31 yo Women with Double Vision

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Dr. Upala does not have any relevant financial relationships with any commercial interests

Learning Objectives

- Review manifestation of Graves' disease
- Review treatment in Graves' ophthalmopathy

HPI

- A 31Yrs female first seen in consultation for hyperthyroidism
- Since 2012 pt p/w tremors, heat insensitivity, weight gain, hair loss, eye dryness
- In June 2014 diagnosis with Graves' disease , labs were not available at that time - on MMI 5mg on and off
- Thyroid uptake and scan: OSH in June 2014, 24h uptake 42% upper nl 24
- Last TSH in December 2014 when she was off MMI was 1.09
- 4day/wk exercise, diet control - lost 7 lbs
- Then she lost follow up

HPI

- She was seen again in March 2017
- Since then she had a baby, no worsening hyperthyroid during pregnancy
- However, she reported that she has been feeling hyperthyroid and exophthalmia after delivery her baby
- Struggled with anxiety and balancing life with new baby and work (as a nurse)
- At that time, TFTs were extremely hyperthyroid (free T4 5.7, TT3 510)
- Plan to have another pregnancy in the next 2-3 years

HPI

- She was started MMI 20mg qd
- US thyroid revealed enlarged hypervascular and heterogeneous appearance of the thyroid gland
- Pt opted for surgery, as RAI was not possible at that time as she was breastfeeding, and planning for another child in the next 1-2 years
- CT orbit prior surgery: lack of optic nerve inflammation and no optic muscle hypertrophy
- She was referred to Dr. Angelos and underwent thyroidectomy in June 2018
- Since having her thyroidectomy, she states that her hyperthyroid symptoms have improved
- She no longer has a tremor nor heat intolerance, she is sleeping better and she has more energy

HPI

- Then, in Aug 2018 patient has developed worsening Graves ophthalmopathy, with double vision with up and down gaze and the L more pronounced than the R as well as mild proptosis, excessive dryness
- Pt was evaluated in Ophthalmology in Sep 2018 by Dr. Shah with acute worsening with protrusion and lid lag

Other History

- Past Medical History
  - Graves' disease
- Past Surgical history
  - S/p thyroidectomy
- Family History
  - Father : Graves' disease
  - Three paternal aunts: Graves' disease
  - Paternal GM : Graves' disease
- Allergy
  - No Known Allergies
- Social History
  - Never smoked
  - No alcohol intake
  - No recreational drugs
- Medication
  - Levothyroxine 100 mcg qd

Review of Systems

- Constitutional: No fevers, night sweats, appetite change, malaise, fatigue
- HEENT: No photophobia, blurred vision**, +eyes protrusion**, no pain, hearing loss, difficulty swallowing, thirst, hoarseness
- Resp: No cough, dyspnea, increase WOB
- CV: No CP, diaphoretic, palpitation, LE edema, no DOE, orthopnea, PND, palpitations,
- GI: No abdominal pain, nausea, vomiting, diarrhea, constipation
- GU: No dysuria, urgency, no polyuria, hematuria
- MSK: No myalgias, joint pain, back pain
- Neuro: No syncope, No numbness, paresthesias, seizures, tremors,
- headaches
- Heme: No adenopathy or easy bruising/bleeding
- Endo: No heat or cold intolerance, dry skin, dry hair, hair loss
- Derm: No rashes, ulcers, abdominal striae, hirsutism, acne
- Psych: No anxiety or depression

Physical Exam

BP: 120/82

Pulse: 74

Resp: 18

Weight: 69.8 kg Height:162.6 cm Body mass index is 26.4 kg/(m^2)

- Generally: a well-appearing female in no acute distress
- Eyes: Non-injected sclera. **Proptosis L eye, lid lag**
- ENT: Clear oropharynx.
- Neck: **non palpable, thyroid thyroidectomy scar**
- Respiratory: Clear to auscultation bilaterally
  Cardiovascular: Regular rate. No lower extremity edema
- Abdomen: Positive bowel sounds. Soft, non-tender, non-distended
- Skin: No rash. No hair loss
- Musculoskeletal: Normal gait and station
- Lymphatic: No lymphadenopathy in the neck
- Psychiatric: Alert and oriented x3. Appropriate mood/affect

Eyes Exam (In Sep 2018)

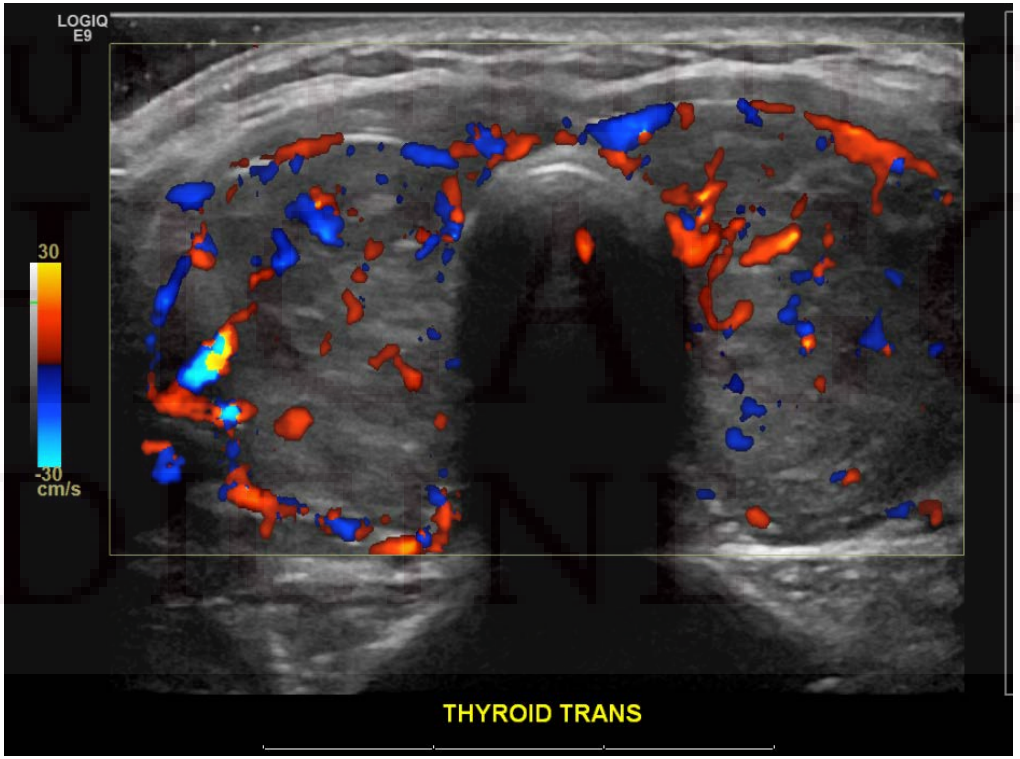
- Slit Lamp Exam

	Right	Left
Lids/Lashes	Normal	**UL retraction**
Conjunctiva/Sclera	White and quiet	**1+ injection**
Cornea	Clear	**Diffuse 1-2 + staining**
Anterior Chamber	Deep and quiet	Deep and quiet
Iris	Round and reactive	Round and reactive
Lens	Clear	Clear
Vitreous	Normal	Normal

