



# Management of Ophthalmopathy and Use of Selenium in Graves' Disease: A Survey of Physicians from the Middle East and Africa

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J Diabetes Endocrine Practice

## Abstract

**Objectives** We explored how physicians in the Middle East and Africa (MEA) assess and manage Graves' ophthalmopathy (GO) and ascertain their perceptions of selenium (Se) in thyroid disease.

**Methods** Two online questionnaires were sent to a sample of physicians from the MEA region. Responses from 183 GO and 102 Se surveys were received and analyzed.

**Results** In the GO survey, 68.6% thought multidisciplinary team (MDT) was very valuable, but fewer participated in MDT (19.0%) or referred patients to MDT (44.2%). Respondents advocated the assessment of visual fields by perimetry (65.9%), magnetic resonance imaging (52.9%), color vision (51.8%), and ultrasonography (14.1%). Autoimmune thyroid diseases (ATDs) were the most common choice (95.1%) for first-line therapy for coexisting hyperthyroidism. Glucocorticoids (GCs) were preferred as the first-line therapy by the majority of respondents; among them, 63.1% chose the intravenous route. The treatment strategy for GO with intravenous GC therapy remains debatable and surgical decompression (31.3%) and radiotherapy (13.1%) were recommended. When diabetes coexists, radiotherapy and orbital decompression are more favored over GCs. Regarding the Se survey, a minority (10.3%) used Se routinely for Graves' disease (GD). However, this increased to 29.1% when GO exists. However, about a quarter needed to be sure/did not know (23.9%) the evidence in GD without GO and 27.4% for GD with GO. In GD without GO on ATDs, 67.5% never recommend Se, whereas 32.5% recommend Se sometimes. Conversely, when GO occurs, 65.0% recommend Se in variable frequencies. Of these, Se is used as an alternative to watchful waiting in patients with mild ocular involvement (22.1%) and as an adjuvant to the established treatment in patients with moderate to severe ocular involvement (20.4%). The dose of 200 mcg/day was recommended by 42.5% of respondents.

**Conclusion** Gaps exist in the physicians' knowledge and practices concerning diagnosis and management of GO. More focused education and training are needed in the MEA region.

## Keywords

- ▶ clinical management
- ▶ Graves' ophthalmopathy
- ▶ Graves' disease
- ▶ selenium
- ▶ thyroid eye disease
- ▶ thyrotoxicosis

DOI <https://doi.org/10.1055/s-0045-1804531>.  
ISSN 2772-7653.

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Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

## Introduction

The management of Graves' ophthalmopathy (GO) is challenging for both patients and endocrinologists. Such patients are ideally managed in a multidisciplinary setting with input from specialist physicians and ophthalmologists. The prognosis is usually unfavorable and requires interdisciplinary collaborations. The most appropriate approach to treat GO has yet to be identified, and using glucocorticoids to treat severe forms of GO remains controversial.<sup>1-3</sup> Several surveys targeting relevant physicians found big differences among thyroid experts in treating GO.<sup>4-9</sup>

The selenium (Se) tissue concentration is the highest of any human tissue, and a number of selenoprotein families protect thyrocytes from excess hydrogen peroxide during thyroid hormone synthesis and act as catalysts for activating thyroid hormone.<sup>10</sup> Adverse effects are clinically evident in severe Se and iodine-deficient areas but may also be detectable in marginal deficiency states.<sup>11,12</sup> Se may be low in patients with autoimmune thyroid disease (ATD).<sup>13</sup>

Data on Se supplementation are limited and equivocal.<sup>14,15</sup> The effect of Se supplementation on either the response to treatment or the recurrence rate in Graves' disease (GD) is uncertain. Also, Se supplementation in a Se-sufficient cohort of patients failed to demonstrate an adjuvant role in the short-term control of hyperthyroidism. Other studies reported a faster remission of GD with Se treatment and even a decrease in serum thyroid-stimulating hormone (TSH) receptor antibody (TRAb) concentrations.<sup>16,17</sup>

Physicians' knowledge and attitudes concerning the management of GO and the role of thyroid function in health and disease may influence the quality of patients' care. International surveys on the management of GO<sup>4-9</sup> and the role of Se in thyroid disease were conducted.<sup>18</sup> However, these surveys had minimal or no representation of the Middle East and Africa (MEA) physicians. Therefore, the findings of these studies may not directly apply to the MEA region. Hence, the present survey was conducted to

explore the perceptions and practices of MEA physicians regarding (1) the GO evaluation and treatment and (2) the role of Se in ATD and GO management.

## Materials and Methods

### Study Design

A cross-sectional study was conducted between 2020 and 2021. The electronic questionnaire service Survey Monkey (SVMK Inc., San Mateo, California, United States) was used to create, disseminate, and analyze the questionnaire. Two separate questionnaires (Graves' Ophthalmopathy Survey and Selenium Survey) were electronically sent to a convenience sample of endocrinologists residing and practicing in the MEA who are likely to be involved in managing thyroid disease. The respondents were not mutually exclusive. The respondents were identified on academic databases of health-related bodies, professional groups, and recent continuous professional development events similar to several previous studies in the region.<sup>19-22</sup> The initial invitation email explained the study's rationale. Reminders were sent for nonresponders and partial responders. The survey service automatically blocked repeat submissions from the same Internet protocol address. ►Table 1 shows respondents' demographic and professional profiles to the two surveys of GO and Se in ATD.

### Survey Questionnaires

The questions were based on previously validated GO management and Se surveys.<sup>4-9,18</sup> Additional questions were added to characterize the demographic and professional profiles of the respondents. The text of the two surveys is provided in ►Supplementary Material S1 and S2. In the first part of the GO survey, participants were asked to give their general impressions of GO in their daily practice. The second part is about managing an index case (►Fig. 1). Questions related to the index case were asked, focusing on GO diagnosis and treatment. The Se survey presented multiple-choice questions to explore respondents' general knowledge about

**Table 1** Demographic and professional profiles of respondents to the two surveys of GO and selenium in ATD

Characteristics		GO survey <sup>a</sup>	Se survey <sup>a</sup>
Respondents	Max number	183	102
Location (region)	Middle East	151 (82.5%)	80 (78.4%)
	Africa	31 (17.5%)	22 (21.6%)
Specialty	Adult endocrinology	137 (74.9%)	80 (78.4%)
	Pediatric Endocrinology	20 (10.9%)	8 (7.8%)
	Ophthalmology	26 (14.2%)	0 (0.0%)
	Others	–	14 (13.7%) <sup>b</sup>
Career stage	Senior	158 (86.3%)	89 (87.3%)
	Mid-grade	25 (13.7%)	13 (12.7%)

Abbreviations: ATD, autoimmune thyroid disease; GO, Graves' ophthalmopathy; Se, selenium.

