



A Korean Clinical Practice Framework for Thyroid Eye Disease: Integrating International Recommendations with Survey-Informed Consensus

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Thyroid eye disease (TED), the most common extrathyroidal manifestation of Graves' disease, requires individualized management that integrates medical, radiotherapeutic, and surgical interventions. In this article, we present a society-endorsed, survey-informed Korean clinical practice framework, including consensus elements, for TED management. This framework integrates the 2022 American Thyroid Association/European Thyroid Association consensus, the 2021 European Group on Graves' Orbitopathy (EUGOGO) guideline, and contemporary Korean specialist practice patterns. A 2025 nationwide survey of 32 members of the Korean Society of Ophthalmic Plastic and Reconstructive Surgery characterized current Korean practice patterns in TED management. Korean oculoplastic surgeons showed high adherence to international recommendations, with 87.5% using both the clinical activity score and EUGOGO severity classification and 96.9% administering intravenous glucocorticoid therapy according to EUGOGO protocols. Distinctive features of Korean practice included frequent use of orbital radiotherapy (90.6%) and regional triamcinolone injections (81.2%) in selected clinical settings. For dysthyroid optic neuropathy, 59.4% of respondents reported using combined intravenous glucocorticoid therapy and orbital radiotherapy as the initial treatment approach. This framework stratifies treatment according to disease activity, severity, and predominant clinical phenotype to support context-adapted therapeutic decision-making. As emerging therapies such as teprotumumab become more accessible, this Korean clinical practice framework may provide practical guidance tailored to local clinical practice and healthcare-system constraints.

Keywords: Graves ophthalmopathy; Thyroid eye disease; Autoimmune diseases; Glucocorticoids; Orbital radiotherapy; Immunosuppressive agents

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INTRODUCTION

Epidemiology of thyroid eye disease

Thyroid eye disease (TED), also referred to as Graves' orbitopathy, is a major extrathyroidal manifestation of autoimmune thyroid disease and is associated with substantial morbidity and impaired quality of life. In Western populations, Bartley et al. [1] evaluated the incidence of TED in Olmsted County, Minnesota, and reported age-adjusted annual incidence rates of 16.0 per 100,000 in women and 2.9 per 100,000 in men. More recent Danish registry data showed a lower mean annual incidence of 5.0 per 100,000 persons, including 8.0 per 100,000 women and 1.9 per 100,000 men [2].

In East Asian populations, Japanese studies have reported an incidence of 7.3–11.1 per 100,000 person-years [3], and a large multicenter Korean cross-sectional study of 1,632 patients with dysthyroid disease reported a 17.3% prevalence of TED. In that study, female sex, younger age, Graves' disease, dermopathy, and prior antithyroid or radioiodine therapy were identified as independent risk factors [4]. Regarding ethnic variation, Lim et al. [5] observed no significant difference in TED prevalence among major Asian ethnic groups (Malays, 35.1%; Chinese, 34%; Indians, 40%; $P=0.928$). In contrast, Tellez et al. [6] reported a markedly higher prevalence of TED among individuals of European ancestry than among Asian populations (42% vs. 7.7%, $P=0.0002$). Collectively, these findings indicate that although TED occurs worldwide, genetic, environmental, and lifestyle factors may contribute to meaningful differences in disease incidence and clinical phenotype across populations.

Although direct comparative data on TED phenotypes across ethnic groups remain limited, several distinctive features have been identified in Korean populations. Unlike Western cohorts, Korean patients often exhibit a “low-CAS but progressive” phenotype, characterized by ongoing remodeling despite minimal overt inflammation. In addition, regional nutritional status substantially influences treatment responsiveness; for example, the absence of a clear benefit from selenium in Korea contrasts with findings from Europe, possibly because of higher baseline dietary intake. These regional characteristics, together with broad access to orbital imaging, support the development of a tailored management framework that integrates international standards with Korean clinical realities.

Classification of TED severity

TED severity should be stratified according to a classification system adapted from the European Group on Graves' Orbitopa-

thy (EUGOGO) guidelines [7,8]. Mild TED is characterized by the absence of sight-threatening features and minimal impact on quality of life and may include lid retraction (<2 mm), mild proptosis (<3 mm), minimal soft-tissue involvement, and either no diplopia or only intermittent diplopia.

Moderate-to-severe TED is characterized by at least two of the following features: moderate-to-severe soft-tissue inflammation, lid retraction (≥ 2 mm), exophthalmos (≥ 3 mm), and inconstant or constant diplopia. This category typically warrants immunosuppressive therapy.

Sight-threatening TED includes severe exposure keratopathy with corneal breakdown or dysthyroid optic neuropathy (DON). DON is caused by enlarged extraocular muscles within the confines of the bony orbit, resulting in deterioration of visual acuity and visual fields and creating an imminent risk of irreversible vision loss.

In Korean clinical practice, this EUGOGO-based severity classification has been widely adopted. In a nationwide survey of Korean Society of Ophthalmic Plastic and Reconstructive Surgery (KSOPRS) subspecialists, 87.5% of respondents reported routinely incorporating this stratification system into their clinical assessment of TED severity [9].

Assessment of disease activity

The clinical activity score (CAS) is the most widely used standardized measure of inflammatory activity in TED. It is based on seven clinical features: spontaneous retrobulbar pain, pain on eye movement, eyelid erythema, conjunctival redness, eyelid swelling, chemosis, and inflammation of the caruncle or plica [10]. A CAS of $\geq 3/7$ is generally considered indicative of active disease and is commonly used to guide decisions regarding immunosuppressive therapy.

According to a survey of KSOPRS subspecialists, 87.5% of Korean oculoplastic surgeons reported using CAS as their primary indicator of disease activity in clinical practice. However, reliance on CAS alone has important limitations, particularly in Asian populations with TED. Studies from Korean and Hong Kong cohorts have shown that many patients exhibit progressive myopathic or fibrotic disease phenotypes despite low CAS values (<3), reflecting relatively limited overt orbital congestion despite ongoing inflammatory remodeling [10,11].

These “low-CAS but progressive” presentations indicate that inflammatory activity and disease progression do not always correlate closely with CAS in Asian patients. Accordingly, comprehensive assessment of disease activity in these populations should integrate CAS with additional parameters, including

changes in ocular motility, thyrotropin receptor antibody (TRAb) levels, and orbital imaging findings, to reduce the risk of under-treatment.

Inactive TED represents a fibrotic phase characterized by stable signs and symptoms, in which residual congestion is driven primarily by chronic tissue remodeling rather than active inflammation. During this stage, rehabilitative surgical interventions may be considered to restore function and address residual deformities. Surgical management is typically staged, beginning with orbital decompression to correct disfiguring or functionally significant proptosis, followed by strabismus surgery once ocular alignment has stabilized, and then eyelid surgery to correct lid retraction and improve corneal protection and cosmesis. Optimal outcomes depend on appropriate timing, and surgery is generally deferred until disease inactivity has been maintained for at least 6 months. Notably, recent evidence indicates that elevated preoperative TRAb levels are independently associated with postoperative recurrence of proptosis after rehabilitative orbital decompression, highlighting the prognostic importance of residual immunologic activity [12].

DEVELOPMENT OF THE KOREAN CLINICAL PRACTICE FRAMEWORK

To provide a standardized clinical framework for TED management in Korea, KSOPRS established a dedicated committee to develop this guidance document. The development process integrated international consensus recommendations, including the 2021 EUGOGO guideline and the 2022 American Thyroid Association (ATA)/European Thyroid Association (ETA) consensus, with contemporary Korean practice patterns characterized through a previously published, nationwide, anonymized online survey [9].