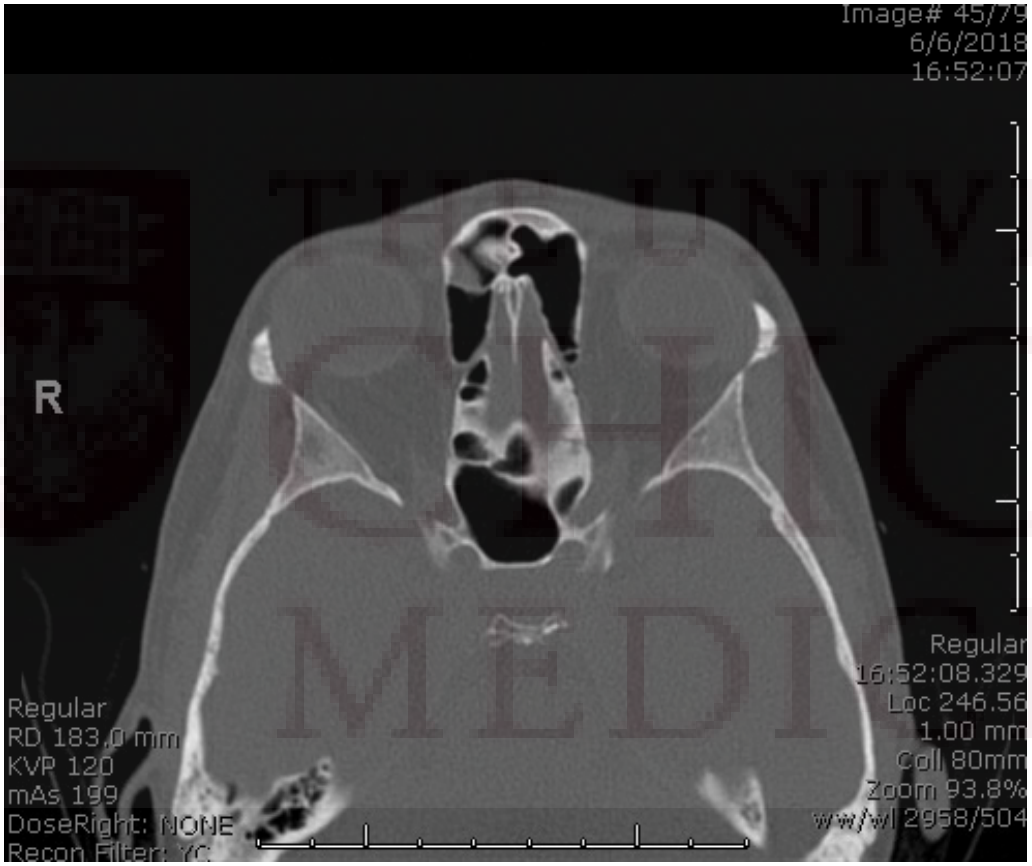
- Fundus Exam : normal

Imaging (US thyroid 1/2018)

- Enlarged hypervascular and heterogeneous appearance of the thyroid gland

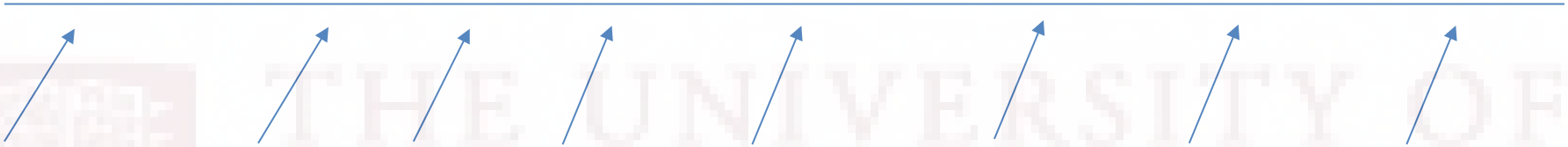


Imaging (CT orbit 6/2018)



CT orbit shows a lack of optic nerve inflammation and no optic muscle hypertrophy

HPI



tremors, heat insensitivity, weight gain, hair loss, eye dryness

Dx with Graves' disease
On MMI 5 mg qd on and off

Loss of follow up

Pregnant
On MMI 20 mg qd (off and on)

Worsening tremor and lid lag
(free T4 5.7, TT3 510)
Increase MMI to 30 mg qd

CT orbit: lack of optic nerve inflammation and no optic muscle hypertrophy

s/p thyroidectomy

Worsening eyes symptoms with double vision and lid lag

Lab

Jan 2018

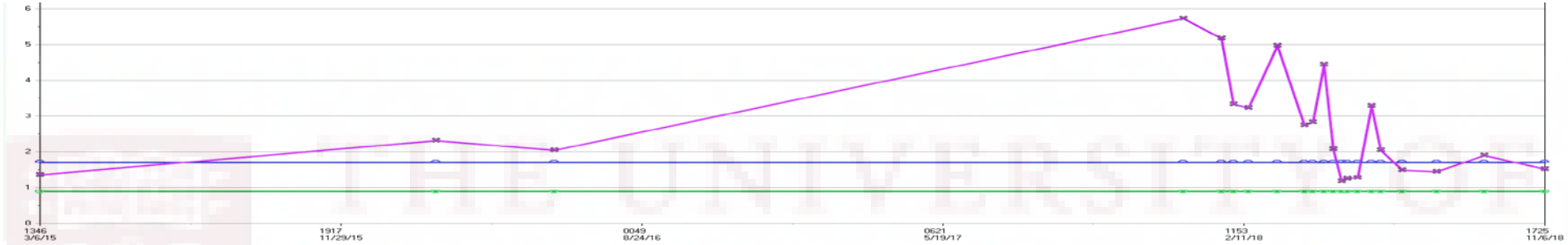
- TG ab : 8.4 (<0.4)
- TSI : 5.5 (<1.3)
- TPO ab: >20
- FT4 : 5.17 (0.9-1.7)
- TSH : 0.01 (0.3-4)
- TT3 : 482 (80-195)

Nov 2018

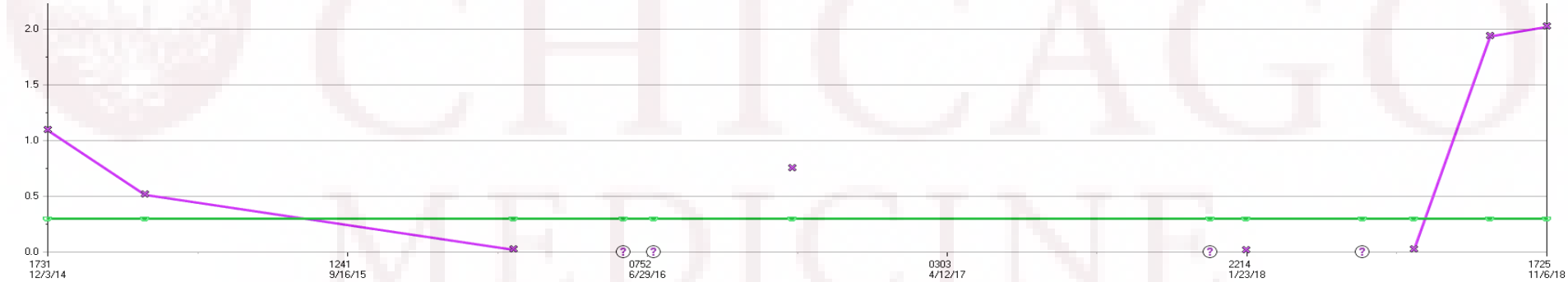
- TSI : 3.5 (<1.3)
- FT4 : 1.51 (0.9-1.7)
- TSH : 2.02 (0.3-4)
- TT3 : 63 (80-195)

TFT

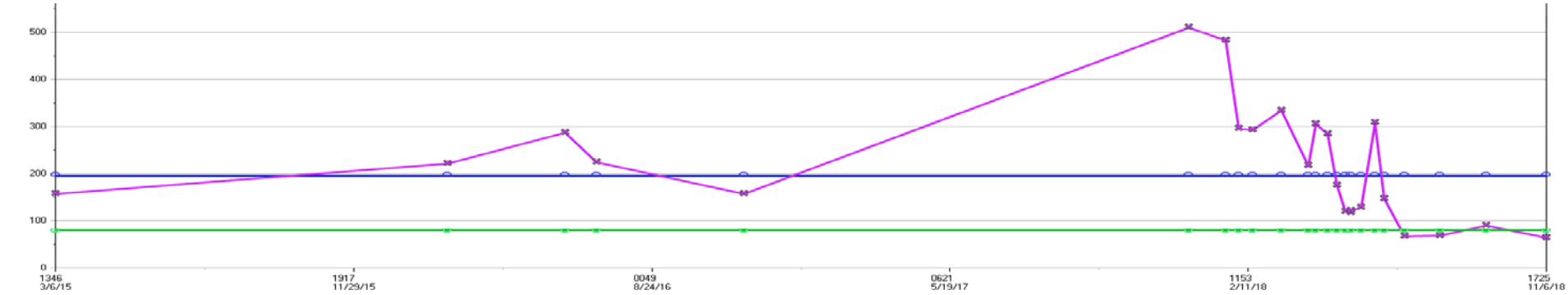
- FT4



- TSH



- TT3



Management

- Next step?