<sup>a</sup>The two sets of respondents are not mutually exclusive.

<sup>b</sup>Included general internal physicians and general physicians with an interest in endocrinology.

A 65-year-old female patient presents with typical symptoms of hyperthyroidism. She also gives a 6-week history of uncomfortable watery eyes, lid swelling in the mornings, and double vision on upward and lateral gaze. She smokes 15-20 cigarettes per day. On examination, she is found to be moderately thyrotoxic. She has an easily palpable but small symmetrical goiter. There is marked periorbital edema, redness of the conjunctiva, bilateral chemosis, and obvious restriction of eye movements on upward gaze, and attempts to look up provoke retro-orbital pain. Proptosis is 19 mm bilaterally. Her visual acuity is normal (6/6-1.0, bilaterally on the Snellen chart). On direct questioning, she admits to being aware that colors appear less bright than they did two weeks earlier. Fundoscopy shows normal optic discs. Biochemistry confirms thyrotoxicosis (free thyroxine 52 pmol/L, normal range 11-23; total triiodothyronine 9.3 nmol/L, normal range 1-2.9; thyroid-stimulating hormone (0.05 mU/L).

**Fig. 1** The index case: patient with moderate to severe Graves' ophthalmopathy (GO) and hyperthyroidism.

Se, its role in ATD, and their attitudes to its use in ATD with and without GO.

### Collection and Summary of Responses

Survey responses were collected anonymously and stored electronically by the survey service provider, accessible and password-protected. Responses from those who met the inclusion criteria only were included (endocrinologists, internal medicine specialists with interest and practice in endocrinology with some ophthalmologists). Survey management service tools were used to examine the results and perform descriptive analysis. We chose to report the findings of the two surveys together since they are closely related.

### Statistical Analysis

The descriptive analysis was prepared using online survey software tools. Summary statistics were prepared for responses to each question. Because not every participant answered all questions, the percentage of respondents providing a given answer was calculated individually for each question, using the number of respondents to that question as the denominator. Differences between groups were tested using the chi-square test.

## Results

### Respondents Profile

Responses from 183 participants in the GO survey and from 102 participants in the Se survey were included. No information is available on nonrespondents, and questionnaires with missing information were excluded due to the nature of the original database. Thus, a response rate could not be calculated. Over three-quarters were from the Middle East and the rest were from Africa. The majority were senior adult endocrinologists (► **Table 1**).

### General Issues

#### Involvement and GO Trends

A small proportion of respondents (3.8%) saw > 20 GO cases, and the majority (62.8%) saw 1 to 5 cases, and 23 and 10.4% saw 6 to 10 and 11 to 20 cases, respectively. The source of the referrals is variable (► **Table 2**). More than half of the

respondents (55.2%) thought the GO prevalence was "unchanged" or "increased" (► **Table 2**).

### Smoking

A perceived prevalence of smoking in patients with GO was reported at 30%. However, only 47 (26.1%) based their answer on data. Over one-third (37.6%) thought that the frequency of smoking has increased or unchanged among patients with GO in the last 10 years (► **Table 1**). Almost all (93.9%) advise their patients with GO to give up smoking, but less than half of their patients have access to a smoking cessation program (► **Table 1**).

### GO-Multidisciplinary Team

Three-quarters of respondents (75.5%) claimed that treating GO in a multidisciplinary approach was highly desirable, but only 23.9% participated in a GO-multidisciplinary team (MDT). Over half (51.7%) refer cases to a GO-MDT (► **Table 2**).

### The Quality of Specialist Services

► **Fig. 2** depicts the respondents' rating of the quality of specialist services their patients receive. The highest levels of satisfaction/availability were reported with diagnostic imaging, and the lowest degree of satisfaction was recorded for orbital surgery.

### The Index Case

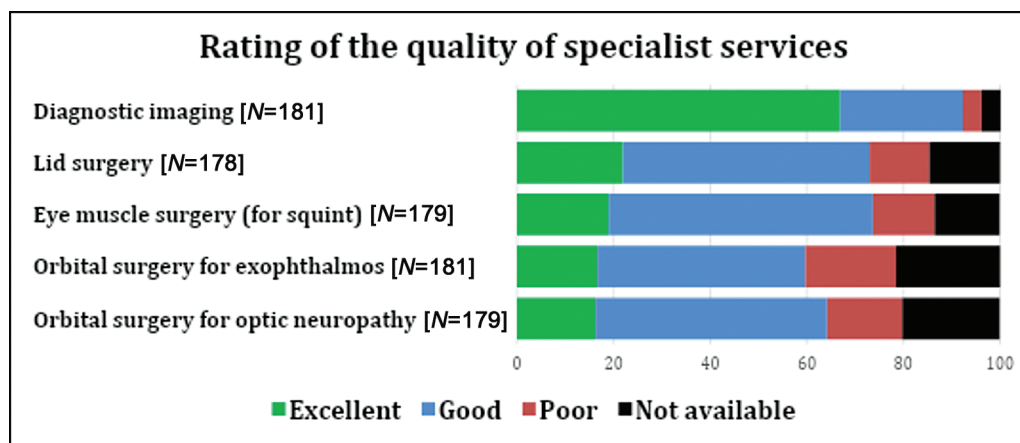
#### Diagnosis of Optic Neuropathy

Given the scenario of active eye disease of recent onset with a history of color desaturation but normal visual acuity (► **Fig. 1**), an urgent referral to an ophthalmologist was judged appropriate by 66.7% of responders, nonurgent referral by 28.2%, and no referral by 5.1%. In response to additional clinical information about optic nerve function (reduction of color vision on Ishihara plates to 12/15 on the right and 14/15 on the left, possible right peripheral field defect, and marginally delayed visual evoked potential responses on the right), while visual acuity was preserved (6/6 or 1 on Snellen chart bilaterally), 78% of the responders felt that the diagnosis of optic neuropathy was very likely (23.1%) or probable (63.2%) and 11.1% unlikely (► **Tables 3 and 4**).