The survey instrument was developed by the committee members and formally reviewed by the KSOPRS board to ensure clinical relevance. Among 226 registered members, 60 active oculoplastic surgeons specializing in TED management were identified as the primary target group, and 32 specialists responded (response rate, 53.3%). Most respondents (68.8%) practiced at tertiary centers and had extensive clinical experience, with 40.6% reporting more than 20 years in practice. Because TED care in Korea is concentrated among a relatively small number of subspecialists, predominantly at tertiary referral centers, the predefined target population was intentionally restricted to oculoplastic surgeons actively involved in TED management. The questionnaire comprehensively assessed diagnos-

tic tools, therapeutic preferences at each disease stage, and perspectives on emerging therapies. Although the survey provides a useful snapshot of contemporary TED care among Korean subspecialists, its findings are best interpreted as reported specialist practice patterns rather than as nationally representative data across all ophthalmic practice settings or as evidence of treatment superiority. Based on the integration of global evidence and these local practice patterns, the final manuscript and treatment algorithms received formal endorsement and official approval from the KSOPRS board. Accordingly, this manuscript should be interpreted not as a formal evidence-graded guideline but as a society-endorsed, survey-informed clinical practice framework with consensus elements for TED management within the Korean healthcare system.

ENDOCRINE CONTEXT OF THERAPEUTIC DECISION-MAKING IN TED

TED is an extrathyroidal manifestation of thyroid autoimmunity in which systemic endocrine factors directly influence orbital disease activity and therapeutic decision-making. TRAbs contribute to orbital fibroblast activation through the thyrotropin receptor (TSHR)–insulin-like growth factor-1 receptor (IGF-1R) signaling complex, supporting their role not only in diagnosis but also in risk stratification, assessment of treatment response, and evaluation of residual immunologic activity [12–14]. Likewise, unstable thyroid function and radioactive iodine (RAI) exposure may exacerbate orbital inflammation, making the maintenance of euthyroidism and careful selection of steroid prophylaxis important components of TED management [14–17]. In addition, dyslipidemia appears to be associated with orbital inflammatory activity and may represent a modifiable factor relevant to disease risk and severity [18–22]. Taken together, these considerations support an endocrine-informed treatment approach in which orbital findings are interpreted alongside TRAb status, thyroid function control, prior or planned RAI exposure, and metabolic profile, particularly in patients with low-CAS but progressive disease [10,11].

INITIAL MANAGEMENT AND SUPPORTIVE CARE

Normalization of thyroid function

Achieving and maintaining a euthyroid state is a cornerstone of TED management. Patients should be managed in close collaboration with endocrinologists to facilitate prompt normalization

of thyroid function. In patients with Graves' disease and active moderate-to-severe TED, antithyroid drugs (ATDs), including propylthiouracil and methimazole, are generally preferred over RAI therapy.

When RAI therapy is being considered, the need for prophylactic corticosteroids should be determined according to TED activity, disease severity, and individual risk factors. Current Korean Thyroid Association recommendations indicate that routine steroid prophylaxis is not required for patients with inactive or mild TED in the absence of risk factors, but it may be considered when factors such as smoking, elevated TRAb titers, or recent disease progression are present [15]. In patients with active moderate-to-severe TED, RAI therapy is generally discouraged because of the substantial risk of disease exacerbation. Nevertheless, when RAI is clinically indicated despite these concerns, prophylactic corticosteroid therapy is recommended, particularly in patients with additional risk factors. In such high-risk cases, oral prednisone or prednisolone at a dose of 0.3 to 0.5 mg/kg/day, initiated on the day of RAI administration and tapered over approximately 12 weeks, is advised [14].

In Korea, ATDs are overwhelmingly favored as first-line therapy for Graves' disease, accounting for approximately 98% of initial treatments and yielding a modest 5-year remission rate of 46.8%. In contrast, RAI therapy, despite achieving a higher 5-year remission rate of 91.0%, is markedly underused, representing only 0.7% of initial treatments, and is used infrequently even after ATD failure [16]. The strong preference for ATDs in Korea likely contributes to the lower incidence of acute RAI-induced inflammatory flares compared with Western populations. However, this chronic management pattern may also contribute to the characteristic "low-CAS but progressive" myopathic phenotype observed in Asian patients, as it may favor a prolonged subclinical remodeling phase over an acute inflammatory spike [17].

Risk factor management

Smoking cessation is essential in all patients with TED, as smoking is associated with greater disease severity, reduced responsiveness to therapy, and an increased risk of DON [23–25]. Patients should be offered structured smoking cessation counseling and pharmacologic support when appropriate.

Beyond its role as a diagnostic marker, TRAb is a central pathophysiological driver of orbital fibroblast activation through the TSHR–IGF-1R signaling complex. Accordingly, monitoring antibody dynamics is important not only for diagnosis but also for predicting therapeutic response and assessing the risk of

long-term recurrence. Measurement of serum TRAb, including thyrotropin-binding inhibitory immunoglobulin (TBII) and thyroid-stimulating immunoglobulin (TSI), is recommended for disease assessment and perioperative planning. In a 2025 KSO-PRS subspecialist survey, 93.8% of respondents reported monitoring TRAb levels, and 90.6% incorporated TBII and/or TSI into decisions regarding the timing of TED surgery. Notably, 56.3% assessed both antibody subtypes, reflecting a Korean practice pattern that emphasizes comprehensive serologic evaluation [9]. For risk stratification, both Korean and international studies consistently identify smoking, uncontrolled hyperthyroidism, and elevated TRAb titers as key predictors of TED development and progression [13]. More recent Korean data have further highlighted potential sex-specific effects and health system-level predictors [26].

Accumulating evidence also implicates dyslipidemia in the pathogenesis and progression of TED. Higher total cholesterol and low-density lipoprotein cholesterol levels have been associated with increased disease risk and greater severity, suggesting that lipid-driven inflammation may contribute to orbital inflammatory activity [18,20]. Recent multicenter Korean data extend these findings by showing that elevated serum triglyceride levels are independently associated with increased TED activity and severity [19].

In the Statins for Graves' orbitopathy (STAGO) phase II randomized clinical trial, adjunctive atorvastatin combined with intravenous glucocorticoids (IVGCs) resulted in significantly improved outcomes compared with glucocorticoid therapy alone in patients with active moderate-to-severe TED and hypercholesterolemia [22]. Complementary epidemiologic studies have further shown that statin use in patients with Graves' disease is associated with a lower incidence of orbitopathy, with hazard ratios of approximately 0.6–0.7 in large national cohorts [21]. Collectively, these findings suggest that optimization of lipid profiles, including consideration of statin therapy, may serve as a useful adjunctive strategy to mitigate disease risk and progression in patients with TED and coexisting dyslipidemia.

MEDICAL MANAGEMENT OF ACTIVE TED

Mild, active TED

In mild active TED, selenium supplementation is supported by international recommendations, whereas the inclusion of oral glucocorticoids and regional steroid injections in this framework reflects context-dependent evidence and Korean practice patterns.

Selenium supplementation

Selenium supplementation is recommended by EUGOGO for patients with mild active TED, based on randomized controlled trials demonstrating improved quality of life and slower disease progression with selenium administered at a dose of 100 µg twice daily for 6 months [27]. However, the Selenium in Graves' Ophthalmopathy in Selenium-Sufficient Area (SeGOSS) trial, a phase III multicenter randomized study conducted in Korea, did not replicate the clinical benefits observed in European cohorts [28,29].

This discrepancy likely reflects geographic differences in baseline dietary selenium intake, as East Asian populations generally have higher dietary selenium intake than European populations, potentially attenuating the incremental benefit of supplementation. Nevertheless, most Korean oculoplastic surgeons continue to recommend selenium supplementation for patients with mild active TED, citing its favorable safety profile and potential antioxidative properties [9]. Collectively, these findings suggest that although selenium represents a low-risk adjunctive therapy, its clinical efficacy may be population dependent and should be interpreted in the context of regional nutritional status.

Ocular surface management

Patients with TED frequently develop exposure-related keratopathy, superior limbic keratoconjunctivitis, and filamentary keratopathy as a result of lid retraction, lagophthalmos, and tear film instability. The prevalence of ocular surface disease in patients with TED has been estimated to range from 65% to 95%, with common symptoms including ocular dryness, foreign-body sensation, and blurred vision. These symptoms are often accompanied by objective findings such as reduced tear breakup time, punctate epithelial staining, and meibomian gland dysfunction [30].

Regular use of preservative-free artificial tears, with nighttime lubricating ointment as needed, is recommended to prevent epithelial breakdown and maintain corneal integrity. A recent systematic review evaluated therapeutic approaches targeting ocular surface disease in TED, including topical and non-topical interventions across seven eligible studies [31]. The review found that treatments such as topical cyclosporine A, vitamin A palmitate gel, and rebamipide were associated with improvements in both subjective symptoms and objective parameters, including tear breakup time and corneal staining, in selected patient cohorts [31].