Management

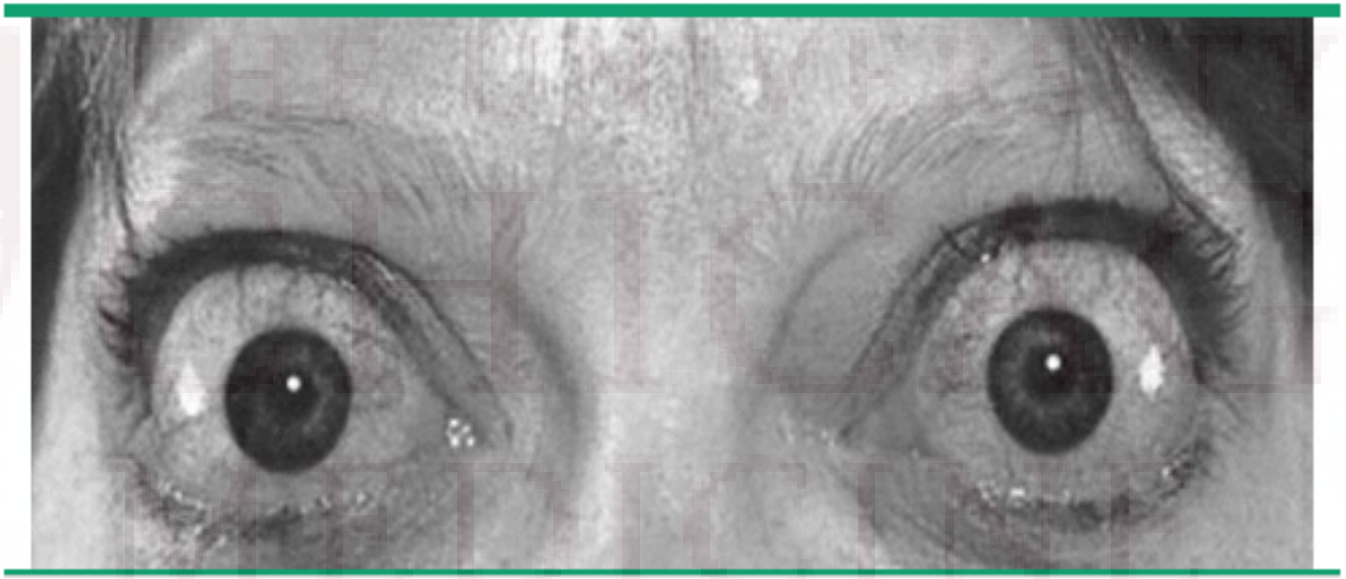
- Steroid infusions were started
- She has 6 weekly infusions of 500 mg solu-medrol so far (now 5/6)
- Protects eye with tape at night, eye drops

Clinical Question

- Treatment of Graves ophthalmopathy?

Graves' Ophthalmopathy

Typical presentation of Graves' orbitopathy showing marked stare, proptosis, and conjunctival inflammation



Courtesy of Terry Davies, MD, FRCP, FACE.

Graphic 116687 Version 1.0

Graves' Orbitopathy Severity Assessment

Graves' orbitopathy severity assessment [1-4]

Grade*	Lid retraction	Soft tissues	Proptosis¶	Diplopia	Corneal exposure	Optic nerve status
Mild	<2 mm	Mild involvement	<3 mm	Transient or absent	Absent	Normal
Moderate	≥2 mm	Moderate involvement	≥3 mm	Inconstant	Mild	Normal
Severe	≥2 mm	Severe involvement	≥3 mm	Constant	Mild	Normal
Sight threatening	–	–	–	–	Severe	Compression
Upper limits of normal						
African American	F/M = 23/24 mm					
White	F/M = 19/21 mm					
Asian	F/M = 16/17 mm (Thai) or 18.6 mm (Chinese)					

F: female; M: male; GO: Graves' orbitopathy.

* Mild GO: patients whose features of GO have only a minor impact on daily life, generally insufficient to justify immunosuppressive or surgical treatment. Moderate-to-severe GO: patients without sight-threatening GO whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive). Sight-threatening GO: patients with dysthyroid optic neuropathy and/or corneal breakdown. This category warrants immediate intervention.

¶ Proptosis refers to the variation compared with the upper limit of normal for each race/sex or the patient's baseline, if available.

References:

1. *de Juan E Jr, Hurley DP, Sapira JD. Racial differences in normal values of proptosis. Arch Intern Med 1980; 140:1230.*
2. *Sarinnapakorn V, Sridama V, Sunthornthepvarakul T. Proptosis in normal Thai samples and thyroid patients. J Med Assoc Thai 2007; 90:679.*
3. *Tsai CC, Kau HC, Kao SC, Hsu WM. Exophthalmos of patients with Graves' disease in Chinese of Taiwan. Eye (Lond) 2006; 20:569.*
4. *Bartalena L, Baldeschi L, Dickinson AJ, et al. Consensus statement of the European group on Graves' orbitopathy (EUGOGO) on management of Graves' orbitopathy. Thyroid 2008; 18:333.*

Graves' Orbitopathy Severity Assessment

Assessment of Graves' orbitopathy: Clinical activity score elements[1,2]

Elements*	Each visit	Comparison with previous visit	Score
Painful feeling behind the globe over last four weeks	X		1
Pain with eye movement during last four weeks	X		1
Redness of the eyelids	X		1
Redness of the conjunctiva	X		1
Swelling of the eyelids	X		1
Chemosis (edema of the conjunctiva)	X		1
Swollen caruncle (flesh body at medial angle of eye)	X		1
Increase in proptosis ≥2 mm		X	1
Decreased eye movements ≥5° any direction		X	1
Decreased visual acuity ≥1 line on Snellen chart		X	1

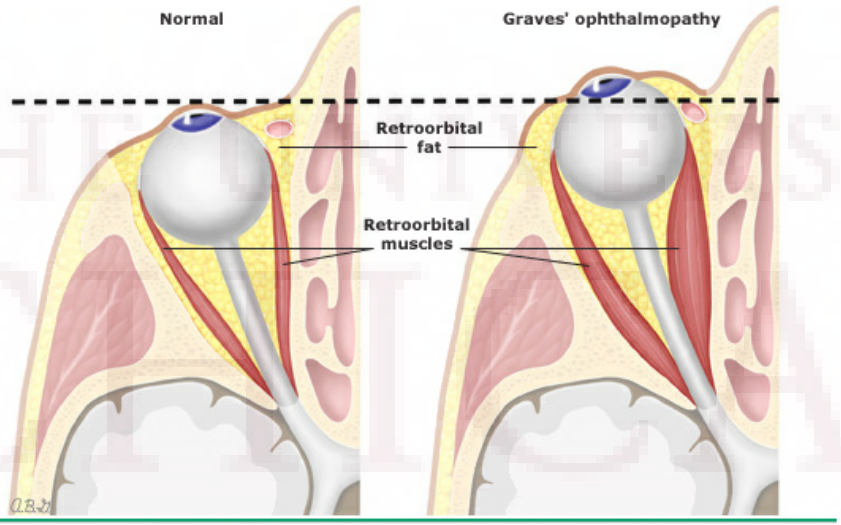
GO: Graves' orbitopathy; CAS: clinical activity score.
* A seven-point scale (excluding the last three elements) is used when no previous assessment is available. GO is considered active in patients with a CAS ≥3.