**Table 2** The extent of experience with GO among respondents and their perceptions of the burden and trend of disease, role of GO-MDT, and impact of smoking

Questions	Answer choices	Responses
How many Graves' disease patients do you see in an average month? [N = 183]	1–5 cases 6–10 cases 11–20 cases > 20 cases	115 (62.8%) 42 (23.0%) 19 (10.4%) 7 (3.8%)
How many NEW cases of GO have you seen over the last 6 months? [Mean; median (min-max)]	Male Female	2.5;2.0 (0–30) 5.5;2.0 (0–200)
What is the source of the majority of your patients with GO referrals [N = 181]	Family doctors Other specialists Self-referrals	56 (30.9%) 76 (42.0%) 49 (27.1%)
Has the number of new cases of GO per annum changed in the last 10 years in the area where you practice? [N = 183]	Unchanged Increased Decreased Not sure	64 (35.0%) 37 (20.2%) 24 (13.1%) 58 (31.7%)
How valuable do you think is a TED-MDT clinic for the management of patients with GO? [N = 181]	Very valuable Moderately Not valuable	137 (75.7%) 38 (21.0%) 6 (3.3%)
Do you participate in a TED-MDT clinic [N = 180]	Yes No	43 (23.9%) 137 (76.1%)
Do you refer some of your patients to a TED-MDT clinic? [N = 180]	Yes No	93 (51.7%) 87 (48.3%)
What is the prevalence of smoking in patients with GO in your practice? [N = 177] [mean (min-max)] %	Mean/Median Min-Max	30.2(30) 0–100
Regarding the above question, was your answer based on data? [N = 180]	Yes No	47 (26.1%) 133 (73.9%)
Do you think the frequency of smoking has changed among patients with GO in the last 10 years in the area where you practice? [N = 181]	Unchanged Increased Decreased Not sure	50 (27.6%) 20 (11.0%) 29 (16.0%) 82 (45.3%)
Do you advise your patients with GO to give up smoking? [N = 180]	Yes No	169 (93.9%) 11 (6.1%)
Do your patients have access to a smoking cessation program? [N = 179]	Yes No	84 (46.9%) 95 (53.1%)

Abbreviations: GO, Graves' ophthalmopathy; TED-MDT, multidisciplinary thyroid eye disease clinic.



**Fig. 2** Respondents' rating of the quality of specialist services that their patients receive (N = 182).

**Treatment for Hyperthyroidism**

The majority of responders were in favor of antithyroid drugs, mostly in a titrated dose as first-line therapy

(► **Table 3**). Radioiodine was the least popular option (1.7%). Thyroidectomy was advocated by 0.9% of responders. Following restoration of euthyroidism, responders were

**Table 3** Respondent's approach to evaluating the "index case" described in ► Fig. 1

1. What investigations would you perform? (you may tick more than one box if you wish) [N = 119]	
Questions	Affirmative responses
Visual fields by perimetry	86 (72.3%)
Color vision testing	67 (56.3%)
MRI scan	67 (56.3%)
CT scan	53 (44.5%)
Orbital ultrasonography	15 (12.6%)
Octreoscan	4 (3.4%)
Other (please specify)	10 (8.4%)
2. Should she have been referred to an ophthalmologist at this stage? [N = 117]	
Referral needed urgently	78 (66.7%)
Referral needed nonurgently	33 (28.2%)
Postpone referral until euthyroid	4 (3.4%)
No referral is required at this stage	2 (1.7%)
3. Do you have a preference regarding first-line treatment for her hyperthyroidism? [N = 117]	
Antithyroid drugs "Titrated dose"	97 (82.9%)
Antithyroid drugs "block and replace"	10 (8.5%)
Radioiodine	2 (1.7%)
Radioiodine + oral steroids	4 (3.4%)
Thyroidectomy	1 (0.9%)
Other (please specify)	3 (2.6%)
4. Assuming the first-line treatment has established euthyroidism, do you have a preference regarding second-line treatments for her hyperthyroidism? [N = 117]	
Radioiodine alone	9 (7.7%)
Radioiodine + oral steroids	38 (32.5%)
Thyroidectomy	63 (53.8%)
Other	7 (6.0%)
<b>5. Optic nerve compression diagnosis:</b> You have arranged for the patient to have additional investigations available 2 weeks later. Visual acuity is still normal (6/6–1.0 on the Snellen chart). Color vision on the Ishihara chart is 12/15 in the right eye and 14/15 in the left. Automated visual fields show a possible peripheral defect on the right. Visually evoked potentials show a slight delay on the right but are within the reference range for a 65-year-old	
Do you think optic nerve compression [N = 117]	
Probable	74 (63.2%)
Very likely	27 (23.1%)
Unlikely	13 (11.1%)
Other	3 (2.6%)
Are other tests required to confirm or exclude the diagnosis of optic nerve compression? [N = 118]	
No	9 (7.8%)
Yes - MRI scan	79 (68.1%)
Yes - CT scan	18 (15.5%)
Yes - Orbital ultrasound	3 (2.6%)
Yes - Octreoscan	4 (3.4%)
Yes - Other	3 (2.6%)

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

**Table 4** Responses concerning managing GO patients with optic nerve compression in the index case and two case variants, including young age and diabetes, are based on optic compression severity in two different clinical contexts