Regional steroid injection

Regional triamcinolone administration represents an important

therapeutic option for patients with mild active TED characterized by soft-tissue inflammation and eyelid retraction [32]. Repeated subconjunctival triamcinolone injections of 20 mg per injection have been shown to reduce eyelid swelling and lid retraction in patients with recent-onset TED [32].

In Korean clinical practice, 81.2% of oculoplastic surgeons report using subconjunctival or eyelid triamcinolone injections for the management of mild active TED, with 69.2% limiting treatment to a maximum of three injections [9]. A recent comparative study further demonstrated that percutaneous paralevator palpebrae superioris injection provides efficacy comparable to that of subconjunctival injection for upper eyelid retraction, while offering the advantage of a significantly lower risk of intraocular pressure elevation [33].

Moderate-to-severe active TED

For moderate-to-severe active TED, treatment selection in this framework is anchored in high-level international evidence for IVGC, teprotumumab (TEP), mycophenolate mofetil (MMF), tocilizumab, and orbital radiotherapy (ORT). The positioning of selected adjunctive or combination approaches, however, reflects context-dependent evidence or Korean practice patterns.

Systemic glucocorticoids

IVGC pulse therapy is recommended as the first-line treatment for patients with moderate-to-severe active TED [7,8]. Although oral glucocorticoids may be effective, the intravenous route is generally preferred because randomized controlled trials have demonstrated higher response rates than oral administration (approximately 77%–88% vs. 51%–63%) and a lower incidence of adverse effects [34,35].

In Korean clinical practice, 96.9% of oculoplastic surgeons administer IVGC pulse therapy in accordance with EUGOGO guidelines, using a total dose of 4.5 g [9]. This regimen consists of intravenous methylprednisolone at a dose of 500 mg weekly for 6 consecutive weeks, followed by 250 mg weekly for an additional 6 weeks, resulting in a cumulative dose of 4.5 g over 12 weeks. The cumulative IVGC dose should not exceed 8.0 g per treatment cycle. During therapy, regular monitoring of liver function, renal function, and serum glucose is required. Infusions should be administered slowly over 1–2 hours with careful monitoring.

Oral prednisone at a dose of 0.5–1.0 mg/kg/day may serve as an alternative in patients who decline intravenous therapy or have contraindications to IVGC. In Korean practice, approximately 50% of oculoplastic surgeons prescribe oral glucocorti-

coids, with distinct patterns of use: 87.5% use oral steroids for tapering after IVGC therapy, whereas 56.3% use them as first-line treatment in patients with mild active TED. This pattern reflects recognition that oral glucocorticoids continue to have a role in milder disease and as consolidation therapy after intravenous treatment.

The 2021 EUGOGO guidelines recommend escalating the dose for particularly severe TED, consisting of intravenous methylprednisolone at 750 mg weekly for 6 weeks, followed by 500 mg weekly for an additional 6 weeks, for a cumulative dose of 7.5 g [8]. However, only 18.8% of Korean oculoplastic surgeons report using a 7.5-g regimen as first-line therapy for severe TED, whereas 62.1% report using concomitant ORT with standard-dose IVGC (4.5 g) from the outset [9].

Higher cumulative glucocorticoid doses are associated with a substantially increased risk of hepatotoxicity, hyperglycemia, immunosuppression, and other systemic adverse effects. Accordingly, the Korean practice pattern of combining ORT with standard-dose IVGC may reflect an attempt to balance treatment intensity against concerns about systemic toxicity, particularly in patients with metabolic or infectious comorbidities. Although the prevalence of hepatitis B virus (HBV) infection has declined substantially following widespread vaccination [36], Korea remains an area of intermediate endemicity, and chronic HBV carriage persists. In patients identified as HBV carriers, prophylactic antiviral therapy and periodic monitoring of liver function and HBV DNA levels should be considered during high-dose glucocorticoid therapy, as immunosuppression may precipitate HBV reactivation [37-39].

Orbital radiotherapy

ORT has demonstrated efficacy in the treatment of TED in multiple randomized controlled trials and retrospective studies [40,41]. When combined with oral glucocorticoids or IVGCs, ORT provides greater improvement in ocular motility than either ORT or glucocorticoid therapy alone [38,42-44]. External-beam radiotherapy is typically delivered to both orbits at a total dose of 20 Gy, fractionated into 10 sessions over 2 weeks.

In Korean series of patients with steroid-resistant TED, ORT has been associated with sustained improvements in inflammatory activity and exophthalmos. Consequently, ORT is commonly used in Korean clinical practice as a second-line treatment option [45,46]. A survey of KSOPRS subspecialists reported that 90.6% of Korean oculoplastic surgeons recommend ORT, making it one of the most frequently used therapeutic modalities for active TED [9].

Among surgeons who use radiotherapy, 96.6% reported recommending ORT when IVGC therapy is ineffective or contraindicated, supporting its role as a commonly used second-line intervention. In addition, 62.1% reported recommending ORT in combination with IVGC as part of initial therapy for patients with prominent extraocular muscle enlargement, indicating that some Korean clinicians integrate ORT early in selected clinical phenotypes.

Mycophenolate

Mycophenolate has emerged as an important immunosuppressive agent in TED management, supported by robust evidence from recent clinical trials. The drug is available globally as MMF and enteric-coated mycophenolate sodium. In the randomized, observer-masked, multicenter moderate-to-severe Graves' orbitopathy (MINGO) trial, Kahaly et al. [47] evaluated the efficacy of IVGC alone versus IVGC combined with mycophenolate sodium in 164 patients with active moderate-to-severe TED. Combination therapy achieved a significantly higher overall response rate than IVGC monotherapy (79% vs. 51%, $P=0.006$).

Adverse events were mild and comparable between the treatment groups, indicating that the addition of mycophenolate improves therapeutic efficacy without compromising tolerability. Based on these findings, the 2021 EUGOGO guidelines recommend IVGC combined with oral mycophenolate sodium as first-line therapy for moderate-to-severe active TED, representing a shift away from glucocorticoid monotherapy.

Despite these recommendations, mycophenolate use in Korea remains limited. A 2025 KSOPRS subspecialist survey reported that immunosuppressive agents were prescribed by 40.6% of clinicians, with MMF (53.8%) and methotrexate (46.2%) being the most frequently selected agents. This pattern likely reflects several challenges specific to the Korean healthcare system, including requirements for institutional review board approval for off-label use and the absence of locally standardized treatment protocols. Accordingly, although MMF is positioned in this framework on the basis of high-level international evidence, in Korean practice it is incorporated more selectively according to treatment response and local feasibility rather than used uniformly as initial combination therapy.

In routine clinical practice, mycophenolate is not typically initiated concurrently with IVGC pulse therapy at 500 mg weekly, but is more often introduced when the response to IVGC alone is inadequate. It may also be used as maintenance therapy, either in combination with tapering oral glucocorticoids or as mono-

therapy, to reduce the risk of disease reactivation after glucocorticoid withdrawal. This practice pattern likely reflects clinical observations that IVGC monotherapy often yields limited improvement in proptosis and may be followed by rebound disease activity, prompting adjunctive use of immunomodulatory agents such as mycophenolate.

Rituximab

Rituximab is a chimeric human–mouse monoclonal antibody targeting the CD20 antigen on B lymphocytes, resulting in B-cell depletion and downstream immunosuppressive effects. Evidence for its efficacy in TED comes from two randomized double-blind trials with discordant outcomes.

In a United States-based trial [48], 25 patients were randomized to receive rituximab, administered as two 1,000-mg doses given 2 weeks apart, or placebo. The study found no significant differences between groups in reduction of CAS or overall disease severity at either 24 or 52 weeks of follow-up. In contrast, an Italian randomized controlled trial [49] reported superior outcomes with rituximab compared with IVGC, including higher rates of disease inactivation at 24 weeks (100% vs. 69%) and lower rates of disease reactivation at 52 weeks (0% vs. 31%).