References:

1. *Mourits MP, Koornneef L, Wiersinga WM, et al. Clinical criteria for the assessment of disease activity in Graves' ophthalmopathy: A novel approach. Br J Ophthalmol 1989; 73:639.*
2. *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.*

Graves' Ophthalmopathy

Graves' ophthalmopathy: Retroorbital fat and muscle

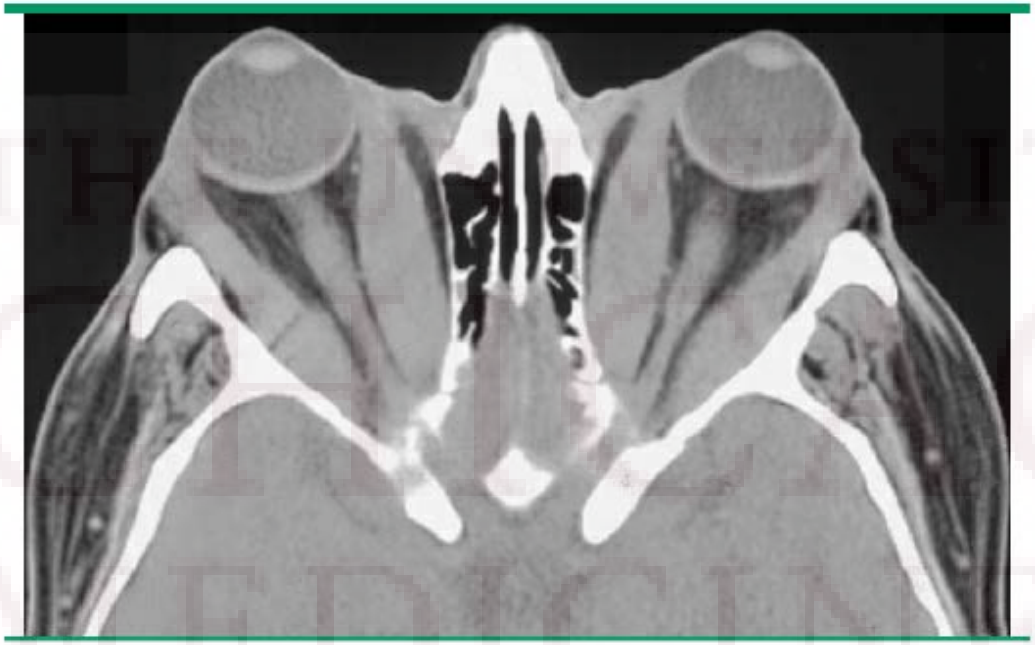


Both the retroorbital fat and muscles are involved in the development of Graves' opthalmopathy. Cytokine released from fibroblast and pre-adipocytes accentuate the secretion of hyaluronic acid-like molecules, which increase the osmotic pressure in the tissues causing fluid accumulation and, in particular, disruption of the muscle bundles. This figure shows the marked swelling of the retroorbital muscles, often well visualized on MRI or CT scanning in such patients. The consequence of retroorbital swelling is proptosis (exophthalmos), not well illustrated here since this may depend on both the anatomy of the orbit and the degree of swelling.

CT: computed tomography; MRI: magnetic resonance imaging.

Graves' Ophthalmopathy: CT Scan

Graves' orbitopathy: Findings on CT scan



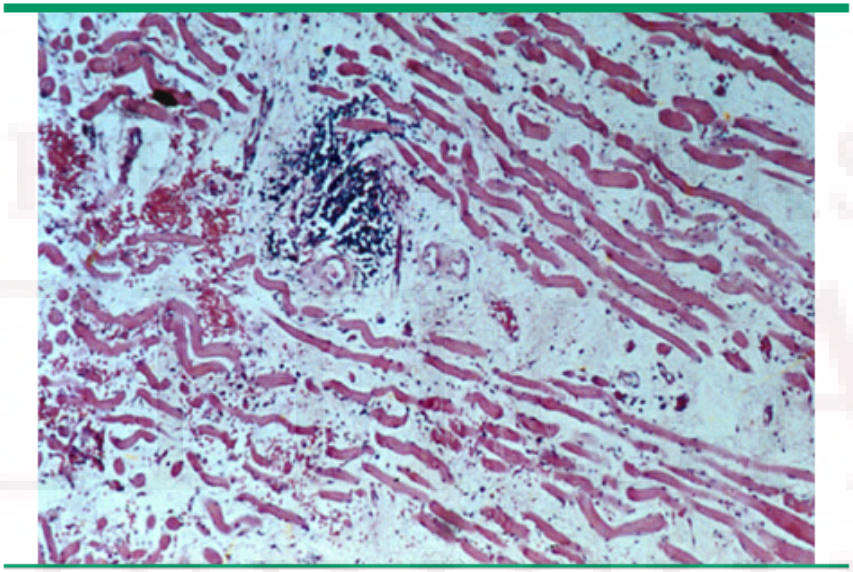
CT scan showing enlarged extra-ocular muscles in a patient with Graves' orbitopathy and resulting proptosis.

CT: computed tomography.

Courtesy of Terry F Davies, MD, FRCP, FACE.

Graves' Eye Pathology

Graves' eye infiltrate: Findings on extraocular muscle biopsy

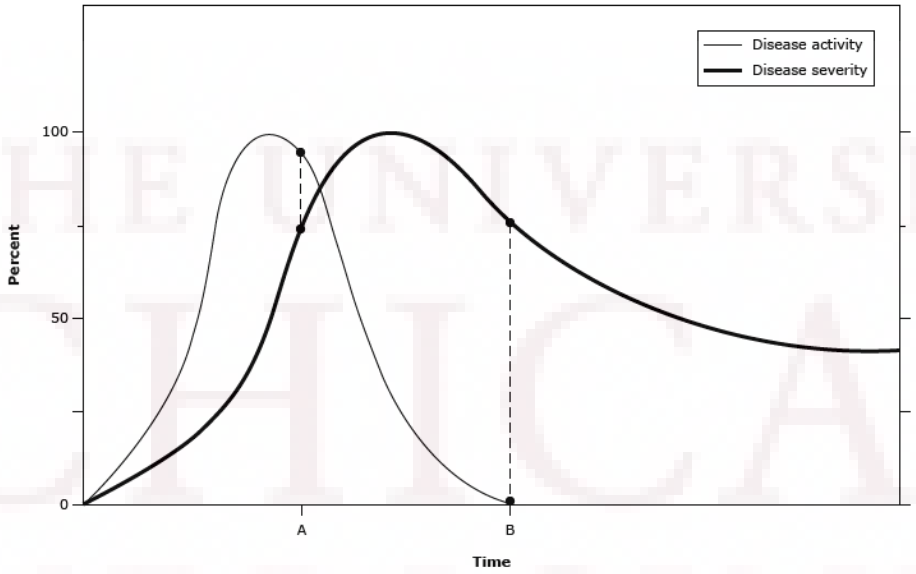


Disrupted muscle fibers and an area of inflammatory cell accumulation in the superior rectus muscle of a patient with ophthalmic Graves' disease. The sample was obtained at the time of decompression surgery. The extraocular muscles are swollen, and some muscle fibers show loss of striation, fragmentation, and infiltration with lymphocytes, most of which are T lymphocytes.

Courtesy of Terry F Davies, MD, FRCP, FACE.

GO Disease and Activity

Hypothetical relationship between GO disease activity and GO severity



Hypothetical relationship between disease activity and severity in the natural history of GO. The disease activity is not synonymous nor coincident with the severity of the disease. "A" represents a point where an individual patient may be just beyond the most active phase of disease but has yet to show the most severe ocular involvement. "B" represents a point where an individual patient may have severe ocular manifestations, but the disease has run its course.

GO: Graves' orbitopathy.