<i>Context A. (following from ►Table 4): Your efforts to contact the patient have failed as she has gone on a week's holiday. Upon her return, she will appear in your outpatient clinic. Her visual acuity is 6/12 (0.5) on the right and 6/9 (0.67) on the left. On fundoscopy, she has a blurred disc margin on the right. What treatment(s) would you institute at this stage for the index case, a similar case aged 32 years and a 65-year-old patient with diabetes? (you may tick more than one if you wish)</i>			
Treatment options	Case variants		
	Index case	32-year-old	Diabetes
Responders (n)	118	118	118
Intravenous steroids	72.0%	63.6%	30.5%
Surgical orbital decompression	29.7%	34.7%	31.4%
Oral steroids	22.0%	28.0%	16.1%
Radiotherapy	14.4%	12.7%	33.1%
Other	8.5%	10.2%	15.3%
Intravenous IgG	6.8%	5.9%	9.3%
Subconjunctival/retrobulbar steroids	5.1%	5.1%	9.3%
Plasmapheresis	2.5%	2.5%	7.6%
Octreotide/Lanreotide	2.5%	2.5%	1.7%
Azathioprine	1.7%	1.7%	6.8%
Cyclosporin	0.0%	2.5%	4.2%
None	0.0%	2.5%	1.7%
<i>Context B. Following extensive discussions, the patient decides to have high-dose intravenous steroids. Three months later, she received three cycles of intravenous steroids and is still on oral prednisolone 40 mg daily. Reduction of oral prednisolone to less than 40 mg daily 2 weeks earlier led to deterioration in visual acuity. On examination, the patient is markedly Cushingoid. Visual acuity is 6/6 (1.0) bilaterally. Color vision (Ishihara chart) is 13/15 on the right and 15/15 on the left. She has a possible relative afferent pupillary defect on the right. The discs look normal. The right orbit feels very "tight" on ballottement. What treatment(s) would you institute at this stage? (You may tick more than one if you wish.) For the index case, is there a similar case aged 32 years and a 65-year-old patient with diabetes?</i>			
Case variant	Index case	32-year-old	Diabetes
Number of respondents	118	116	115
Surgical orbital decompression	40.5%	43.1%	40.0%
Radiotherapy	33.6%	23.3%	33.9%
Withdraw steroids	22.4%	15.5%	26.1%
Continue the same dose of oral steroids	15.5%	12.9%	7.0%
Other	11.2%	11.2%	11.3%
Intravenous steroids	10.3%	15.5%	7.0%
Azathioprine	10.3%	11.2%	11.3%
Cyclosporin	6.9%	5.2%	5.2%
Plasmapheresis	6.9%	6.0%	5.2%
Subconjunctival/retrobulbar steroids	3.4%	7.8%	4.3%
Intravenous IgG	3.4%	3.4%	3.5%
Octreotide/Lanreotide	0.9%	1.7%	1.7%

Abbreviations: GO, Graves' ophthalmopathy; IgG, immunoglobulin G.

asked if they would prefer a second-line treatment of hyperthyroidism. Four options were offered: radioiodine alone, radioiodine with prophylactic steroids, thyroidectomy, and "other." There was a major shift in favor of the use of radioiodine with steroid prophylaxis (from 3.4 to 32.5%,  $p < 0.001$ ) and thyroidectomy (from 0.9 to 53.8%,  $p < 0.001$ ) (►Table 3).

#### Treatment of Optic Neuropathy

Most responders recommended a steroid (oral, intravenous, or subconjunctival/retrobulbar) (►Table 4, Context A). Intravenous steroids (alone or in combination with other treatments) were the most frequently chosen treatment (72.0%), followed by oral steroids alone or in combination



**Table 5** Respondents' basic knowledge of selenium status and supplementation in general and the use of selenium supplements in thyroid patients

Question	Answer choices	Responses N (%)
1. Do you use Se supplements in patients with thyroid disease? [N = 101]	Never Only in clinical trials Rarely/Occasionally Frequently/Always	40 (39.6%) 3 (3.0%) 38 (37.6%) 20 (19.8%)
2. Do you ask about using dietary supplements containing Se before recommending Se supplementation? [N = 101]	Generally Occasionally Never	18 (17.8%) 27 (26.7%) 56 (55.4%)
3. Does the Se status of the general population influence your decision to recommend Se supplementation in a given patient? [N = 100]	Yes, generally Yes, occasionally No Do not know	11 (11.0%) 9 (9.0%) 53 (53.0%) 27 (27.0%)
4. Do you measure Se status in a given patient before recommending Se supplementation? [N = 100]	Generally Occasionally Never	4 (4.0%) 11 (11.0%) 85 (85.0%)
5. Does the Iodine status of the general population in your country of residence influence your decision to recommend Se supplementation in a given patient? (Choose one or more options) [N = 101]	Yes, Iodine deficiency would make my decision to recommend Se supplementation more likely Yes, Iodine deficiency would make my decision to recommend Se supplementation less likely Yes, adequate Iodine intake would make my decision to recommend Se supplementation more likely Yes, adequate Iodine intake would make my decision to recommend Se supplementation less likely Yes, and Iodine excess would make my decision to recommend Se supplementation more likely Yes, an excess of Iodine would make my decision to recommend Se supplementation less likely No, Iodine status of the population does not influence my decision on Se supplementation Do not know	11 (10.9%) 4 (4.0%) 3 (3.0%) 3 (3.0%) 2 (2.0%) 1 (1.0%) 45 (44.6%) 38 (37.6%)
6. What type of Se compound do you generally prefer when recommending Se supplementation? [N = 101]	Organic Se compound Inorganic Se compound Different depending on the indication Different depending on the price No preference Do not know	16 (15.8%) 9 (8.9%) 6 (5.9%) 9 (8.9%) 30 (29.7%) 31 (30.7%)
7. In your country of practice, do you also make a prescription when you recommend Se supplementation? <sup>a</sup> [N = 102]	Yes, always, Se is exclusively POM Yes, sometimes, Se is a POM in high doses only Yes, sometimes, when I strongly recommend Se supplementation No, Se is sold as an OTC medicine (No prescription is needed) Do not know	9 (8.8%) 7 (6.9%) 26 (25.5%) 33 (32.4%) 27 (26.5%)

Abbreviations: OTC, over-the-counter; POM, prescription-only medicine; Se, selenium.

with other treatments (22.0%), radiotherapy (alone or in combination with other treatments) by 14.4% of responders, and surgical decompression (alone or in combination with other treatments) by 29.7% of responders (► **Table 5**).

A younger age (32 years compared to 65 years) did not influence the choice of treatments (► **Table 6**). The presence of diabetes led to a significant reduction in the use of steroids (intravenous: 72.0–30.5%; oral: 22.0–16.1%), an increase in the use of orbital irradiation (from 14.4 to 33.3%), more use of surgical decompression (from 29.7 to 31.4.8%), and more use of cyclosporine (0.0–4.2%) and azathioprine (from 1.7 to 6.8%) (► **Table 5**).