These discrepant results may be explained by differences in patient selection, particularly disease duration and baseline inflammatory activity, which were shorter and more pronounced, respectively, in the Italian cohort than in the United States cohort. Reported adverse events included rare but clinically significant complications, such as cytokine release syndrome and isolated cases of DON and vasculitis.

More recently, a prospective nonrandomized study using a low-dose rituximab regimen consisting of a single 100-mg infusion achieved disease inactivation in >90% of patients within 12 weeks, with no relapse over 76 weeks of follow-up and minimal infusion-related toxicity [50]. Collectively, these findings suggest that rituximab may be effective in carefully selected patients with early active TED, while emphasizing that optimal dosing strategies and patient selection are critical for consistent efficacy and safety. In Korea, off-label use of rituximab remains uncommon, at 3.1% in the 2025 KSOPRS survey, likely because of regulatory constraints and reimbursement limitations.

Tocilizumab

Tocilizumab, a humanized monoclonal antibody targeting the interleukin-6 receptor, is an effective second-line therapy for moderate-to-severe corticosteroid-resistant TED [8]. Interleukin-6 promotes orbital fibroblast activation and adipogenesis,

thereby contributing to soft-tissue expansion and inflammation.

In a pivotal randomized controlled trial of 32 patients with steroid-resistant TED, intravenous tocilizumab, administered at 8 mg/kg every 4 weeks for 4 doses, achieved disease inactivation (CAS <3) in 86% of treated patients compared with 35% in the placebo group ($P<0.005$), with substantial improvement in soft-tissue inflammation [51]. Tocilizumab was generally well tolerated; infections and headache occurred more frequently than with placebo, and effects on proptosis were modest.

Consistent benefits have also been reported in observational cohorts using monthly intravenous or weekly subcutaneous regimens [52,53]. In Korea, however, off-label use remains limited (6.2%), primarily because of access and reimbursement constraints despite increasing supportive evidence.

Teprotumumab

TEP is a fully human monoclonal antibody targeting IGF-1R, a critical mediator of TSHR–IGF-1R signaling in TED pathogenesis. It received U.S. Food and Drug Administration approval in 2020 and remains the only approved therapy for active moderate-to-severe TED in adults.

TEP is administered as eight intravenous infusions every 3 weeks, with an initial dose of 10 mg/kg followed by 20 mg/kg. Its efficacy was established in two randomized placebo-controlled trials, a phase 2 trial and the phase 3 Treatment of Graves' Orbitopathy (Thyroid Eye Disease) to Reduce Proptosis with Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study (OPTIC) trial, that enrolled a total of 170 patients with active TED [54,55]. In pooled analyses, mean proptosis reduction at 24 weeks was approximately 3 mm with TEP compared with <0.5 mm with placebo [56], and diplopia improved in 70% versus 31% of patients, respectively.

These findings were replicated in the Japanese trial, in which 89% of patients achieved a ≥ 2 -mm reduction in proptosis and mean CAS decreased by 4.6 ± 1.8 points compared with 1.1 ± 1.5 points in the placebo group [57]. Long-term pooled follow-up across three trials (phase 2, OPTIC, and Treatment of Graves' Orbitopathy to Reduce Proptosis with Teprotumumab Infusions in an Open-Label Clinical Extension Study [OPTIC-X]), demonstrated sustained benefit at 72 weeks, with maintained improvements in CAS, diplopia, and proptosis. However, 17.9% of patients required additional therapy by 99 weeks, indicating possible late reactivation [58].

The introduction of TEP has been associated with a significant reduction in orbital decompression rates [59,60]. A recent meta-analysis reported superior efficacy over IVGC, including

greater proptosis reduction and higher diplopia response rates [61].

The 2021 EUGOGO guideline recommended TEP as a second-line option, pending confirmation of long-term effectiveness, cost-effectiveness, and accessibility [8]. In contrast, the 2022 ATA/ETA consensus statement recognized TEP as the preferred therapy for active proptosis-dominant TED, contingent on regulatory approval and affordability [14].

Common adverse events include muscle spasms (25%), nausea (17%), alopecia (13%), diarrhea (12%), fatigue (12%), hearing impairment or ototoxicity (10%), and hyperglycemia (10%) [54–56]. Most events are mild to moderate, although rare serious adverse events have been reported, including exacerbation of inflammatory bowel disease, infusion reaction, and Hashimoto encephalopathy with confusion. TEP is relatively contraindicated during pregnancy, and caution is warranted in those with inflammatory bowel disease, metabolic comorbidities, such as diabetes mellitus or impaired glucose tolerance, and preexisting auditory dysfunction. Given its high cost, real-world adoption will depend on reimbursement policies and risk-benefit considerations.

Within the Korean healthcare system, where the high cost of TEP remains a major barrier to immediate widespread adoption, strategic prioritization is essential. Based on the 2025 KSOPRS survey, Korean specialists prioritized TEP in the following clinical scenarios: active TED with an inadequate response to IVGC (mean rank, 2.09), active TED as a potent first-line alternative for patients seeking nonsurgical proptosis reduction (mean rank, 2.13), and active TED refractory to both IVGC and ORT (mean rank, 2.28) [9]. Alongside these priorities, rigorous long-term safety monitoring for adverse effects such as hearing impairment and hyperglycemia will be crucial to establish TEP as a sustainable therapeutic option in the local clinical setting.

Sight-threatening TED

In sight-threatening TED, urgent IVGC therapy and early decompression are grounded in high-level international recommendations, whereas upfront combination therapy with IVGC and ORT reflects a survey-informed Korean practice pattern.

DON is an ophthalmic emergency that requires immediate administration of high-dose IVGC to prevent irreversible vision loss. The recommended regimen is intravenous methylprednisolone 500 to 1,000 mg daily for 3 consecutive days, with a maximum cumulative dose of 8 g, to achieve rapid reduction of orbital inflammation and optic nerve compression [8].

The 2022 ATA/ETA consensus statement likewise recom-

mends prompt initiation of high-dose IVGC in a hospital setting under close ophthalmologic and endocrine supervision [14]. If visual function fails to improve after a second IVGC cycle within 2 weeks, urgent orbital decompression is recommended to relieve mechanical compression at the orbital apex [8,14].

Upfront combination therapy with IVGC and ORT may be considered in selected cases of compressive optic neuropathy, as ORT can reduce extraocular muscle enlargement [38,62,63]. This combined approach is used in selected Korean practice settings to pair the immediate anti-inflammatory effects of IVGC with the delayed but potentially complementary effects of ORT on extraocular muscle enlargement. In the 2025 KSOPRS survey, 59.4% of oculoplastic surgeons reported using combined IVGC and ORT as the initial treatment approach for DON, whereas 40.6% reported using IVGC alone [9]. Furthermore, 90.6% proceeded to orbital decompression within 2 weeks in the absence of treatment response, reflecting timely escalation of care and adherence to international guidelines.

Consistent with EUGOGO and ATA/ETA recommendations, functional parameters are prioritized over anatomical findings when evaluating treatment response in DON. In the KSOPRS survey, Korean specialists ranked visual acuity and relative afferent pupillary defect as the most important indicators, followed by color vision and visual field testing, whereas radiologic apical crowding and optic disc swelling were assigned lower priority. TEP and other biologic agents may have adjunctive roles in selected circumstances, but they should not delay definitive surgical decompression in rapidly progressive cases.

MANAGEMENT OF INACTIVE TED

Inactive TED is defined by stable or minimally progressive clinical findings with minimal signs of inflammation ($CAS \leq 2/7$) maintained for at least 6 months. This phase represents the fibrotic endpoint of TED, in which inflammatory processes have largely resolved. Most patients with inactive TED require only observation and supportive ocular surface care. Periodic ophthalmologic examinations at 6–12-month intervals are appropriate to confirm disease stability.

Surgical intervention is indicated only in inactive disease with persistent cosmetically or functionally significant sequelae. Rehabilitative surgery may include orbital decompression, strabismus surgery, and eyelid procedures for eyelid retraction or residual cosmetic deformity. Orbital decompression is indicated for persistent exophthalmos associated with cosmetic concern or congestive symptoms related to elevated orbital pressure.

Various surgical approaches, including medial, lateral, and inferior wall decompression, may be selected according to imaging findings and the pattern of extraocular muscle involvement. In Korean practice, 71.9% of oculoplastic surgeons report performing orbital decompression [9].

