THE ROLE OF THYROID EYE DISEASE AND OTHER FACTORS IN THE OVERCORRECTION OF HYPOTROPIA FOLLOWING UNILATERAL ADJUSTABLE SUTURE RECESSION OF THE INFERIOR RECTUS (AN AMERICAN OPHTHALMOLOGICAL SOCIETY THESIS)

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ABSTRACT

Purpose: Overcorrection of hypotropia subsequent to adjustable suture surgery following inferior rectus recession is undesirable, often resulting in persistent diplopia and reoperation. I hypothesized that overcorrection shift after suture adjustment may be unique to thyroid eye disease, and the use of a nonabsorbable suture may reduce the occurrence of overcorrection.

Methods: A retrospective chart review of adult patients who had undergone eye muscle surgery with an adjustable suture technique was performed. Overcorrection shifts that occurred between the time of suture adjustment and 2 months postoperatively were examined. Descriptive statistics, linear regression, Anderson-Darling tests, generalized Pareto distributions, odds ratios, and Fisher tests were performed for two overcorrection shift thresholds (>2 and >5 prism diopters [PD]).

Results: Seventy-seven patients were found: 34 had thyroid eye disease and inferior rectus recession, 30 had no thyroid eye disease and inferior rectus recession, and 13 patients had thyroid eye disease and medial rectus recession. Eighteen cases exceeded the 2 PD threshold, and 12 exceeded the 5 PD threshold. Statistical analyses indicated that overcorrection was associated with thyroid eye disease (P=6.7E-06), inferior rectus surgery (P=6.7E-06), and absorbable sutures (>2 PD: OR=3.7, 95% CI=0.4-35.0, P=0.19; and >5 PD: OR=6.0, 95% CI=1.1-33.5, P=0.041).

Conclusions: After unilateral muscle recession for hypotropia, overcorrection shifts are associated with thyroid eye disease, surgery of the inferior rectus, and use of absorbable sutures. Surgeons performing unilateral inferior rectus recession on adjustable suture in the setting of thyroid eye disease should consider using a nonabsorbable suture to reduce the incidence of postoperative overcorrection.

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INTRODUCTION

EARLY DESCRIPTIONS AND WORK IN THYROID EYE DISEASE

Thyroid goiter was known to be associated with eye disease as early as the 12th century.[1] In the early 1800s, the triad of hyperthyroidism, diffuse nodular goiter, and ophthalmopathy was described[2] and Graves' name was given to the disease, even though Graves ascribed the protrusion of the globe seen in thyroid eye disease to enlargement of the globe itself.[1] In 1845, Von Basedow[3] correctly described the basic pathology of the disease as "intumescence of the cellular tissue behind the bulbus." Von Graefe[4] expounded on the clinical signs associated with thyroid eye disease, bringing this disease to the attention of ophthalmologists. The discovery of iodine and its protein-binding properties in the 19th century laid the foundation for understanding the pathophysiology of thyroid eye disease.[1] In the first half of the 20th century, overproduction of thyroid-stimulating hormone (TSH) from the anterior pituitary was linked to hyperthyroidism and eye findings in thyroid eye disease.[5] An immune-mediated mechanism became apparent, as the excessive production of TSH was found to result from stimulation of the thyroid cell membrane by the immunoglobulin thyroid-stimulating antibody.[1]

Our modern understanding of clinical thyroid eye disease (also called Graves' disease or ophthalmopathy, thyroid ophthalmopathy, thyroid-related ophthalmopathy, or thyroid orbitopathy) was facilitated by description of the "NO SPECS" classification of clinical staging for eye changes[6]:

0. **N**o signs or symptoms
1. **O**nly signs (upper lid retraction and stare), no symptoms
2. **S**oft tissue involvement (lid edema, chemosis, congestion)
3. **P**roptosis
4. **E**xtraocular muscle involvement
5. **C**orneal involvement
6. **S**ight loss

Following the report of this classification scheme in 1969,[6] the publication of studies regarding the class 4 stage of thyroid eye disease—extraocular muscle involvement—proliferated. Our understanding of the pathophysiology, natural history, and treatment of thyroid eye disease entered its current state in the 1970s, and the following summary describes our current understanding of strabismus associated with thyroid eye disease.

PATHOPHYSIOLOGY OF STRABISMUS IN THYROID EYE DISEASE

Thyroid eye disease is a secondary immunologic manifestation of the primary autoimmune disease directed at the thyroid gland. The hallmark of thyroid eye disease is extraocular muscle enlargement, which can result in strabismus and diplopia. The immune-mediated process resulting in extraocular muscle enlargement is, as yet, poorly understood[7] and is likely influenced by genetic, environmental, hormonal, and other factors.[8] Primary Graves' disease occurs when T cells, in a process that is not entirely understood, target the TSH

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receptor on the thyrocyte. Interaction between the anti-TSH receptor antibodies and T cells stimulates thyroid hormone production that is not regulated by the hypothalamic-pituitary-thyroid axis. Of the extrathyroidal manifestations of Graves' disease, the orbital disease is the most debilitating. Activated T cells infiltrate the orbit, stimulating cytokine-mediated inflammatory response. Though there are probably common antigenic proteins between thyrocytes and the secondarily affected tissues in the orbit, those specific antigen(s) remain unidentified. A likely candidate for the target of the T-cell mediated reaction is the expression of TSH epitopes on the orbital preadipocyte fibroblast.[9-11]

During the early stages of thyroid eye disease, before restrictive strabismus is noted, microscopy of the extraocular muscles reveals infiltration between the extraocular muscle fibers with mononuclear inflammatory cells.[12] Interfibrillar spaces are enlarged and contain an amorphous material, which, in turn, contains hyaluronic acid. Acute muscle enlargement may also be mediated by raised muscle tension secondary to transition from slow to fast muscle types induced by the hyperthyroid state.[13] Following infiltration of the endomysial space of the muscle by lymphocytes, macrophages, and neutrophils, muscle cells decrease in numbers, and the contractile properties of the affected muscles may be compromised.[12] Stimulated fibroblasts produce increased levels of glycosaminoglycans (including hyaluronic acid), which attract water osmotically, contributing to interstitial edema.[14] Collagen synthesis and deposition occurs in interfascicular membranes and extraocular muscle sheaths.[15,16] At the cellular level, there is a marked expansion of the endomysial space in the extraocular muscles of patients with recently inactive thyroid eye disease.[17] In the healing phase of thyroid eye disease, the muscles become fibrotic and inelastic, resulting in permanently restricted eye movement.[12]

CLINICAL PRESENTATION OF STRABISMUS IN THYROID EYE DISEASE

Strabismus occurs in 15% of all patients with thyroid eye disease.[18] In one study, 9.2% of all patients with thyroid eye disease had strabismus surgery.[19] Though most patients with thyroid eye disease and strabismus have a history of hyperthyroidism, they may be euthyroid, hyperthyroid, or hypothyroid at the time of presentation. Thyroid dysfunction has usually been present for 5 years before strabismus and the accompanying diplopia become manifest, with a reported range of 0 to 11 years for the appearance of diplopia after the onset of thyroid dysfunction.[20] Signs and symptoms of thyroid eye disease typically start 2 years prior to the onset of diplopia. Exophthalmos usually precedes diplopia. This time course confounds discussions of the role decompressions play in the development of diplopia, as an estimated 6.7% of all patients with thyroid eye disease undergo decompressions.[19] The natural history of diplopia in thyroid eye disease is such that a certain number of these were likely to develop whether or not the patient had a decompression early in the course of their disease. The average age of patients experiencing diplopia in thyroid eye disease is 50.[20] Though women are more likely to be affected by a margin of 4 or 5 to 1,[21] older patients, white males, and cigarette smokers tend to have a more severe course of the disease.[22-24] Younger patients are less likely to develop strabismus with thyroid eye disease.[25,26]

Common patterns of strabismus in thyroid eye disease are hypotropia secondary to inferior rectus restriction (Figure 1), esotropia secondary to medial rectus restriction, hypertropia secondary to superior rectus restriction, hypertropia after recession of the inferior rectus, and A-pattern exotropia. Also common to the strabismus of thyroid eye disease is tremendous variability noted from patient to patient with regard to presentation, findings, and response to treatment. Most frustrating to the strabismus surgeon is the frequency with which variable and seemingly unpredictable responses occur with surgical treatment. In particular, surgery of the inferior rectus has proven particularly challenging with regard to variable outcomes.

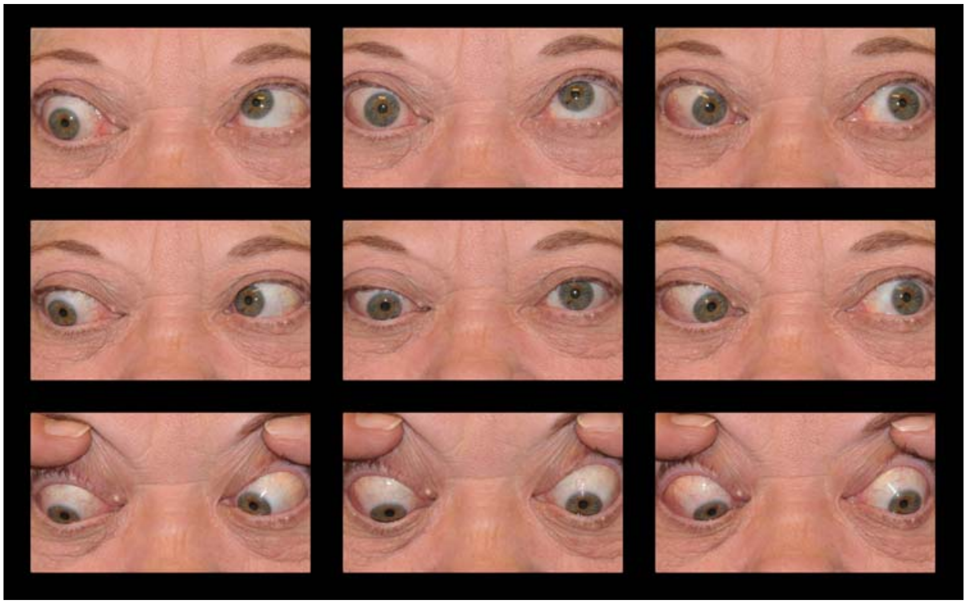

FIGURE 1

Left hypertropia/right hypotropia secondary to right inferior rectus restriction in the setting of thyroid eye disease.

SURGICAL TREATMENT OF STRABISMUS OF THYROID EYE DISEASE

Tracing the modern history of surgical treatment for diplopia in thyroid eye disease affords an understanding of the topic addressed in my study. In the 1940s, the limitation of upgaze so common in class 4 thyroid eye disease was incorrectly attributed to superior rectus and inferior oblique paralysis.[27-30] In 1953, Braley[31] reported intraocular pressure differences in primary gaze and downgaze in patients with thyroid orbitopathy (as measured with Schiøtz tonometer), which he correctly attributed to inelasticity of the opposing muscle—in this case, the inferior rectus. In 1961 and 1965, Miller and coworkers[32,33] showed that patients with upgaze deficiencies secondary to thyroid eye disease could be successfully managed with a single inferior rectus muscle recession, and proposed the etiology of hypotropia in thyroid eye disease as it is understood today: hypotropia in thyroid eye disease is secondary to inferior rectus restriction.

In 1976, John Dyer[34] published his American Ophthalmological Society thesis entitled "The Oculorotary Muscles in Graves' Disease." He reported 116 patients undergoing eye muscle surgery for diplopia and thyroid eye disease between 1968 and 1975. He used fixed sutures and reported a reoperation rate of 45%. He also investigated the use of scleral spacers to relax the inferior rectus muscle, noting one case with progressive postoperative overcorrection. Also of interest to the contemporary strabismus surgeon, he discussed the "team effort" to successful outcomes for these patients, recognizing advances in decompression surgery (transantral-ethmoidal instead of transfrontal), and advocating for decompression of the proptotic orbit before muscle surgery, as well as lid surgery following eye muscle surgery for the effects of lid retraction and exposure. He reported recessions of bilateral inferior recti and the need to alter the amount of recession performed for patients with thyroid eye disease. He recommended larger-than-usual recessions and based the amount of surgery performed on the excursion of the globe, not the measurement in primary gaze.

In a series of 30 patients published in 1979, Forrest Ellis[35] reported a reoperation rate of only 17% and attributed his success to the use of adjustable sutures. Like Dyer, he advocated a larger-than-usual amount of recession in thyroid eye disease. However, he found no reason to advocate for muscle extensions (such as scleral spacers). In 1981, Scott and Thalacker[36] published a series of 25 patients undergoing treatment for diplopia in order to highlight the special difficulties encountered in thyroid disease. Though they mentioned that adjustable sutures would be ideal, they did not state the technique used (adjustable or fixed) and with what frequency. They did point out four overcorrections and discussed possible mechanisms, including progression of the disease, undetected involvement of the ipsilateral superior rectus, or both. In 1983, Evans and Kennerdell[37] advocated marginal myotomies in addition to recession using a fixed suture and determining the amount of myotomy by forced ductions at the time of surgery. They noted that 5 of 45 patients had a postoperative overcorrection but did not specify whether these were inferior or medial recti. In 1984, Skov and Mazow[18] advocated the use of adjustable sutures (with "generous" recession) for muscles with considerable "spring back into the orbit once released from their insertions." However, concerns for undercorrection (rather than overcorrection) led them to recommend a fixed suture for the fibrotic muscle that remains near its insertion after release, so that the muscle would not reattach at the original insertion. In 1992, Lueder and associates[38] reported 47 patients treated with adjustable sutures, noting a reoperation rate of 15% and alleviation of diplopia in primary and/or reading position in 91% of the patients. Although this was a report of long-term follow-up, no mention was made of overcorrection after inferior rectus recession. However, within a few years of the publication of this study, overcorrection after inferior rectus recession in thyroid eye disease became a well-published phenomenon.

OVERCORRECTION OF HYPOTROPIA FOLLOWING INFERIOR RECTUS RECESSION

Progressive overcorrection after inferior rectus recession (dubbed POAIRR by Sharma and Reinecke[39]), also called late overcorrection after inferior rectus recession, is one of the most common sources of recurrent postoperative diplopia in thyroid eye disease (Figure 2), with a reported incidence as high as 50%.[40] Overcorrection in the weeks or months following inferior rectus recession is particularly bothersome, as it cannot, by virtue of the time of its occurrence, be prevented by the use of adjustable sutures in the immediate postoperative period, and it leaves the patient in need of prism glasses or reoperation. The specific etiology of progressive overcorrection after inferior rectus recession is probably dependent upon the timing of its occurrence. Overcorrection that occurs between the first few postoperative days and 2 months after the surgery is likely due to change that occurs with the healing process after muscle surgery, specifically adherence of the muscle to the globe. Overcorrection that occurs 2 months or more after the surgery is more likely due to long-term changes in the orbit(s), such as increases in antagonist or yoke muscle contracture.[41]

The variability of vertical strabismus in thyroid eye disease, even without surgery, may also play a role in the unpredictable outcomes of vertical strabismus surgery in thyroid eye disease.[42] Compounding the confusion regarding the etiology of this problem is progressive overcorrection after inferior rectus recession occurring in patients without thyroid eye disease[43] and undercorrections reported as commonly as overcorrections.[44] No predictive factors have been found for postoperative overcorrections.[44]

Clarifying the factors associated with progressive overcorrection after inferior rectus recession in thyroid eye disease is important, as it suggests possible solutions. If failure of muscle adherence to the globe postoperatively is at fault,[43] then using a nonabsorbable suture may improve results.[39] If the problem is ipsilateral superior rectus contracture[41] or contralateral inferior rectus contracture,[45] then recessing additional muscles at the first surgery on the inferior rectus may improve outcomes.

PURPOSE OF THE STUDY

The purpose of this study is to determine the factors contributing to progressive overcorrection after inferior rectus recession in thyroid disease and to test one possible solution for this problem. Data on the postoperative course and preoperative information from patients with thyroid eye disease undergoing unilateral inferior rectus muscle surgery on adjustable suture were collected and analyzed. Additionally, to understand the contributions of factors other than thyroid eye disease to overcorrection shift, unilateral inferior rectus recessions on adjustable sutures from patients who had other etiologies for their vertical strabismus were analyzed with regard to progressive overcorrection after inferior rectus recession. To understand whether or not the inferior rectus has unique features that predispose it to progressive overcorrection (such as its special anatomical features), unilateral medial rectus recessions on adjustable sutures from patients with thyroid eye disease were also studied. By examining overcorrection shift between postoperative day 1 (POD 1) after suture adjustment and 2 months in these patients, factors associated with progressive overcorrection after inferior rectus recession were determined. The factors chosen for analysis in this study were chosen because they have been proposed by other investigators as playing a role in progressive overcorrection after inferior rectus recession (discussed and referenced below). They include the effect of thyroid eye disease on postoperative overcorrection, the unique behavior of the inferior rectus muscle (as opposed to the medial rectus with thyroid eye disease), and other operative factors, such as the amount of recession performed. Absorbable vs nonabsorbable sutures were evaluated to determine their effect on progressive overcorrection after inferior rectus recession.

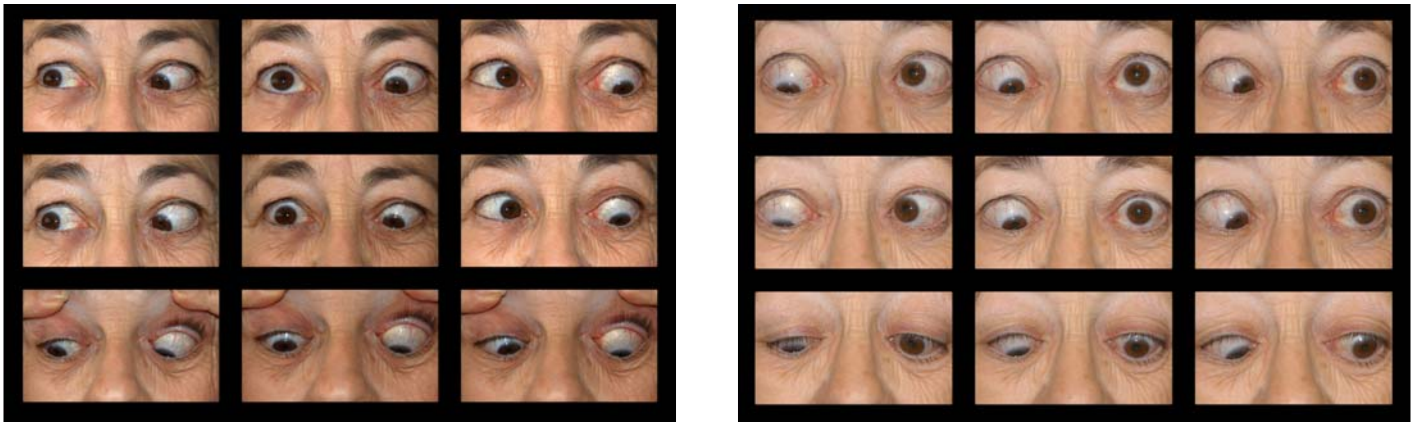

FIGURE 2

Left, Initial presentation of right hypertropia/left hypotropia secondary to left inferior rectus recession in the setting of thyroid eye disease. Right, Overcorrection after left inferior rectus recession on adjustable suture resulting in a left hypertropia/right hypotropia.