Responders were asked whether their treatment choice would alter in the light of marked Cushingoid side effects and ongoing threat of optic neuropathy (visual acuity is 6/6 or 1

bilaterally, color vision on Ishihara plates 13/15 on the right and 15/15 on the left, a possible relative afferent pupillary defect on the right, normal looking optic discs, and the right orbit feeling very “tight” on ballottement). There was a major shift away from the use of steroids and a rise in the use of orbital irradiation (33.6%) and surgical decompression (40.5%) (► **Table 5**, Context B).

A younger age (32 years) led to a slight reduction in the use of orbital irradiation (23.3% vs. 33.6%) and a slight increase in the use of steroids (► **Table 6**). However, the diagnosis of diabetes resulted in a significant reduction in the use of oral steroids. There was no difference in the use of other immunosuppressive therapies and no change in the use of orbital irradiation (► **Table 5**).

Regarding perceptions of the role of orbital radiotherapy in managing GO, 149/181 (82.3%) participants lacked

**Table 6** Respondents reported the use of selenium for thyroid disease with and without GO

Question	Answer choices	GO absent	GO present
1. Do you think that the available evidence warrants the use of Se supplementation in GD? [N = 102]	Yes, I recommend it routinely No, I never recommend it No, but I think it is effective, I recommend it routinely No, but I recommend it occasionally Other Do not know	11 (10.8%) 28 (27.5%) 6 (5.9%) 24 (23.5%) 6 (5.9%) 27 (26.5%)	27 (26.5%) 13 (12.7%) 12 (11.8%) 14 (13.7%) 7 (6.9%) 29 (28.4%)
2. In a patient with GD receiving antithyroid medication? [N = 102]	Never Sometimes Frequently Always	70 (68.6%) 23 (22.5%) 5 (4.9%) 4 (3.9%)	39 (38.2%) 31 (30.4%) 16 (15.7%) 16 (15.7%)
3. (a) If recommended sometimes, frequently, or always (in 2 above), Why do you suggest Se supplementation for this patient group (one or more options)? [N = 97]	Induce disease remission Improve the quality of life Reduce TRAb levels Reduce the risk of relapse Improve thyroid texture Reduce ATD dose Other Do not know	14 (14.4%) 14 (14.4%) 13 (13.4%) 11 (11.3%) 5 (5.2%) 4 (4.1%) 7 (7.2%) 56 (57.7%)	
3. (b) If recommended sometimes, frequently, or always (in 2 above), why do you suggest Se supplementation for this patient group (Choose one or more options)? [N = 98]	Induce disease remission As an alternative to doing nothing in mild GO As an alternative to other treatment modalities in patients with moderate to severe GO As a supplement to other treatment modalities in patients with moderate to severe GO Improve the quality of life Other Do not know		11 (11.2%) 21 (21.4%) 1 (1.0%) 21 (21.4%) 7 (7.1%) 6 (6.1%) 31 (31.6%)
4. If recommended sometimes, frequently, or always (in 2 above), which daily amount of Se supplementation do you recommend for this patient group? (Choose one option) [N = 94]	< 100 mcg/day 100 mcg/day 200 mcg/day > 200 mcg/day Other Do not know	6 (6.4%) 18 (19.1%) 31 (33.0%) 3 (3.2%) - 36 (38.3%)	5 (5.1%) 15 (15.3%) 42 (42.9%) 5 (5.1%) 2 (2.0%) 29 (29.6%)
5. If recommended sometimes, frequently, or always (in 2 above), how long would you recommend this patient take Se supplementation? (Choose one option) [N = 94, 98]	Weeks to months, and then reevaluate Years, and then reevaluate As long as ATD is needed Indefinitely Other Do not know	42 (44.7%) 2 (2.1%) 11 (11.7%) 2 (2.1%) 2 (2.1%) 35 (37.2%)	53 (54.1%) 5 (5.1%) - 2 (2.0%) 4 (4.1%) 34 (34.7%)

Abbreviations: ATD, autoimmune thyroid disease; GD, Graves' disease; GO, Graves' ophthalmopathy; Se, selenium; TRAb, thyroid-stimulating hormone receptor antibody.

knowledge of the details of the radiotherapy regimens. Over the last 3 years, 86/180 respondents stated that they are less likely to use orbital irradiation as monotherapy for moderately severe GO, and the use of orbital irradiation in combination with high-dose steroids for severe GO has not changed, according to 81/178 (45.5%) respondents.

**Comparisons with Previous Studies**

► **Supplementary Material S3** provides a narrative comparison of the present study and previous studies. For the treatment of Graves' ophthalmology (noting that multiple options are allowed), the number of respondents favoring steroids is similar. European respondents slightly favor orbital irradiation, whereas MEA, Chinese, and Latin American respondents favor surgical decompression. Concerning the treatment for comorbid thyrotoxicosis, the antithyroid drugs

were preferred as a single option but relatively less so by the Chinese respondents. Radioiodine was more favored by the Chinese respondents (16.1%) and least favored by the Europeans (2.0%). Thyroidectomy was more favored by the Chinese respondents (9.7%) than others.

**General Knowledge of Se Supplementation**

► **Table 5** provides general statements on the use of Se supplements in thyroid patients. Se supplements are never used by 39.6%, rarely/occasionally used by 37.6%, or used frequently/always by 19.8% of the respondents. A smaller proportion (17.8%) generally ask about using dietary supplements containing Se before recommending Se supplementation, whereas 26.7% occasionally do, and more than half (55.4%) never ask. The Se status of the general population does not influence the decision by over half of respondents



(53.0%) to recommend Se supplementation in a given patient (27.0%). Most (85%) only measure Se status in patients after recommending Se supplementation. The iodine status of the general population in a country does not influence the decision to recommend Se supplementation in a given patient by the majority (44.6%), whereas over a third (37.6%) admitted their ignorance. About 30% had no preference for the Se compound type, and a similar proportion needed to gain knowledge. About 25.5% of the respondents provide prescriptions occasionally when they strongly recommend Se supplementation, 32.4% stated that Se is sold as an over-the-counter (OTC) medicine, and 26.5% did not know.

