti-inflammatory diet" OR "ketogenic diet" OR "Mediterranean diet") AND ("autoimmune thyroid disease" OR "Hashimoto's thyroiditis" OR "Graves' disease"). English search strategy: ("Dietary intervention" OR "Nutritional intervention" OR "Gluten-free diet" OR "Low-carbohydrate diet" OR "Anti-inflammatory diet" OR "Ketogenic diet" OR "Mediterranean diet") AND ("Autoimmune thyroid disease" OR "Hashimoto's thyroiditis" OR "Graves' disease"). The search timeframe covered database inception to March 1, 2025.

1.3 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Study subjects were diagnosed AIT patients; (2) Studies involved dietary intervention or dietary therapy and evaluated clinical effects on AIT patients; (3) Studies provided specific dietary intervention protocols and assessed impacts on thyroid function, immune markers, or quality of life; (4) Included study designs comprised randomized controlled trials (RCTs), non-randomized controlled trials, cohort studies, case-control studies, etc.; (5) Only studies investigating overall dietary patterns were included.

Exclusion criteria: (1) Studies on non-dietary interventions (e.g., medica-

tions, surgery); (2) Studies analyzing single nutrients or nutritional supplements; (3) Animal studies; (4) Studies with unavailable full text or incomplete data.

1.4 Literature Screening and Data Extraction

All literature screening was performed using NoteExpress 3.7 software for deduplication. The screening process was conducted independently by two researchers, first based on titles and abstracts to exclude non-compliant literature. Disagreements were resolved by a third researcher to finalize included studies. The following key information was extracted from included studies: basic study information, participant characteristics, intervention measures, research methods, outcome indicators, and mechanism exploration.

1.5 Risk of Bias Assessment

Scoping review is a knowledge synthesis methodology, and currently there are no strict requirements for the types and quality of included information. Furthermore, neither the scoping review framework by HILARY et al.[6] nor the 2018 PRISMA-ScR statement[9] explicitly mandates bias risk assessment. Therefore, this study did not conduct formal risk of bias assessment for included studies, but evaluated the quality of included literature to ensure reliability of findings.

Results

2.1 Literature Search Results

The initial search retrieved 846 articles: 70 from CNKI (Chinese and English), 105 from VIP database, 24 from Wanfang Data, 108 from Chinese Biomedical Literature Database, 447 from PubMed, and 92 from Web of Science. After software deduplication, 629 articles remained, and manual screening further reduced this to 469 articles. Title and abstract screening excluded 314 irrelevant studies, 47 animal experiments, 34 with inappropriate study types, and 7 conference abstracts, leaving 67 articles. Full-text review excluded 37 studies with incomplete interventions or mismatched objectives, 3 non-Chinese/English articles, 4 duplicate publications, and 2 articles with unavailable full text, resulting in 23 included studies (see Table 1).

2.2 Study Types and Geographic Distribution

This study included 23 articles: 12 RCTs[10-21], 3 cross-sectional studies[22-24], 3 pilot studies[25-27], 2 non-randomized controlled studies[28-29], 2 cohort studies[30-31], and 1 case-control study[32].

The geographic distribution showed significant bias, concentrated in high-income European and North American countries. Europe contributed 15 studies (8 from Poland, 4 from Italy), North America contributed 2 studies (both from the United States), while low- and middle-income countries contributed only 6 studies (4 from Asia, 1 from Africa), indicating relatively

insufficient research in dietary interventions in developing countries (see Table 1).

2.3 Researcher Characteristics

The 23 included studies comprised 1,450 AIT patients, with individual study sample sizes ranging from 17 to 180 (median: 62). Participants were predominantly female, aged 18-72 years with a mean age of (38.5$±$9.2) years, consistent with the epidemiological characteristic of AIT being more prevalent in women of reproductive age. Only 3 studies explicitly reported that patients had normal thyroid function; the remaining studies did not stratify by thyroid function status.

2.4 Intervention Methods and Outcome Measures

This study analyzed intervention effects of various dietary patterns. Primary intervention modalities included: nutrition education and personalized dietary planning (mostly provided by physicians or dietitians)[8], offline interventions (including dietary intake recording and regular follow-up), digital combined interventions (dietary monitoring and remote guidance via mobile health technology), and comprehensive lifestyle interventions[23] (combining diet with exercise and stress management). Intervention duration ranged from 3 weeks to 12 months. Primary outcome measures included: thyroid function, immune markers, metabolic indicators, inflammatory markers, oxidative stress indicators, quality of life, and mental health status[22,27].