PATIENTS AND METHODS

The University of Tennessee Health Science Center Institutional Review Board reviewed and approved this retrospective chart review study. Adherence to Health Information Portability and Accountability Act of 1996 (HIPAA) regulations regarding patient information was maintained. Inclusion criteria were any inferior rectus muscle recessions or eye muscle surgery for thyroid eye disease on adult patients from the University of Tennessee Health Science Center Department of Ophthalmology's Pediatric Ophthalmology and Strabismus service. Cases were identified by review of an automated billing record from 2001 to 2008 and surgical logs from 1994 to 2001. Cases were excluded for any of the following: bilateral or multiple vertical or horizontal rectus recessions, previous surgery on the operated muscle, lack of a recorded prism and alternate cover measurement of the deviation at distance after adjustment on POD 1, failure to follow up 2 months after surgery, poor visual acuity, or use of fixed sutures. Seventy-seven cases remained for study that had single inferior rectus muscle recession on adjustable suture or single medial rectus recession on adjustable suture and thyroid eye disease. Thirty-four cases of unilateral inferior rectus surgery with thyroid eye disease met inclusion criteria and were designated as Group 1. Nonabsorbable sutures were used in eight of the 34 cases of unilateral inferior rectus surgery with thyroid eye disease. Thirty cases of unilateral inferior rectus recession from patients without thyroid eye disease (Group 2) met inclusion criteria. Nonabsorbable sutures were used in 11 of the 30 cases comprising Group 2. Thirteen cases of unilateral medial rectus recession on adjustable, absorbable suture from patients with thyroid eye disease were identified and met criteria for inclusion (Group 3).

Preoperative data recorded for this study included patient identification number, date of birth, date of first visit, preoperative diagnosis (or diagnoses) or etiology of the motility disorder, and preoperative measurement of ocular deviation. Also, for the patients with thyroid eye disease, history of prior orbital decompression surgery was noted. Clinical assessment of proptosis was noted. These data are shown per group in Tables 1A, 2, and 3A. Exophthalmometry was not measured preoperatively and postoperatively for strabismus surgery. It would be interesting to assess whether patients who experienced a shift in proptosis after inferior rectus surgery were more likely to experience overcorrection. However, the study establishing the phenomenon of increased proptosis after muscle recession in thyroid ophthalmopathy, by Gomi and associates,[46] was not published until 2007, and most of our cases were performed well before then. Gomi and associates' study makes no assessment of outcome for the strabismus surgery, only the effect of inferior rectus recession on proptosis.

TABLE 1A. DATA RETRIEVED FROM PATIENT RECORDS FOR GROUP 1 (THYROID EYE DISEASE, INFERIOR RECTUS SURGERY)

SURGERY ID	GENDER	PRIOR ORBITAL DECOMPRESSION	AGE IN YEARS	DIPLOPIA	PROPTOSIS	NUMBER OF MUSCLES RECESSED	SUTURE TYPE	AMOUNT OF RECESSION (mm)	PREOPERATIVE MEASUREMENT (PD)	POSTOPERATIVE MEASUREMENT (PD) DAY 1*	POSTOPERATIVE MEASUREMENT (PD) 2 MONTHS	SHIFT (PD)†
1	Female	Yes	40.4	Yes	Yes	2	Absorbable	5.0	14.0 RHT	0.0	0.0	0.0
2	Female	Yes	44.7	Yes	Yes	3	Absorbable	6.0	12.0 RHT	0.0	8.0 LHT	8.0
3	Female	Yes	47.0	No	Yes	2	Absorbable	7.0	35.0 RHT	2.0 RHT	15.0 RHT	-13.0
4	Female	No	52.7	Yes	Yes	1	Absorbable	6.0	15.0 RHT	4.0 RHT	3.0 RHT	1.0
5	Female	No	53.6	Yes	No	1	Absorbable	7.0	25.0 RHT	0.0	0.0	0.0
6	Female	Yes	54.7	Yes	Yes	1	Absorbable	10.0	25.0 RHT	5.0 RHT	8.0 RHT	-3.0
7	Female	Yes	55.6	Yes	Yes	2	Absorbable	5.0	8.0 RHT	0.0	0.0	0.0
8	Male	Yes	56.1	Yes	Yes	3	Absorbable	7.0	12.0 RHT	15.0 RHT	30.0 RHT	15.0
9	Male	No	56.7	Yes	Yes	1	Absorbable	10.0	35.0 RHT	15.0 LHT	15.0 RHT	30.0
10	Female	Yes	57.8	No	Yes	2	Absorbable	6.5	20.0 LHT	1.0 LHT	2.0 RHT	3.0
11	Female	No	58.0	Yes	No	1	Absorbable	4.0	6.0 RHT	0.0	0.0	0.0
12	Female	Yes	58.5	Yes	Yes	1	Absorbable	8.0	30.0 RHT	8.0 LHT	10.0 LHT	-2.0
13	Female	Yes	63.1	No	Yes	1	Absorbable	10.0	30.0 RHT	8.0 RHT	4.0 LHT	12.0
14	Female	No	64.3	Yes	No	1	Absorbable	10.0	25.0 RHT	0.0	0.0	0.0
15	Male	Yes	64.7	Yes	Yes	2	Absorbable	4.0	5.0 RHT	0.0	0.0	0.0
16	Female	Yes	65.1	Yes	Yes	2	Absorbable	6.0	6.0 RHT	8.0 RHT	20.0 RHT	12.0
17	Female	No	65.6	Yes	No	2	Absorbable	10.0	70.0 RHT	20.0 LHT	12.0 RHT	32.0
18	Female	No	66.9	Yes	Yes	1	Absorbable	7.0	14.0 RHT	2.0 LHT	2.0 LHT	0.0
19	Male	Yes	67.4	Yes	Yes	3	Absorbable	10.0	20.0 RHT	0.0	8.0 RHT	8.0
20	Male	No	67.8	Yes	No	2	Absorbable	6.0	12.0 RHT	0.0	2.0 RHT	2.0
21	Female	No	68.3	Yes	Yes	1	Absorbable	10.0	20.0 RHT	10.0 LHT	3.0 RHT	-13.0
22	Male	No	69.0	Yes	No	1	Absorbable	5.0	10.0 RHT	4.0 RHT	0.0	-4.0
23	Female	No	69.5	Yes	No	1	Absorbable	10.0	25.0 LHT	10.0 LHT	8.0 RHT	18.0
24	Female	Yes	71.6	Yes	Yes	1	Absorbable	10.0	35.0 RHT	15.0 LHT	6.0 LHT	9.0
25	Male	No	72.4	Yes	No	2	Absorbable	6.0	12.0 RHT	0.0	0.0	0.0
26	Female	No	73.2	Yes	No	2	Absorbable	6.0	12.0 RHT	4.0 LHT	10.0 LHT	6.0
27	Female	Yes	54.4	No	Yes	2	Nonabsorbable	7.5	20.0 RHT	6.0 LHT	2.0 RHT	-8.0
28	Female	No	57.0	Yes	No	2	Nonabsorbable	3.5	11.0 ET	0.0	0.0	0.0
29	Female	No	58.2	Yes	Yes	1	Nonabsorbable	10.0	30.0 LHT	4.0 LHT	0.0	4.0
30	Female	No	60.9	Yes	Yes	1	Nonabsorbable	10.0	20.0 LHT	2.0 LHT	0.0	2.0
31	Male	No	62.7	Yes	Yes	1	Nonabsorbable	10.0	40.0 RHT	0.0	0.0	0.0
32	Female	Yes	65.2	Yes	Yes	2	Nonabsorbable	7.5	15.0 LHT	0.0	0.0	0.0
33	Female	No	67.9	Yes	No	2	Nonabsorbable	10.0	15.0 LHT	4.0 LHT	0.0	4.0
34	Female	Yes	74.1	Yes	No	2	Nonabsorbable	8.0	20.0 RHT	0.0	2.0 RHT	-2.0

ET, esotropia; LHT, left hypotropia; PD, prism diopters; RHT, right hypotropia.

[*] Postadjustment.

†Negative numbers indicate undercorrection.

TABLE 1B. TIME COURSE OF DISEASE AND TREATMENT FOR GROUP 1 (THYROID EYE DISEASE, INFERIOR RECTUS SURGERY)

	ELAPSED TIME IN YEARS				
SURGERY ID	**SYSTEMIC HYPERTHYROIDISM TO THYROID EYE DISEASE ONSET***	**THYROID EYE DISEASE ONSET TO ORBITAL DECOMPRESSION†**	**ORBITAL DECOMPRESSION TO STRABISMUS SURGERY**	**THYROID EYE DISEASE ONSET TO DIPLOPIA SYMPTOM ONSET‡**	**DIPLOPIA SYMPTOM ONSET TO STRABISMUS SURGERY§**
1	0.0	3.5	1.0	1.0	3.5
2	0.1	1.0	0.4	0.0	1.4
3			0.3		
4	5.3			1.1	1.3
5	0.0			6.0	1.1
6	0.0	5.1	0.3	4.0	1.4
7	1.3	1.0	0.3	0.4	0.9
8	0.7	0.6	0.4	0.0	1.0
9	21.8			0.0	1.1
10			0.7		
11	3.5			0.0	1.6
12	-1.1	1.5	0.5	1.1	0.9
13	0.0	1.6	0.3		
14	0.7			0.4	0.3
15	2.0	0.4	1.5	1.0	0.8
16	0.3	0.6	0.4	0.2	0.7
17	0.9			0.0	1.5
18	11.8			1.9	0.8
19	0.0			0.0	1.3
20	2.0			1.4	6.8
21	0.5			3.8	1.0
22	9.0			0.0	1.8
23					
24	7.9	3.9	0.4	0.3	4.0
25	0.0			0.0	7.2
26	1.0			0.0	5.3
27			7.1		
28					2.9
29					0.8
30					0.7
31					4.1
32			1.2		1.9
33					1.3
34			0.4		0.8

*Blank cells indicate no date of thyroid eye disease onset was recorded.
†Blank cells indicate no orbital decompression and/or no thyroid eye disease onset was recorded.
‡Blank cells indicate no date for diplopia and/or thyroid eye disease onset was recorded.
§Blank cells indicate no date fore diplopia onset was recorded.

TABLE 2. DATA RETRIEVED FROM PATIENT RECORDS FOR GROUP 2 (NO THYROID EYE DISEASE, INFERIOR RECTUS SURGERY)

SURGERY ID	GENDER	AGE IN YEARS	NUMBER OF MUSCLES RECESSED	SUTURE TYPE	AMOUNT OF RECESSION (mm)	PREOPERATIVE MEASUREMENT (PD)	POSTOPERATIVE MEASUREMENT (PD) DAY 1	POSTOPERATIVE MEASUREMENT (PD) 2 MONTHS	SHIFT (PD)*
35	Female	60.8	2	Absorbable	5.0	12.0 LHT[b]	0.0	8.0 LHT	-8.0[c]
36	Male	75.9	2	Absorbable	6.0	12.0 LHT	0.0	4.0 LHT	-4.0
37	Female	76.2	1	Absorbable	4.0	12.0 LHT	0.0	4.0 LHT	-4.0
38	Male	73.0	1	Absorbable	4.0	16.0 LHT	0.0	2.5 LHT	-2.5
39	Male	55.9	2	Absorbable	6.0	15.0 LHT	2.0 LHT	4.0 LHT	-2.0
40	Male	82.8	1	Absorbable	8.5	12.0 RHT[d]	2.0 RHT	4.0 RHT	-2.0
41	Female	55.6	1	Absorbable	4.5	6.0 LHT	0.0	0.0	0.0
42	Female	53.3	1	Absorbable	10.0	30.0 LHT	0.0	0.0	0.0
43	Female	57.0	1	Absorbable	4.0	2.0 LHT	0.0	0.0	0.0
44	Male	63.8	1	Absorbable	8.0	15.0 LHT	0.0	0.0	0.0
45	Female	44.2	1	Absorbable	4.0	7.0 RHT	0.0	0.0	0.0
46	Female	92.3	1	Absorbable	7.5	16.0 RHT	0.0	0.0	0.0
47	Male	62.5	1	Absorbable	7.5	15.0 LHT	0.0	0.0	0.0
48	Male	46.0	1	Absorbable	6.0	10.0 LHT	1.0 LHT	0.0	1.0
49	Male	60.8	2	Absorbable	10.0	20.0 LHT	9.0 LHT	8.0 LHT	1.0
50	Male	68.0	1	Absorbable	7.0	15.0 LHT	2.0 LHT	0.0	2.0
51	Male	73.9	1	Absorbable	8.0	20.0 RHT	2.0 RHT	4.0 LHT	6.0
52	Male	75.6	1	Absorbable	2.0	2.0 RHT	0.0	2.0 RHT	-2.0
53	Female	75.3	1	Absorbable	4.0	5.0 LHT	0.0	0.0	0.0
54	Male	49.1	3	Nonabsorbable	4.0	5.0 LHT	0.0	4.0 LHT	-4.0
55	Male	35.1	1	Nonabsorbable	7.5	13.0 RHT	2.0 RHT	6.0 RHT	-4.0
56	Female	47.4	3	Nonabsorbable	8.0	10.0 RHT	4.0 LHT	0.0	-4.0
57	Female	54.4	2	Nonabsorbable	5.0	8.0 LHT	0.0	0.0	0.0
58	Female	33.7	2	Nonabsorbable	7.5	20.0 RHT	0.0	1.5 RHT	-1.5
59	Male	40.3	1	Nonabsorbable	5.5	17.5 LHT	2.0 LHT	0.0	2.0
60	Female	78.8	1	Nonabsorbable	7.0	14.0 RHT	2.0 RHT	0.0	2.0
61	Female	50.8	1	Nonabsorbable	4.0	25.0 RHT	1.0 RHT	1.0 LHT	2.0
62	Female	28.1	2	Nonabsorbable	6.0	20.0 LHT	3.0 LHT	0.0	3.0
63	Male	33.5	1	Nonabsorbable	10.0	40.0 LHT	4.0 LHT	0.0	4.0
64	Male	63.7	1	Nonabsorbable	6.5	13.0 LHT	0.0	0.0	0.0

LHT, left hypertropia; PD, prism diopters; RHT, right hypertropia.
*Negative numbers indicate undercorrection.

TABLE 3A. DATA RETRIEVED FROM PATIENT RECORDS FOR GROUP 3 (THYROID EYE DISEASE, MEDIAL RECTUS SURGERY, ABSORBABLE SUTURES)

SURGERY ID	GENDER	PRIOR ORBITAL DECOMPRESSION	AGE IN YEARS	PROPTOSIS	NUMBER OF MUSCLES RECESSED	AMOUNT OF RECESSION (mm)	PREOPERATIVE MEASUREMENT (PD)	POSTOPERATIVE MEASUREMENT (PD) DAY 1*	POSTOPERATIVE MEASUREMENT (PD) 2 MONTHS	SHIFT (PD)†^{C}
65	Female	Yes	40.4	Yes	2	5.0	16.0 ET	10.0 ET	12.0 ET	-2.0
66	Female	Yes	47.0	Yes	2	3.0	12.0 ET	0.0	12.0 ET	-12.0
67	Female	Yes	54.4	Yes	2	7.0	15.0 ET	8.0 ET	6.0	2.0
68	Female	Yes	55.6	Yes	2	5.0	16.0 ET	0.0	0.0	0.0
69	Female	Yes	55.6	Yes	1	8.0	40.0 ET	0.0	4.0 ET	-4.0
70	Female	No	57.0	No	2	4.0	9.0 ET	0.0	2.0 ET	-2.0
71	Female	Yes	57.8	Yes	2	7.0	25.0 ET	0.0	2.0 XT	2.0
72	Male	Yes	64.7	Yes	2	7.0	30.0 ET	15.0 ET	20.0 ET	-5.0
73	Female	Yes	65.1	Yes	2	6.5	40.0 ET	20.0 ET	20.0 ET	0.0
74	Female	No	65.6	No	2	4.0	10.0 ET	6.0 ET	10.0 ET	-4.0
75	Male	No	67.8	No	2	6.0	15.0 ET	0.0	1.0 ET	-1.0
76	Male	Yes	71.9	Yes	2	7.0	55.0 ET	30.0 ET	20.0 ET	10.0
77	Female	Yes	74.1	No	2	5.0	15.0 ET	4.0 ET	0.0	4.0

ET, esotropia; PD, prism diopters; XT, exotropia.
*Postadjustment.
†Negative numbers indicate undercorrection.

TABLE 3B. PREOPERATIVE AND POSTOPERATIVE MEASUREMENTS FOR GROUP 3 (THYROID EYE DISEASE, MEDIAL RECTUS SURGERY, ABSORBABLE SUTURES)

	ELAPSED TIME IN YEARS				
SURGERY ID	SYSTEMIC HYPERTHYROIDISM TO THYROID EYE DISEASE ONSET*	THYROID EYE DISEASE ONSET TO ORBITAL DECOMPRESSION†	ORBITAL DECOMPRESSION TO STRABISMUS SURGERY	THYROID EYE DISEASE ONSET TO DIPLOPIA SYMPTOM ONSET‡	DIPLOPIA SYMPTOM ONSET TO STRABISMUS SURGERY§
65	0.0	3.5	1.0	1.0	3.5
66			0.3		
67			7.1		
68	4.0	1.1	0.4	0.4	1.0
69	1.3	1.0	0.3	0.4	0.9
70		0.0	0.0		2.9
71			0.7		
72	2.0	0.4	1.5	1.0	0.8
73	0.3	0.6	0.4	0.2	0.7
74	0.9	0.0	0.0	0.0	1.5
75	2.0	0.0	0.0	1.4	6.8
76		1.1	4.9	0.0	6.0
77			0.4		0.8

*Blank cells indicate no date of thyroid eye disease onset was recorded.
†Blank cells indicate no orbital decompression and/or no date for thyroid eye disease onset was recorded.
‡Blank cells indicate no date for diplopia and/or thyroid eye disease onset was recorded.
§Blank cells indicate no date for diplopia onset was recorded.