### Se Supplementation in GD without GO

For patients with GD not associated with GO, 11 out of 102 respondents (40.4%) answered that the available evidence does not warrant using Se. Over two-thirds of respondents (68.6%) affirmed that they never prescribed it. Thirty-two clinicians (31.3%) suggested using Se. Regardless of their use, the most frequent reasons for their recommendation were to induce disease remission (14.4%), improve the quality of life (14.4%), and reduce TRAb levels (13.4%). However, over half (57.7%) admitted ignorance (note that more than one answer was allowed). The most frequently suggested doses for Se supplementation were nearly equally distributed between 200 and 100 µg/day (by 33.0 and 19.1% of respondents, respectively), and 38.3% of respondents did not know the dose. Furthermore, the recommended length of treatment was from a few weeks to months for 42 of 94 respondents (44.5%). The other respondents were evenly distributed among the different possible options: "as long as antithyroid medication is needed," "years," or "indefinitely." Again, over one-third (37.2%) admitted ignorance.

### Se Supplementation for GO

For Graves' patients with GO, 26.5% of respondents declared that the available evidence supports using Se supplementation. A substantial proportion, 39 (38.2%), answered that there is no evidence in favor of this treatment. However, 26 (25.5%) respondents affirmed that they prescribed Se even if they recognized the available scientific evidence as insufficient (lack of knowledge was admitted by 27; 26.5% of respondents). Furthermore, the majority (63; 61.8%) of respondents recommended Se use in GO, namely, 31 "sometimes" (30.4%), 16 "frequently" (15.7%), and 16 "always" (15.7%).

Se supplementation was recommended by 21 respondents (21.4%) as an alternative to surveillance alone in patients with mild ocular involvement and by 21 (21.4%) as a supplement to the established treatment modalities in patients with moderate to severe GO (more than one answer was allowed). The preferred dose was 200 µg/day for 42 (42.9%), and 29 (29.6%) admitted lack of knowledge. Se treatment for a few weeks to months and a subsequent reassessment of the patient for evaluating the effect of Se supplementation was recommended by 54.1% of respondents, whereas 34.7% were unsure or did not know.

## Discussion

We explored perceptions and self-reported practices relating to the management of GO and the role of Se in thyroid disease aspects with a view to guiding future education, guidelines, and research in MEA.

We have employed the same case scenario as the one used in the previous surveys.<sup>4-9</sup> Her visual acuity and funduscopy showed normal optic discs. However, her other complaints of disturbed color vision indicated that she was probably having early optic nerve compression. Two-thirds of MEA respondents would urgently refer this GO patient to an ophthalmologist because of symptoms similar to those in the European study.<sup>4</sup> This may be reassuring that these respondents recognized the disease's seriousness.

For patients with mild GO, Se administration significantly improved quality of life, reduced ocular involvement, and slowed disease progression.<sup>23</sup> Moderate to severe GO can be effectively treated with glucocorticoids, orbital irradiation, or both. High-dose intravenous glucocorticoids should be immediately administered to patients with optic neuropathy.<sup>24</sup> This is likely well-accepted by respondents from the MEA region and those from Europe, Latin America, and China. More than 70% of respondents chose intravenous glucocorticoids as the first-line therapy for the patient.<sup>4-9</sup>

The duration and dose of glucocorticoid treatment have always been contentious.<sup>24</sup> Several randomized and uncontrolled trials, consensus statements, systematic reviews, and meta-analyses elucidated the efficacy and adverse effects of intravenous glucocorticoid therapy in GO. The current first-line treatment for active, moderate-to-severe GO was a 12-week course of high-dose intravenous glucocorticoid pulses. The 12-week intravenous glucocorticoid group patients had a higher treatment response at 3 months than oral glucocorticoids (72% vs. 49%,  $p < 0.001$ ). The intravenous regimen's efficacy is also well recognized by nearly three-quarters of the respondents in the present study. Intravenous glucocorticoids have been thought to have a significant advantage over oral treatment and cause significantly fewer adverse events.<sup>25,26</sup> Our questionnaire survey revealed that glucocorticoids were preferentially administered intravenously for treating GO in the MEA region (72% vs. 22%), similar to the European study. Further training is required for clinicians on the standardized use of glucocorticoids to manage GO with clearly defined roles of endocrinologists and ophthalmologists, preferably within an MDT.

Significant increases in the ocular manifestations of GD followed radioiodine therapy for hyperthyroidism when compared with surgical thyroidectomy and ATD treatment.<sup>27,28</sup> Radioiodine is considered the first-line treatment for GD in many institutions, particularly in North America. In the present survey, the proportion of MEA respondents preferring radioiodine therapy for hyperthyroidism in the case was similar to Latin American, higher than in Europe, and less than in China (**► Supplementary Material S3**). Radioiodine therapy could induce the onset or progression of GO in approximately 15 to 20% of patients,<sup>29</sup> particularly when they have a history of cigarette smoking.<sup>30</sup>

Glucocorticoid prophylaxis is highly effective in preventing the deterioration of eye disease in patients with preexisting ophthalmopathy compared with radioiodine therapy without glucocorticoids.<sup>31</sup> This was recommended by almost one-third (32.5%) of MEA respondents. Lower doses of oral prednisone could effectively prevent GO exacerbation without the adverse effects of high-dose intravenous glucocorticoids.<sup>32</sup>

Knowledge of present practice by specialists who manage patients with GO is valuable in identifying deficits in training, education, and expertise and planning services for patients with this condition. The response rates to our questionnaire could not be confidently calculated based on the wide net recruited. Therefore, it is challenging to be certain that the views expressed are representative of relevant specialists in the MEA region. However, it is likely that most of those who did not reply were either clinically inactive or managed very few patients with GO. Therefore, the opinions expressed by the respondents affect many patients with GO in the MEA region.

This survey has identified several potential inadequacies of clinical services, particularly orbital surgery available to patients with GO in MEA, as illustrated by the following findings: (1) specialist orbital surgery for optic neuropathy was not readily available, and (2) when the index case developed troublesome Cushingoid features, while the optic nerves were still threatened, 40.5% of the responders chose surgical decompression. These findings suggest that specialist training in assessing and interpreting diagnostic tests in patients with GO is lacking across the region. Regional professional organizations should address this through targeted educational activities to implement evidence-based practice in collaboration with international bodies.<sup>33</sup>

Se supplementation has been proposed as a potential adjuvant treatment for accelerating the remission of hyperthyroidism and, when present, for improving the symptoms and signs of GO. Although the scientific evidence is still limited and somewhat controversial, its empirical use is not infrequently considered in clinical practice.<sup>18</sup> For these reasons, the second survey explored physicians' practice patterns across the MEA region.