Glucocorticoids for Graves' Disease

Ocular involvement	Activity	Treatment
Nonsevere	Active	Supportive measures
Nonsevere	Inactive	Supportive measures
Severe	Active	Glucocorticoids
		Orbital radiotherapy
		Orbital decompression*
Severe	Inactive	Orbital decompression
		Strabismus surgery
		Eyelid retraction surgery

*Only in the setting of compressive optic neuropathy that has not resolved with maximal medical management, (Bartalena L, Pinchera A, Marcocci C. Management of Graves' ophthalmopathy: reality and perspectives. Endocr Rev 2000;21(2):168-99)

Glucocorticoids for Graves' Disease

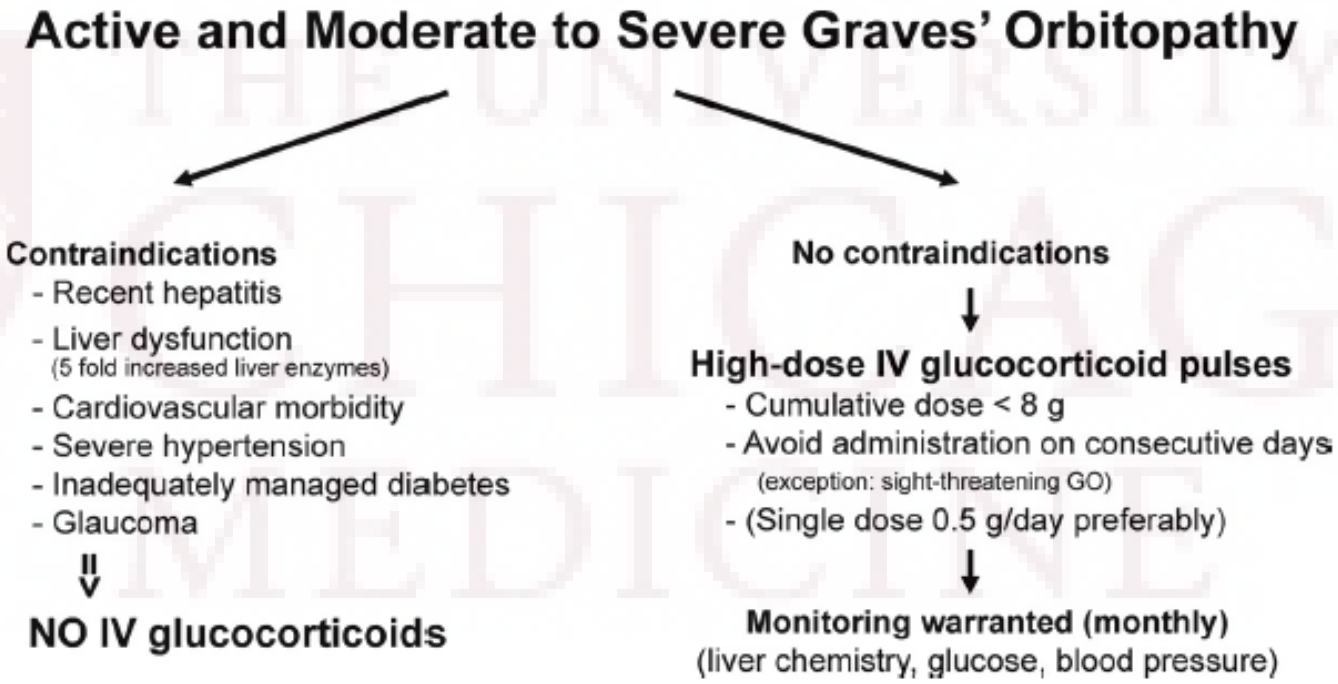


FIG. 2. Algorithm for the iv glucocorticoid treatment in active and severe GO.

IV Glucocorticoid Pulse Therapy

- Moderate-to-severe GO is a 6-12 wks course of high-dose iv glucocorticoid pulses
- The response rate is approximately 80%
- IV glucocorticoids have a statistically significant advantage over oral treatment and cause significantly fewer adverse events
- The morbidity and mortality of iv glucocorticoid therapy are 6.5 and 0.6%, respectively
- Before iv glucocorticoid administration, patients should be screened for recent hepatitis, liver dysfunction, cardiovascular morbidity, severe hypertension, inadequately managed diabetes, and glaucoma

J Clin Endocrinol Metab 90: 5234–5240, 2005

High Dose of Oral Prednisone

- Some clinicians initiate therapy with a high dose of oral prednisone, such as 80 to 100 mg/day.
- However, doses of 30 to 40 mg/day appear to be as effective for moderate orbitopathy and have fewer side effects
- Improvement usually occurs within four weeks. Approximately one-half of patients have a good response to prednisone by the end of six months; those patients with less muscle swelling are more likely to respond
- Other approaches should be considered if the patient does not respond in 4 to 6 weeks. If a good response occurs, the daily dose should be decreased to the lowest dose at which improvement is maintained

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids

- Designs: randomized control trial over 12 wk with 6-month follow-up
- Patients: 70 euthyroid patients with untreated, severe orbitopathy randomly assigned to receive once-weekly IV methylprednisolone (0.5 g, then 0.25 g, weekly for six weeks each) or a high dose of oral prednisone (100 mg per day, tapering by 10 mg per week)
- Setting: university joint thyroid and ophthalmic clinics
- Main outcome measures: at 3 months, the primary end point was a composite of improvements in proptosis, lid fissure width, and rate of diplopia in primary gaze, visual acuity, eye muscle thickness, and patient's quality of life

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids

TABLE 1. Demographic and clinical data of the 70 patients with untreated, active, and severe GO

	Oral prednisolone	Intravenous methylprednisolone	Oral *vs.* IV $P^{[a]}$
n	35	35	
Age (yr)	48 (25–75)	52 (31–72)	0.607
Duration of thyroid disease (months)	4 (0–6)	5 (0–7)	0.646
Duration of GO (months)	3 (0–5)	4 (0–6)	0.941
Clinical activity score of GO	5 (3–7)	5 (3–7)	1.000
Female (n, %)	24 (69%)	25 (71%)	1.000
Euthyroidism	35	35	1.000
Graves' disease (n, %)	35	33 (94%)	0.774
Hashimoto's thyroiditis	0	2 (6%)	0.493
Smokers (n, %)	20 (57%)	21 (60%)	1.000
1–19/d	15 (43%)	14 (40%)	1.000
>20/d	5 (14%)	7 (20%)	0.822
Orbital pain (n, %)	16 (46%)	20 (57%)	0.473
Conjunctivitis (n, %)	26 (74%)	29 (83%)	0.561
Chemosis (n, %)	15 (43%)	23 (66%)	0.092
Optic neuropathy (n, %)	3 (9%)	5 (14%)	0.710
Diplopia			
Constant (n, %)	21 (60%)	23 (66%)	0.805
Inconstant (n, %)	2 (6%)	3 (9%)	1.000
Intermittent (n, %)	1 (3%)	0 (0%)	1.000

Median values and range are shown.
[a] The Fisher's exact test was applied.