Measurement of ocular deviations was accomplished using the alternate prism and cover test in primary position at distance with best refractive correction. Although one classification scheme describes strabismus in terms of ductions graded by light reflexes,[47] this system is not standard practice for strabismus evaluation and would be poorly suited for quantifying primary gaze deviations, particularly when 2 prism diopters (PD) makes a difference in the assessment of outcome. All patients were evaluated at least twice before surgery at 2-month intervals and found to have stable measurements greater than 6 months from any event that might incite change in ocular motility (such as orbital surgery or thyroid ablation) or change in symptoms.[48] The muscle recessed, amount of recession, and suture material used were recorded.

Surgery was performed only after all signs of acute thyroid eye disease had resolved, all anticipated orbital surgery had been completed, 6 months had elapsed between orbital surgery or any other factor that might cause a change in strabismus (eg, instability in thyroid function or change in thyroid medication dosages),[49] and two sets of ocular motility measurements separated by at least 2 months were deemed stable. All inferior rectus recessions prior to 2005 were performed with absorbable 5-0 Vicryl suture (polyglactin; Ethicon, Inc, Somerville, New Jersey). Since 2005, all inferior rectus recessions have been performed with 5-0 Mersilene suture (polyester; Ethicon, Inc, Somerville, New Jersey). This change in suture was stimulated after listening to a workshop entitled "Thyroid Ophthalmopathy: Evaluation and Therapeutic Options" at the 2005 American Association for Pediatric Ophthalmology and Strabismus meeting. Factors associated with poor outcomes following strabismus surgery in Graves' disease were discussed by the panel and informally after the panel session. Rather than expose my patients to bilateral inferior rectus surgery when only one inferior rectus was clinically restricted (as was advocated by Cruz[45]), it seemed prudent to develop a way to address the likely (though unproven) mechanism for postadjustment overcorrections: slippage of the muscle after dissolution of the absorbable suture. Operating on the single offending inferior rectus is important for my approach to surgical correction of hypotropias in Graves' disease, as I may need to reoperate after a very large (>20 PD) hypotropia has been addressed with inferior rectus surgery. Having an unoperated inferior rectus on the less affected eye often proves quite valuable, as reoperating a tight and previously recessed inferior rectus to advance it if there is an overcorrection is technically more difficult and unpredictable with regard to outcome (personal observation).

Other than the type of knot used (bow tie for nonabsorbable and noose for absorbable, both closed with a square knot at the conclusion of the adjustment), no other aspect of surgical care (including surgical technique or postoperative care), other than the type of suture used, was changed in 2005. All medial rectus recessions were performed with 5-0 absorbable Vicryl suture and a noose closed with a square knot at the time of adjustment. In all cases hang-back sutures were fixed at the original insertion, not at any point posterior to the original insertion. Patients had either local anesthesia with intravenous sedation or general anesthesia. All patients had adjustment within 24 hours of surgery ("two-stage adjustable suture" technique). The primary surgeons used a standard follow-up protocol of 2 weeks and then 2 months after muscle recession. The amount of recession (in millimeters) varied according to the individual patients and their preoperative measurement. Minimal dissection of the recessed muscle was performed, with only blunt dissection of the inferior lid retractors away from the inferior rectus when large recessions were performed.

Patients were not gender- or age-matched. The age of patients in this series ranged from 28 to 92 years. The average age of all patients was 60.1±12.1 years. The average age for each group of patients was as follows: Group 1 (thyroid eye disease, inferior rectus surgery), 61.3±8.2 years; Group 2 (nonthyroid eye disease, inferior rectus surgery), 58.9±16.3 years; and Group 3 (thyroid eye disease, medial rectus surgery), 59.8±9.6 years. Overall, there were 27 men and 50 women included in the study. Group 1 had 8 men and 26 women, Group 2 had 16 men and 14 women, and Group 3 had 3 men and 10 women. There were 72 self-described white patients and 5 self-described African American patients. Three of the 47 patients with thyroid eye disease (Groups 1 and 3) were African American, and 2 of the 30 patients without thyroid eye disease (Group 2) were African American.

Preoperative diagnoses for Group 2 patients (without thyroid eye disease) were cranial nerve palsies, paralytic and neurologic conditions (including bilateral skew deviation and internuclear ophthalmoplegia), restrictive or orbital disease, nonstrabismic eye surgery, and childhood strabismus (Table 4). Some patients had more than one diagnosis accounting for their vertical eye misalignment. The most common preoperative etiology for all patients was cranial nerve palsy.

The appropriateness of combining patients who had different disease entities that cause hypotropia and who underwent single inferior rectus recession on adjustable suture into Group 2 might be questioned. According to current literature, grouping patients with multiple diseases that cause a vertical deviation is common practice. For muscle-specific surgery, combining multiple diagnostic entities in the same case series in order to examine the outcome of surgical technique is typical. Studies that address surgical outcomes after treatment for specific conditions (eg, thyroid eye disease, diplopia after cataract surgery, superior oblique palsy) include muscle surgery to a variety of muscles using a variety of techniques (such as fixed and adjustable sutures) in the same study group. Little exists in the literature to ascertain whether such groupings are appropriate to study outcomes, and the results of these studies may not be helpful when managing a specific muscle problem in a specific disease because of the heterogeneous study groups that exist in the literature. This study examines a specific technique for a specific muscle (inferior rectus) in a specific disease (thyroid eye disease) to address a specific problem (postoperative overcorrection). One might argue against the appropriateness of combining different etiologies in Group 2, but there is no literature to suggest that I should expect different outcomes for surgery in these entities. For example, Ken Wright[43] published a series of 7 patients, all with late overcorrection after inferior rectus recession. Two patients had congenital superior oblique palsy, one had a floor fracture, one had retina surgery, one had traumatic superior oblique palsy, one had sinus surgery with orbital fracture, and one had retrobulbar injection with cataract surgery. Another report, published in 2000, addresses late overcorrections in inferior rectus muscle surgery for vertical strabismus.[50] The study sample is composed of congenital superior oblique palsies, thyroid eye disease, blowout fractures, and double elevator palsy. All patients except a child had adjustable suture. Five of 21 patients experienced postoperative overcorrection between 1 month and 3 months. The average amount of overcorrection was 9.6 PD. None of the dysthyroid patients had overcorrections, despite larger-than-average recessions. All overcorrections were in the superior oblique palsy group. Citations were made pointing out that late overcorrections have not been reported after surgery for double elevator palsy[51] or vertical strabismus after cataract surgery.[52,53] Clearly, reports of outcome following inferior rectus recessions are somewhat idiosyncratic and provide no clear answer as to the implications of combining patients in Group 2. All of the diseases that comprise the etiologies in Group 2 have both paralytic/hypocontractile and restrictive/hypoelastic features. Even cranial nerve palsies and other causes of paralytic muscles often have a secondary antagonist contractured muscle, and strabismus after cataract surgery and inferior orbital fractures can have hypocontractile and hypoelastic extraocular muscles affecting motility. Thus, there is no obvious anatomical reason to suspect that inferior rectus muscle surgery may have different effects in the Group 2 patients with different etiologies and reject the grouping of these patients. There are, however, very significant orbital and extraocular muscle abnormalities in thyroid eye disease that are disease-specific and specific to the operated/recessed inferior rectus muscle, and those issues will be addressed in the "Discussion" section.

TABLE 4. ETIOLOGIES OF STRABISMUS IN NONTHYROID PATIENTS UNDERGOING INFERIOR RECTUS RECESSION (GROUP 2)*

ETIOLOGY	ALL PATIENTS WITH INFERIOR RECTUS RECESSION (n=31)	INFERIOR RECTUS RECESSION WITH NONABSORBABLE SUTURES (n=11)	INFERIOR RECTUS RECESSION WITH ABSORBABLE SUTURES (n=20)
Cranial nerve palsy			
CN III	2	1	1
CN IV	14	8	6
Paralytic/neurologic	12	5	7
Restrictive/orbit (excluding thyroid eye disease)	8	1	7
Eye surgery (not involving muscles/orbit)	5	1	4
Childhood strabismus	9	6	3

*Some patients had multiple etiologies.

Overall, the range for inferior rectus recession was 2 to 10 mm, with an average of 7.0 mm. For Group 1 (inferior recti with thyroid eye disease), the inferior rectus recessions performed with absorbable sutures ranged in amount of recession from 4 to 10 mm, with an average of 7.4 mm. The amount of recession for inferior rectus recessions performed with nonabsorbable sutures ranged from 3.5 to 10 mm, with an average of 8.3 mm. The range for inferior rectus recession in Group 2 (inferior recti without thyroid eye disease) was 2 to 10 mm, with an average of 6.2 mm. For surgeries performed with absorbable sutures in Group 2, the amount of recession ranged from 2 to 10 mm, with an average of 6.1 mm. The amount of recession for inferior rectus recessions performed with nonabsorbable sutures ranged from 4 to 10 mm, with an average of 6.5 mm. For purposes of surgical planning, we anticipated correction of 2 PD hypotropia per millimeter of recession performed on inferior recti in all cases. For Group 3 (medial recti with thyroid eye disease), absorbable suture was used for all procedures. The range of recession was 3 to 8 mm, with an average of 5.7 mm. The anticipated correction was 3.5 PD per millimeter for medial rectus recessions. The surgeon did not intentionally undercorrect or overcorrect the patient during adjustment of the suture, though no vertical muscle was recessed more than 10 mm (both absorbable and nonabsorbable suture), and no medial rectus was recessed more than 7 mm, no matter how large the preoperative deviation or undercorrection at the time of postoperative adjustment.

The primary surgeon determined the postoperative measurements in all cases (reported in Tables 1B, 2, and 3B). Patients were adjusted within the first 24 hours postoperatively. The primary surgeon measured the deviation of ocular alignment at that time. Measurements prior to adjustment (if the patient's suture was adjusted) were not recorded due to the process of adjustment. If the patient was determined undercorrected after maximal recession, then no further recession was performed and the measurement at that time was recorded. If the patient was overcorrected, he or she was adjusted to orthotropia (or as near as possible) and that measurement postadjustment was recorded. If the patient was orthotropic upon intial evaluation, then no adjustment was performed and the measurement recorded. Subsequent measurements were recorded at 2 weeks, 2 months, and the most recent postoperative visit. Any patient who did not comply with standard postoperative follow-up visits was excluded from the study. All postoperative measurements used for analysis were taken in the primary position of gaze.

For patients with thyroid eye disease, 26 of 47 (55%) had had prior orbital decompression surgery. Sixteen of 34 (47%) in Group 1 (inferior rectus recessions) and 10 of 13 (77%) in Group 3 (medial rectus recessions) had had prior orbital decompression.

Of all 77 cases, 38 (49%) had no concurrent muscle surgery at the time of the surgical event included in this study (ie, there was only a single muscle operated). Thirty-four (44%) had one other muscle operated concurrently, and 5 patients (6%) had three muscles operated at the studied event. Note that, given the exclusion criteria for this study, if the patient was included for an inferior rectus surgery, then the other muscle operated had to have been a horizontal rectus, and if the medial rectus was the studied surgical event, then the other operated muscle was a vertical rectus. In Group 1, 18 (of 34, 53%) had concurrent horizontal muscle surgery, and in Group 2, 9 (of 30, 30%) had concurrent horizontal muscle surgery. In Group 3, 12 (of 13, 92%) had concurrent vertical muscle surgery. Summation of the data collected for analysis is presented per group in Tables 1, 2, and 3.

STATISTICAL ANALYSES

The purpose of this study was to characterize the factors (variables) associated with the phenomenon of overcorrection after muscle recession. In this study, the single response variable of interest, overcorrection shift, was collected via retrospective chart review. Several plausible explanatory variables for the observed outcome of postoperative, postadjustment overcorrection shift were investigated, including both categorical variables (eg, suture type) and continuous variables (eg, age). The possible association of explanatory variables with postoperative overcorrection shift was initially screened using a test for normality. Variables that do not correlate with outliers (ie, overcorrection shifts) would be expected to show normally distributed postoperative shifts, whereas variables that correlate with the outlier overcorrection shifts would be expected to show a nonnormal, positively skewed (ie, extreme value) distribution.

The two thresholds analyzed, >2 and >5 PD, were chosen because of previous studies. The >5 PD threshold has common usage in the literature dealing with strabismus surgery in inferior rectus and/or thyroid eye disease studies.[39,54-56] The >2 PD threshold was chosen for two reasons. First, some studies used restoration of single binocular vision/relief of diplopia as their measure of success.[12,38,41,57] Second, because of limited vertical fusion in adult patients who are susceptible to postoperative diplopia if the postoperative alignment shifts more than 2 PD, it seemed to be a conservative and reasonable alignment threshold to allow comparison to these studies and provide further insight into clinically important overcorrection shifts.

The next step was to analyze explanatory variables to determine which combinations of them were correlated with the overcorrection shifts. These variables were identified previously in the literature as potentially contributing or causally related factors in the severity of strabismus in thyroid eye disease and/or its response to treatment. The explanatory variables included age,[22] thyroid eye disease,[40,41] preoperative deviation,[58] muscle recessed,[40,43,44,59,60,] type of suture,[39,60,61] amount of recession,[58] number of muscles operated,[40] prior history of orbital decompression,[57,62,63,] and proptosis.[64]

A comment on the usefulness of the normality tests as a screening tool for extreme outlier overcorrection shift is in order. One of the key results of this study, discussed below, is that the distribution of overcorrection shift in the identified subpopulations is not simply a result of a normally distributed population shifted to a higher mean and higher standard deviation. Instead, the bulk of the subpopulation retains a normal distribution while outliers drift to higher values postoperatively. The resulting distribution is not gaussian. The impact of this phenomenon on the statistical treatment is twofold: first, the distribution of outliers is best handled with the tools of extreme value theory; and second, a test for normality becomes a good screening tool to help identify factors that may be associated with outlier overcorrection shift.

Techniques used to screen for normal distribution, ie, find the variables associated with the outlying overcorrection, included the Anderson-Darling test and box-and-whiskers plots. The Anderson-Darling test generates a *P* value to indicate the likelihood that the sample is drawn from a normal distribution. It was used to identify variables that show a nonnormal distribution with respect to overcorrection shift and, thus, may be candidates for further analysis. Binomial variables such as presence or absence of thyroid eye disease and prior history of orbital decompression were tested. The Anderson-Darling test is preferable to other tests for normality, such as the Kolmogorov-Smirnov test, for the current study because it is more sensitive to deviations in the tails of the distribution.[65] It was also utilized to evaluate whether a shifted log-normal distribution would explain the distribution of the data normally.

Box-and-whiskers plots succinctly convey a wealth of information about the distribution of the dependent variable. The "box" part of the plot shows the 25th to 75th percentile range of the data, also known as the interquartile range (IQR). The "whiskers" of the plot typically represent ±1.5 times IQR below the 25th or above the 75th percentile (unless the minimum and/or maximum of the data are within the ±1.5 times IQR limits, in which case the whisker tips represent the actual minimum and/or maximum of the data). Points falling outside the whiskers' limits are considered "outliers" and, for small samples, are also indicators of nonnormality. Therefore, box-and-whiskers plots can be used to identify data sets that are candidates for fitting with an extreme value distribution function. An advantage of the boxplot is that it makes no assumption about the distribution of the sample (ie, it is nonparametric). It is a graphic technique and allows for a subjective identification of those factors that are associated with outliers, though no quantitative assessment is rendered. Box-and-whiskers plots were constructed for postoperative shift as functions of explanatory variables, singly and in combination.

We chose to perform linear regressions on three continuous explanatory variables of interest (age, amount of recession, and preoperative measurement) because the Anderson-Darling test is difficult to apply to continuous variables. The regressions were performed one by one. Then, building on these regressions, multivariate linear models involving all the explanatory variables (both continuous and categorical) were constructed. Pearson's product moment coefficient (PPMC) was used as the measure of the correlation between two variables. It is widely used in the sciences as a measure of the strength of linear dependence between two variables. We used it to find out if there was a relationship between overcorrection shift and several continuous explanatory variables. However, the PPMC suffers from a lack of distributional robustness when outliers are present. As a cross-check for the results of the regression analysis, scatterplots were created and inspected for drift vs continuous explanatory variables. Inspection of the scatterplot will typically reveal when lack of robustness is an issue for the PPMC. The correlation of the continuous explanatory independent variables (age, amount of muscle recession, and preoperative deviation) with overcorrection shift was analyzed by linear regression analysis. The Pearson product moment correlation, *R*, was used to generate an R^2 value for the linear regression plot and estimate the variance in the dependent variable (overcorrection shift) explained by each independent variable. As mentioned above, however, linear regression models do not capture the tail of the shift distribution well.

As illustrated by the histogram shown in Figure 3, the majority of the cases in our series had no significant (≥2 PD) undercorrection or overcorrection shifts. The cases of interest for my study, ie, the overcorrected ones, clustered in the top quartile of the data series. The basic problem with approaching the phenomenon of overcorrection shift with a linear model is that measures of central tendency, such as sample mean and median, are not adequate for comparing the tails of distributions for different groups, which are just the portions of data I needed to compare (ie, the positive tail of the shift distribution for thyroid eye disease with the positive tail of the shift distribution for no thyroid eye disease). The best-known techniques of statistical analysis are based on the mean and variance of random variables. The central limit theorem states that the mean of a sufficiently large number of independent random variables, each with finite mean and variance, will be asymptotically normally distributed. Tests based on the normality of the underlying population variable (such as Student's *t* test and analysis of variance) are popular and generally uncontroversial tools for statistical analysis. These tests are powerful tools for determining whether two or more samples are drawn from the same or different populations. It is important to recognize, however, that these tests focus on measures of central tendency (ie, the sample mean) and on dispersion about the mean (ie, the standard deviation) and thus tend to be insensitive to the outliers of a sample.