Corrective extraocular muscle surgery may be performed to address restrictive strabismus and diplopia after 6–12 months of documented disease stability following the active phase. Eyelid retraction correction, such as levator recession, Müller muscle recession, lower eyelid spacer graft placement, or other tailored procedures, may be undertaken for cosmetically significant or functionally impairing eyelid abnormalities in stable disease. In Korea, 84.4% of oculoplastic surgeons perform eyelid retraction surgery, and blepharoplasty is also commonly performed (87.5%) [9].

Emerging evidence suggests that TEP may demonstrate sustained efficacy in selected patients with long-standing or inactive TED, particularly for proptosis reduction, thereby expanding therapeutic options beyond the traditional active-disease paradigm. In the OPTIC-X extension study, 89.2% (33/37) of patients previously assigned to placebo achieved a mean proptosis reduction of 3.5 ± 1.7 mm following TEP treatment, despite having a longer disease duration than patients in the primary OPTIC trial (12.9 months vs. 6.3 months) [64]. Furthermore, a retrospective analysis of 31 patients with chronic inactive TED (median disease duration, 81 months; CAS ≤ 1) demonstrated a mean proptosis reduction of 3.5 mm [65]. In addition, a recent randomized controlled trial showed that TEP significantly reduced proptosis by a mean of 2.4 mm in patients with chronic inactive TED [66]. Collectively, these data suggest that TEP may represent a medical alternative for selected patients with established proptosis for whom surgical decompression has traditionally been the primary definitive option, particularly those who are poor surgical candidates or prefer to avoid invasive procedures.

IMAGING APPROACH

Imaging plays a central role in confirming orbital involvement and assessing disease severity and activity in TED. In Korean clinical practice, 96.9% of oculoplastic surgeons use at least one imaging modality for TED evaluation, with computed tomography (CT) being the most commonly used modality (84.4%). CT provides reliable assessment of extraocular muscle enlargement, orbital fat expansion, and apical crowding, all of which are critical for phenotype classification and identification of patients at

risk for DON. Its wide availability and rapid acquisition facilitate timely evaluation of patients presenting with diplopia or suspected DON, thereby supporting prompt clinical decision-making.

Magnetic resonance imaging (MRI), used by 12.5% of respondents, is valued for its superior soft-tissue contrast, ability to assess inflammatory activity, and usefulness in excluding alternative diagnoses. Previous studies have shown that the signal intensity ratio on short tau inversion recovery sequences and the T2 relaxation time of extraocular muscles correlate with disease activity and help distinguish active inflammation from fibrotic change [67–69]. More recently, diffusion-weighted imaging parameters, including the apparent diffusion coefficient of extraocular muscles, have also been shown to correlate with CAS and overall disease severity in TED [70], offering a quantitative MRI-based biomarker of orbital inflammation.

SPECIAL CONSIDERATIONS IN KOREAN TED MANAGEMENT

The 2025 KSOPRS subspecialist survey showed that ORT is used frequently in Korean clinical practice, with 90.6% of oculoplastic surgeons recommending this modality. This pattern may reflect accumulated clinical experience with ORT in Korea and broad access to radiotherapy resources within the Korean healthcare system. In Korea, where access to biologic agents remains limited because of cost and reimbursement constraints, ORT may serve as a practical therapeutic option for patients with steroid-resistant TED. A Korean study demonstrated sustained clinical benefit of ORT in steroid-refractory TED, with CAS declining progressively from baseline through 12 months after treatment, supporting its role as an effective salvage therapy [45]. Careful patient selection remains essential, particularly with respect to age-related radiation-associated malignancy risk and avoidance of radiotherapy in patients with uncontrolled diabetes, hypertensive retinopathy, or diabetic retinopathy, to ensure optimal safety.

For DON, the 2025 KSOPRS survey showed that 59.4% of Korean oculoplastic surgeons reported using combined IVGC and ORT as the initial treatment approach, whereas 40.6% reported using IVGC alone. Because DON requires urgent intervention to prevent irreversible vision loss, IVGC can be initiated immediately without delays related to insurance authorization. This contrasts with biologic agents such as TEP, which often require prolonged reimbursement approval. Although ORT does not have an immediate therapeutic effect, combination

therapy may provide complementary benefits by combining rapid corticosteroid-induced immunosuppression with delayed radiotherapy-mediated control of orbital inflammation.

The 2025 KSOPRS survey further showed that 81.2% of Korean oculoplastic surgeons use subconjunctival or eyelid triamcinolone injections for mild active TED [9]. Among these clinicians, 69.2% limit treatment to three injections, reflecting a cautious approach to repeated local corticosteroid exposure. In more severe cases with prominent retrobulbar inflammation, ultrasonography-guided retrobulbar injection may be considered; however, only 6.2% of respondents reported using this technique, likely reflecting a preference for the safer subconjunctival or eyelid route. Careful attention to anatomic placement and injection volume reduces the risk of complications, including intraocular pressure elevation. Regional triamcinolone injections may be considered as adjunctive therapy within a comprehensive treatment strategy that incorporates systemic immunosuppression, supportive care, and radiotherapy when indicated.

In Korean practice, immunosuppressive agents are prescribed by 40.6% of physicians, with MMF accounting for 53.8% of immunosuppressant use. Off-label use of tocilizumab and rituximab remains uncommon (6.2% and 3.1%, respectively), likely reflecting limited access, reimbursement barriers, and the absence of nationally standardized treatment protocols, despite increasing international evidence supporting their efficacy in steroid-refractory TED.

TEP has demonstrated substantial efficacy in moderate-to-severe TED and remains the only medical therapy with consistent evidence for proptosis reduction. In the 2025 KSOPRS survey, Korean oculoplastic surgeons tended to prioritize TEP for patients with active TED, particularly when conventional therapies such as IVGC had failed. Mean priority ranks were 2.09 ± 0.73 for active TED with poor response to IVGC, 2.13 ± 0.89 for active TED as first-line therapy, and 2.28 ± 0.91 for active TED refractory to both IVGC and ORT, whereas TEP was deprioritized for inactive TED with mild proptosis (mean rank, 3.31 ± 0.97) [9]. As TEP availability increases and long-term outcome data accumulate in Korea, the development of consensus-based utilization criteria may facilitate more consistent, evidence-informed adoption.

A distinctive feature of Korean TED management is the extensive use of serologic evaluation [9]. In the 2025 KSOPRS survey, 93.8% of respondents monitored TRAb levels, and 90.6% incorporated TBII or TSI measurements into decisions regarding surgical timing. This practice suggests that Korean clinicians frequently use immunologic profiling to guide orbital

decompression planning. In addition, 43.8% of physicians reported considering total thyroidectomy in patients with persistently elevated TRAb levels, which may indicate a more proactive thyroid ablation strategy in refractory cases.

PRACTICAL CLINICAL DECISION FRAMEWORK FOR TED MANAGEMENT

To facilitate practical application of this Korean clinical practice framework, treatment selection should proceed stepwise according to disease severity, activity, predominant phenotype, and patient-specific context. Table 1 summarizes the overall framework, and the following text-based algorithm provides a concise clinical pathway for decision-making.

Step 1: Determine whether TED is sight-threatening or non-sight-threatening.

Step 2: In non-sight-threatening TED, assess disease activity (active vs. inactive) and severity (mild vs. moderate-to-severe).

Step 3: In active mild TED, prioritize supportive care and selected adjunctive measures; in active moderate-to-severe TED, consider systemic treatment.

Step 4: In active moderate-to-severe TED, select treatment according to the predominant phenotype; IVGC-based therapy for inflammation-predominant disease, TEP for proptosis-dominant disease when available and feasible, and ORT for restrictive myopathy or progressive diplopia.

Step 5: Modify treatment selection according to patient context, including thyroid functional status, TRAb level, prior or planned RAI exposure, metabolic comorbidities, cost, reimbursement, and local treatment availability.

Step 6: In inactive TED, manage residual sequelae with staged rehabilitative surgery, typically orbital decompression, followed by strabismus surgery and then eyelid correction.