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids

TABLE 2. Ophthalmic clinical signs of severity of GO and ultrasound measurements of the sum of the four rectus eye muscles at baseline (0) and at 12 wk in the oral prednisolone and intravenous methylprednisolone groups

	Oral (n = 35)			Intravenous (n = 35)			Oral *vs.* iv
	0	12 wk	*P* value	0	12 wk	*P* value	*P* value
Lid width (mm)							
Median	12	11	0.05[a]	13	11	0.01[a]	0.005[b]
Range	10–14	9–13		9–17	7–14		
Proptosis (mm)							
Median	23	22	0.05[a]	24	22	0.02[a]	0.011[b]
Range	18–26	18–25		19–28	17–25		
Visual acuity							
Median	0.5	0.6	0.368[a]	0.4	0.6	0.02[a]	0.01[b]
Range	0.1–0.9	0.3–1		0.05–1	0.35–1		
Ocular pressure (mm Hg)							
Median	22	21.5	0.219[a]	25	22	0.01[a]	0.005[b]
Range	12–35	11–30		18–32	14–28		
Muscle thickness (mm)							
Median	25.7	24.3	0.062[a]	26.6	22.7	0.03[a]	0.01[b]
Range	16–36	16–31		20–37	15–28		
Diplopia (n)							
Constant	21	14	0.016[c]	23	10	<0.001[c]	0.112[d]
Inconstant	2	6	0.125[c]	3	7	0.125[c]	1.000[d]
Intermittent	1	2	1.000[c]	0	3		0.614[d]
Optic neuropathy (n)	3	2	1.000[c]	5	0		0.198[d]

The following statistical tests have been performed when appropriate:
[a] Wilcoxon signed rank test within either the oral or the iv group (dependent samples)—metric variables.
[b] *U* test between the oral and the iv group (independent samples)—metric variables.
[c] McNemar test within either the oral or the iv group (dependent samples)—dichotomous variables.
[d] Fisher's exact test between the oral and the iv group (independent samples)—dichotomous variables.
Pre-post comparisons were performed within groups, and delta values were used for comparisons between groups (treatment groups).

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids

TABLE 3. Ophthalmic symptoms and signs of disease activity as well as serological findings at baseline (0) and at 12 wk in the oral prednisolone and iv methylprednisolone groups

	Oral (n = 35)			Intravenous (n = 35)			Oral *vs.* iv
	0	12 wk	*P* value	0	12 wk	*P* value	*P* value
Chemosis (n)	15	12	0.250[a]	23	9	<0.001[a]	0.002[b]
Conjunctivitis (n)	26	22	0.125[a]	29	14	<0.001[a]	0.003[b]
Orbital pain (n)	16	11	0.063[a]	20	9	0.001[a]	0.088[b]
Clinical activity score							
Median	5	3	0.05[c]	5	2	0.01[c]	0.007[d]
Range	3–7	2–7		3–7	1–5		
TSH-R-Abs (IU/liter)							
Median	28	23	0.146[c]	31	14	0.006[c]	0.0003[d]
Range	5–97	5–41		6–83	0–36		

The following statistical tests have been performed when appropriate:
[a] McNemar test within either the oral or the iv group (dependent samples)—dichotomous variables.
[b] Fisher's exact test between the oral and the iv group (independent samples)—dichotomous variables.
[c] Wilcoxon signed rank test within either the oral or the iv group (dependent samples)—metric variables.
[d] *U* test between the oral and the iv group (independent samples)—metric variables.
Pre-post comparisons were performed within groups, and delta values were used for comparisons between groups (treatment groups).

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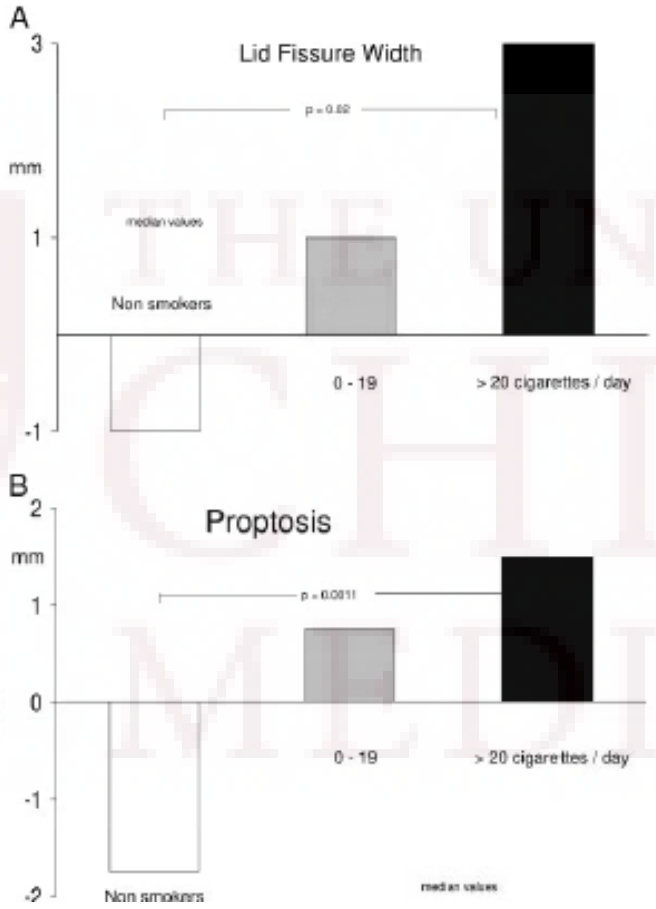
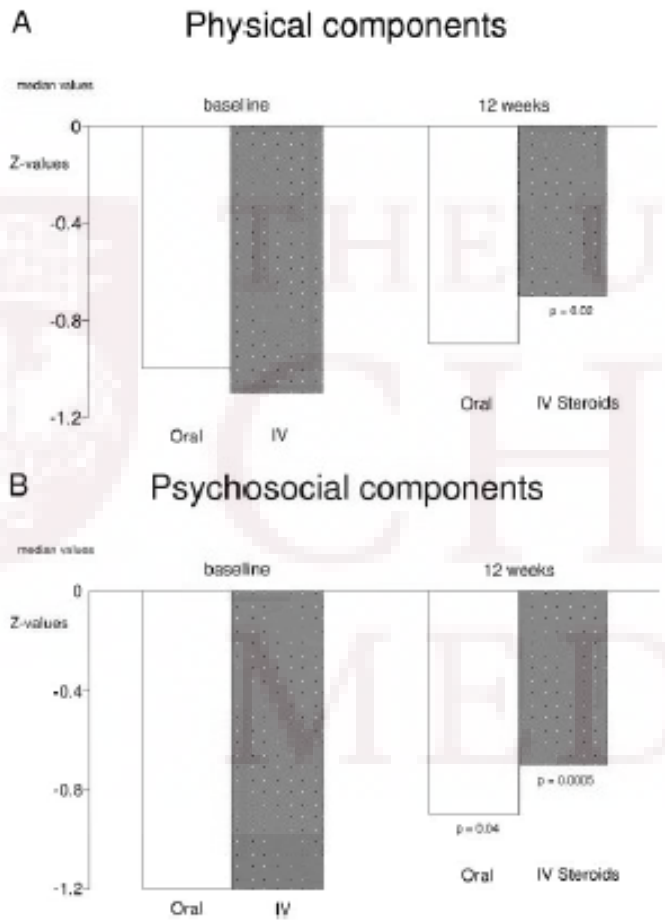
IV vs PO Steroids



- Effect of smoking: none (41%), less than 20 cigarettes/d (41%), or more than 20 cigarettes/d (18%) on the response to glucocorticoid therapy
- The increment and/or decline (median value) in clinically relevant and objective ophthalmic parameters (e.g. lid fissure width, proptosis, and intraocular pressure in up gaze) during steroid therapy are shown in the three panels

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids



- Physical and psychosocial components of the SF-36 questionnaire evaluating health-related QL both at baseline as well as after completion of glucocorticoid therapy in the two iv and oral study groups (A and B)
- Age- and gender-adapted and transformed z-values (median) are shown

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids

TABLE 4. Adverse events of glucocorticoid monotherapy

	Oral prednisolone	Intravenous methylprednisolone	*P* value
Number of events	29	8	<0.001
Patients with events	18/35 (51%)	6/35 (17%)	0.005
Female with events	13/24 (54%)	4/25	0.007
Male with events	5/11 (45%)	2/10	0.361
Major events	2	0	
Weight gain (>3 kg)	9 (26%)	1	0.006
Gastrointestinal	6 (17%)	1	0.106
Sleeplessness	5 (14%)	2	0.428
Myalgias	3	0	
Hypertension	2	0	
Hirsutism	2	0	
Depression	1	0	
Palpitations	1	4	0.356

The exact test of Fisher (two-tailed) was performed.