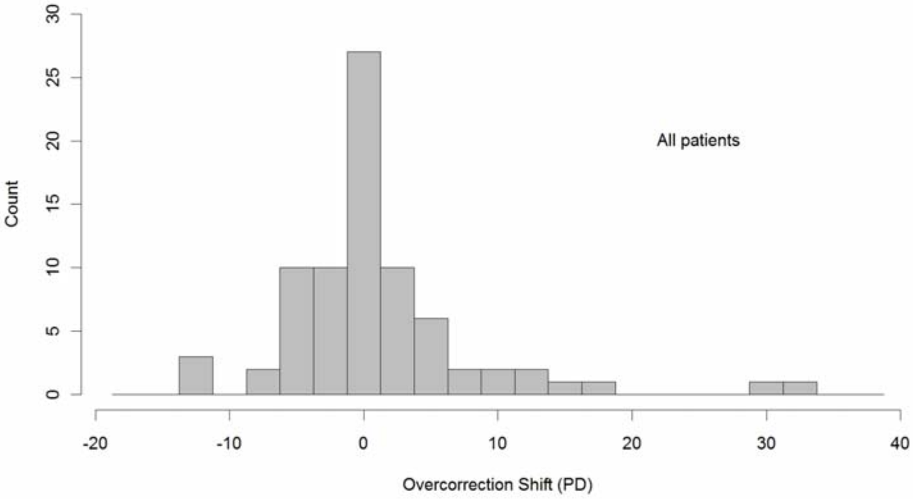

FIGURE 3

Histogram depicting frequency distribution of overcorrection shift for all patients. Note the positively skewed overcorrection tail.

Statistical analysis that is analogous to testing based on a normal population exists to study the problem faced when some phenomenon of interest is characterized not by the central values of a distribution, but rather by the extreme values. This is the case in my current study. Less well known but equally accepted as the central limit theorem, the branch of statistics known as "extreme value theory" has developed the appropriate tools to deal with this situation.[66,67] Extreme value theory has found numerous applications in hydrology, meteorology, finance, gerontology, engineering, and many branches of science.

The fundamental result of extreme value theory is that samples drawn from the extreme values of a probability distribution asymptotically approach one of three functional forms. With the addition of a single adjustable parameter, those functional forms can be unified into a single form called the generalized extreme value distribution. Of course, certain technical requirements must be met, just as with the central limit theorem, but the techniques are broadly applicable.

One way to apply extreme value theory is to truncate a data set so that only values above some threshold are considered. This is called the "peak over threshold," or POT, method. In POT, the distribution of values exceeding the threshold can be shown to converge to a member of the generalized Pareto family of distributions. In this study, the techniques of extreme value theory, in particular the POT method, are used to find which variables contribute to postsurgical overcorrection shift.

The distribution function, *F(x)*, also called the cumulative distribution function or cumulative frequency function, describes the probability that a variable, *X*, takes on a value less than or equal to a number, *x*.[68] As noted above, the postoperative shift distribution for the entire sample shows a long tail for overcorrections. This high tail is well modeled with extreme value theory, eg, fitting a generalized Pareto distribution using the POT approach.[66,67] The distribution of extreme values exceeding a specified threshold approaches a generalized Pareto distribution. Thus, the relationship of the generalized Pareto distribution to extreme values is analogous to the relationship of the normal distribution function to averaged values. The cumulative distribution function for the generalized Pareto distribution is

$$F_{\mu,\sigma,\xi}(\chi)=1-(1+\xi(x-\mu)/\sigma)^{-1/\xi},$$

where μ is the threshold parameter, ξ is the shape parameter, and σ is the scale parameter. In this study, *x* is the overcorrection shift in PD and σ is a dimensional parameter, also in PD, that provides a scale for *x* (the overcorrection shift). Thus, the ratio *x*/σ is dimensionless. The generalized Pareto distribution *F(x),* when plotted vs *x*, has a shape that is quantified by the dimensionless parameter ξ. The threshold μ provides a lower bound to the overcorrection shifts to be fitted to the generalized Pareto distribution. Values of overcorrection shift below the threshold μ are, thus, not analyzed.

The usual approach to fitting a generalized Pareto distribution using the peak-over-threshold method is to vary the threshold μ over a range of values and examine a plot of shape (ξ) and scale (σ) parameters and their uncertainties. These plots are called "threshold choice" plots. Typically, the threshold choice plots will show a bias for smaller values of the threshold μ (ie, inconsistent results because some points are included that are not "extreme enough") together with growing uncertainty (error bars) as the threshold μ is raised. The threshold choice plots are used to estimate the threshold μ that gives the "best" tradeoff of bias and uncertainty. Threshold choice plots for shape (ξ) and scale (σ) of the generalized Pareto distribution generated for the data set accumulated in the course of this study show that thresholds in the range of 2 to 5 PD are quite reasonable. The threshold choice plots for scale and shape for the entire sample are shown in Figure 4. Both provided good fits to a generalized Pareto distribution (Figures 5 and 6).

The explanatory independent variables that demonstrated a nonnormal distribution by means of the Anderson-Darling test and the box-and-whiskers plots were identified as the ones best suited to be modeled with extreme value theory by fitting the aforementioned generalized Pareto distribution using the POT approach.

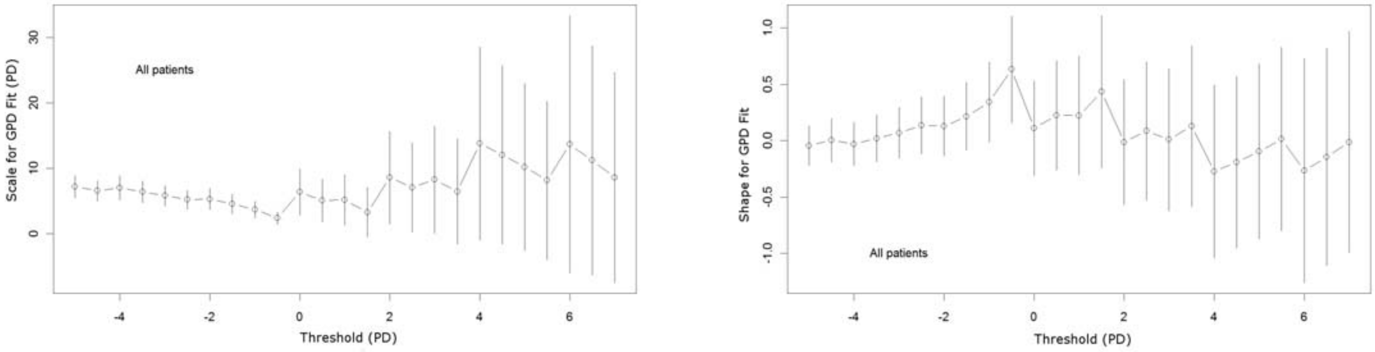

FIGURE 4

Left, Threshold choice plot for scale of the generalized Pareto distribution (GPD). Right, Threshold choice plot for shape of the generalized Pareto distribution. Wider vertical lines (uncertainty bands) indicate greater uncertainty. As can be seen, uncertainty increases between 0 and 5 PD for both the shape and fit of the model, indicating that the thresholds of >2 and >5 PD are reasonable choices for this data set.

The Mann-Whitney *U* test was used to determine if differences in the study sample composition could explain the difference found in results between patients operated with absorbable sutures and those operated with nonabsorbable sutures. As will be shown in the course of my analyses, a different behavior in the amount of postoperative overcorrection shift existed within Group 1 between patients operated with nonabsorbable sutures and those operated with absorbable sutures. Therefore, to analyze the possible impact of other explanatory independent variables on overcorrection shift within these two study subsamples stratified by suture type, the distributions of these explanatory independent variables were compared using the Mann-Whitney *U* test. The *U* test is useful in the same situations as the independent samples Student *t* test. Though slightly less efficient than the Student *t* for large samples from normal populations, the *U* test is less likely than a *t* test to indicate significance spuriously in the presence of outliers.

I also sought to estimate the likelihood of developing an overcorrection shift as a function of the type of suture used. Odds ratios (ORs) were estimated with a 2×2 table approach for both the >2 PD and the >5 PD threshold. Because one of the cells in the 2×2 table had a zero value (see "Results" section), the odds ratio and its 95% confidence interval (CI) were calculated using the null hypothesis to provide these estimates.[47] Under the null hypothesis that treatment with a nonabsorbable suture has no effect on outcome, the difference between the observed number of overcorrections and their expected number would have zero difference and variance. Though more difficult to interpret than a risk ratio, this approach permits having zero value cells without generating an infinity odds ratio value (which was encountered in my data). To verify the tendency of the estimates based on my case series, I performed a pooled analysis merging this data with data from the literature, which was available in a limited fashion for the >5 PD threshold.

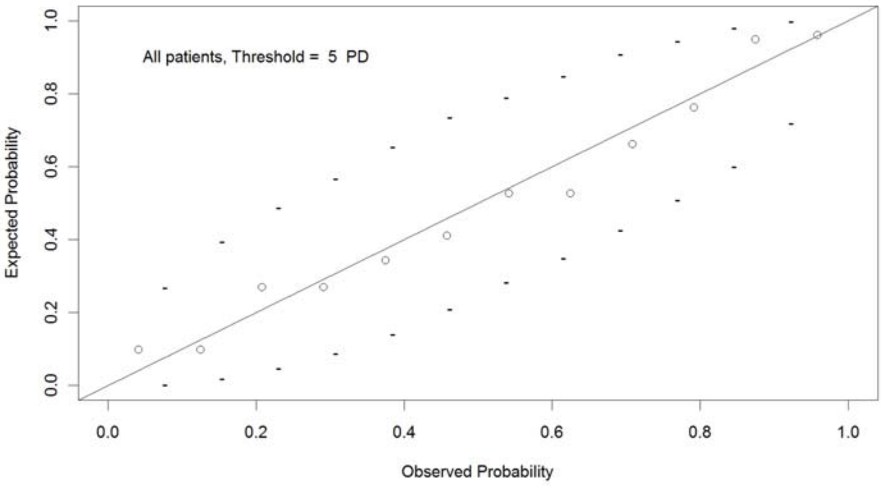

FIGURE 5

Fits of threshold to the generalized Pareto distribution for >5 PD. The dotted lines represent the 95% CI for the fit to a general Pareto distribution, and all data points lie within the 95% CI and all the plotted data points are near the line of equivalence between *x* (observed probability for overcorrection shift) and *y* (fitted probability for overcorrection shift, based on the general Pareto distribution model).

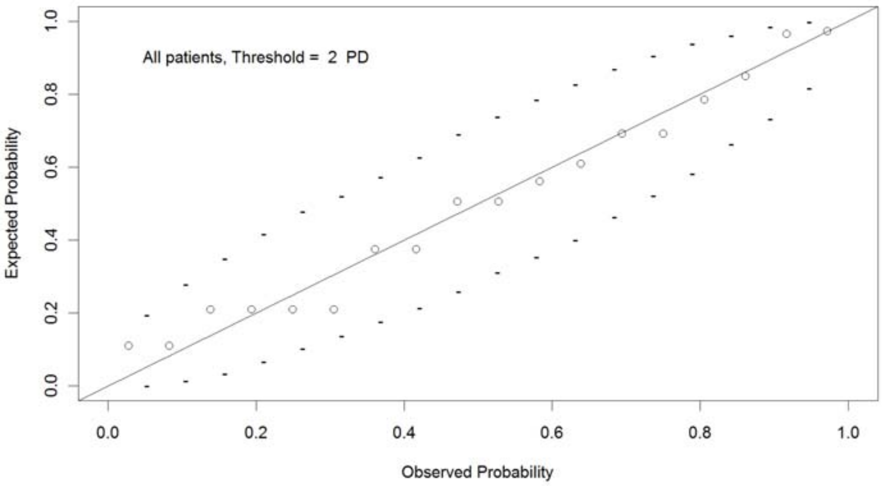

FIGURE 6

Fits of threshold to the generalized Pareto distribution for >2 PD. The dotted lines represent the 95% CI for the fit to a general Pareto distribution, and all data points lie within the 95% CI and all the plotted data points are near the line of equivalence between x (observed probability for overcorrection shift) and y (fitted probability for shift, based on the general Pareto distribution model).

Odds ratios were also calculated in my sample of patients with thyroid disease (Groups 1 and 3) for the time course of their disease and the outcome of overcorrection shift >5 PD as well as proptosis and the outcome of overcorrection shift ≥5 PD. Elapsed times were calculated for (Tables 1B and 3B):

1. onset of systemic hyperthyroidism to onset of thyroid eye disease;
2. onset of thyroid eye disease to date of orbital decompression (subsample: patients who underwent orbital decompression);

3. date of orbital decompression to date of strabismus surgery (subsample: patients who underwent orbital decompression);
4. onset of thyroid eye disease to onset of diplopia symptoms (subsample: patients without orbital decompression); and
5. onset of diplopia to date of strabismus surgery.

The sample of thyroid patients was split into two groups: those whose elapsed time for one of these clinic course data points was above average and those whose elapsed time was below average. A 2×2 table was then constructed for above/below elapsed time measures and overcorrection shift/no overcorrection shift. The Gart correction was used because some cells contained a zero value.[69] A 2×2 table was also constructed for proptosis (present or not present) and overcorrection shift ≥5 PD for all patients with thyroid eye disease (Groups 1 and 3) and just inferior rectus recessions and thyroid eye disease (Group 1). An OR was calculated for each matrix, as well as a 95% CI and a Fisher exact test *P* value.

Descriptive statistics were performed with Microsoft Excel (2000 and 2007). Tests for normality[70] and generalized Pareto distributions with POT method[71] were performed in R—a free software for statistical computing and graphics (www.r-project.org). Odds ratio and Fisher's test statistical computations were performed with SAS software, v. 9.0 (SAS Statistical Institute, Cary, North Carolina). Results were considered statistically significant for $P\leq 0.05$. Different techniques exist for adjusting the *P* value chosen based on the number of comparisons run, generally using a smaller *P* value for a large number of comparisons. However, a type I error rate for the numerous comparisons made in order to screen for candidate factors influencing overcorrection shifts is acceptable given their use as a screening tool, not a final determinant of significance for the study. Additionally, using the larger *P* value minimizes the type II false negative error (ie, missing a true positive), which is important in the search for factors contributing to overcorrection. As noted previously, the box-and-whiskers plot was used as a check for the results of the Anderson-Darling test, and the scatter plot was used as a cross-check for the PPMC, both screening tests that were then evaluated by the methods of extreme value theory.

RESULTS

DISTRIBUTION OF RETRIEVED DATA

Analysis using >2 PD of overcorrection as the threshold value yielded 18 cases of overcorrection (23.1% of 77). A total of 12 patients (15.8% of 77) had outcomes in excess of the threshold value of >5 PD of overcorrection shift after muscle recession.

To deal with the long positive tail of the frequency distribution of overcorrection shifts, we performed a log-normal or "shifted" log-normal distribution, ie, one in which arbitrary fixed values are added to the raw data to offset the fact that there are negative values for overcorrection shifts. We used the Anderson-Darling goodness-of-fit test on our shifted data because of the small sample size. Fitting a log-normal distribution with offsets from 15 PD to 100 PD did not produce a normal distribution. The best fit to a shifted log-normal distribution occurred with the addition of 26 PD (Figure 7), but the Anderson-Darling test indicated that the fit was still not log-normally distributed (P=2.80E-8). Fitting the data to a log-normal distribution did not result in a normal distribution because of the large number of shift results that were at or near zero. The excess kurtosis of the best fit log-normal was 2.8 (compared to a value of 0 if the distribution had been normal). While there were a large number of successful results with no substantial shift, there was a positively skewed data distribution with regard to overcorrection shift.

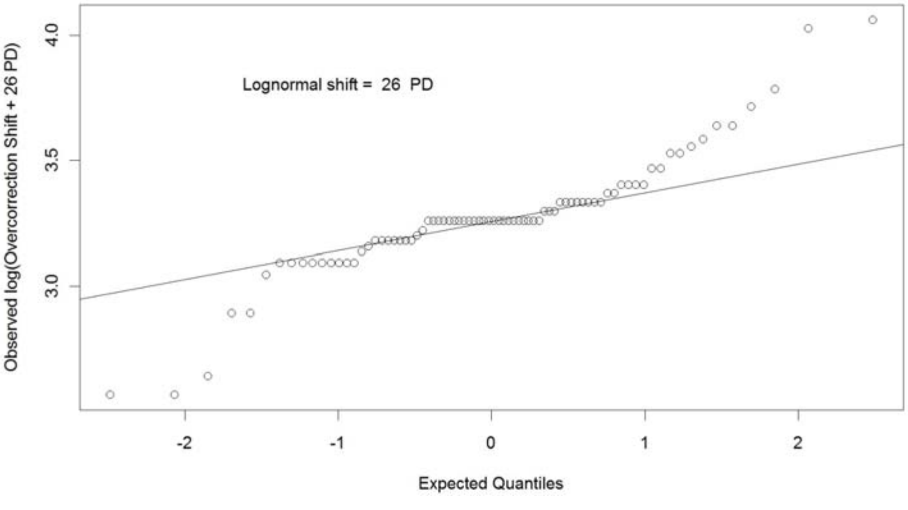

FIGURE 7

Best fit log-normal distribution at +26 PD. As can be seen from the outliers at either end, the distribution is not normal.

Screening for normal distribution of the continuous variables in this study was problematic, as there were not enough data points in my study to analyze the shift distribution at each value of the continuous variable for normality, or even for binned data with useful bin sizes. Attempts were made to bisect the sample at various crossover points of the continuous variables. For example, the subsample for amount of recession less than or equal to 5 mm was compared to the subsample for amount of recession greater than 5 mm, with both subsamples screened for normality. Using the Anderson-Darling test for normality (where a small sample is deemed normally distributed when $P>0.05$), the result was $P=5.0E\text{-}4$ for recessions less than or equal to 5 mm and $P=2.0E\text{-}7$ for recessions greater than 5 mm. The lack of normality on both sides of the bisection point indicated that amount of recession was not likely to be a useful explanatory variable for overcorrection shift. Similar negative results were obtained for age and preoperative measurement. Anderson-Darling *P* values and box-and-whiskers plots for age and preoperative measurement were nonnormally distributed. The *P* value for above median age was 8.26e-06 and for sample below median age was 6.29e-07. The *P* value for preoperative measurement above the median was 4.07e-05 and for preoperative measurement below the median was 3.12e-05.