DISTINCTION FROM INTERNATIONAL RECOMMENDATIONS

Although this Korean clinical practice framework adheres to the fundamental principles of the 2021 EUGOGO guideline and the 2022 ATA/ETA recommendations, it incorporates several features tailored to the Korean clinical landscape. First, in mild active TED, regional triamcinolone injection is used more prominently to address eyelid retraction. Second, in DON, combination therapy with IVGC and ORT is more commonly used as the initial approach in Korean practice. Third, ORT is more fully integrated into both primary and secondary treatment algo-

Table 1. Korean Clinical Practice Framework for TED Management Integrating the 2022 ATA/ETA Consensus with Survey-Informed Korean Practice Patterns

Initial management					
Thyroid function control (A), smoking cessation (A), ocular surface management (A)					
Mild TED					
Main problem		Active phase/Progression		Inactive phase	
Eyelid swelling with retraction		Watchful monitoring (A) Selenium (B) OGC (C) Regional TA (B)		Eyelid surgery (A)	
Proptosis		Watchful monitoring (A) Selenium (B) OGC (C)		Decompression (A)	
Moderate-to-severe TED					
Main problem	Active phase/progression				Inactive phase
	Nonsurgical treatment			Other treatment	Surgical intervention and others
	First-line	Second-line	May be considered		
Proptosis	TEP (A) ^a	IVGC (A) MMF (B) ^a			Decompression (A) TEP (B) ^a
Soft-tissue inflammation	IVGC (A)	TEP (A) ^a MMF (A) ^a OGC (B) ORT (A)	TCZ (A) ^a RTX (B) ^a		Decompression (A) Eyelid surgery (A)
Diplopia due to restrictive myopathy	ORT (A) TEP (A) ^a IVGC+ORT (C)	IVGC (B) MMF (B) ^a OGC (B)		Prism glasses (A)	Strabismus surgery (A) Prism glasses (A)
Eyelid retraction				Regional TA (B) Botulinum injection (B)	Eyelid surgery (A)
Sight-threatening TED					
Diagnosis	Active phase/progression				Surgical intervention
	Nonsurgical treatment				
	First-line	Second-line			
DON	IVGC (A) IVGC+ORT (C)				Decompression (A)
Corneal breakdown					Decompression (A) Eyelid surgery, including tarsorrhaphy (A)

(A) High-level evidence supported by international guidelines and/or randomized trials/meta-analyses; (B) Supportive clinical evidence with context-dependent applicability; (C) Survey-informed expert consensus or contemporary Korean practice pattern, used when the positioning in this framework is based primarily on national survey findings or expert consensus.

TED, thyroid eye disease; ATA, American Thyroid Association; ETA, European Thyroid Association; OGC, oral glucocorticoid; TA, triamcinolone acetonide; TEP, teprotumumab; IVGC, intravenous glucocorticoid; MMF, mycophenolate mofetil; ORT, orbital radiotherapy; TCZ, tocilizumab; RTX, rituximab; DON, dysthyroid optic neuropathy.

^aAdministered when available.

rhythms, reflecting its high accessibility. Fourth, surgical timing is often informed by comprehensive serologic profiling, including TBII and TSI titers. Finally, because of current reimbursement constraints, emerging biologic agents may be prioritized for steroid-refractory or proptosis-dominant cases. Taken to-

gether, these features suggest that this survey-informed framework is not merely a regional adaptation of global standards, but a practical framework tailored to the Korean clinical setting.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS FOR TED MANAGEMENT IN KOREA

Korean oculoplastic practice has evolved over several decades, resulting in a distinctive treatment paradigm. IVGC has remained a widely used first-line medical therapy, while ORT has complemented this approach by reducing disease reactivation and improving diplopia, particularly in muscle-predominant moderate-to-severe TED. The frequent use of combined IVGC and ORT as first-line therapy for severe extraocular muscle involvement is consistent with this dual-modality practice pattern. Following the 2021 EUGOGO guideline update, MMF has been increasingly incorporated, either as part of initial combination therapy with IVGC or added according to early treatment response. In contrast, biologic agents, including rituximab and tocilizumab, remain largely inaccessible in Korea because of cost, regulatory approval, and reimbursement barriers, which constitute defining features of the current national treatment landscape.

Despite the effectiveness of medical and radiotherapeutic therapies in controlling inflammatory activity, their effect on proptosis remains limited. Consequently, many Korean clinicians proceed to orbital decompression once TED has entered an inactive, stable phase and responses to nonsurgical therapies have plateaued. Orbital decompression reliably reduces proptosis and is associated with high patient satisfaction; however, its invasive nature carries meaningful risks, including postoperative diplopia and perioperative morbidity. As a result, many patients defer surgery because of concerns about complications and invasiveness, leading to persistent impairment in quality of life despite otherwise stable disease.

The approval of TEP by the U.S. Food and Drug Administration in 2020, followed by approval in Japan in 2024 and ongoing regulatory review in other countries, represents a major shift in the TED therapeutic landscape. Unlike conventional medical therapies, TEP has demonstrated robust efficacy in reducing proptosis without surgery, offering a noninvasive alternative with the potential to substantially alter patient outcomes. Approval of TEP in Korea may benefit patients with disfiguring proptosis and impaired quality of life who are reluctant to undergo decompression surgery. Nevertheless, clinicians must carefully assess the risk-benefit profile of TEP, including the need to monitor adverse effects such as hearing impairment, and critically evaluate its cost-effectiveness within the Korean healthcare system. To support optimal integration of TEP into

clinical practice, continued appraisal of evolving TED guidelines, long-term efficacy and safety data, and comparative effectiveness studies is essential. Such efforts will facilitate consistent, evidence-based application of medical, radiotherapeutic, surgical, and biologic therapies tailored to individual patient characteristics and treatment goals.

CONCLUSIONS

Management of TED requires an individualized approach that integrates thyroid function control, supportive ocular care, and appropriately sequenced medical and surgical interventions. We present a Korean clinical practice framework for TED management that uses the 2022 ATA/ETA consensus as its foundation, with treatment algorithms informed by a 2025 survey of KSO-PRS subspecialists reflecting contemporary clinical practice. Korean oculoplastic surgeons show substantial adherence to international standards, with 87.5% using both CAS and the EUGOGO severity classification and 96.9% administering IVGC pulse therapy in accordance with EUGOGO recommendations for moderate-to-severe TED. At the same time, Korean practice exhibits distinctive patterns shaped by local clinical experience and healthcare infrastructure, particularly the high use of ORT and regional triamcinolone injections. Broad access to orbital imaging in Korea enables reliable differentiation between fat-predominant and muscle-predominant disease in most patients, facilitating phenotype-based treatment selection. Because therapeutic response varies according to disease phenotype, phenotype-guided treatment stratification is a core component of this clinical practice framework.

To our knowledge, this clinical practice framework represents the first comprehensive national framework for TED management developed in Korea. As emerging therapies such as TEP become more accessible, regular updates to this framework that integrate global evidence with local regulatory and healthcare constraints will be essential to support patient-centered care. Future clinical trials and cost-effectiveness analyses will further refine this framework and inform optimal context-specific management strategies for TED.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