J Clin Endocrinol Metab 90: 5234–5240, 2005

IV vs PO Steroids

- At 3 months, 27 of 35 patients (77 percent) in the IV group had a treatment response compared with 18 of 35 (51 percent) in the oral group
- Conclusions: in patients with active and severe GO, iv glucocorticoids were more effective and better tolerated than oral steroids
- Improvements over baseline for visual acuity, chemosis, and quality of life were greater in the IV group
- Additional treatment was required less frequently in the IV group
- Adverse events were less frequent with IV glucocorticoids

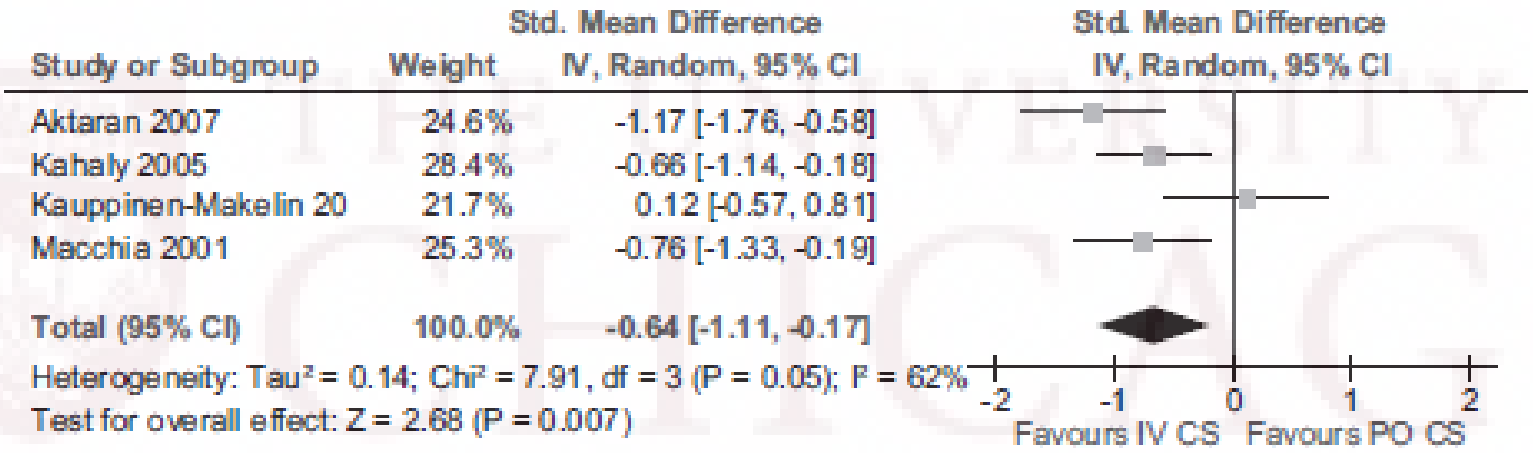
J Clin Endocrinol Metab 90: 5234–5240, 2005

Management

- Designs: systematic review and meta-analysis of randomized, controlled trials comparing treatment modalities for GO *vs.* placebo, no intervention, or other treatments
- Primary outcome: the clinical activity score (CAS)
- Numbers: 33 trials evaluating 1,367 patients

J Clin Endocrinol Metab 94: 2708–2716, 2009

Management



IV - intravenous, PO - per os, CS - corticosteroids, CAS - clinical activity score.

FIG. 2. Intravenous corticosteroids *vs.* oral corticosteroids. The outcome was CAS at the end of follow-up. PO, Per os; CS, corticosteroids.

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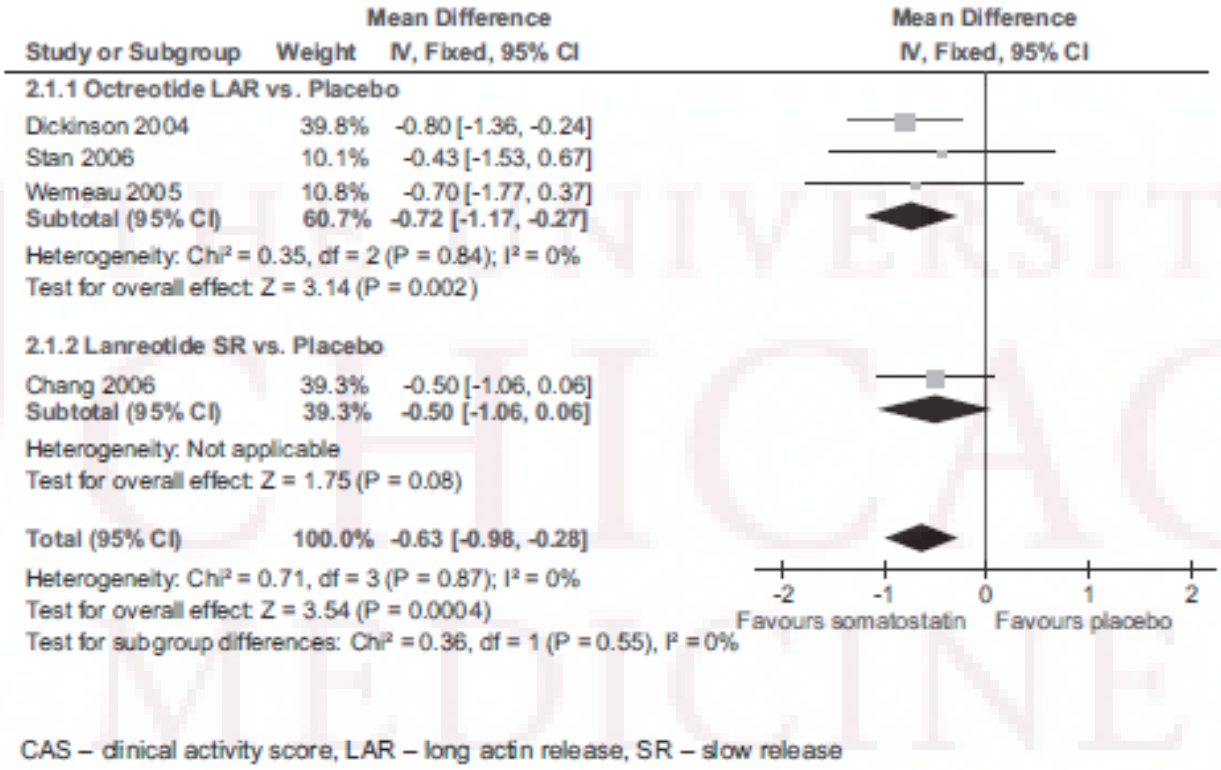

FIG. 3. Somatostatin analogs *vs.* placebo. The outcome was CAS at the end of follow-up.