Anderson-Darling tests showed that the total sample (n=77) did not follow a normal distribution with regard to amount of shift ($P=7.5E\text{-}12$). Distribution of shift in subsets of proposed explanatory variables that showed a nonnormal distribution (ie, had an overcorrection tail) included thyroid eye disease ($P=6.7E\text{-}06$), absorbable suture ($P=1.7E\text{-}09$), and inferior rectus recession ($P=2.2E\text{-}11$), whereas no thyroid eye disease ($P=0.06$), nonabsorbable suture ($P=0.14$), and medial rectus recession ($P=0.45$) showed a normal distribution (ie, no overcorrection tail). Thus, thyroid eye disease, absorbable suture, and inferior rectus recession were variables showing a possible association with overcorrection shifts.

For pairs of explanatory variables where both variables showed nonnormal distributions (eg, sex and race), there was no difference noted for these variables with regard to an overcorrection tail; overcorrections were represented equally in both variables in the tested pair, making these variables unlikely candidates for being associated with overcorrection shifts. Prior orbital decompression for patients with thyroid eye disease, constituting Groups 1 and 3, showed a normal distribution for a history of orbital decompression ($P=0.25$), whereas its paired variable, overcorrection shift in thyroid eye disease patients without a history of orbital decompression, had an overcorrection shift tail and nonnormal distribution ($P=1.8E\text{-}06$). These analyses indicate that patients without a history of orbital decompression showed a tendency toward overcorrection shift, whereas those with a history of decompression showed no such tendency.

For the number of muscles operated, both single-muscle surgery ($P=3.5E\text{-}09$), and two-muscle surgery ($P=3.3E\text{-}05$) were associated with a nonnormal distribution. Thus, there is no evidence to indicate a difference between these groups with regard to overcorrection shifts. Three-muscle surgery could not be analyzed using Anderson-Darling normality tests, as there were fewer than seven data points (n=5).

Group 1 (thyroid patients undergoing inferior rectus recession) showed a nonnormal distribution ($P=1.1E\text{-}04$). Subdividing this group further, patients in Group 1 with absorbable sutures had a nonnormal distribution/overcorrection tail ($P=0.0042$), whereas patients from this group with nonabsorbable suture had a normal distribution and no overcorrection tail ($P=0.16$). Group 2 (nonthyroid patients undergoing inferior rectus recession) showed a normal distribution ($P=0.063$). Group 3 (thyroid patients undergoing medial rectus recession) had a normal distribution with $P=0.45$. Thus, within Group 1, absorbable suture showed a tendency toward overcorrection shifts, whereas nonabsorbable suture showed no such tendency.

CORRELATIONS WITH OVERCORRECTION SHIFTS

Linear regression analysis was performed to determine the correlation between three continuous patient-related variables and overcorrection shift: age (Figure 8), preoperative measurement (Figure 9), and amount of recession (Figure 10). The dotted lines on the plot represent the central 95% CI for the regressed model. Pearson's product moment correlation showed no correlation for age and overcorrection shift ($R^2=0.01$, $P=0.38$) and a weak correlation for preoperative measurement ($R^2=0.17$, $P=0.0002$) and amount of recession ($R^2=0.13$, $P=0.001$). Looking at the linear regression plots (Figures 8 through 10), it becomes apparent that the extreme values of overcorrection shift were not accounted for by the correlation. Additionally, given the long period of time over which the study patients were accumulated and concern that overcorrections could be positively or negatively correlated with the surgeons' experience over time, linear regression analysis was performed plotting date of patient encounter with postoperative shift. If increased experience of the surgeons resulted in better outcomes, a correlation would have been expected between overcorrection and earlier surgery dates and fewer overcorrections for the later dates. No correlation was found ($R^2=0.000877$, $P=0.84$).

Box-and-whiskers plots, as described in the "Patients and Methods" section, confirmed outlier overcorrection shifts in thyroid disease (Figure 11), with absorbable suture use (Figure 12), and in inferior rectus recession (Figure 13). Additionally, outlier overcorrection shift was noted in patients with thyroid eye disease who had muscle recession but never had orbital decompression (Figure 14).

Fitting a generalized Pareto distribution using the POT method for the suture type, we found that extreme value theory models the overcorrection shifts seen in patients with absorbable sutures (Figures 15 and 16). However, no such fit could be calculated for the patients with nonabsorbable sutures because there was no extreme value tail for overcorrection shift. All patients (n=12, 100%) who had an overcorrection shift >5 PD had surgery with an absorbable suture. Fourteen of 18 (78%) who had an overcorrection shift threshold >2 PD had surgery with an absorbable suture. With regard to muscle type, extreme value theory also models the overcorrection shift extreme value tail seen in inferior rectus recessions (Figures 17 and 18). Eleven of 12 cases (92%) with overcorrection shift >5 PD were performed on inferior recti, and 16 of 18 cases (89%) with overcorrection shift >2 PD were performed on inferior recti. No such plot could be made for medial recti (Group 3), as there was no overcorrection shift tail associated with this group.

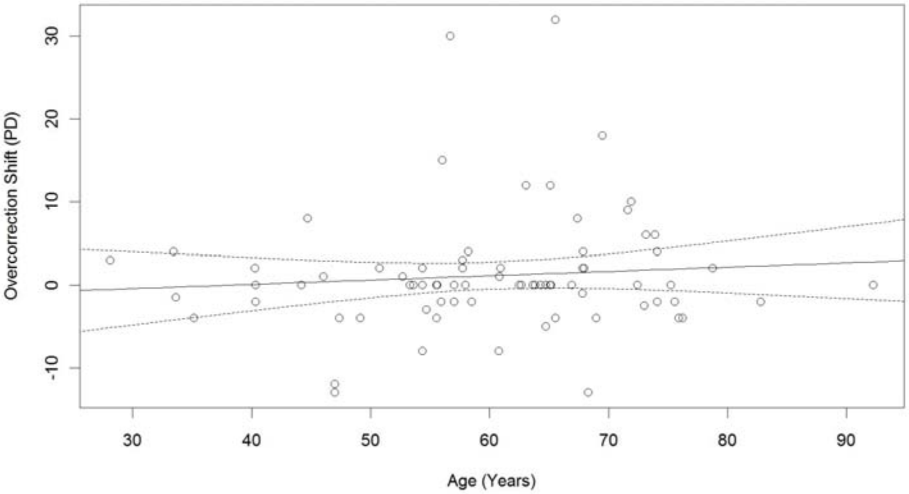

FIGURE 8

Linear regression of age (years) vs overcorrection shift (PD). The dotted lines on the plot represent the central 95% CI for the regressed model. Pearson's product moment correlation showed no correlation for age and overcorrection shift (R2=0.0077).

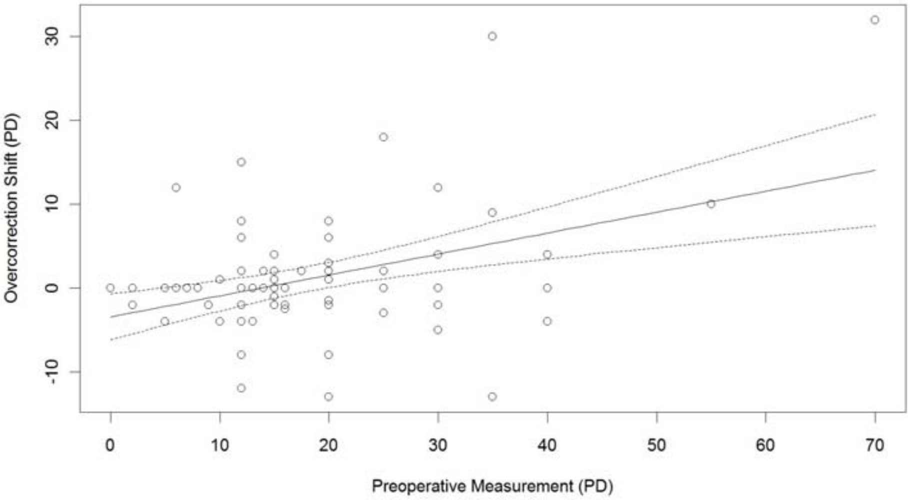

FIGURE 9

Linear regression of the preoperative measurement (in PD) vs overcorrection shift (PD). The dotted lines on the plot represent the central 95% CI for the regressed model. Pearson's product moment correlation showed a weak correlation for preoperative deviation and overcorrection shift (R2=0.13).

The presence of thyroid disease was associated with the overcorrection tail in 11 of 12 cases (92%) for threshold value of 5 PD and 15 of 18 cases (83%) for threshold value of 2 PD overcorrection shift. Thus for thyroid disease, extreme value theory modeled the positive extreme value tail seen in this study population (Figures 19 and 20). A generalized Pareto distribution fit could not be obtained for patients without thyroid disease, as that categorical variable had fewer and smaller overcorrection shifts. A generalized Pareto distribution fit was not stable for the extreme values noted in the box-and-whiskers plot for prior orbital decompression (Figure 14), as there were only four patients in this subgroup with overcorrection >5 PD.

COMPARING ABSORBABLE AND NONABSORBABLE SUTURES

Understanding that surgery of the inferior rectus muscle in the setting of thyroid eye disease with absorbable suture was associated with overcorrection shifts, whereas surgery on the inferior rectus muscle in patients without thyroid eye disease (Group 2) and surgery on the medial rectus muscle in the setting of thyroid eye disease (Group 3) were not associated with overcorrection shifts, the at-risk population for overcorrection shifts in the first 2 months after surgery was patients who underwent inferior rectus surgery in the setting of thyroid eye disease. However, in that same setting but utilizing nonabsorbable sutures, there were no overcorrection shifts greater than 5 PD, and only three cases of overcorrection shift between 2 and 5 PD. To verify that these two study subpopulations (Group 1 with absorbable vs Group 1 with nonabsorbable) were comparable except for suture type so that nonabsorbable suture was the only identifiable factor in this study that was strongly correlated with the absence of overcorrection in this at-risk group, the Mann-Whitney

U test was used to compare the two subpopulations for (a) amount of preoperative deviation and (b) amount of recession, as these factors were also found to be associated with overcorrection shift. No significant difference was found with respect to amount of recession performed in these two groups (P=0.21). The average recession performed in the nonabsorbable group was slightly larger than in the absorbable group (8.3±2.27 mm vs 7.4±2.14 mm). With regard to preoperative measurements, the nonabsorbable group had an average 20.0±11.65 PD deviation preoperatively, whereas the absorbable group measured on average 20.5±13.8 PD (P=0.68). Thus, suture type was the only variable in this study that explained the difference in the number of overcorrection shifts between the Group 1 (inferior rectus recession with thyroid disease) patients operated with nonabsorbable and those operated with absorbable sutures.

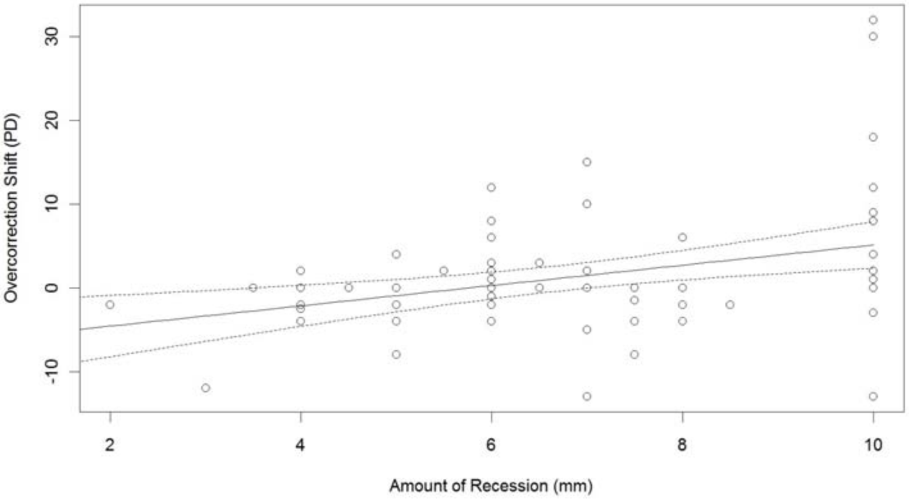

FIGURE 10

Linear regression of the amount of recession (mm) vs overcorrection shift (PD). The dotted lines on the plot represent the central 95% CI for the regressed model. Pearson’s product moment correlation showed a weak correlation for amount of recession and overcorrection shift (R^2=0.17).

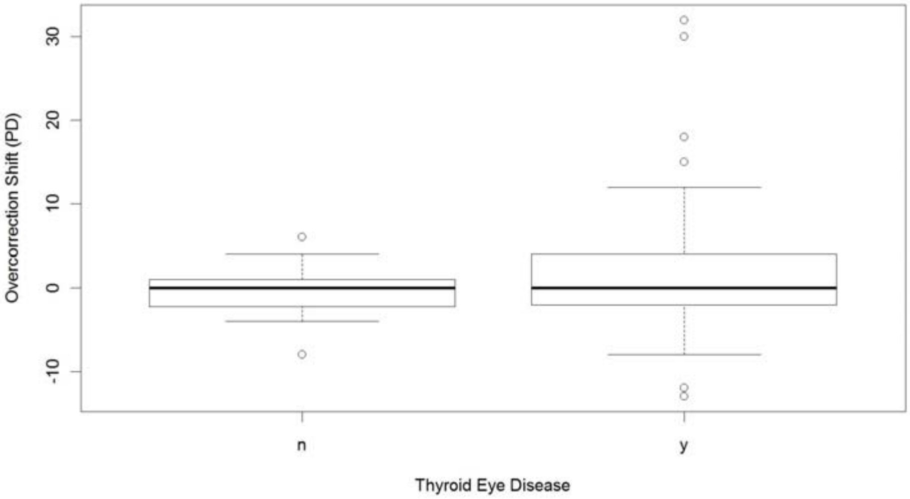

FIGURE 11

Box-and-whiskers plot for the presence (“y”) or absence (“n”) of thyroid eye disease. Outliers (±2 SD limits, indicated by the whiskers) are noted with greater frequency in the thyroid eye disease group than those without thyroid eye disease.

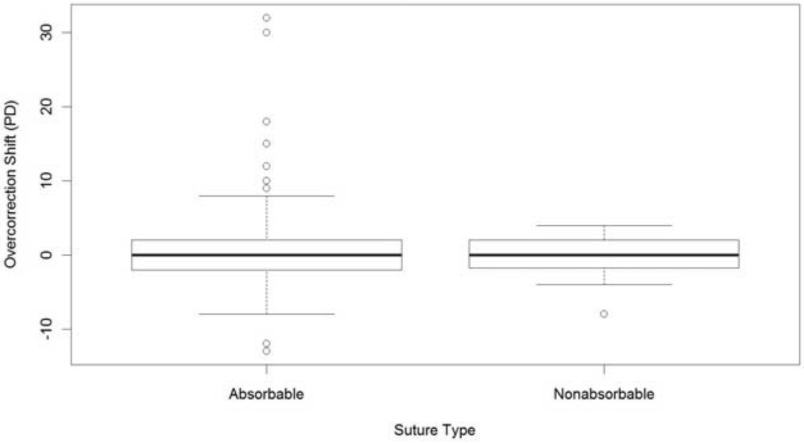

FIGURE 12

Box-and-whiskers plot for the suture type used in the recession. High shift outliers (±2 SD limits, indicated by the whiskers) are noted in the absorbable suture group but not in the nonabsorbable suture group.

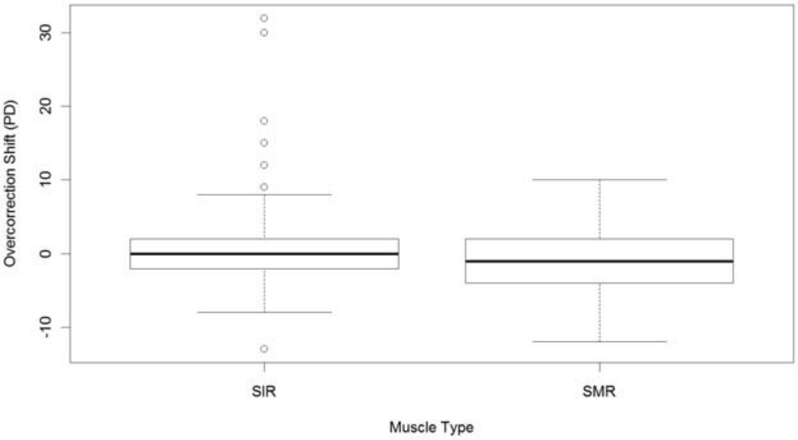

FIGURE 13

Box-and-whiskers plot for the type of muscle recessed: single inferior rectus (SIR) or single medial rectus (SMR). Outliers (±2 SD limits, indicated by the whiskers) are noted in the SIR group but not the SMR group.

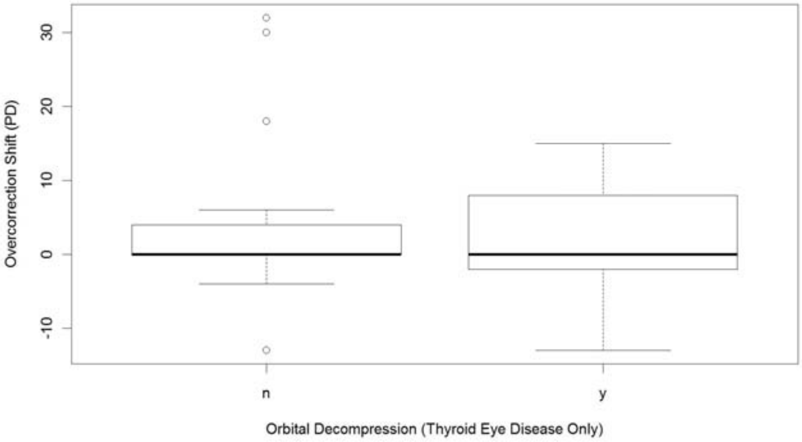

FIGURE 14

Box-and-whiskers plot for the presence ("y") or absence ("n") of a history of orbital decompression prior to muscle surgery in patients with thyroid eye disease. Outliers (±2 SD limits, indicated by the whiskers) are noted with greater frequency in the eyes without a history of orbital decompression.