- Bartley GB, Fatourehchi V, Kadrmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA, et al. The incidence of Graves' ophthalmopathy in Olmsted County, Minnesota. *Am J Ophthalmol* 1995; 120:511-7.
- Boulakh L, Nygaard B, Bek T, Faber J, Heegaard S, Toft PB, et al. Nationwide incidence of thyroid eye disease and cumulative incidence of strabismus and surgical interventions in Denmark. *JAMA Ophthalmol* 2022;140:667-73.
- Watanabe N, Kozaki A, Inoue K, Narimatsu H, Shinohara M, LoPresti MG. Prevalence, incidence, and clinical characteristics of thyroid eye disease in Japan. *J Endocr Soc* 2023;8: bvad148.
- Woo KI, Kim YD, Lee SY. Prevalence and risk factors for thyroid eye disease among Korean dysthyroid patients. *Korean J Ophthalmol* 2013;27:397-404.
- Lim SL, Lim AK, Mumtaz M, Hussein E, Wan Bebakar WM, Khir AS. Prevalence, risk factors, and clinical features of thyroid-associated ophthalmopathy in multiethnic Malaysian patients with Graves' disease. *Thyroid* 2008;18:1297-301.
- Tellez M, Cooper J, Edmonds C. Graves' ophthalmopathy in relation to cigarette smoking and ethnic origin. *Clin Endocrinol (Oxf)* 1992;36:291-4.
- Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, et al. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy guidelines for the management of Graves' orbitopathy. *Eur Thyroid J* 2016; 5:9-26.
- Bartalena L, Kahaly GJ, Baldeschi L, Dayan CM, Eckstein A, Marcocci C, et al. The 2021 European Group on Graves' Orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. *Eur J Endocrinol* 2021;185:G43-67.
- Surl D, Ko J, Yang J, Yoon JS. A nationwide survey by the Korean Society of Ophthalmic Plastic and Reconstructive Surgery (KSOPRS) on the management of thyroid eye disease in South Korea. *Korean J Ophthalmol* 2025;39:532-41.
- Mourits MP, Prummel MF, Wiersinga WM, Koornneef L. Clinical activity score as a guide in the management of patients with Graves' ophthalmopathy. *Clin Endocrinol (Oxf)* 1997;47:9-14.
- Kim JW, Woo YJ, Yoon JS. Is modified clinical activity score an accurate indicator of diplopia progression in Graves' orbitopathy patients? *Endocr J* 2016;63:1133-40.
- Byeon HJ, Ko J, Kikkawa DO, Yoon JS. Preoperative risk factors for proptosis recurrence after rehabilitative orbital decompression in Graves' orbitopathy patients. *Am J Ophthalmol* 2024;258:110-8.
- Lee MH, Chin YH, Ng CH, Nistala KR, Ow ZG, Sundar G, et al. Risk factors of thyroid eye disease. *Endocr Pract* 2021; 27:245-53.
- Burch HB, Perros P, Bednarczuk T, Cooper DS, Dolman PJ, Leung AM, et al. Management of thyroid eye disease: a consensus statement by the American Thyroid Association and the European Thyroid Association. *Thyroid* 2022;32:1439-70.
- Kim KJ, Song E, Kim M, Kwon H, Ku EJ, Kwon HW, et al. 2025 Korean Thyroid Association management guidelines for radioactive iodine therapy in patients with hyperthyroidism. *Endocrinol Metab (Seoul)* 2025;40:342-56.
- Kim KJ, Choi J, Shin SM, Kim JA, Kim KJ, Kim SG. Treatment patterns and preferences for Graves' disease in Korea: insights from a nationwide cohort study. *Endocrinol Metab (Seoul)* 2024;39:659-63.
- Ahn HY, Lee J, Kim M, Lee JK. Risk factors and outcomes of Graves' orbitopathy after radioactive iodine therapy. *Endocrine* 2025;90:248-55.
- Sabini E, Mazzi B, Profilo MA, Mautone T, Casini G, Rocchi R, et al. High serum cholesterol is a novel risk factor for Graves' orbitopathy: results of a cross-sectional study. *Thyroid* 2018;28:386-94.
- Park J, Yoon JS, Choung H, Lew H; Korean Society of Ophthalmic Plastic and Reconstructive Surg group; KSOPRS group. Triglycerides as a predictor of activity and severity in thyroid eye disease: a multicentre study. *Br J Ophthalmol* 2026;110:721-8.
- Lanzolla G, Sabini E, Profilo MA, Mazzi B, Sframeli A, Rocchi R, et al. Relationship between serum cholesterol and Graves' orbitopathy (GO): a confirmatory study. *J Endocrinol Invest* 2018;41:1417-23.
- Barnett MJ, Casipit C, Lam J, Rivadeneira A. Statins and thyroid eye disease: a propensity score-matched retrospective cohort analysis. *Cureus* 2025;17:e83243.
- Lanzolla G, Sabini E, Leo M, Menconi F, Rocchi R, Sframeli A, et al. Statins for Graves' orbitopathy (STAGO): a phase

- 2, open-label, adaptive, single centre, randomised clinical trial. *Lancet Diabetes Endocrinol* 2021;9:733-42.
23. Sadeghi-Tari A, Jamshidian-Tehrani M, Nabavi A, Sharif-Kashani S, Elhami E, Hassanpour N, et al. Effect of smoking on retrobulbar blood flow in thyroid eye disease. *Eye (Lond)* 2016;30:1573-8.
24. Blandford AD, Zhang D, Chundury RV, Perry JD. Dys thyroid optic neuropathy: update on pathogenesis, diagnosis, and management. *Expert Rev Ophthalmol* 2017;12:111-21.
25. Kemchoknatee P, Thongsawangchai N, Srisombut T, Tangon D, Chantra S. Predictive factors of development of dys thyroid optic neuropathy among individuals with thyroid eye disease. *Eur J Ophthalmol* 2024;34:834-42.
26. Lee J, Kang J, Ahn HY, Lee JK. Sex-specific risk factors associated with Graves' orbitopathy in Korean patients with newly diagnosed Graves' disease. *Eye (Lond)* 2023;37:3382-91.
27. Marcocci C, Kahaly GJ, Krassas GE, Bartalena L, Prummel M, Stahl M, et al. Selenium and the course of mild Graves' orbitopathy. *N Engl J Med* 2011;364:1920-31.
28. Ahn HY, Lee MJ, Jung KY, Kim HJ, Jung EH, Chung CW, et al. Selenium vs control for Graves ophthalmopathy in a selenium-sufficient area: a randomized clinical trial. *JAMA Ophthalmol* 2025;143:287-94.
29. Chung CW, Jung KY, Jung EH, Lee MJ, Park YJ, Lee JK, et al. Efficacy of selenium supplementation for mild-to-moderate Graves' ophthalmopathy in a selenium-sufficient area (SeGOSS trial): study protocol for a phase III, multicenter, open-label, randomized, controlled intervention trial. *Trials* 2023;24:272.
30. Rana HS, Akella SS, Clabeaux CE, Skurski ZP, Aakalu VK. Ocular surface disease in thyroid eye disease: a narrative review. *Ocul Surf* 2022;24:67-73.
31. Wong AS, Chelnis JG. Systematic review of ocular surface treatments in the setting of thyroid eye disease. *Front Ophthalmol (Lausanne)* 2024;4:1352355.
32. Lee SJ, Rim TH, Jang SY, Kim CY, Shin DY, Lee EJ, et al. Treatment of upper eyelid retraction related to thyroid-associated ophthalmopathy using subconjunctival triamcinolone injections. *Graefes Arch Clin Exp Ophthalmol* 2013;251:261-70.
33. Wang M, Luan Y, Qian Z, Wang Y, Fang W. Percutaneous para-levator palpebrae superioris and subconjunctival injection of triamcinolone acetate for upper eyelid retraction in thyroid-associated ophthalmopathy. *Front Med (Lausanne)* 2025;12:1679057.
34. Marcocci C, Bartalena L, Tanda ML, Manetti L, Dell'Unto E, Rocchi R, et al. Comparison of the effectiveness and tolerability of intravenous or oral glucocorticoids associated with orbital radiotherapy in the management of severe Graves' ophthalmopathy: results of a prospective, single-blind, randomized study. *J Clin Endocrinol Metab* 2001;86:3562-7.
35. Kahaly GJ, Pitz S, Hommel G, Dittmar M. Randomized, single blind trial of intravenous versus oral steroid monotherapy in Graves' orbitopathy. *J Clin Endocrinol Metab* 2005;90:5234-40.
36. Yim SY, Kim JH. The epidemiology of hepatitis B virus infection in Korea. *Korean J Intern Med* 2019;34:945-53.
37. Yoon EL. Prophylactic antiviral treatment in immunosuppressed chronic hepatitis B patients. *Korean J Gastroenterol* 2019;74:258-66.
38. Kim JW, Han SH, Son BJ, Rim TH, Keum KC, Yoon JS. Efficacy of combined orbital radiation and systemic steroids in the management of Graves' orbitopathy. *Graefes Arch Clin Exp Ophthalmol* 2016;254:991-8.
39. Choi J, Lim YS. Characteristics, prevention, and management of hepatitis B virus (HBV) reactivation in HBV-infected patients who require immunosuppressive therapy. *J Infect Dis* 2017;216(suppl 8):S778-84.
40. Mourits MP, van Kempen-Hartevel ML, Garcia MB, Koppe-schaar HP, Tick L, Terwee CB. Radiotherapy for Graves' orbitopathy: randomised placebo-controlled study. *Lancet* 2000;355:1505-9.
41. Prummel MF, Terwee CB, Gerding MN, Baldeschi L, Mourits MP, Blank L, et al. A randomized controlled trial of orbital radiotherapy versus sham irradiation in patients with mild Graves' ophthalmopathy. *J Clin Endocrinol Metab* 2004;89:15-20.
42. Prummel MF, Mourits MP, Blank L, Berghout A, Koornneef L, Wiersinga WM. Randomized double-blind trial of prednisone versus radiotherapy in Graves' ophthalmopathy. *Lancet* 1993;342:949-54.
43. Bartalena L, Marcocci C, Chiovato L, Laddaga M, Lepri G, Andreani D, et al. Orbital cobalt irradiation combined with systemic corticosteroids for Graves' ophthalmopathy: comparison with systemic corticosteroids alone. *J Clin Endocrinol Metab* 1983;56:1139-44.
44. Oeverhaus M, Witteler T, Lax H, Esser J, Fuhrer D, Eckstein A. Combination therapy of intravenous steroids and orbital irradiation is more effective than intravenous steroids alone in patients with Graves' orbitopathy. *Horm Metab Res* 2017;49:739-47.

