



Floppy Eyelid Syndrome: an Overlooked Comorbidity Among Bariatric Patients

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Abstract

Purpose Floppy eyelid syndrome (FES) is a clinical entity characterized by palpebral hyperlaxity and chronic conjunctivitis. Patients' eyelids evert ("flip inside out"), leading to eye irritation, dryness, grittiness, and tearing. More severe cases can lead to significant ocular complications, such as keratoconus and impaired eyesight. Research has revealed an association between FES and obstructive sleep apnea syndrome (OSAS). OSAS is also one of the most common comorbidities among patients with obesity and an indication for bariatric surgery. This is one of the first studies to explore FES in a group of patients who have undergone bariatric surgery.

Materials and Methods This was a retrospective study. A total of 88 patients completed a survey by mail or telephone. Additional data on demographics and baseline preoperative clinical information was extracted from the online medical records and the MBSAQIP database.

Results Thirty-nine patients (44%) recalled having chronic ocular symptoms before their bariatric surgery, among whom six reported palpebral laxity and/or an established diagnosis of FES. The majority of them (67%) rated their symptoms postoperatively as "somewhat" or "significantly improved." The patients that reported improvement in their ocular symptoms also experienced an improvement in their OSAS severity.

Conclusion Bariatric surgery might affect the clinical course of FES and the severity of symptoms. Treating OSAS, the underlying mechanism of FES, is a possible mechanism of how bariatric surgery can help patients. It is also critical for bariatric surgeons to consider FES when patients with obesity, particularly those with OSAS, present with chronic eye symptoms.

Keywords Bariatric surgery · Floppy eyelid syndrome · Chronic papillary conjunctivitis · Obstructive sleep apnea

Key Points

- Floppy eyelid syndrome (FES) is a common yet underdiagnosed clinical entity.
- FES is related to obstructive sleep apnea, which also affects bariatric patients.
- The present study is one of the first to explore FES among bariatric patients.
- This study aims to raise awareness of FES among bariatric surgeons.

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Introduction

Floppy eyelid syndrome is a palpebral laxity disorder that Culbertson and Ostler first described in 1981 [1]. It is characterized by the presence of a lax ("floppy") upper eyelid that everts spontaneously during sleep, although the lower lid can be affected too. This nocturnal eyelid eversion and

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subsequent conjunctival exposure can lead to chronic conjunctivitis [1]. In addition, physical irritation of the ocular surface by eye rubbing and repetitive microtrauma has been proposed as one possible mechanism contributing to the pathogenesis of FES keratoconjunctivitis [2]. Eyelid hyperlaxity has also been associated with a higher risk of severe ocular surface disease symptoms [3], including corneal dryness [4].

The prevalence of FES among adults has been estimated to fall between 3.8 and 15.8% [3, 4]. However, this disorder remains largely underdiagnosed, and therefore, the aforementioned numbers are likely an underestimation. FES is a syndrome of tarsal papillary conjunctivitis. Hence, patients can present with eye redness, foreign body sensation, tearing, mucus discharge, and/or blurred vision. Symptoms are usually worse in the morning upon waking up and can be either unilateral or bilateral. Notably, symptoms are often more pronounced on the side the patient usually sleeps [5]. Various ocular findings have been associated with FES, including blepharitis, entropion, ectropion, dermatochalasis, corneal scarring/ulceration [6], and keratoconus [7, 8].

Even though the pathophysiology and underlying mechanism of FES are not yet fully elucidated, previous research has revealed an association between FES and obstructive sleep apnea syndrome (OSAS) [9]. FES and OSAS share important risk factors, namely male gender and obesity. The prevalence of OSAS in patients with FES has, in fact, been estimated to be as high as 90–100% [2]. OSAS is a well-known comorbidity of patients with obesity [10] and is one of the indications for bariatric surgery referral, according to the American Society for Metabolic and Bariatric Surgery (ASMBS). Studies exploring the association between FES and obesity have generated mixed results. One study showed an increased lid hyperlaxity in patients with OSAS and high BMI compared to patients with OSAS and low BMI [6]. Another study demonstrated no association between FES and BMI [6]. To our knowledge, this study is one of the first to explore the prevalence of FES in bariatric patients and examine the potential effect of bariatric surgery on FES symptoms. Based on the background described above, our working hypothesis was that bariatric surgery might lead to improvement or resolution of FES.

Materials and Methods

We sought to obtain retrospective data from patients who underwent bariatric surgery at Beth Israel Deaconess Medical Center (BIDMC) between January 1, 2016, and December 31, 2021. All patients were 18 years or older at the time of the surgery. A survey packet, including the prospective agreement, the survey questionnaire, and a pre-stamped envelope for returning the completed material

to the researchers, was mailed to the patients. The survey was prepopulated, and unique identifier codes were used to ensure anonymity. Telephone follow-up was conducted for patients that had neither returned a completed survey nor refused participation. The survey elicited information about patients' demographics, self-reported eye symptoms preoperatively, and postoperative symptom evolution (Table 1). Additional clinical information, including baseline (preoperative) comorbidities (Table 2), was abstracted from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement (MBSAQIP) database.