Discussion

3.1 Gluten-Free Diet (Grade B Recommendation)

Gluten-free diet (GFD) is a dietary approach that excludes all gluten-containing foods. Gluten is a protein found in grains such as wheat, barley, and rye. In certain populations, particularly patients with celiac disease (CD) or gluten sensitivity, consumption of gluten triggers immune responses or intestinal damage. GFD primarily includes naturally gluten-free foods such as rice, corn, quinoa, potatoes, vegetables, fruits, meat, and fish, while avoiding processed foods and gluten-containing grains and their derivatives like bread, biscuits, and pasta. For patients with gluten-related disorders, such as CD and non-celiac gluten sensitivity, GFD is an essential therapeutic intervention.

3.1.1 Core Mechanism—Immune Modulation and Intestinal Repair

The efficacy of GFD is closely related to its modulation of immune responses and intestinal microecology. Gluten intake may activate thyroid autoimmunity through molecular mimicry. In genetically susceptible individuals, gluten proteins share epitope structures similar to thyroid peroxidase and other autoantigens, potentially triggering cross-immune reactions and elevating TPOAb

levels. In AIT patients with comorbid CD, GFD can significantly reduce anti-tissue TGAb levels, indirectly decreasing TPOAb cross-reactivity[36-39]. Additionally, ALEKSANDRA et al.[12] reported that after 8 weeks of GFD intervention, intestinal permeability markers decreased by 40% and Lactobacillus abundance increased 2.3-fold in AIT patients, suggesting GFD may indirectly improve thyroid autoimmunity by restoring intestinal barrier integrity and suppressing systemic inflammatory responses. However, GFD's impact on gut microbiota is double-edged: while beneficial bacteria like Lactobacillus increase, long-term GFD may reduce Firmicutes phylum, subsequently affecting trace element absorption such as selenium. This paradoxical effect requires careful consideration in clinical application.

3.1.2 High-Quality RCT Evidence Supporting GFD Efficacy in AIT Patients with Comorbid CD Existing RCTs have primarily focused on GFD efficacy in AIT patients with comorbid CD or metabolic abnormalities. SAARA et al.[30] conducted a prospective RCT including 62 AIT patients with CD, demonstrating that after 1 year of GFD intervention, thyroid volume decreased by 18.7%, TPOAb levels dropped by 32.5%, and intestinal symptoms improved significantly. However, in non-CD patients, no statistically significant differences were observed between GFD and control groups in thyroid volume or antibody levels, indicating strong population specificity of GFD efficacy. Another RCT by JAKUB et al.[13] further validated GFD's limitations, enrolling 89 AIT patients (including 24 with CD). While GFD enhanced LT4 absorption rate (serum LT4 levels increased by 15%), its direct effects on TSH, FT3, and FT4 were limited, suggesting its role concentrates more on immune regulation rather than direct thyroid function correction. These high-quality RCT results indicate that GFD clinical benefits should be strictly limited to AIT patients with comorbid CD or gluten sensitivity, and expanding indications blindly may increase treatment burden unnecessarily.

3.1.3 Combined Intervention Strategies for Synergistic Enhancement The limitations of single GFD necessitate exploration of combined nutritional intervention strategies. ROBERT et al.[25] conducted an RCT including 45 AIT patients with CD, showing that after 6 months of GFD combined with vitamin D (4,000 IU/d), TPOAb decreased by 41.2%, significantly higher than the 22.1% reduction in the GFD-only group, suggesting vitamin D may enhance GFD's antibody-suppressive effects through modulation of Th1/Th2 immune balance. Another randomized controlled study by MALGORZATA et al.[11] further confirmed the potential of combined strategies, integrating GFD with EPA/DHA supplementation (2 g/d). After 12 weeks of intervention, serum CRP levels decreased by 1.8 mg/L and anti-inflammatory cytokine IL-10 secretion increased by 35%, compared to only 0.6 mg/L reduction in the GFD-only group. These results indicate that synergistic effects of GFD and anti-inflammatory nutrients may suppress inflammatory responses through multiple pathways, though long-term efficacy and comprehensive impacts on thyroid function require validation

in larger RCTs.