As a main finding, a nonnegligible minority (31.4%) of clinicians recommend Se use in GD not associated with symptoms or signs of GO. Conversely, nearly two-thirds (61.8%) of clinicians recommend Se supplementation in mild GO either always, frequently, or sometimes. However, too many admitted their ignorance of the rationale for its use.

The widely variable approaches of MEA physicians are probably the consequence of the limited and partly conflicting available clinical data. The described approaches differ from the recommendations and guidelines.<sup>1-3</sup> This surprisingly high number of people recommend Se use based on a wish to offer complementary treatment to patients affected by a debilitating or progressively worsening disease. Further reasons could be pressure from pharmaceutical companies and the patients' requests due to the widespread availability of Web-based information on various, frequently uncontrolled, social media.

For more than half of clinicians who recommend Se treatment, the main perceived benefit was the potential decrease in serum TRAb levels. For this purpose, most recommended a dose between 100 and 200  $\mu\text{g}/\text{day}$ , supplementing Se for a few weeks to months, and then reevaluating the patient. Interestingly, the reduction in TRAb levels was reported only in a single recent trial, limited to a series of 41 patients.<sup>18</sup>

Thus, confirmatory data and clear guidelines for relevant regional physicians are needed. The current guidelines on the management of GO and GD included Se supplementation as a suggested treatment for mild forms of GO.<sup>1-4</sup> Interestingly, whereas only half of the clinicians stated that the available evidence warrants Se supplementation, the vast majority (over 90%) recommended this treatment in GO. Mostly, Se is used as an alternative therapeutic option to simple surveillance in patients with mild ocular involvement, by European Thyroid Association (ETA) guidelines. However, almost half of the clinicians state that they use Se as a therapeutic adjuvant to the established treatment modalities in moderate to severe GO, which conflicts with the ETA guidelines.<sup>4,5</sup>

A U-shaped link between Se status and disease has been established, indicating that subjects who might benefit from supplementation are those with Se deficiency.<sup>34</sup> However, surprisingly, for most respondents, Se status in the general population of their region was unknown, and Se status was rarely evaluated before recommending supplementation. However, most respondents asked the patients about their use of dietary, potentially Se-containing, supplements. Thus, overall, in many, if not most, patients, it was unknown whether the patients had Se deficiency and, if treated, which Se level was reached. In published studies recruiting patients with GD and GO, the Se dose mostly ranged from 200 to 300  $\mu\text{g}/\text{day}$ . Notably, nearly no respondent suggested a dose exceeding 200  $\mu\text{g}/\text{day}$ . This clinical approach appears sound. The recommended daily intake for adults is 70 and 60  $\mu\text{g}/\text{day}$  for men and women, respectively.<sup>35</sup>

A remarkably high proportion of respondents admitted ignorance about key questions on Se and thyroid. Due to the limited knowledge of Se status among respondents, nearly two-thirds of respondents in this survey did not state any preference regarding the formulation of Se or did not respond at all. More respondents recommended an organic Se compound over an inorganic compound (15.8% vs. 8.9%).

The strength of this study lies in its novelty in the region, the respondents being from a wide region, and the use of previously established instruments. On the other hand, the number of analyzed responses could be big enough to draw firm conclusions, and the small number of thyroidologists from each country who made any comparison between countries is unreliable. The uneven distribution of answers between various parts of the region and the lack of both content and construct validation of the questionnaire are other limitations to the interpretation of the data. The selection bias of respondents may skew the results toward both an overestimation and an underestimation of the recommendation for Se supplementation. Thus, we need to determine whether these physicians represent practice

patterns in the MEA region. Also, the fact that Se is an OTC product in most countries suggests that many patients are independent of the advice of their physicians and may be easy targets of other sources of information, particularly in the digital age.

## Conclusion

The appropriate treatment for patients with GO remains controversial, even among MEA endocrinologists. Some potential deficiencies in the diagnosis and management of GO were observed in our survey. In Graves' hyperthyroidism without GO, 32.5% of respondents recommend Se supplementation. Conversely, Se is recommended by 65.0% of respondents in GO, both in patients with mild and moderate to severe ocular involvement. Regarding the use of Se, clinical practice disagrees with current treatment guidelines and is at variance with previous surveys. The findings highlight the need for further training of thyroid specialists, easier access of patients to multidisciplinary centers, and the establishment of practice guidelines required to manage this condition. In-depth education and focused training are needed to improve the perceptions and practices of endocrinologists in developing regions such as the MEA region.

### Authors' Contributions

S.A.B. adapted the questionnaire and managed the online survey. All other authors reviewed the data and contributed to the data analysis and interpretation, drafting and revising of the manuscript, and approval of its final version.

### Compliance with Ethical Principles

The study was approved by the Institutional Review Board of Sheikh Khalifa Medical City, Abu Dhabi. Respondents provided informed consent digitally before they could answer the survey questions and all data were analyzed anonymously.

### Funding

None.

### Conflict of Interest

None declared.

### Acknowledgment

We are grateful to all the colleagues who responded to the survey.