While we extensively reviewed the existing literature and the work of researchers that have studied FES, we found no standardized questionnaires for this particular group of patients. Therefore, we decided to structure our survey in a way that could help us collect key anamnestic details and findings that may suggest the diagnosis of FES. We asked patients to reflect on the 6 months prior to their weight loss surgery and to respond whether they had, more often than not, symptoms suggestive of FES, including eye redness, grittiness, dryness, and mucus discharge. We also asked

Table 1 Respondents' demographic data

Demographic	<i>n</i>
Sex	
Male	26
Female	62
Ethnicity	
Hispanic or Latino	19
Not Hispanic or Latino	69
Race	
White	56
Black or African American	25
American Indian or Alaskan Native	1
More than one race	3
Other	2

Table 2 Respondents' baseline comorbidities

Comorbidity	<i>n</i>	<i>N%</i>
Obstructive sleep apnea (OSA)	55	62.5
Use of sleep apnea machine (e.g., CPAP)	45	51.13
Dyslipidemia	31	35.22
Hypertension	48	54.54
Diabetes		
With complications	7	7.95
Without complications	19	21.59
Ophthalmologic disease	9	10.22
Autoimmune disease	7	7.95
Allergy/allergic disease	16	18.18

CPAP continuous positive airway pressure

about the localization of symptoms (unilateral versus bilateral) and when these were more pronounced (upon waking up/throughout the day/towards the end of the day). We included more direct questions as well, asking patients whether they had ever noticed (or had been told) their eyelids were “floppy” and whether they were diagnosed with FES prior to surgery. Finally, we asked patients to reflect on how their eye symptoms have changed after their weight loss surgery (significantly improved/somewhat improved/no change/somewhat worsened/significantly worsened). The full questionnaire is included in Fig. 1.

Results

In total, 88 patients completed the survey, 31 by mail and 57 by phone. An additional 24 patients could not be contacted due to changes in their contact information that

were not updated on our records, while 7 refused participation. The respondents’ demographics and baseline (pre-operative) comorbidities can be seen in Tables 1 and 2, respectively. The mean age was 48.4 years. The mean body mass index (BMI) was 44.7 preoperatively and 33.3 post-operatively (Δ BMI = - 11.4, mean % excess weight loss (%EWL) = 57.8). The mean weight reduction was 27.3 kg (60.2 lbs). Thirty-nine patients recalled having at least one ocular symptom, more often than not, in the period immediately prior to their bariatric surgery, with more than half of these patients (24 patients) reporting seeing an ophthalmologist for their ocular symptoms. Among these 39 patients, three had noticed and/or had been told that their eyelids felt “loose”/flipped over (Fig. 2) during sleep, two had both noticed/had been told that their eyelids felt “loose” and had been diagnosed with FES, and one had been diagnosed with FES, without self-reporting having “loose” eyelids. As this is a retrospective study, patients recall that having “loose,”

Fig. 1 Questionnaire

SURVEY

Today’s date: _____

Please answer each question by checking the box that best describes you.

Q1. What is your current weight (in pounds)? _____ pounds

Q2. Before having your weight loss surgery, were you diagnosed with high blood pressure?

Yes No

Q3. Before having your weight loss surgery, were you diagnosed with Obstructive Sleep Apnea?

Yes No

Q4. If you answered yes to the previous question, did you use a Sleep Apnea machine?

Yes No

Q5. Have you ever noticed or been told that you have “loose” eyelids that “flip over” during sleep?

Yes No

Q6. Before having your weight loss surgery, were you diagnosed with Floppy Eyelid Syndrome?

Yes No

Q7. In the last 6 months before your weight loss surgery, more often than not, did you experience any of the following eye symptoms?

Eye redness	<input type="radio"/> Yes	<input type="radio"/> No
Dryness	<input type="radio"/> Yes	<input type="radio"/> No
Grittiness (feeling like there is sand in the eye)	<input type="radio"/> Yes	<input type="radio"/> No
Tearing	<input type="radio"/> Yes	<input type="radio"/> No
Mucus discharge (“sticky” eyes)	<input type="radio"/> Yes	<input type="radio"/> No
Blurry vision	<input type="radio"/> Yes	<input type="radio"/> No
Other eye symptoms	<input type="radio"/> Yes	<input type="radio"/> No

Please describe what other eye problems you experienced: _____

Fig. 1 (continued)

Q8. If you answered yes to any of the options in question Q7, did you have this/ese symptom/s in one or both eyes?