3.1.4 Clinical Recommendations and Risk-Stratified Management Based on the aforementioned evidence, GFD clinical application requires precise stratification principles. For AIT patients with comorbid CD (Grade B recommendation), GFD is a fundamental therapeutic approach requiring strict gluten avoidance and regular monitoring of iron, zinc, and B-vitamin levels[28,40], with serum trace elements and TPOAb recommended for testing every 3 months. However, potential risks of GFD in non-CD patients cannot be ignored: ALEKSANDRA et al.[12] follow-up studies showed long-term GFD may reduce Firmicutes abundance by 50%, subsequently affecting selenium absorption (serum selenium levels decreased by 12%), and selenium deficiency may exacerbate thyroid oxidative stress. Therefore, for general AIT patients without CD, no high-quality RCT currently supports routine GFD application. Clinical decisions must comprehensively consider patient immune characteristics, nutritional status, and adherence to avoid over-intervention.

3.2 Mediterranean Diet (Grade B Recommendation)

The Mediterranean diet (MD) is a dietary pattern based on traditional eating habits of Mediterranean regions, emphasizing high consumption of vegetables, fruits, whole grains, nuts, legumes, and olive oil, with moderate intake of fish and seafood, and limited red meat and processed foods[41-42]. This dietary pattern is rich in monounsaturated fatty acids, antioxidants, fiber, and trace elements, conferring significant anti-inflammatory, antioxidant, and cardiovascular protective effects[43-44]. In recent years, MD has been extensively studied for its regulatory roles in metabolic syndrome, chronic inflammation, and autoimmune diseases, and has been gradually integrated into AIT nutritional intervention systems[20,21,24].

3.2.1 Core Mechanism—Metabolic Regulation and Immune Homeostasis MD's efficacy primarily stems from its multi-target regulation of metabolism and immune systems. First, the high proportion of monounsaturated fatty acids in MD can improve insulin sensitivity by activating the PPAR-γ pathway. FILIPPIS et al.[44] RCT demonstrated that after 12 weeks of MD intervention, fasting insulin levels decreased by 18.7% and HOMA-IR index reduced by 22.3% in AIT patients, an effect closely associated with a 2.1-fold increase in Roseburia abundance, a short-chain fatty acid-producing gut microbe. Second, abundant polyphenols in MD can reduce pro-inflammatory cytokine release by inhibiting the NF- B pathway. MARTINA et al.[19] RCT showed serum IL-6 levels decreased by 35% from baseline in the MD group, compared to only 12% in the GFD group, confirming MD's specific anti-inflammatory advantage. Additionally, adequate selenium, zinc, and other trace elements in MD directly support thyroid peroxidase function, optimizing the hormonal synthesis microenvironment.

3.2.2 High-Quality RCT Evidence Supporting Metabolic and Thyroid Benefits Multiple RCTs have validated stratified efficacy of MD in specific AIT populations. MANAL et al.[33] pilot RCT included 40 AIT patients with metabolic syndrome, showing that after 12 weeks of MD intervention, FT3 levels increased by 0.32 pg/mL (11.4% increase) and TPOAb decreased by 24.8%, suggesting MD may indirectly regulate function by improving thyroid hormone synthesis efficiency and antioxidant status. However, another RCT by WERONIKA et al.[21] (n=62) showed that although MD combined with physical activity significantly reduced BMI (-1.39 kg/m2) and waist circumference (-3.3 cm), no statistically significant changes were observed in TSH or antibody levels, indicating metabolic improvement and immune regulation may be decoupled. This paradox was further elucidated in ROSARIA et al.[24] study, where high-adherence MD (MedDiet score $ $9) reduced advanced glycation end-products (AGEs) by 28%, increased glutathione peroxidase (GPx) activity by 41%, and improved thyroid ultrasound echo uniformity by 2.17-fold compared to controls, suggesting MD's antioxidant effects may indirectly protect thyroid function by reducing tissue oxidative damage rather than directly suppressing autoantibodies.

3.2.3 Combined Lifestyle Intervention for Synergistic Effects Combined strategies of MD with exercise and nutritional supplementation can further amplify clinical benefits. MUTLU et al.[20] RCT combined MD with 150 minutes of moderate-intensity exercise weekly, and after 3 months of intervention, AIT patients' visceral fat area decreased by 12.5% and FT4 levels increased by 9.2%, compared to only 3.8% increase in the MD-only group, suggesting exercise may enhance metabolic efficiency by promoting peripheral T4-to-T3 conversion. Subgroup analysis by MARTINA et al.[19] demonstrated that MD combined with selenium supplementation (200 g/d) increased TPOAb reduction from 18.4% in the MD-only group to 29.7%, with GPx activity further increasing by 23%, highlighting the synergistic antioxidant potential of selenium with MD polyphenols.