Finally, an OR was calculated to determine the likelihood of absorbable suture resulting in overcorrection shift in Group 1 patients for a >2 PD threshold and a >5 PD threshold as compared to the nonabsorbable suture. For the >5 PD threshold, the OR was 6.0 (95% CI=1.1 to 33.5) with a Fisher's test *P*=0.041. For the >2 PD threshold the odds ratio was 3.7 (95% CI=0.4 to 35.0) with a Fisher's test *P*=0.19. In other words, on average, absorbable sutures were associated with an almost fourfold increased chance of overcorrection >2 PD (though not statistically significant) and a sixfold increased chance of an overcorrection >5 PD (statistically significant). Note that to estimate the OR for the >5 PD overcorrection shifts, the null hypothesis had to be used, since no patient operated with the nonabsorbable suture experienced an overcorrection above the 5 PD threshold; hence, my caution in overemphasizing the statistically significant outcome of the >5 PD analysis.[72]

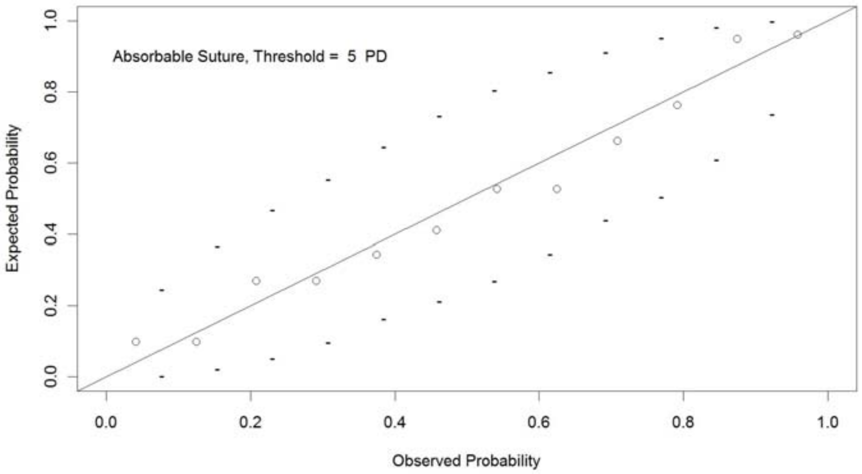

FIGURE 15

Peak-over-threshold plot fitting of a generalized Pareto distribution for the absorbable suture type using a >5 PD threshold. The dotted lines represent the 95% CI for the model, and all 12 of the overcorrection shift values exceeding threshold fall within those lines.

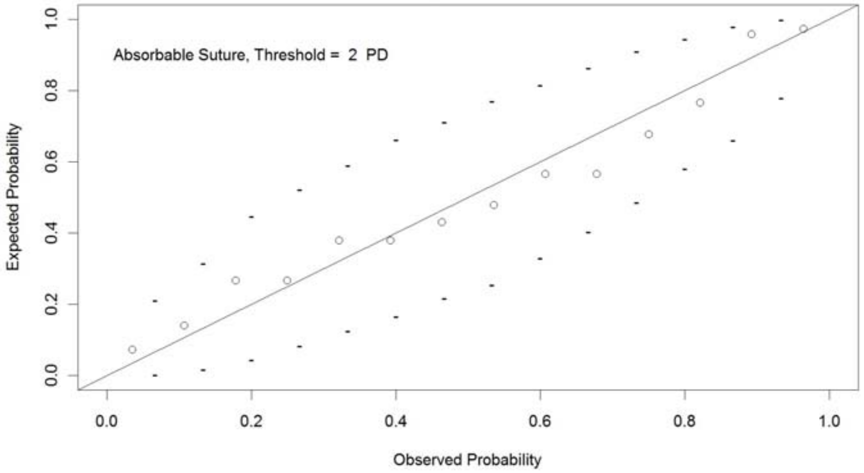

FIGURE 16

Peak-over-threshold plot fitting of a generalized Pareto distribution for the absorbable suture type using a >2 PD threshold. The dotted lines represent the 95% CI for the model, and all 14 of the overcorrection shift values for absorbable suture exceeding threshold fall within those lines.

To verify the tendency of the ORs from this case series, a pooled analysis of the data with published data (available in a limited fashion for the >5 PD threshold) was performed. Specifically, we pooled the nonabsorbable data (n=8) with the series operated with another type of nonabsorbable suture by Sharma and Reinecke (n=7, 2 overcorrections),[39] and the absorbable data (n=26) with the reports from Sprunger and Helveston (n=18, 9 overcorrections),[40] Scotcher and coworkers (n=2, 2 overcorrections),[44] Ruttum (n=9, 5 overcorrections),[73] and Rauz and Govan (n=1, 0 overcorrections).[74] The data used for the pooled estimate is summarized in Table 5. The OR estimated from this pooled data analysis was 5.6 (95% CI=1.2-27.3). This OR is statistically significant (*P*=0.015) and indicates that, on average, an overcorrection >5 PD is approximately five times more likely to occur when using an absorbable suture for adjustable inferior rectus recessions in thyroid eye disease. Figure 21 graphically illustrates the overall consistency of the ORs calculated from my data for the >2 PD and the >5 PD thresholds and for the pooled data analysis, indicating the increased likelihood of overcorrections when using an absorbable suture.

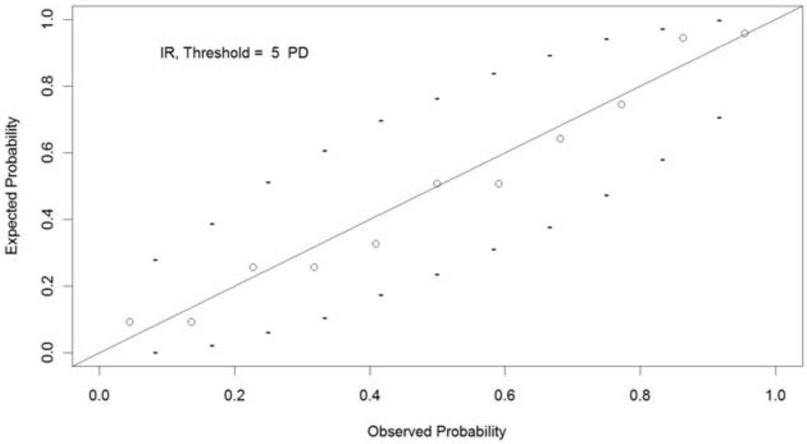

FIGURE 17

Peak-over-threshold plot fitting of a generalized Pareto distribution for the inferior rectus (IR) muscles using a >5 PD threshold. The dotted lines represent the 95% CI for the model, and the 11 overcorrection shift values for inferior rectus muscles exceeding threshold for inferior rectus muscles fall within those lines.

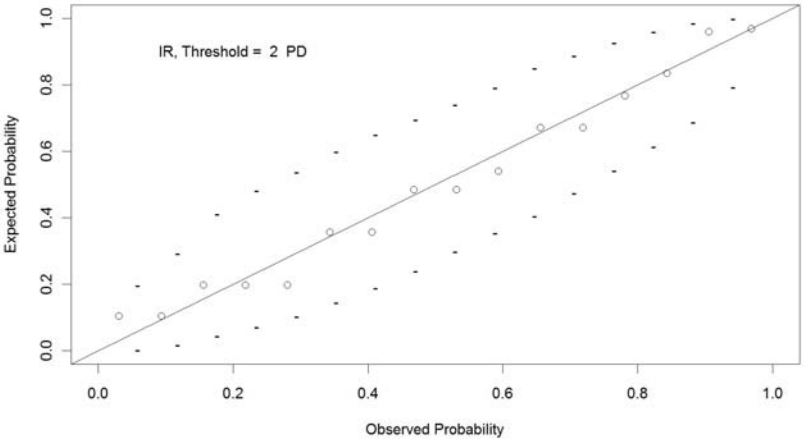

FIGURE 18

Peak-over-threshold plot of a generalized Pareto distribution for the inferior rectus (IR) muscles using a >2 PD threshold. The dotted lines represent the 95% CI for the model, and all 16 of the overcorrection shift values for inferior rectus muscles exceeding threshold fall within those lines.

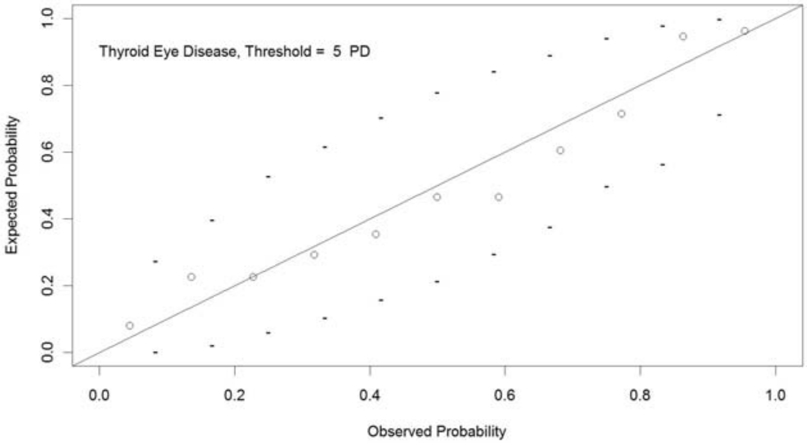

FIGURE 19

Peak-over-threshold plot of a generalized Pareto distribution for thyroid eye disease using a >5 PD threshold. The dotted lines represent the 95% CI for the model, and all 11 of the overcorrection shift values exceeding threshold fall within those lines.

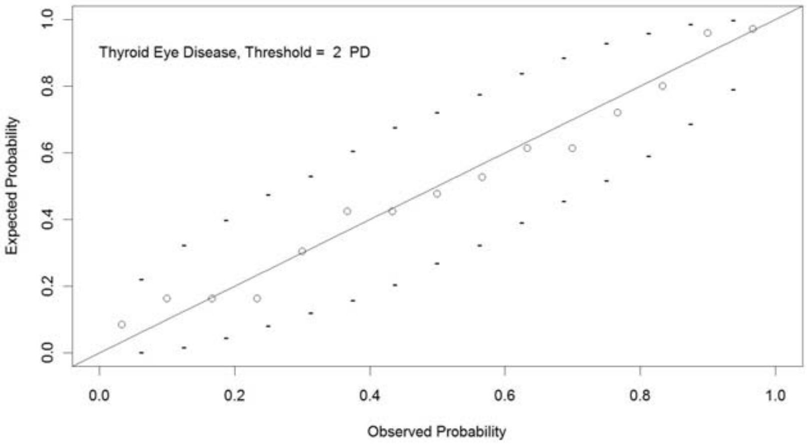

FIGURE 20

Peak-over-threshold plot of a generalized Pareto distribution for thyroid eye disease using a >2 PD threshold. The dotted lines represent the 95% CI for the model, and all 15 of the overcorrection shift values exceeding threshold fall within those lines.

TABLE 5. POOLED DATA FOR >5 PD OVERCORRECTION SHIFT FOLLOWING INFERIOR RECTUS RECESSIONS ON ADJUSTABLE SUTURE IN THYROID EYE DISEASE

STUDY	SAMPLE SIZE	ABSORBABLE SUTURE		NONABSORBABLE SUTURE	
	(n)	≤5 PD	>5 PD	≤5 PD	>5 PD
Present study	34	16	10	8	0
Sharma and Reinecke[39]	7	N/A	N/A	5	2
Sprunger and Helveston[40]	18	9	9	N/A	N/A
Scotcher and coworkers[44]	2	0	2	N/A	N/A
Ruttum[73]	9	4	5	N/A	N/A
Rauz and Govan[74]	1	1	0	N/A	N/A
Total	71	30	26	13	2

PD, prism diopters; N/A, data not available or not reported.

TIME COURSE OF DISEASE AND OVERCORRECTION SHIFT

We report in Tables 1B and 3B various time courses of disease for the patients with thyroid disease (Groups 1 and 3). The average elapsed time for all thyroid patients between onset of systemic hyperthyroidism and thyroid eye disease was 2.6±4.7 years (n=30, range -1.1 to 22 years); the patient with onset of systemic hyperthyroidism to thyroid eye disease with a negative number was not diagnosed with systemic hyperthyroidism until 1.1 years after the onset of thyroid eye disease. The average elapsed time for onset of thyroid eye disease to orbital decompression was 1.7±1.5 years (n=16, range 0.4 to 5.1 years). The elapsed time from the date of orbital decompression to date of strabismus surgery was 1.3±2.0 years (n=25, range 0.3 to 7.1 years) and from the onset of thyroid eye disease to onset of diplopia was 1.1±1.7 years (n=15, range 0.0 to 6.0 years); patients with onset of thyroid eye disease to onset of diplopia of 0 presented with diplopia as the initial manifestation of thyroid eye disease. Finally, the average elapsed time from the onset of diplopia to the date of strabismus surgery was 2.1±1.9 years (n=39, range 0.3 to 7.2 years).

Calculating an odds ratio for the elapsed time data points comparing overcorrection shift >5 PD and no overcorrection shift vs above and below the average elapsed time yielded no statistically significant differences. For elapsed time between onset of systemic hyperthyroidism and thyroid eye disease, OR=1.0 (95% CI=0.18 to 5.6, *P*=0.36), for onset of thyroid eye disease to orbital decompression, OR=0.6 (95% CI=0.06 to 5.3, *P*=0.40), date of orbital decompression to date of strabismus surgery, OR=0.9 (95% CI=0.12 to 7.6, *P*=0.44), date of thyroid eye disease to onset of diplopia, OR=0.09 (95% CI=0.004 to 2.2, *P*=0.09), and onset of diplopia to date of strabismus surgery OR=1.4 (95% CI=0.31 to 6.5, *P*=0.29).

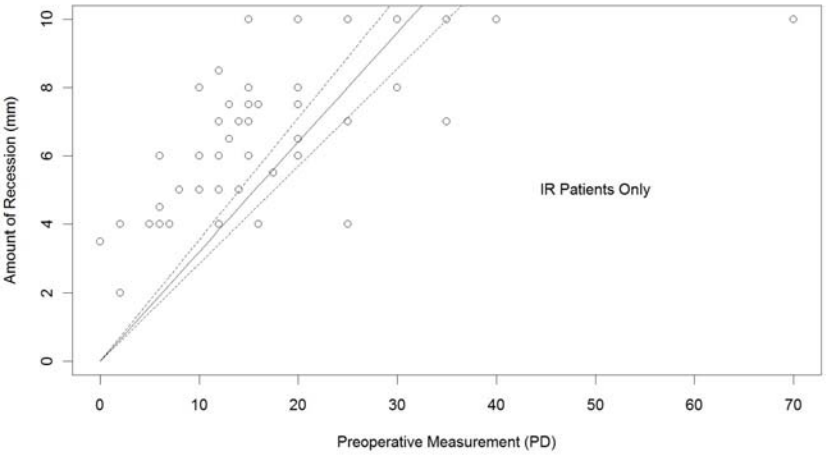

FIGURE 21

Odds ratio calculations for the current study, >2 PD and >5 PD, and pooled data with other studies. Lower limits of confidence interval >1.0 (vertical line) are statistically significant. The x-axis has been transformed to a log scale to improve visualization of the upper and lower limits of the 95% CI.

PROPTOSIS AND OVERCORRECTION SHIFT

Thirty-one of 47 patients in Groups 1 and 3 (thyroid eye disease, both medial and inferior rectus surgery) had clinical proptosis. Twenty of 34 in Group 1 (inferior rectus surgery with thyroid eye disease) had clinical proptosis. For overcorrection shift >5 PD, the OR for all thyroid patients with proptosis was 1.40 (95% CI=0.34 to 5.73, *P*=0.08). The OR for thyroid patients undergoing inferior rectus surgery and a >5 PD overcorrection shift was 1.31 (95% CI=0.29 to 5.91, *P*=0.12). Thus, the correlation between proptosis and overcorrection shift was not significant.

DISCUSSION

Overcorrection after inferior rectus recession has been described in multiple studies drawn from patient series with a mixture of underlying diseases. Commonly cited is Sprunger and Helveston's 1993 study,[40] in which 14 of 67 patients (21%) undergoing inferior rectus recessions developed progressive overcorrection after inferior rectus recession. However, in the 18 patients who had thyroid eye disease, nine (50%) developed progressive overcorrection after inferior rectus recession. A 6-0 absorbable suture was used in this series. Overcorrections were noted between the 1-week and 1-month follow-up, with a minimum follow-up for inclusion in the study of 3 months. Overcorrection was defined as >5 PD. In 1996, Rauz and Govan[74] published a series of seven patients undergoing inferior rectus surgery on adjustable suture (absorbable) and found no cases of progressive overcorrection 3 months after surgery. However, only one patient (14%) had thyroid eye disease. Scotcher and coworkers[44] published a series of 21 patients undergoing inferior rectus surgery, 18 (86%) of whom were on an adjustable suture. With a planned undercorrection of 6 to 8 PD, the two patients (10%) with thyroid eye disease had overcorrection shifts at 3 months of 6 and 8 PD. Sharma and Reinecke[39] reported 12 patients undergoing single-stage adjustable suture surgery for restrictive strabismus. Seven (58%) had thyroid eye disease. A 6-0 silicon-treated polyester (nonabsorbable) suture, which is no longer available, was used. Two of the seven patients (29%) with thyroid eye disease developed overcorrection by 6 to 12 weeks after the surgery. One had an initial preoperative vertical deviation of 75 PD, and the other had a vertical deviation of 19 PD. The amount of progressive overcorrection after inferior rectus recession was 12 PD and 15 PD, respectively. None of the other five patients had progressive overcorrection after inferior rectus recession. The investigators suggested that use of the nonabsorbable suture reduced the incidence of progressive overcorrection after inferior rectus recession in their series when compared to Sprunger and Helveston's report of a 50% incidence of progressive overcorrection after inferior rectus recession in thyroid eye disease when absorbable suture was used.[40]

In comparison, my study included 64 cases of single inferior rectus recession on adjustable suture, 34 (of 65, 52%) with thyroid eye disease. Twenty-six (of 34, 76%) thyroid eye disease patients were operated with absorbable sutures and eight (of 34, 24%) with nonabsorbable sutures. Ten (of 26, 38.5%) thyroid eye disease patients with absorbable suture experienced overcorrection shift of >5 PD, whereas no patients (of 8, 0%) operated with nonabsorbable suture had shift >5 PD. The incidence of overcorrection shift with absorbable suture is less than that reported by Sprunger and Helveston (50%)[40] and Scotcher and associates (100%).[44] However, I also reported fewer overcorrection shifts (0%) for nonabsorbable sutures, as did Sharma and Reinecke (28.5%).[39] Most significantly, when the data from these other studies is pooled with the data from the current study (Table 5, Figure 21), the OR for overcorrection >5 PD for absorbable suture (vs nonabsorbable) in inferior rectus recessions on adjustable suture was 5.6 and reached statistical significance, consistent with my single-series data, indicating a statistically significant 5.5-fold increase in the likelihood of overcorrections when using absorbable sutures.