In one eye only In both eyes

Q9. If you answered yes to any of the options in question Q7, when were the symptom/s most severe?

Upon waking up Throughout the day Towards the end of the day

Q10. If you answered yes to any of the options in question Q7, did you do any of the following to address your eye symptom/s?

Visit an eye doctor Yes No

Use eye drops Yes No

Use eye cream Yes No

Use a night mask Yes No

Eyelid taping Yes No

Q11. For each of the following questions, place an "X" in the box that best describes how the following have changed compared to before getting your weight loss surgery:

	Significantly improved	Somewhat improved	No change	Somewhat worsened	Significantly worsened
a. Your high blood pressure has	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Your obstructive sleep apnea has	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Your eye symptoms have	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

General Information

Which of the following best describes your ethnicity? Hispanic or Latino Not Hispanic or Latino

Which of the following best describes your race?

White Black or African American Native Hawaiian or Pacific Islander American Indian or Alaska Native Asian More than one race

Other: _____

Which of the following best describes your current marital status?

Single, never married Married/ Partnered, living together Separated/ Divorced Widowed

End of the survey. Thank you for your participation!

floppy eyelids and/or a diagnosis of FES was the strongest information we could rely on to assume that these patients possibly had the syndrome. Of these six patients, three were women, and three were men.

Five patients reported suffering from OSA before their surgery; four also used a sleep apnea machine. Regarding their postoperative state, three patients evaluated both their OSA and their ocular symptoms as “significantly improved,” one as both conditions “somewhat improved,” and one responded that there had been no change in the severity of their OSA, while their eye symptoms had “significantly worsened” (Table 3). One patient, who had no prior diagnosis of OSA, reported no change in their ocular symptoms (Table 3). Notably, a patient commented that his desire to improve his FES symptoms was one of the reasons

he decided to have bariatric surgery, as their physician advised. Of the remaining 33 patients who recalled chronic ocular symptoms before surgery but had not observed eyelid laxity nor had a diagnosis of FES, 19 responded that they had seen no change in their symptoms after surgery. Four evaluated them as “somewhat improved” and three as “significantly improved.” In contrast, four other patients reported that their ocular symptoms have “somewhat worsened,” and one patient reported them as “significantly worsened.” Two patients did not fill out the survey section regarding their postoperative outcomes. Although many of these patients describe symptom profiles that could be attributed to FES, it would be precarious to assume so. In many cases, the symptoms could be due to dry eye syndrome or a particular subset of this named Sjögren’s syndrome.



Fig. 2 Flipped eyelid

Discussion

This is the first study to our knowledge that explores FES in a group of bariatric patients. FES is an important and relatively common cause of ocular irritation. Nevertheless, it can be easily misdiagnosed in clinical practice. As discussed above, even though FES has not been linked directly to obesity, it is strongly associated with OSAS, with the majority of patients with FES suffering from OSAS.

The mechanism of FES is not well understood. One hypothesis to explain the association between FES and OSAS is that chronic sleep fragmentation, microtrauma [11], and alternating states of tissue ischemia and reperfusion [12], as seen in OSAS, can lead to overexpression of elastolytic proteases (e.g., matrix metalloproteinases) and subsequently loss of elastin and hyperlaxity of the palpebral tissue [13]. In addition, a case–control study revealed that FES patients were more likely to suffer from conditions related to metalloproteinase dysfunction (e.g., hernias, dermatologic, or rheumatological diseases), suggesting that they might represent a unique phenotype among patients presenting with OSA [14]. As many of these proteases depend on cofactors such as metal ions, it is worth mentioning that none of the six patients with FES had any nutritional deficiencies, according to their medical records. All six took standard multivitamin supplements, as noted in their medication list. Furthermore, a decrease in cortical arousability and reflex response to noxious stimuli can be seen in patients with OSAS. This feature may exacerbate mechanical injury to palpebral tissue during sleep as the patient can often tolerate significant mechanical stress that would have

normally prompted the individual to wake up and reposition [7]. Interestingly, the use of continuous positive airway pressure (CPAP) therapy in patients with OSAS resulted in an improvement of their FES symptoms when these were also present [2, 15]. This reinforces the likely causal relationship between OSAS and FES.

OSAS is highly prevalent among populations with obesity and is an indication for bariatric surgery for patients with a BMI of 35 or higher. Weight loss surgery has been shown to improve or lead to complete resolution of OSAS, with post-surgical remission in as many as 80% of the cases [16]. This raises the question of whether bariatric surgery has an effect on FES symptoms. Although the design of our study does not allow us to reach definitive conclusions, our findings can be considered hypothesis-generating. Additional research is needed to examine whether improvement of FES is one of the benefits a patient can anticipate after their weight loss surgery (WLS). Improvement of FES could indirectly be linked to bariatric surgery by improving OSA severity.