3.2.4 Clinical Recommendations and Risk-Stratified Management Based on current evidence, MD clinical application must balance efficacy with regional feasibility. For AIT patients with metabolic syndrome (BMI $ $25 kg/m2 or waist circumference $ 90$cminmen/$ $80 cm in women) or high oxidative stress (AGEs $ 12U/mL), $MDisrecommendedasthepreferreddietarypattern(GradeB)$, $withadaptedversionstoaccon$ $richseafoodsuchasseaweedandnori$[45−46].$Duringimplementation$, $MedDietadherencescoreshouldbeassess$ considered adequate), with monitoring of thyroid function, inflammatory markers, and body composition changes. Notably, MD's antibody-suppressive effects are weaker in non-obese AIT patients; for this population, immune-targeted interventions should be prioritized over dietary adjustments alone.

3.3 Other Dietary Patterns with Insufficient Evidence (Grade C/D Recommendation)

Although multiple dietary patterns have been applied in AIT auxiliary intervention research in recent years, such as low-carbohydrate diet (LCD), anti-inflammatory diet (AID), lactose-free diet (LFD), low-calorie diet (CAL), autoimmune protocol diet (AIP), low-iodine diet (LID), and qualitative diets, these patterns generally suffer from small sample sizes, non-rigorous study designs, and short intervention durations. Most studies are observational or pilot studies, lacking multi-center, long-term RCT support, making systematic evaluation of their stability and broad applicability in AIT management difficult. Therefore, current evidence levels are low (Grade C or D), and caution is advised before incorporating them into routine clinical pathways.

3.3.1 Low-Carbohydrate Diet (Grade C Recommendation) Low-carbohydrate diet (LCD) typically restricts daily carbohydrate intake to less than 50 g to promote fat metabolism, improve insulin sensitivity, and control body weight, offering theoretical advantages in AIT patients with metabolic syndrome. Some small-sample studies suggest LCD can reduce BMI, HOMA-IR index, and CRP levels, but its direct effects on thyroid function and antibody levels remain unclear[16]. Additionally, carbohydrate restriction may suppress T3 production, inducing "low T3 syndrome," and long-term implementation may interfere with thyroid hormone synthesis and the hypothalamic-pituitary-thyroid axis. As existing studies are mostly observational or short-term interventions lacking systematic evaluation of specific immune indicators such as TPOAb and TGAb, LCD is currently not recommended as routine intervention. Its application should be limited to short-term metabolic remodeling stages in individuals with severe metabolic abnormalities, under dietitian guidance, with close monitoring of thyroid function and energy metabolism.

3.3.2 Anti-Inflammatory Diet (Grade C Recommendation) Anti-inflammatory diet (AID) emphasizes consumption of natural foods rich in n-3 fatty acids, polyphenols, and vitamins C and E, while limiting high-sugar, high-fat processed foods to reduce systemic inflammation. Theoretically, it may indirectly intervene in AIT immune activation by suppressing pro-inflammatory cytokine release through modulation of NF- B and NLRP3 inflammatory pathways[23]. However, research on AID in AIT populations is extremely limited, with only a few small-sample pilot studies showing mild improvement trends in TPOAb levels and fatigue scores, and no high-quality RCTs support its long-term efficacy[32]. It may serve as an auxiliary adjustment principle in clinical practice but is not recommended as routine intervention.

3.3.3 Lactose-Free Diet (Grade C Recommendation) Lactose-free diet (LFD) avoids lactose intake to alleviate intestinal intolerance-related symptoms, theoretically improving gut-immune axis dysfunction. Some AIT patients with

comorbid lactose intolerance frequently report bloating, diarrhea, and other symptoms, and LFD can improve quality of life and intestinal barrier function to some extent. Individual retrospective studies suggest LFD may indirectly influence thyroid immune responses by reducing intestinal inflammatory load, but relevant data rely heavily on subjective symptom scales and lack objective measurements of antibody levels or hormonal indicators[29,31]. Notably, long-term LFD may affect nutrient intake such as calcium and vitamin D, increasing bone metabolism risks, particularly requiring careful assessment in hypothyroid populations. Therefore, LFD is mainly applicable to AIT patients with comorbid lactose intolerance or IBS symptoms, serving as an auxiliary measure for intestinal symptom management rather than core intervention for thyroid immunity.