EARLY VS LATE OVERCORRECTION OF HYPOTROPIA FOLLOWING INFERIOR RECTUS RECESSION

Inferior rectus overcorrection examined in this study was early overcorrection occurring in the first 2 months after surgery, not the later overcorrections (between 2 and 5 months postoperatively) as reported by Hudson and Feldon.[41] In their series of 12 patients undergoing unilateral inferior rectus surgery for hypotropia in thyroid eye disease, five (42%) were found to have overcorrection that did not stabilize until 9 weeks or more after surgery. These five patients had increased proptosis and superior rectus muscle volume on the ipsilateral side when compared to a group that did not have overcorrection after unilateral inferior rectus recession, indicating that the contractured superior rectus was a causative factor. Though proptosis was not found to be a predictive factor for overcorrection in my study, superior rectus muscle volume was not evaluated.

Additionally, the overcorrections that occur within the first 2 months after surgery are probably not due to the spontaneous changes in vertical deviations that have been reported in thyroid eye disease. Frueh and Berger[42] reported two cases of spontaneous resolution of vertical diplopia. One case resolved 1 week after the initial visit, and the other case resolved 16 months after initial presentation. The use of a 6-month or greater period of stability prior to surgery and the relatively narrow 2-month postoperative window in this study should reduce the effect seen from fluctuation in the disease process itself (as opposed to postsurgical effects).

OVERCORRECTION AND PREVIOUS ORBITAL DECOMPRESSION

The effect of orbital decompression on strabismus in thyroid eye disease has been widely studied over the years. The incidence of new diplopia following orbital decompression may be as high as 41% to 73%.[75] Subdividing patients into those with normal versions on motility examination and no diplopia prior to decompression (type 1) and those with motility problems prior to decompression (type 2), Nunery and colleagues[75] found that the incidence of new diplopia after decompression was only 4% for type 1 patients, but 50% for type 2 patients. Of the type 2 patients who already had primary position diplopia, there was significant worsening of both esotropia and vertical deviations after decompression. Shorr and associates[76] had similarly found that more severely diseased orbits were more likely to have significant strabismus after decompression, and endoscopic techniques produce similar results.[77] Prior orbital decompression was not found to have an effect on strabismus surgery outcome in a study by Mourits and associates,[62] where fixed sutures (suture material not specified) were employed, and 13 of 27 patients had had prior orbital decompression. Single binocular vision was obtained in 71% of patients after one surgery, and in another 18% after two surgeries, resulting in an overall success rate of 89%.

Overall, of the 11 patients in my study with overcorrection shift >5 PD and thyroid eye disease, four had no prior decompression and seven had prior decompression (including one case of unilateral medial rectus recession). So, assuming that more severely affected patients in the present study would have been the ones who had had prior orbital decompression (and thus strabismus after their decompressions), I was surprised to find that the two largest overcorrections (30 and 32 PD) occurred in patients with no prior decompression. However, if proptosis correlates with superior rectus muscle volume as Hudson and Feldon have suggested,[41] undecompressed orbits may face significant forces generating upward tension, as well as proptosis contributing to the decreased arc of contact of the inferior rectus (see discussion to follow on anatomical and physiologic attributes of the inferior rectus contributing to overcorrection shifts). Thus, although patients who have had orbital decompression may have had more severe orbital disease, some of the factors associated with overcorrection in inferior rectus recession may actually be worse in undecompressed orbits. I did not find the presence or absence of clinical proptosis to increase the risk of overcorrection in my patient sample.

It has been proposed that the severity of orbitopathy and thus poorer outcomes after strabismus surgery would be predicted by the duration of thyroid eye disease.[78] Neither the duration of thyroid eye disease prior to strabismus surgery nor any other measure of the disease's time course relative to surgical intervention predicted overcorrection in my patients. This is similar to findings of Oguz and associates.[78] A previous study[48] of early strabismus surgery in thyroid eye disease found an overcorrection rate of 25% for inferior rectus recessions, so the time course of the disease before surgery, either waiting a longer or shorter time, does not seem to impact the outcome for inferior rectus overcorrection.

EFFECT OF AMOUNT OF RECESSION AND SIZE OF PREOPERATIVE DEVIATION

In this study, the amount of recession and size of the preoperative deviation are not unrelated, as I use an estimate of 2 PD of correction per millimeter of recession in surgical planning for vertical muscles (Figure 22). The R^2 value for this plot is 0.84, with a P for the slope of 2.2E-16. Thus, if the amount of preoperative deviation correlates with overcorrection shift, then the amount of recession should correlate with overcorrection shift, which is, in fact, what I found (Figures 9 and 10). The R^2 value for the size of the deviation was 0.17 (P=0.001), indicating that 17% of the overcorrection shift is attributable to preoperative deviation, with larger deviations showing a greater tendency for postoperative overcorrection. However, knowing that patients operated with absorbable sutures populated the data set for overcorrection shift, further analysis was performed. The correlation R^2 value for absorbable sutures and preoperative size of deviation was 0.19 (P=0.006), whereas the R^2 value for the nonabsorbable suture was only 0.13 (P=0.13). Similarly, the R^2 value for amount of recession was 0.13 (P=0.001). However, stratifying the absorbable suture data reveals an R^2 value of 0.17 (P=0.0009) for absorbable suture and 0.05 (P=0.34) for the nonabsorbable suture. Thus, the correlation between overcorrection shift and larger amount for recession/larger preoperative deviations holds for absorbable sutures, not nonabsorbable sutures. Yan and Zhang[79] published a series of patients with large-angle strabismus undergoing muscle recession in Graves' ophthalmopathy with similar results. They used adjustable absorbable suture, large posterior dissection, and 5- to 7-mm recessions (although they also performed free tenotomies, but only on superior recti). They reported an overcorrection rate for inferior recti of 27% (4/15) occurring days to years after surgery. This lends support to the hypothesis that nonapposition to the globe contributes to the phenomenon of postoperative overcorrection when suspended absorbable sutures are used in the setting of inferior rectus surgery for patients with thyroid eye disease (see next section on anatomical and physiologic attributes of the inferior rectus contributing to overcorrection shifts). More nonapposition occurs when there is more recession, and when the absorbable suture dissolves over the course of the first 2 months after surgery, the inferior rectus that is not in proper apposition to the globe results in a stretched scar[80] or slippage.[81] This increased tension is due to the forces that are unique to the inferior rectus and thyroid eye disease and will be discussed in the next section: a contractured superior rectus, Bell's reflex, rigid capsulopalpebral head/lid retractor attachments pulling on the inferior rectus in downgaze, and proptosis.

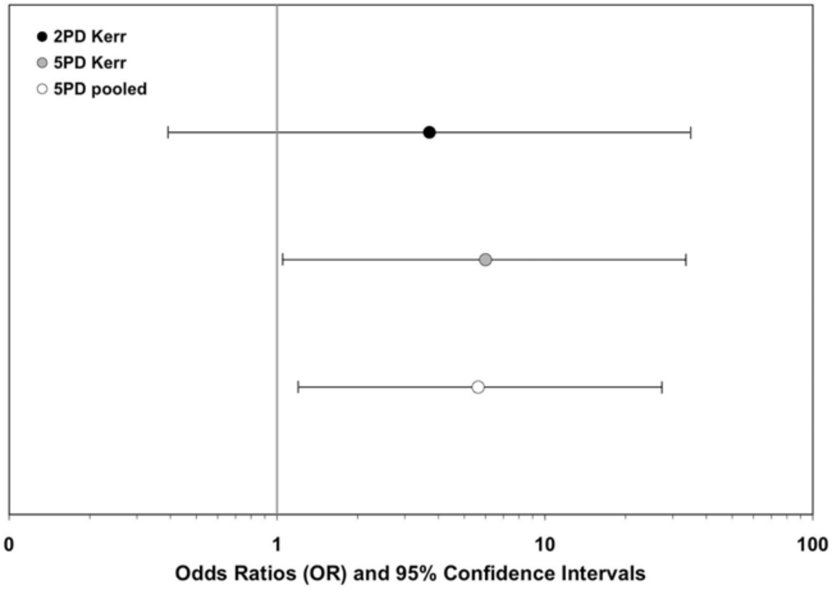

FIGURE 22

Plot of amount of recession vs preoperative measurement (R2=0.84, P=2.2E-16). This indicates that 84% of the variance of the amount of recession was accounted for by measurement of the preoperative deviation. This relationship would be anticipated given the formula used for planning surgery on the vertical recti of 2 PD correction for each millimeter recession, with an upper limit of 10 mm recession.

The observation that size of preoperative deviation and amount of recession correlate positively with postoperative overcorrection may be a phenomenon of suspended sutures. In the literature for fixed sutures in thyroid eye disease, some investigators recommend larger-than-usual recessions,[18,34,35] whereas others have limited the size of inferior rectus recessions to 5 mm or less, with varying reports of overcorrection.[62,82] Before adjustable sutures were commonly used,[34,82] reports of overcorrection were unusual. Reporting of progressive overcorrection after inferior rectus recession began when adjustable sutures appeared in the literature on eye muscle surgery. However, the causal relationship remains unclear in the absence of a randomized trial comparing fixed and adjustable sutures for inferior rectus surgery in thyroid eye disease.[83]

ANATOMICAL AND PHYSIOLOGIC FACTORS CONTRIBUTING TO PROGRESSIVE OVERCORRECTION FOLLOWING INFERIOR RECTUS RECESSION

My finding that a nonabsorbable suture eliminated postoperative overcorrection shift for inferior rectus surgery in the setting of thyroid eye disease suggests not only a therapeutic option for this problem but also an etiology. This study indicates that the inferior rectus is unique in its propensity for postoperative overcorrection shift in the setting of thyroid eye disease. Patients undergoing medial rectus recessions did not experience the same incidence of overcorrection as the inferior recti cases. In my series, 47 patients had thyroid eye disease: 34 undergoing unilateral inferior rectus surgery and 13 undergoing unilateral medial rectus recessions. As discussed, 10 of 34 (29.4%) inferior rectus surgeries with thyroid eye disease resulted in overcorrection >5 PD, whereas only one of 13 (7.7%) patients with medial rectus surgery had an overcorrection shift of >5 PD. Similarly, Ruttum (1995)[73] found that overcorrections of esotropia with adjustable suture recessions of the medial recti were uncommon in thyroid eye disease (one of 19 cases had exotropia after single or bilateral medial rectus recession). Other studies have found that superior rectus surgery does not produce the same overcorrection shifts seen in inferior recti recessions in nonthyroid patients.[40,84]

What is unique about the unilateral inferior rectus in thyroid eye disease operated with an absorbable suture in the first 2 months after adjustable suture surgery that results in the observed overcorrection shift? This question can be addressed by discussing the unique anatomical and physiologic attributes of the inferior rectus as it relates to the issue of progressive overcorrection after inferior rectus recession, and how these factors may be synergistic when using adjustable, absorbable sutures in the setting of thyroid eye disease. Thus, we may arrive at a clearer understanding of how best to surgically manage this special set of patients.

In the literature on inferior rectus recessions in patients without thyroid eye disease, Vazquez and Munoz[85] reported five of 20 patients with overcorrection after adjustable suture in patients without thyroid eye disease undergoing unilateral inferior rectus recession. Wright[43] reported seven patients (out of a series of approximately 60 patients, ~12%) without thyroid eye disease who experienced an overcorrection shift after inferior rectus recession. Three had fixed suture placement and four had adjustable sutures, all on a 6-0 polyglactin absorbable suture. Overcorrection of 12 to 25 PD occurred between 4 and 6 weeks after surgery. On reoperation, no slippage was detected, and no superior rectus restriction was noted on forced ductions. However, there was extensive scarring of the Lockwood ligament and the capsulopalpebral head. Wright postulated that the scarring was due to his posterior dissection of the inferior rectus (10 mm). The resulting adhesion caused a slackening of the inferior rectus anterior to this adhesion, affecting a "pseudo-inferior rectus paresis" that theoretically should (and did) appear during fibrosis and scar contracture, which is 4 to 6 weeks after surgery. He suggested a strategy of limited posterior dissection. This is in contrast to published studies suggesting extensive posterior dissection to prevent inferior lid retraction.[36,37] An additional reason to do extensive posterior dissection in patients with thyroid disease is the theoretical possibility that there is increased rigidity of the capsulopalpebral head, so force applied by the inferior eyelid retractors could direct the insecurely attached inferior rectus muscle away from the globe. So, although strabismus surgeons often do extensive posterior dissection to free the capsulopalpebral head in thyroid eye disease in an attempt to avoid lid retraction and this should, theoretically, diminish the force of the lid retractors pulling the muscle away from the globe, postoperative adhesion of the capsulopalpebral head to the Lockwood ligament (and also adhesion of the capsulopalpebral head back to the lid retractors after surgery) may play a role in postoperative overcorrection shifts that extensive posterior dissection will not correct.

Wright's strategy of limited posterior dissection[43] was followed, in my study, with results that his hypothesis predicted: reduced overcorrection shifts in the patients without thyroid eye disease. Of 31 patients without thyroid eye disease in my study, only one (3%) had an overcorrection shift of >5 PD after undergoing unilateral inferior rectus recession with an adjustable suture. And there are descriptions of inferior lid retractor lysis that do not involve manipulating the capsulopalpebral head if one needs to prevent inferior scleral show postoperatively at the time of inferior rectus recession.[86] So the practice of extensive posterior dissection in inferior rectus recession may be unnecessary and, actually, undesirable for multiple reasons.

Sharma and Reinecke[39] suggested another causal factor for the relatively high incidence of inferior rectus surgery overcorrection shifts as compared to recession of other muscles: Bell's phenomenon results in increased tension on the inferior rectus for as many hours during each day as one sleeps, and affects the inferior rectus but not the other muscles. They suggested using a nonabsorbable suture to prevent slippage, which did alleviate the problem of overcorrection shifts in my study of unilateral inferior rectus recessions in patients with thyroid eye disease.

Postoperative slippage creating overcorrections was reported by Ludwig[80] in her American Ophthalmological Society thesis, "Scar Remodeling After Strabismus Surgery." She examined 198 muscles during the course of 134 procedures where postoperative overcorrection had occurred. Most were medial recti resulting in consecutive exotropia (148 muscles), but other muscles included seven inferior recti cases and patients with thyroid disease (number unspecified). Those who overcorrected within 4 months after surgery were deemed as having "probable early stretching." Reoperation to correct stretched scars (early and late overcorrections) was more successful when nonabsorbable sutures were used ("restretching" in 4 of 70 cases, 6%) than when absorbable sutures were used (restretching in 27 of 64 cases, 42%). The difference in restretch (which would be synonymous with overcorrection in my series) was, on average, 5.5 PD between the absorbable and nonabsorbable groups. Of cases with single-muscle or symmetrical original surgery, large overcorrection shifts of >10 PD were more common in the absorbable suture group (12 of 44, 27%) than in the nonabsorbable group (6 of 55, 11%). These were patients who had already had one stretched scar and, thus, were believed to be predisposed to having scar-remodeling issues. This belief was supported by the high incidence of restretch after reoperation in these patients.

There were many explanations offered for the stretched scar phenomenon in Ludwig's report,[80] but in the animal studies she conducted, increased prolonged tension on the operated muscle resulted in scar elongation. The tension resulting in scar elongation in her study, 27 gm, was much lower than reported tensions required for rupture (resulting in slipped muscles), which are commonly referenced in deciding when scars are at risk for changing and altering postoperative outcome.[87] When horizontal muscles are placed in extreme gaze, they exert more than 40 gm of tension on the insertion,[88] and the inferior rectus has been demonstrated to exert more than 90 gm of tension on the superior rectus in thyroid eye disease.[89] It seems plausible that increased prolonged tension (from Bell's phenomenon and an ipsilateral enlarged and contractured superior rectus, thought to be present in thyroid eye disease[41]) exerted on the postoperative inferior rectus as it fibroses to form its adhesion to the globe may result in a stretched scar and overcorrection when absorbable sutures are used.

The anatomy of the inferior rectus as it relates to shifts after surgery has also been explored by high-resolution magnetic resonance orbital imaging.[59] Multipositional imaging was obtained for normal eyes, patients with thyroid eye disease, and patients with thyroid eye disease on POD 1 after rectus recessions performed with a suspension (adjustable-style) technique. Chatzistefanou and coworkers[59] found that the medial and inferior recti have a smaller wraparound effect (as determined by the muscle's arc of contact between the insertion and point of tangency), which may be a contributing factor in the increased incidence of lost muscles in medial and inferior recti. But this may not be a factor in overcorrection shifts in my study, as the patients who had medial rectus recessions (Group 3) did not have a high incidence of overcorrection (8%). However, their finding of decreased apposition to the globe for suspended inferior rectus in postoperative thyroid eye disease patients is relevant to my study. Based on their normal patient measurements, a recession of 6 mm or less of the inferior rectus should not result in loss of arc of contact. However, in the unoperated thyroid eye disease patients, the altered anatomy indicated that even small recessions could result in loss of arc of contact. In fact, when measuring the arc of contact on POD 1 for two patients with thyroid eye disease undergoing inferior rectus recessions of 4 mm on a suspended suture, nonapposition to the globe was found. This may predispose the patient to slipped muscles or muscle creep.[80,90] Also, given that we had average recessions of inferior recti greater than 6 mm in all groups and subgoups, it is doubtful that the small differences among the subgroups impacted the results of the study.

In this same study utilizing magnetic resonance imaging findings, Chatzistefanou and coworkers[59] observed that the downgaze position is particularly problematic with regard to nonadherence in inferior rectus surgery, stating that it is the most frequently used gaze position and places the suspended (operated) inferior rectus further away from the globe. It is arguable, according to Sharma and Reinecke,[39] that Bell's phenomenon (placing the eye in tonic and prolonged upgaze) is as important as, if not more important than, downgaze in the etiology of progressive overcorrection after inferior rectus recession. The findings of Chatzistefanou and coworkers[59] suggest one reason why overcorrection shifts were seen in patients undergoing inferior rectus recession with thyroid eye disease but not in patients without thyroid eye disease. The reduced arc of contact that occurs with the orbital changes in thyroid eye disease may predispose the eye to problems with muscle reattachment to the globe after suspension on an absorbable suture. Several investigators[1,39,60,81] have suggested use of a nonabsorbable suture to address this issue. Currently, however, only two studies have been published that present data from inferior rectus surgery using nonabsorbable sutures,[39,60] and neither of these studies has focused on the patient with thyroid eye disease.