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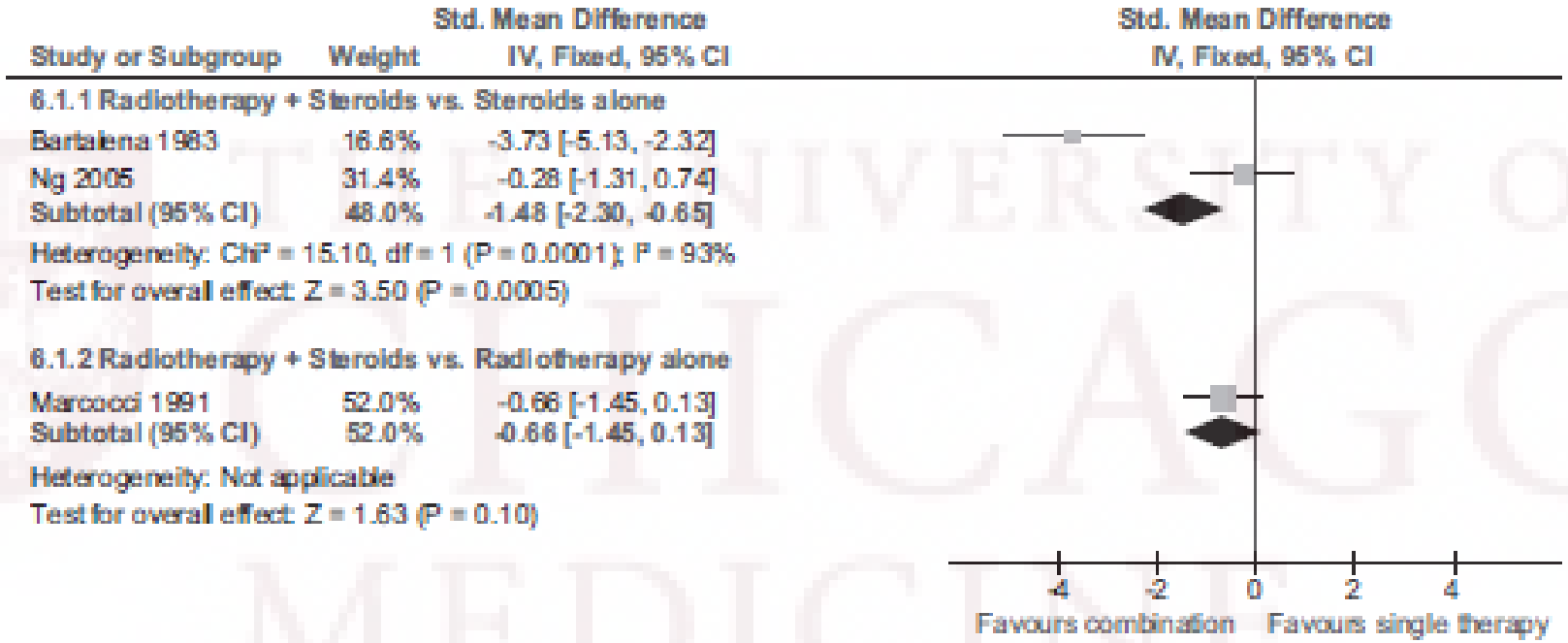

FIG. 4. Orbital radiotherapy plus corticosteroids *vs.* either treatment alone. The outcome was OI/TES at the end of follow-up.

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Management

- IV pulse corticosteroids therapy has a small but statistically significant advantage oral therapy and causes significantly fewer adverse events
- Somatostatin analogs have marginal clinical efficacy
- The efficacy of orbital radiotherapy as single therapy remains unclear, whereas the combination of radiotherapy with corticosteroids has better efficacy than either radiotherapy or oral corticosteroids alone
- The advantage was mostly due to improvements in patients with severe orbitopathy

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Clinical Question

- Steroids non-responsive?

Potential Therapy in GO

Table 1

Potential Therapeutic Targets in Graves' Ophthalmopathy.*

Target	Current Agent	Description	Potential Benefit	Reference
TNF	Infliximab, adalimumab	TNF-specific monoclonal antibodies	Reduction in inflammation, leukocyte recruitment, and hyaluronan production	Feldmann,[92] Durrani et al.[95]
TNF receptor	Etanercept	TNF receptor–IgG Fc fusion molecule	Reduction in inflammation, leukocyte recruitment, and hyaluronan production	Feldmann,[92] Paridaens et al.[96]
Interleukin-1 receptor	Anakinra	Interleukin-1–receptor antagonist	Reduction in inflammation, leukocyte recruitment, and hyaluronan production	Mertens and Singh,[97] Tan et al.[98]
Interleukin-6 receptor	Tocilizumab	Interleukin-6 receptor–specific mono-clonal antibody	Reduction in inflammation, leukocyte recruitment, and hyaluronan production	Smolen et al.[99]
TGF-β	Lerdelimumab, GC1008	TGF-β–specific monoclonal antibodies	Reduction in fibrosis	Pohlers et al.[100]
Oxygen free radicals	Selenium	Essential trace element	Antiinflammatory activity	Wertenbruch et al.[101]
CD20	Rituximab, ocrelizumab, ofatumumab	Partially or fully humanized CD20-specific monoclonal antibodies	Decreased antigen presentation and T-cell activation; possible modulation of anti–thyrotropin-receptor antibody production	Tsokos,[102] El Fassi et al.,[103] Kwan-Morley and Albert,[104] Salvi et al.[105]
CD3	ChAglyCD3	Fc-mutated CD3-specific monoclonal antibody	Induction of tolerance	Keymeulen et al.[106]
CD28	Abatacept	CTLA-4–immunoglobulin recombinant protein	Modulation of costimulatory pathways	Kremer et al.[107]
CD154	IDEC-131	Humanized CD154-specific monoclonal antibody	Modulation of costimulatory pathways	Kalunian et al.[108]
PPAR-γ	Selective PPAR modulators	Novel selective PPAR-γ antagonists	Reduction in inflammation and orbital adipogenesis	Knouff and Auwerx,[109] Straus and Glass[110]
Somatostatin receptor	SOM230	Synthetic high-affinity somatostatin analogue	Inhibition of orbital preadipocyte proliferation	Cozma et al.[111]
Thyrotropin receptor	NIDDK/CEB-52	Low-molecular-weight thyrotropin-receptor antagonist	Inhibition of orbital adipogenesis and hyaluronan production	Neumann et al.[112]

*CTLA denotes cytotoxic T-lymphocyte–associated antigen 4, PPAR peroxisome-proliferator–activated receptor, TGF transforming growth factor, and TNF tumor necrosis factor.

Orbital Decompression Surgery

Orbital decompression surgery anatomy

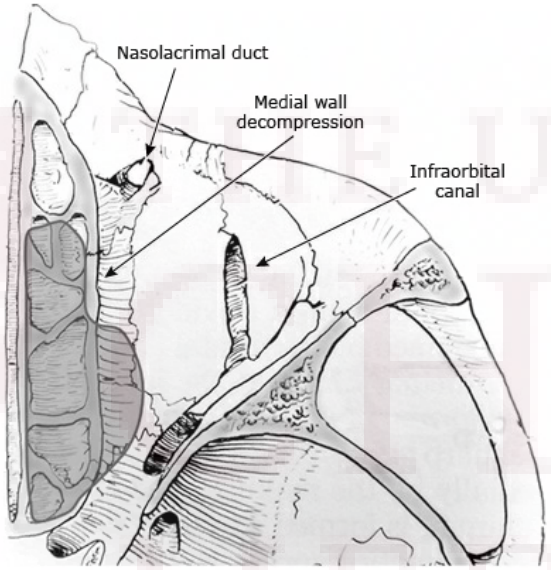

Diagram to show extent of medial wall orbital decompression. Note, to achieve an effective decompression, the posterior half of the bony bar ("strut") between the maxillary antrum and the ethmoid air cells should be removed.

Indications for orbital decompression surgery include

- Optic neuropathy caused by enlarged extraocular muscles not responsive to high-dose corticosteroids
- Severe orbital inflammation
- Excessive proptosis leading to exposure keratitis, corneal ulceration, or debilitating cosmetic defect
- Pain relief
- Progressive orbitopathy not responding to other measures

Garrity JA. Am J Ophthalmol 1993; 116:533.

Patient Course

- Pt was evaluated in ophthalmology and considering the acute worsening with protrusion and lid lag, steroid infusions were started
- She has 6 weekly infusions of 500mg solu-medrol so far (now 5/6)
- Protects eye with tape at night, eye drops
- Pt feels under a lot of personal stress, sees a therapist
- Weight gain in setting of steroids - ~12lbs

Eyes Exam (In Nov 2018, after IV steroids x4)

- Slit Lamp Exam

	Right	Left
Lids/Lashes	Normal	**UL retraction**
Conjunctiva/Sclera	White and quiet	**1+ injection, inf temp conjunc staining**
Cornea	Clear	**Scatter 1+ staining , lasix flap**
Anterior Chamber	Deep and quiet	Deep and quiet
Iris	Round and reactive	Round and reactive
Lens	Clear	Clear
Vitreous	Normal	Normal

- Fundus Exam : normal

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31 yo Women with Double Vision

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December 13, 2018

Dr. Upala does not have any relevant financial relationships with any commercial interests