3.3.4 Low-Calorie Diet (Grade C Recommendation) Low-calorie diet (CAL) typically restricts daily energy intake to 1000-1500 kcal, aiming for rapid weight control and improved insulin sensitivity. In obese AIT patients or those with prominent metabolic abnormalities, CAL can reduce body weight, BMI, and fasting insulin levels, thereby alleviating chronic low-grade inflammation. However, existing studies have focused primarily on metabolic parameter improvement, lacking systematic observation of thyroid function or antibody levels. Excessive calorie restriction may also lead to insufficient protein intake and nutrient deficiencies, subsequently affecting thyroid hormone synthesis and immune regulation, and even inducing reactive changes such as elevated TSH or decreased FT3[17]. Therefore, CAL is only recommended for obese AIT patients, requiring combined nutrient fortification and professional monitoring, and is not suitable for promotion as a long-term foundational intervention model.

3.3.5 Autoimmune Protocol Diet (Grade D Recommendation) Autoimmune Protocol diet (AIP) is an enhanced elimination diet based on the Paleo diet, removing all potentially immune-triggering foods including grains, dairy, legumes, etc., theoretically reducing immune activation through a "food antigen removal" mechanism[27]. AIP has preliminary evidence in autoimmune diseases such as inflammatory bowel disease and rheumatoid arthritis, but research in AIT populations is extremely limited. Only a handful of case series reports suggest possible improvements in autoantibody levels and fatigue scores, yet none employed controlled designs or randomization[22]. This diet involves numerous restrictions, is difficult to implement, and easily leads to insufficient protein and micronutrient intake, raising concerns about long-term adherence and nutritional safety. AIP is currently not recommended as a routine dietary plan for AIT patients, except in special populations with identified food triggers, and only for short-term trials after individualized assessment by professional dietitians.

3.3.6 Low-Iodine Diet (Grade D Recommendation) Low-iodine diet (LID) is typically used before radioactive iodine therapy to reduce intrathyroidal

iodine stores and enhance iodine-131 uptake efficiency. Its core mechanism is not targeted at autoimmune regulation but rather treatment strategy optimization[47]. In AIT patients with comorbid hyperthyroidism, Graves' disease, or toxic nodules requiring radioactive iodine therapy, short-term LID application can improve therapeutic efficacy[18]. However, in most AIT patients, particularly those presenting with hypothyroidism, long-term low iodine intake may suppress thyroid hormone synthesis, worsen hypothyroid symptoms, or induce elevated TSH. In most regions of China, residents have transitioned from iodine deficiency to adequate or mildly excessive iodine status[3], making LID unfounded as routine dietary intervention and potentially causing adverse consequences. Therefore, LID is only recommended for short-term use by endocrinology specialists in specific therapeutic contexts, and is not applicable to daily management pathways for AIT.

3.3.7 Qualitative Diet (Grade D Recommendation) Qualitative diet is a personalized elimination protocol based on individual food sensitivity, microecological status, or IgG antibody test results, predicated on the assumption that "specific foods activate the immune system, triggering autoimmunity." Although this concept is widely referenced in functional medicine, no high-quality RCTs have confirmed that IgG food antibody levels directly correlate with AIT progression. Related studies are mostly retrospective or self-reported interventions with substantial subjective bias, making it difficult to establish clear causal relationships[14]. Furthermore, qualitative diet development lacks standardized protocols, with significant variations in testing methods, poor reproducibility, and inconsistent clinical interpretations, easily leading to unnecessary broad eliminations and nutritional structure disruption. Currently, routine implementation of such interventions in AIT patients is not recommended; indications must be strictly controlled, and it should only serve as an exploratory auxiliary tool for patients with dietary tolerance disorders.