A correlation might also exist between FES and leptin hormone levels. A case series showed that plasma leptin levels were elevated in FES patients, implying that hyperleptinemia might play a role in FES pathogenesis [17]. Although leptin is primarily produced by adipocytes, the stomach is another identified production site [18]. In this context, bariatric surgery, which alters the stomach anatomy, might affect FES through mechanisms related to leptin. More data are warranted.

The small number of patients with potential or diagnosed FES we identified in this study does not allow for further correlation analysis. However, the relationship between bariatric surgery and FES, as well as risk factors and predictive markers, are likely to be further elucidated as research continues to shed light on the pathophysiology of FES. We also hope that this effort will help raise awareness about FES among medical professionals. Many specialists, including ophthalmologists, sleep physicians, and bariatric surgeons, should keep a high level of suspicion and refer these patients to appropriate resources for further evaluation and treatment.

Limitations

We acknowledge that our study presents a number of limitations. First of all, due to our retrospective design, the risk of recall bias cannot be excluded. We relied on a self-reported diagnosis of FES and/or history of eyelid laxity, but we cannot exclude nor confirm the presence of FES among the rest of the patients reporting chronic eye symptoms. Furthermore, there is a risk of selection bias, as we were not able to contact all patients due to changes in contact information that were not updated properly in our patient records. Finally, our survey included patients from a single WLS

Table 3 Demographic, preoperative, and postoperative information of the patients with FES symptoms

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Sex	F	F	F	M	M	M
Age	62	66	50	50	50	46
Preoperative comorbidities and ocular symptoms						
OSA	Yes	Yes	No	Yes	Yes	Yes
OSA machine	Yes	Yes	-	Yes	No	Yes
HTN	Yes	No	No	Yes	No	Yes
Diabetes	No	No	No	Yes, no complications	No	No
Eye disease	No	Yes (cataract)	No	No	No	Yes
Autoimmune disease	No	No	Yes (RA)	No	No	No
Seasonal allergy	Yes	Yes	No	Yes	No	No
“Loose” eyelids preoperatively	Yes	Yes	Yes	Yes	Yes	No
Preoperative FES diagnosis	Yes	No	Yes	No	No	Yes
Redness	Yes	No	Yes	No	Yes	No
Dryness	Yes	Yes	Yes	Yes	Yes	Yes
Grittiness	Yes	Yes	Yes	Yes	Yes	Yes
Tearing	No	No	Yes	No	Yes	No
“Sticky” eyes	No	No	Yes	Yes	No	No
Blurry vision	No	No	Yes	No	Yes	No
Unilateral/bilateral symptoms	Unilateral	Bilateral	Bilateral	Unilateral	Bilateral	Bilateral
When were the eye symptoms most prominent?	Throughout the day	Throughout the day	Throughout the day	Upon waking up	Throughout the day	Could not recall
Measures taken	Dr. visit, eye drops, eye cream	Dr. visit, eye drops	Dr. visit, eye drops	Dr. visit, eye drops	Dr. visit, eye drops	Dr. visit
Postoperative outcomes						
ΔBMI	−8.91	−8.41	−4.73	−18.71	−10.18	−10.65
ΔWeight (lbs)	−51.9	−49	−28	−138	−73	−68
OSA outcomes	↓	No change		↓↓	↓↓	↓↓
Ocular outcomes	↓	↑↑	No change	↓↓	↓↓	↓↓

OSA obstructive sleep apnea, HTN hypertension, FES floppy eyelid syndrome, BMI body mass index, ΔBMI=postop BMI−initial BMI, ΔWeight=postop weight−initial weight, ↓ somewhat improved, ↓↓ significantly improved, ↑↑ significantly worsened

center in Boston, and the patients who responded had all undergone sleeve gastrectomy. Therefore, the generalizability of our findings is limited.

Conclusions

FES is a common yet underdiagnosed condition that can be associated with significant ocular symptoms. Therefore, it is critical to consider FES when patients with high BMI, particularly those with OSA, present with nonspecific ocular symptoms, such as eye irritation. The present study explores the possible effects of bariatric surgery on FES symptoms.

Further research, including prospective studies with patients with an established diagnosis of FES, is needed and will allow for more definitive conclusions.

Data Availability The data supporting this study's findings are available on request from the corresponding author, TZ. The data are not publicly available due to containing information that could compromise the privacy of research participants.

Declarations

Ethics Approval and Consent to Participate The study was approved by institutional review boards (IRB) at BIDMC. All procedures performed in studies involving human participants were in accordance with the

ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of Interest Dr. Daniel Jones is a member of the advisory board of Allurion Technologies.

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