45. Park J, Lee JE. The efficacy of radiotherapy for steroid-resistant thyroid eye disease: clinical outcomes in orbital inflammation and exophthalmos. *Radiat Oncol J* 2025;43:88-98.
46. Choi JH, Lee JK. Efficacy of orbital radiotherapy in moderate-to-severe active Graves' orbitopathy including long-lasting disease: a retrospective analysis. *Radiat Oncol* 2020;15:220.
47. Kahaly GJ, Riedl M, Konig J, Pitz S, Ponto K, Diana T, et al. Mycophenolate plus methylprednisolone versus methylprednisolone alone in active, moderate-to-severe Graves' orbitopathy (MINGO): a randomised, observer-masked, multicentre trial. *Lancet Diabetes Endocrinol* 2018;6:287-98.
48. Stan MN, Garrity JA, Carranza Leon BG, Prabin T, Bradley EA, Bahn RS. Randomized controlled trial of rituximab in patients with Graves' orbitopathy. *J Clin Endocrinol Metab* 2015;100:432-41.
49. Salvi M, Vannucchi G, Curro N, Campi I, Covelli D, Dazzi D, et al. Efficacy of B-cell targeted therapy with rituximab in patients with active moderate to severe Graves' orbitopathy: a randomized controlled study. *J Clin Endocrinol Metab* 2015;100:422-31.
50. Vannucchi G, Campi I, Covelli D, Curro N, Lazzaroni E, Palomba A, et al. Efficacy profile and safety of very low-dose rituximab in patients with Graves' orbitopathy. *Thyroid* 2021;31:821-8.
51. Perez-Moreiras JV, Gomez-Reino JJ, Maneiro JR, Perez-Pampin E, Romo Lopez A, Rodriguez Alvarez FM, et al. Efficacy of tocilizumab in patients with moderate-to-severe corticosteroid-resistant graves orbitopathy: a randomized clinical trial. *Am J Ophthalmol* 2018;195:181-90.
52. Sanchez-Bilbao L, Martinez-Lopez D, Revenga M, Lopez-Vazquez A, Valls-Pascual E, Atienza-Mateo B, et al. Anti-IL-6 receptor tocilizumab in refractory Graves' orbitopathy: national multicenter observational study of 48 patients. *J Clin Med* 2020;9:2816.
53. Perez-Moreiras JV, Varela-Agra M, Prada-Sanchez MC, Prada-Ramallal G. Steroid-resistant Graves' orbitopathy treated with tocilizumab in real-world clinical practice: a 9-year single-center experience. *J Clin Med* 2021;10:706.
54. Smith TJ, Kahaly GJ, Ezra DG, Fleming JC, Dailey RA, Tang RA, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med* 2017;376:1748-61.
55. Douglas RS, Kahaly GJ, Patel A, Sile S, Thompson EH, Perdok R, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Engl J Med* 2020;382:341-52.
56. Kahaly GJ, Douglas RS, Holt RJ, Sile S, Smith TJ. Teprotumumab for patients with active thyroid eye disease: a pooled data analysis, subgroup analyses, and off-treatment follow-up results from two randomised, double-masked, placebo-controlled, multicentre trials. *Lancet Diabetes Endocrinol* 2021;9:360-72.
57. Hiromatsu Y, Ishikawa E, Kozaki A, Takahashi Y, Tanabe M, Hayashi K, et al. A randomised, double-masked, placebo-controlled trial evaluating the efficacy and safety of teprotumumab for active thyroid eye disease in Japanese patients. *Lancet Reg Health West Pac* 2025;55:101464.
58. Kahaly GJ, Subramanian PS, Conrad E, Holt RJ, Smith TJ. Long-term efficacy of teprotumumab in thyroid eye disease: follow-up outcomes in three clinical trials. *Thyroid* 2024;34:880-9.
59. Bhat AM, Soler ZM, Schlosser RJ, Metson RB, Rathi VK. Orbital decompression surgery among Medicare beneficiaries in the post-teprotumumab era. *Int Forum Allergy Rhinol* 2024;14:1505-9.
60. Topilow NJ, Pentead RC, Ting M, Al-Sharif E, Villatoro GA, Yoon JS, et al. Orbital decompression following treatment with teprotumumab for thyroid eye disease. *Can J Ophthalmol* 2025;60:e59-64.
61. Douglas RS, Dailey R, Subramanian PS, Barbesino G, Ugradar S, Batten R, et al. Proptosis and diplopia response with teprotumumab and placebo vs the recommended treatment regimen with intravenous methylprednisolone in moderate to severe thyroid eye disease: a meta-analysis and matching-adjusted indirect comparison. *JAMA Ophthalmol* 2022;140:328-35.
62. Gold KG, Scofield S, Isaacson SR, Stewart MW, Kazim M. Orbital radiotherapy combined with corticosteroid treatment for thyroid eye disease-compressive optic neuropathy. *Ophthalmic Plast Reconstr Surg* 2018;34:172-7.
63. Shams PN, Ma R, Pickles T, Rootman J, Dolman PJ. Reduced risk of compressive optic neuropathy using orbital radiotherapy in patients with active thyroid eye disease. *Am J Ophthalmol* 2014;157:1299-305.
64. Douglas RS, Kahaly GJ, Ugradar S, Elflein H, Ponto KA, Fowler BT, et al. Teprotumumab efficacy, safety, and durability in longer-duration thyroid eye disease and re-treatment: OPTIC-X Study. *Ophthalmology* 2022;129:438-49.
65. Ugradar S, Kang J, Kossler AL, Zimmerman E, Braun J, Harrison AR, et al. Teprotumumab for the treatment of chronic thyroid eye disease. *Eye (Lond)* 2022;36:1553-9.

66. Douglas RS, Couch S, Wester ST, Fowler BT, Liu CY, Subramanian PS, et al. Efficacy and safety of teprotumumab in patients with thyroid eye disease of long duration and low disease activity. *J Clin Endocrinol Metab* 2023;109:25-35.
67. Das T, Roos JC, Patterson AJ, Graves MJ, Murthy R. T2-relaxation mapping and fat fraction assessment to objectively quantify clinical activity in thyroid eye disease: an initial feasibility study. *Eye (Lond)* 2019;33:235-43.
68. Song C, Luo Y, Yu G, Chen H, Shen J. Current insights of applying MRI in Graves' ophthalmopathy. *Front Endocrinol (Lausanne)* 2022;13:991588.
69. Li Z, Luo Y, Feng X, Zhang Q, Zhong Q, Weng C, et al. Application of multiparameter quantitative magnetic resonance imaging in the evaluation of Graves' ophthalmopathy. *J Magn Reson Imaging* 2023;58:1279-89.
70. George NM, Feeney C, Lee V, Avari P, Ali A, Madani G, et al. Extraocular muscle diffusion weighted imaging as a quantitative metric of posterior orbital involvement in thyroid associated orbitopathy. *Insights Imaging* 2024;15:183.