Mechanisms and Individualized Strategies

4.1 Potential Mechanisms Underlying Variable Efficacy of Dietary Interventions

Although numerous studies demonstrate the potential of dietary interventions in improving AIT, results across different studies exhibit considerable heterogeneity. These variations may stem from multiple factors, including individual characteristics such as immune status, metabolic health, and dietary adherence, as well as study design differences like RCT blinding and control group settings. Individual physiological differences may be key to differential efficacy. In-depth analysis of these mechanistic variations helps better understand effects of different dietary patterns, specifically including: (1) Individual differences in immune modulation: The core pathological mechanism of AIT is thyroid-specific autoimmune response, and dietary patterns influence AIT progression by modulating immune responses and inflammation levels. GFD significantly reduces

TPOAb in CD patients by alleviating intestinal inflammation, but has limited effects in non-sensitive patients. MD and AID primarily reduce systemic inflammation through antioxidant effects but fail to significantly modulate thyroid immunity, resulting in weaker TPOAb improvement. (2) Double-edged sword effects of metabolic modulation: Dietary interventions indirectly affect immune responses by improving metabolic health. LCD enhances insulin sensitivity to reduce metabolic burden, but long-term carbohydrate restriction may inhibit T4-to-T3 conversion, subsequently affecting thyroid function. This explains why LCD can reduce TPOAb in obese patients while potentially elevating TSH levels in euthyroid individuals. (3) Regulatory role of gut microbiota: Different dietary patterns influence AIT treatment efficacy by modulating gut microbiota. GFD reduces immune activation by decreasing pro-inflammatory bacteria such as Prevotella, but shows limited effects in Firmicutes-dominated patients; MD helps increase beneficial bacteria like Lactobacillus and improve intestinal barrier function, but its effects vary across different patient populations. These mechanistic differences provide possible biological explanations for inconsistent dietary intervention effects and emphasize the importance of individualized therapy in AIT management.

4.2 Individualized Recommendation Strategies

This review included nine dietary patterns, with related studies demonstrating diverse intervention mechanisms and pathways. However, evidence levels vary considerably across dietary protocols, with inconsistent research quality and clinical applicability. Comprehensive literature analysis indicates GFD and MD are currently the most evidence-supported interventions, with numerous RCTs and prospective follow-up data supporting their relatively well-defined mechanisms. In contrast, dietary patterns such as LCD, AID, and AIP, while showing potential value in some studies, are limited by small sample sizes, non-rigorous study designs, and short intervention periods, with evidence grades mostly at C or D levels. To enhance clinical guidance value, this article categorized dietary patterns into three recommendation levels based on existing evidence and clinical adaptability, integrating a four-step management framework of "assessment-decision-intervention-monitoring" to provide systematic, dynamically adjustable clinical decision support tailored to patients' immune, metabolic, and gut microecological characteristics, as shown in Figure 2 [Figure 2: see original paper].

First-level recommendation: Grade B, sufficient evidence. For high-risk populations with clear benefits, the following dietary patterns are recommended: GFD is suitable for AIT patients with comorbid CD; these patients should strictly avoid wheat, barley, rye, and their products, with regular monitoring of iron, zinc, vitamin B12, and other nutrients to prevent deficiencies. MD is suitable for AIT patients with BMI $ $25 kg/m2 or insulin resistance; patients are advised to increase intake of olive oil, deep-sea fish, and whole grains, with Asian populations able to substitute tea oil, algae, and brown rice.

Second-level recommendation: Grade C, evidence insufficient, long-term safety requiring validation. LCD is suitable for AIT patients requiring weight control. LFD is suitable for AIT patients with lactose intolerance and TSH>4.0 mIU/L; patients may choose lactose-free dairy products or calcium-fortified plant-based milk, with regular bone density monitoring. AID is suitable for AIT patients with high inflammatory status (CRP $ $3 mg/L or IL-6 $ $5 pg/mL), with concurrent avoidance of processed meats, refined sugars, and trans fats, and selenium yeast supplementation to enhance antioxidant capacity.

Third-level recommendation: Grade D, weak evidence, suitable for experimental interventions or specific patient populations. AIP is suitable for AIT patients unresponsive to conventional interventions with multiple food sensitivities ($ $3 IgG antibody positives), but long-term use may cause TPOAb rebound due to nutritional imbalance; phased implementation with gradual food reintroduction is recommended, with strict monitoring of symptoms and nutritional status. LID is suitable for AIT patients with excessive iodine intake, not applicable in iodine-sufficient or deficient regions; patients should avoid high-iodine foods, combined with urinary iodine monitoring and regular thyroid function assessment to ensure therapeutic efficacy. Qualitative diet may improve quality of life, but its direct effects on thyroid function or antibody levels remain unclear and is still in the exploratory stage; patients should increase intake of fresh vegetables, fruits, whole grains, and plant-based foods while reducing refined processed foods, sugar, and trans fats.