## References

- Bartalena L, Baldeschi L, Boboridis K, et al; European Group on Graves' Orbitopathy (EUGOGO) The 2016 European Thyroid Association/European Group on Graves' Orbitopathy guidelines for the management of Graves' orbitopathy. *Eur Thyroid J* 2016;5(01):9–26
- Kahaly GJ, Bartalena L, Hegedüs L, Leenhardt L, Poppe K, Pearce SH. 2018 European Thyroid Association guideline for the management of Graves' hyperthyroidism. *Eur Thyroid J* 2018;7(04):167–186
- Bartalena L, Kahaly GJ, Baldeschi L, et al; EUGOGO † The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. *Eur J Endocrinol* 2021;185(04):G43–G67
- Perros P, Baldeschi L, Boboridis K, et al; European Group of Graves' Orbitopathy. A questionnaire survey on the management of Graves' orbitopathy in Europe. *Eur J Endocrinol* 2006;155(02):207–211
- Brito JP, Nagy EV, Singh Ospina N, et al. A survey on the management of thyroid eye disease among American and European Thyroid Association members. *Thyroid* 2022;32(12):1535–1546
- Ramos HE, Diehl LA, Camacho CP, Perros P, Graf H Latin American Thyroid Society. Management of Graves' orbitopathy in Latin America: an international questionnaire study compared with Europe. *Clin Endocrinol (Oxf)* 2008;69(06):951–956
- Xu SH, Li XJ, Chen GF, et al. A questionnaire survey on the management of Graves' orbitopathy in China: a comparison with Europe and Latin-America. *Chronic Dis Transl Med* 2015;1(02):117–123
- Chen J, Li C, Teng W, et al. A Chinese survey of clinical practice on the management of thyroid eye disease. *Eur Thyroid J* 2024;13(03):e230269
- Pradhan A, Ganguly A, Naik MN, Nair AG, Desai S, Rath S. Thyroid eye disease survey: an anonymous web-based survey in the Indian subcontinent. *Indian J Ophthalmol* 2020;68(08):1609–1614
- Duntas LH, Benvenega S. Selenium: an element for life. *Endocrine* 2015;48(03):756–775
- Contempre B, Dumont JE, Ngo B, Thilly CH, Diplock AT, Vanderpas J. Effect of selenium supplementation in hypothyroid subjects of an iodine and selenium deficient area: the possible danger of indiscriminate supplementation of iodine-deficient subjects with selenium. *J Clin Endocrinol Metab* 1991;73(01):213–215
- Winther KH, Bonnema SJ, Cold F, et al. Does selenium supplementation affect thyroid function? Results from a randomized, controlled, double-blinded trial in a Danish population. *Eur J Endocrinol* 2015;172(06):657–667
- Bülow Pedersen I, Knudsen N, Carlé A, et al. Serum selenium is low in newly diagnosed Graves' disease: a population-based study. *Clin Endocrinol (Oxf)* 2013;79(04):584–590
- Kahaly GJ, Riedl M, König J, Diana T, Schomburg L. Double-blind, placebo-controlled, randomized trial of selenium in Graves hyperthyroidism. *J Clin Endocrinol Metab* 2017;102(11):4333–4341
- Leo M, Bartalena L, Rotondo Dottore G, et al. Effects of selenium on short-term control of hyperthyroidism due to Graves' disease treated with methimazole: results of a randomized clinical trial. *J Endocrinol Invest* 2017;40(03):281–287
- Wang L, Wang B, Chen SR, et al. Effect of selenium supplementation on recurrent hyperthyroidism caused by Graves' disease: a prospective pilot study. *Horm Metab Res* 2016;48(09):559–564
- Calissendorff J, Mikulski E, Larsen EH, Möller M. A prospective investigation of Graves' disease and selenium: thyroid hormones, auto-antibodies and self-rated symptoms. *Eur Thyroid J* 2015;4(02):93–98
- Negro R, Hegedüs L, Attanasio R, Papini E, Winther KH. A 2018 European Thyroid Association survey on the use of selenium supplementation in Graves' hyperthyroidism and Graves' orbitopathy. *Eur Thyroid J* 2019;8(01):7–15
- Beshyah SA, Sherif IH, Mustafa HE, et al. Patterns of clinical management of hypothyroidism in adults: an electronic survey of physicians from the Middle East and Africa. *J Diabetes Endocr Pract* 2021;4:75–82
- Beshyah SA, Ali KF. Management of adrenal insufficiency: a survey of perceptions and practices of physicians from the Middle East and North Africa. *J Diabetes Endocr Pract* 2021;4:125–130
- Beshyah SA, Khalil AB. Clinical practice patterns in managing thyroid nodules: the first survey from the Middle East and Africa. *J Diabetes Endocr Pract* 2021;4:167–174
- Beshyah SA, Bashir M, Hafidh K, et al. Impact of patient age on management of hypothyroidism: a survey of physicians from three developing regions. *J Diabetes Endocr Pract* 2024;7(03):135–144

- 23 Coulter I, Frewin S, Krassas GE, Perros P. Psychological implications of Graves' orbitopathy. *Eur J Endocrinol* 2007;157(02): 127–131
- 24 Marcocci C, Altea MA, Leo M. Treatment options for Graves' orbitopathy. *Expert Opin Pharmacother* 2012;13(06):795–806
- 25 Tanda ML, Bartalena L. Efficacy and safety of orbital radiotherapy for Graves' orbitopathy. *J Clin Endocrinol Metab* 2012;97(11): 3857–3865
- 26 Soeters MR, van Zeijl CJ, Boelen A, et al. Optimal management of Graves orbitopathy: a multidisciplinary approach. *Neth J Med* 2011;69(07):302–308
- 27 Bartalena L, Marcocci C, Bogazzi F, et al. Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy. *N Engl J Med* 1998;338(02):73–78
- 28 Sisson JC, Schipper MJ, Nelson CC, Freitas JE, Frueh BR. Radioiodine therapy and Graves' ophthalmopathy. *J Nucl Med* 2008;49(06): 923–930
- 29 Hegedüs L, Bonnema SJ, Smith TJ, Brix TH. Treating the thyroid in the presence of Graves' ophthalmopathy. *Best Pract Res Clin Endocrinol Metab* 2012;26(03):313–324
- 30 Träisk F, Tallstedt L, Abraham-Nordling M, et al; Thyroid Study Group of TT 96. Thyroid-associated ophthalmopathy after treatment for Graves' hyperthyroidism with antithyroid drugs or iodine-131. *J Clin Endocrinol Metab* 2009;94(10):3700–3707
- 31 Acharya SH, Avenell A, Philip S, Burr J, Bevan JS, Abraham P. Radioiodine therapy (RAI) for Graves' disease (GD) and the effect on ophthalmopathy: a systematic review. *Clin Endocrinol (Oxf)* 2008;69(06):943–950
- 32 Lai A, Sassi L, Compri E, et al. Lower dose prednisone prevents radioiodine-associated exacerbation of initially mild or absent graves' orbitopathy: a retrospective cohort study. *J Clin Endocrinol Metab* 2010;95(03):1333–1337
- 33 Wakelkamp IM, Tan H, Saeed P, et al. Orbital irradiation for Graves' ophthalmopathy: is it safe? A long-term follow-up study. *Ophthalmology* 2004;111(08):1557–1562
- 34 Shulhai AM, Rotondo R, Petraroli M, et al. The role of nutrition on thyroid function. *Nutrients* 2024;16(15):2496
- 35 Kipp AP, Strohm D, Brigelius-Flohé R, et al; German Nutrition Society (DGE) Revised reference values for selenium intake. *J Trace Elem Med Biol* 2015;32:195–199