As suggested by the imaging studies of postoperative patients with thyroid eye disease after recession,[59] the adjustable suture technique of hanging the suture back may play a role in the overcorrection phenomenon seen in thyroid eye disease not encountered in patients without thyroid eye disease. Although in Ludwig's study of stretched scars, no difference was observed in the scars from the seven adjustable cases compared to the scars resulting from fixed sutures,[80] the attachment properties of a hang-back (suspended/adjustable) absorbable suture have been shown to be different from those of a fixed suture. Hertle and coworkers[91] showed in animal models that the force required for disinsertion of vertical muscles when absorbable sutures are used is significantly less for suspended sutures than for fixed sutures. One week after fixed suture placement, the disinsertion force for an inferior rectus was 300 gm, whereas a suspension-recessed muscle could be disinserted with 50 gm at 1 week. By 2 weeks, the disinsertion force was still only 200 gm. Given a normal rotational force of 30 gm,[91] these disinsertion values are felt to be sufficient for secure reattachment before suture absorption. However, the relative weakness of the suspended suture as compared to the fixed suture when there are increased forces and tensions, as in thyroid eye disease, and when stretch, as opposed to rupture/disinsertion, has been shown to occur at significantly lower tension levels, may explain why there have been studies showing little to no benefit from adjustable sutures in inferior rectus recessions, especially in patients with thyroid disease.

Superior rectus restriction has often been blamed for late overcorrection of hypotropia in thyroid eye disease after inferior rectus recession, and superior rectus restriction (subclinical prior to inferior rectus recession) is one mechanism that may explain the difference in outcomes of adjustable inferior rectus surgery in patients with and without thyroid eye disease.[40] Adjustable sutures should actually confer a significant advantage in thyroid eye disease where the relative inelasticity and contractile properties of the muscle make prediction of response to surgery difficult[18] and where the need to adjust more frequently has been demonstrated.[38,56]

SURGICAL APPROACHES TO LIMITING OVERCORRECTIONS

Ruttum[73] found no advantage with adjustable sutures in inferior rectus surgery in patients with thyroid eye disease, noting that overcorrection shifts could be reduced with fixed sutures. Similarly, a technique using fixed sutures showed improved outcomes when correcting duction abnormalities as opposed to preoperative deviation in patients with thyroid eye disease.[54] The relevance of this study to our discussion of inferior rectus surgery in thyroid eye disease is limited owing to the inclusion of all muscles and bilateral cases in this series. However, it allows us some insight in understanding the pros and cons of fixed vs adjustable sutures for thyroid eye disease. Using a success criteria of <5 PD deviation in primary gaze at last follow-up (>30 days), Nguyen and coworkers[54] found a 74% success rate for duction-based surgery, whereas only 44% of patients had a successful outcome using their standard recession based on preoperative deviation. Thomas and Cruz[56] showed that the improvement seen in the Nguyen study with fixed sutures and duction-based surgery is negated by the use of adjustable sutures. Thomas and Cruz[56] compared the two techniques of duction- and deviation-based surgery in patients with thyroid eye disease but used adjustable sutures (6-0 absorbable). They found a 72% successful outcome (<5 PD deviation at 30 to 180 days) for the duction-based surgeries and 66% for the deviation-based surgeries. So, adjustable sutures afford improved outcomes via a "second-look" mechanism, allowing adjustment for factors such as elasticity and contractility, whose effects cannot be quantified preoperatively. However, the outcomes when using an absorbable suture on patients with thyroid eye disease were still not as good as for patients without thyroid eye disease, presumably because of the overcorrection shifts seen in my study and others.[39,40]

Another approach taken to reduce unwanted overcorrections after inferior rectus recession in thyroid eye disease is to perform asymmetric bilateral inferior recti recessions. Cruz and Davitt[45] published a series of eight patients with thyroid eye disease and hypotropia ranging from 10 to 20 PD in primary gaze. The suture material used was not specified but was presumably a 6-0 absorbable. An adjustable suture technique was used. The idea driving the adoption of this technique was the suggestion by Hudson and Feldon[41] that asymmetric superior rectus tension creates anomalous reattachment of the inferior rectus. Additionally, since this is a bilateral condition, it has been suggested that the contralateral inferior rectus is also restricted, and releasing the tighter inferior rectus will unmask the restriction of the other inferior rectus, resulting in a contralateral hypotropia or apparent ipsilateral overcorrection shift.[92] Of the eight patients reported by Cruz and Davitt,[45] six patients were aligned to within 5 PD of orthotropia and two patients required reoperation for undercorrection (not overcorrection).

Although bilateral inferior rectus surgery is desirable when there is significant bilateral restriction to upgaze on ductions, and performed frequently by the contributing surgeons in this study, performing bilateral surgery when there is only one clinically restricted inferior rectus is not as attractive as performing unilateral surgery, provided the outcome is desirable. First, a unilateral surgery can be performed under local anesthesia with intravenous sedation, sparing the patient general anesthesia. Second, if there is an unwanted overcorrection, there is still an unoperated contralateral inferior rectus. As has been commented upon previously, reoperating a large inferior rectus recession for advancement is a difficult surgery.[34] A more predictable surgery is to have a previously unoperated contralateral inferior rectus to recess in case of overcorrection—not an option in bilateral surgery. The incidence of unwanted outcomes (reoperation/undercorrection) in Cruz and Davitt's study was 25%.[45] There were 12 of 26 patients (46%) with unwanted outcomes in my currently reported series of unilateral inferior rectus patients with thyroid eye disease (both overcorrections and undercorrections >5 PD). Thus, the outcome of the bilateral surgery is better than unilateral surgery with an absorbable suture. However, of the eight patients who underwent unilateral inferior rectus surgery with adjustable, nonabsorbable suture in my study, only one (13%) had a significant undercorrection and there were no cases of significant overcorrection—results comparable to or better than the bilateral surgery reported by Cruz and Davitt,[45] but with the benefits conferred by operating on just one inferior rectus.

Another technique to improve outcomes following eye muscle surgery for thyroid eye disease is the "relaxed muscle technique" described by Dal Canto and associates.[93] The investigators published results from 24 patients who had had a variety of muscle recessions (bilateral and unilateral, horizontal and vertical). There were nine patients with a single vertical inferior rectus recession. Preoperative deviations in this subset of patients ranged from 6 to 30 PD hypotropia, and recessions ranged from 4.0 to 7.0 mm. All of the patients were orthotropic at last follow-up (range, 2 to 12 months). Though the correlation between amount of recession and preoperative deviation for all patients was not strong (R^2=0.7292), and even weaker for single vertical recessions (n=7, R^2=0.5583), when I recalculated the R^2 for the nine patients who had unilateral inferior rectus recessions (which included some patients with concomitant horizontal muscle surgery, as was the protocol in the present study), and forced the regression through the origin, I found that there was a strong correlation between the amount of surgery and preoperative deviation (R^2=0.9429) in Dal Canto and associates' study. However, the slope of the line indicated that they averaged 1 mm recession to correct 4 PD of hypotropia, whereas our protocol is to recess 1 mm for each 2 PD of hypotropia. Thus, with a fixed, absorbable suture and smaller as opposed to larger recessions, Dal Canto and associates were able to achieve excellent results with no overcorrections. To date, other surgeons have not reported results replicating or refuting their study.

LIMITATIONS OF THE STUDY

One of the limitations of this study is its sample size. For factors where we did not find a contribution to overcorrection shift, it could be that my sample size was too small to detect an effect. Most previous studies of surgical outcomes in patients with thyroid eye disease undergoing inferior rectus surgery and/or the correction of hypotropia are much smaller,[33,39,44,56] or the studies consist of mixed populations and the data are not segregated by etiology (thyroid and nonthyroid patients grouped together),[60] anatomy (all types of muscles grouped together in studies of strabismus in thyroid eye disease),[35] or surgical technique (fixed and adjustable grouped together).[18,73] This creates difficulty understanding the role that each of these specific factors plays in determining response to surgical treatment of the inferior rectus in thyroid eye disease.

This retrospective study, like most retrospective studies, was nonorthogonal, meaning that we could not isolate one variable for study (such as suture type) while holding all other factors the same (such as the amount of recession performed or the amount of deviation needing to be corrected). Graves' disease is a multidimensional disease that cannot be captured in a cross-sectional study. Given this limitation, the best this study can offer is conditional probabilities. Thus, someone else conducting a similar study may encounter different results if their set of patient conditions differs from those of my patient population.

Limitations of this study also include those found in any restrospective study: the evidence generated is circumstantial. It would require a randomized prospective treatment trial to conclusively say that nonabsorbable suture reduces the incidence of postoperative overcorrection shift for inferior rectus surgery. This is in agreement with Kraus and Bullock,[83] who concluded in 1993 that it would require a randomized prospective controlled trial of adjustable vs fixed sutures in thyroid eye disease to conclusively decide which technique is more efficacious. However, no such study has been performed, owing to (1) the relatively infrequent occurrence of this entity, even in the subspecialist's practice, which limits the ability to generate large numbers of study patients in a single practice; and (2) the problematic nature of doing surgical trials in a multicenter fashion due to variation in surgical technique from surgeon to surgeon. However, the current study does suggest ways to structure future trials. First, the patients who have the unwanted outcome of overcorrections are those with thyroid eye disease. The number of postoperative overcorrection shifts in patients without thyroid disease is low, so they are not useful for studying the effect of nonabsorbable suture on overcorrection shift and overcorrections. Second, the study should include only inferior rectus recessions. Other muscles, though theoretically at risk for overcorrection shift in thyroid eye disease,[59] have not been shown to have a significant problem with overcorrections in this and other studies.[40,84] Whether or not to include bilateral inferior rectus recessions in such a study is debatable, but given the preliminary evidence that the bilateral technique reduces overcorrections of hypotropias in thyroid eye disease,[56] that technique should probably be studied separately.

Additionally, in this sequential series of patients, it could be argued that the increased experience of the surgeons over the course of the study resulted in improved outcomes and, thus, the technique utilized later in the study of a nonabsorbable suture resulted in improved results due to surgeon expertise, not due to the change in suture material. However, this potential limitation may be addressed two ways, both of which make this alternative explanation of the observed results unlikely. First, I was the ophthalmologist performing most of the surgeries and had been performing these surgeries since 1991. Thus by 2005, I had 14 years of experience. The additional 3 years of experience after which the change in suture occurred is unlikely to have had a significant effect on outcome due to any additional expertise of the surgeon. Second, visual inspection of the plot for date of strabismus evaluation vs overcorrection shift (Figure 23) does not lend support to the idea that experience of the surgeons played a role. Rather, following adoption of nonabsorbable suture (red line), the incidence of overcorrection shift dropped dramatically.

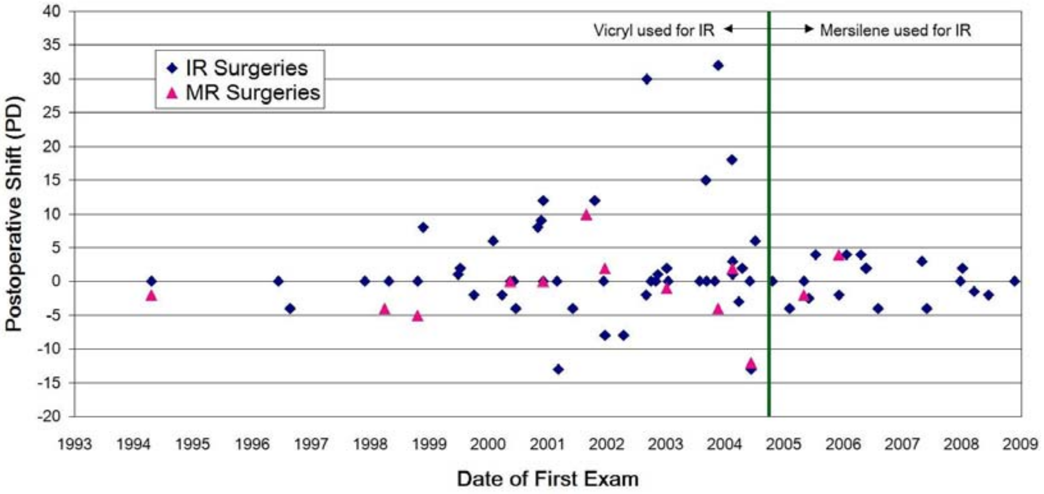

FIGURE 23

Comparison of date of first examination to amount of postoperative shift. The green line indicates the point in time when a nonabsorbable suture was adopted. There is no trend toward improved outcome with surgeons' experience until the suture change occurred.

There are drawbacks to the use of a unilateral inferior rectus recession for hypotropia in thyroid eye disease. When there is a large degree of asymmetry in inferior rectus restriction, which is an indication for ipsilateral (unilateral) single vertical muscle surgery, with normal or near normal motility in the contralateral eye, then the vertical deviation is likely large and the amount of recession indicated will be large. Even though my data suggests that the positive correlation that I found for the amount of recession and overcorrection shift can be reduced or eliminated by the use of a nonabsorbable suture, there is still the possibility of creating hypertropia of the operated eye in reading position as well as increased lower lid retraction and exposure.[38] Also, nonabsorbable adjustable sutures are difficult to cover with conjunctiva, and they are irritating when exposed (Figures 24 and 25). Even when covered with conjunctiva, they remain a foreign body in the eye. I have encountered one patient who had a subconjunctival abscess of the well-covered suture 1 year postoperatively with no other inciting factors identified. And then the question remains: if the effect of a permanent suture is to reduce overcorrection in the first 2 months following recession, how long must it stay in place to maintain this effect? I have cut the knot of a permanent suture on an inferior rectus recession at 2 months when it was irritating a patient. There was no subsequent change in ocular deviation. However, I have encouraged most of my patients to wait 6 months or more after surgery before having the exposed knot removed, as evidence suggests scar remodeling may occur for up to a year.[80]

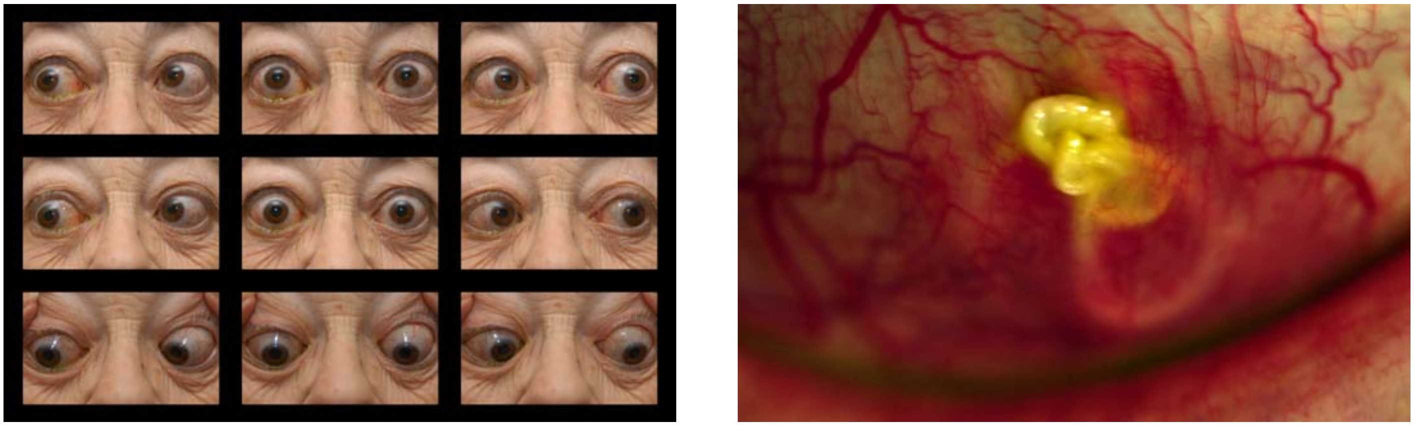

FIGURE 24

Left, Final result for patient depicted in Figure 2 following recession of the right inferior rectus on adjustable nonabsorbable suture (orthotropic in primary gaze with a large area of single binocular vision). Right, Nonabsorbable suture knot that has eroded through conjunctiva 2 months after surgery, creating symptoms of irritation and localized injection of the conjunctiva.

FIGURE 25

Left, Preoperative photos showing right hypertropia/left hypotropia secondary to left inferior rectus restriction in the setting of thyroid eye disease. Middle, Final result following left inferior rectus recession on adjustable nonabsorbable suture. Patient was orthotropic in primary gaze with no diplopia reported in any field of gaze. Right, Exposed nonabsorbable suture knot at the 2-month overcorrection visit associated with conjunctival injection and irritation. Also note the increased left lower lid retraction following left inferior rectus recession.

CONCLUSIONS

The most impactful element on the results of overcorrection shift in this study was the use of nonabsorbable suture for patients with thyroid eye disease. Other elements discussed (but not proven by this study) included limited posterior dissection of the muscle, smaller recessions (<4 mm, which are not usually clinically relevant to the management of strabismus in thyroid eye disease), and reducing tension or stretch on the inferior rectus (ie, orbital decompression). Finally, there are the fairly well-established elements of patient management that impact results of muscle surgery in thyroid eye disease, such as operating on noninflamed muscles with stable clinical measurements after all orbital surgery is complete.

In conclusion, I would like to answer a question for the reader: What have I learned from this study that has impacted my practice and surgical technique?

- I will continue to offer unilateral inferior rectus recession on adjustable suture to patients with thyroid eye disease when there is asymmetry of inferior rectus restriction with a significant vertical deviation in primary gaze, especially if their medical history or personal preference indicates a need for local anesthesia.
- I will continue to use a nonabsorbable suture for unilateral inferior rectus recessions on adjustable suture for patients with thyroid eye disease, though I will revert back to an absorbable suture for nonthyroid cases.
- I will continue to use absorbable suture for recessions of muscles other than inferior recti in patients with thyroid eye disease, as my results do not indicate a problem with late overcorrections in nonthyroid patients.
- I will continue to perform minimal posterior dissection when recessing the inferior rectus.[43]
- I will continue to warn my patients undergoing unilateral inferior rectus recession (as well as surgery on any other muscle) in the setting of thyroid eye disease that further surgery may be indicated, including surgery on the other ("good" or better) eye.

Following eye muscle surgery with adjustable sutures, my experience has been that 90% of patients with thyroid eye disease and diplopia will achieve single binocular vision in primary and reading position without prism.[92] Other studies report similarly good results.[38,62] With continued study and innovation, changing the suture type in appropriate settings may reduce the number of surgeries required to achieve acceptable outcomes. This will reduce the discomfort, inconvenience, anxiety, and risk to the patient requiring surgical intervention to treat the vertical diplopia associated with hypotropia as a result of thyroid eye disease.

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