4.2.1 Multi-Dimensional Assessment Dietary intervention selection should be based on individualized patient assessment, focusing on evaluating thyroid function, metabolic status, dietary habits, intestinal health, and other factors. Through modified thyroid-specific quality of life questionnaires[48] combined with precise assessments like food sensitivity IgG antibody analysis, clinicians can understand patients' immune and metabolic characteristics, thereby providing a basis for subsequent dietary pattern selection.

4.2.2 Precision Dietary Pattern Recommendations The selection of dietary patterns should be guided by evidence levels and patient characteristics. Since current evidence for all dietary patterns has not reached Grade A recommendation standards, this framework focuses primarily on Grade B, C, and D recommendations. The decision path directs patients to different intervention pathways based on dietary pattern recommendations and adaptability.

4.2.3 Intervention and Monitoring Dietary pattern intervention and monitoring are crucial in AIT patient management, and developing systematic intervention pathways helps ensure effectiveness and optimize long-term management. First, intervention implementation requires close multidisciplinary team collaboration to ensure scientific validity and feasibility. Endocrinologists monitor thyroid function, immune indicators, and metabolic status; dietitians

develop dietary plans based on individual needs; gastroenterologists assess intestinal health and food intolerance; and mental health management aims to improve patient adherence and quality of life. Second, intelligent monitoring and data-driven personalized adjustments are key to enhancing intervention effectiveness. Through intelligent health management platforms, patients can record dietary intake, weight changes, and symptom scores, which clinicians and dietitians analyze regularly to adjust intervention strategies based on biomarkers. For patients with poor adherence or unclear intervention effects, management can be optimized through intensive follow-up, personalized nutrition education, and behavioral interventions. Additionally, combining short-term monitoring with long-term follow-up helps ensure sustained intervention effectiveness. During the initial intervention phase, re-evaluation every 4-8 weeks is recommended to monitor dietary adherence and biochemical indicators, with corresponding adjustments. For dietary patterns requiring longer timeframes for effect, at least 12 weeks of follow-up is necessary. In the long-term follow-up phase, comprehensive assessment of thyroid function and metabolic indicators is recommended every 3-6 months, with further optimization of intervention protocols using intelligent tools.

4.3 From Research to Clinical Practice

4.3.1 Challenges in Promoting Current Research Current research results on different dietary patterns remain controversial. Some studies show GFD can reduce TPOAb, but not all patients benefit. MD is noted for anti-inflammatory effects, but its target population is not clearly defined, while LCD may affect thyroid hormone conversion with uncertain long-term safety. Additionally, long-term dietary adherence among AIT patients is low, with strictly restrictive diets being particularly difficult to maintain long-term. When promoting dietary interventions for AIT, how to optimize protocols for different populations and improve adherence are core issues currently faced.

4.3.2 Regional Challenges in Clinical Translation Genetic backgrounds, iodine intake levels, and dietary structures across different regions also affect the applicability of dietary interventions. In China, the salt iodization policy has led to chronic high iodine intake in some populations, while the role of LID in AIT patients has not been adequately validated. Additionally, the Chinese diet is carbohydrate-centric, limiting GFD implementation and questioning LCD applicability. Compared to Western dietary structures, Chinese residents' fat intake primarily comes from vegetable oils, with relatively low fish and nut consumption, affecting MD's actual intervention efficacy. Global research results cannot be directly applied to Chinese patients and require adaptation based on local population characteristics.

4.3.3 Adaptive Optimization and Future Promotion Strategies For different regional realities, AIT dietary intervention promotion should prioritize individualized management and feasibility. In northern China where wheat is

staple, GFD adherence is low, while LCD may be more promotable. In southern coastal populations with high seafood intake, LID feasibility is low, but MD may be more adaptable. Additionally, iodine nutrition assessment should be strengthened in AIT patients, exploring long-term safety of LID in high-iodine regions. Improving feasibility and adherence of dietary interventions is also a future promotion priority; clinically, AI can be integrated to track dietary intake and improve patient persistence with intervention protocols. Simultaneously, more flexible dietary protocols should be explored, such as simplified AIP or phased LCD, to balance efficacy and adherence. Finally, multi-center clinical pathway pilot studies are needed to evaluate the applicability of individualized recommendation protocols across different patient populations, prioritizing large-sample, multi-center, long-term follow-up intervention trials for Mediterranean and gluten-free diets to further clarify optimal implementation pathways, combined nutrition protocols, and individualized target populations, ensuring dietary intervention pathways can be effectively translated into clinical practice and further promoting the dissemination and application of AIT dietary interventions.

Future Directions

5.1 Current Research Limitations

Although existing research suggests dietary interventions have potential benefits for AIT patients, current studies still have numerous limitations, mainly reflected in: (1) Short follow-up duration with questionable long-term efficacy and safety. Most studies have intervention periods of only 6-12 months, lacking long-term data to assess sustained dietary impact on AIT disease course, and research has primarily focused on biochemical indicators without ultrasound follow-up of thyroid tissue changes, making it difficult to determine whether diets alter natural disease progression. (2) Study design biases and inadequate control of key variables. RCT sample sizes are generally small with limited statistical power, and studies are concentrated in European and American countries, with significant differences in dietary patterns and genetic backgrounds in Asian, African, and other regions, limiting generalizability of findings. Additionally, factors such as iodine intake, BMI, insulin resistance, and LT4 use may all affect dietary intervention efficacy, but most studies have not conducted systematic stratified analyses. (3) Insufficient research on combined dietary interventions. Nutrients such as selenium and vitamin D may reduce TPOAb levels, but their synergistic effects with different dietary patterns remain unclear, limiting development of precise intervention strategies. (4) Unclear mechanisms of dietary effects on immune regulation and gut microbiota. The core mechanism of AIT involves immune abnormalities, and diets may influence immune tolerance by modulating gut microbiota; current research has focused primarily on biochemical indicators, lacking in-depth exploration of the gut microbiota-immune axis, affecting scientific explanatory power of dietary interventions. (5) Heterogeneity of study results limits clinical promotion. Intervention results across different

dietary patterns remain controversial, and some stricter dietary patterns with numerous restrictions have low adherence, making them difficult to promote as long-term management protocols.

5.2 Future Research Directions

Addressing these limitations, future research should focus on: (1) Strengthening long-term follow-up to clarify sustained dietary efficacy. Future prospective multi-center RCTs with $ $24 months duration should be conducted, focusing on evaluating long-term effects of different dietary patterns on AIT antibodies, thyroid function, metabolic health, and clinical symptoms. Additionally, high-resolution thyroid ultrasound is recommended to monitor whether dietary interventions affect thyroid volume changes, echo characteristics, and fibrosis degree to clarify their role in disease progression. (2) Optimizing RCT design to improve applicability and scientific rigor. Sample sizes $ $300 are recommended, with multi-center, multi-ethnic cohort studies to enhance result generalizability. Strict control of confounding factors is needed, particularly stratified analysis of iodine intake, BMI, insulin resistance, and LT4 use to reduce potential interference. (3) Exploring combined dietary and medication/nutrient therapeutic models. Future studies should conduct dietary+LT4+selenium/vitamin D combination RCTs with pharmacokinetic studies combined with TSH and FT4 monitoring to clarify effects of different combinations on AIT antibody levels, thyroid function, and metabolic health. (4) In-depth exploration of dietary effects on immune regulation and gut microbiota. Using 16S rRNA sequencing plus short-chain fatty acid analysis to study how different diets affect gut microbiota composition and metabolites, and evaluating whether specific microbiota can serve as biomarkers for predicting efficacy. Future research should prioritize establishing precise, feasible individualized dietary management protocols to optimize comprehensive AIT treatment strategies. Integration of high-quality clinical trials and basic research will help improve treatment efficacy and quality of life for AIT patients and provide solid evidence-based medical evidence for personalized medicine application in AIT management.

Dietary intervention is an important strategy in comprehensive AIT management. This article systematically reviewed research evidence and applicable populations for nine dietary patterns in AIT patients. Comprehensive analysis indicates GFD and MD are currently the two most research-supported interventions, suitable for patient groups with comorbid CD or metabolic abnormalities, respectively, with clear mechanisms and relatively high adherence, recommended as priority foundational intervention strategies. In contrast, LCD, AID, and others, due to lower evidence grades, are currently not recommended for routine use and are suitable as individualized supplementary interventions in specific populations. To enhance practicality and continuity of dietary interventions, clinical application should integrate dynamic management concepts of "assessment-decision-intervention-monitoring" to implement individualized nutrition pathways based on patients' immune, metabolic, and nutritional char-

acteristics. Future research should prioritize multi-center, long-term follow-up trials of high-grade dietary patterns and explore synergistic applications with nutrient supplementation, behavioral interventions, and digital management tools to promote standardized implementation of dietary interventions in precision AIT management.

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Note: Figure translations are in progress. See original paper for figures.