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A New Treatment Protocol of Micro-Focused Ultrasound for Lower Eyelid Fat Bulging

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ABSTRACT

Background: Micro-focused ultrasound (MFU) causes tissue tightening by producing thermal injury zones and is used to treat various age-related changes including lower eyelid fat bulging.

Objectives: To investigate the efficacy of a new treatment protocol of MFU for lower eyelid fat bulging.

Materials and Methods: We reviewed the medical records of all patients who began MFU for lower eyelid fat bulging from March 2017 to September 2018. MFU was performed in two steps to tighten the lower eyelid dermis and orbital septum. Data on age, sex, bulging severity, and the number of treatment sessions were obtained. Associations of these variables with treatment response were determined through an ordinal logistic regression analysis.

Results: Among 191 enrolled patients, 119 (62.3%) and 47 (24.6%) achieved fair and good responses, respectively. In the multivariable analysis, multiple treatment sessions (odds ratio [OR] 6.618; 95% confidence interval [CI] 3.242-13.513; P<0.001), moderate bulging (OR 4.328; 95% CI 1.755-10.671; P=0.001), and severe bulging (OR 7.570; 95% CI 2.537-22.585; P<0.001) were associated with greater treatment response. There were no serious adverse events.

Conclusion: The new treatment protocol of MFU is an effective and safe strategy for lower eyelid fat bulging.

KEY WORDS: Eyelids, rejuvenation, skin aging, ultrasonic therapy/methods

INTRODUCTION

As aging progresses, lower eyelid fat bulging becomes prominent because of age-related changes in the soft tissue and bony orbit.[1] One of its major causes is the loosening of the orbital septum that supports orbital fat. Lower blepharoplasty can be performed for correction, but problems such as scarring, long recovery time, and overcorrection might occur. Thus, effective but non-to-minimal invasive methods for managing lower eyelid fat bulging have been required. Recently, non-surgical treatments such as ablative and non-ablative fractional laser, radiofrequency, and micro-focused ultrasound (MFU) have been used.[2, 3, 4, 5]

MFU produces discrete thermal injury zones to targeted areas, which results in shrinkage and tissue tightening.[6] Moreover, it can raise the temperature of the targeted adipose tissue while sparing the surrounding tissue, and no damage to intervening nerves or arterioles was observed within the path of the ultrasound pulse.[7] Given that the power density of the converging ultrasound beam is much lower as it passes through the path above the target point,[8] MFU is believed to be safe when used off-label for orbital fat treatment, and no serious adverse events have been reported in human eyelid studies.[5, 9]

However, when the orbital septum is deeply located, energy delivery to the orbital septum is limited in the conventional protocol.[5, 9] Also, the shape and location of orbital fat of most patients are not consistent in the supine position compared to the sitting position. In this study, we reported the efficacy of a new two-step protocol of MFU that tightens both lower eyelid dermis and orbital septum for correcting lower eyelid fat bulging.

METHODS

Study Population and Variables

We reviewed the medical records of patients with lower eyelid fat bulging who started MFU at the The Seoul Dermatology Clinic from March 2017 to September 2018. All patients were followed up until we confirmed that no further treatment is needed, until they were lost to follow-up, or until October 15, 2018 (date of scheduled data extraction), whichever arrived earlier. Patients who were lost to follow-up after the first treatment were excluded. Age, sex, and the number of treatment sessions were obtained from the medical records.

Evaluating Bulging Severity and Treatment Results

High-resolution digital photographs taken with a Canon EOS D30 camera (en face; Canon, Lake Success, NY, USA) were used to assess bulging severity and treatment response. Baseline bulging severity was scored from 1 to 5 using photographs taken before initial treatment, with 1 indicating mild bulging and 5 indicating most severe bulging. The severity scores were converted into a single ordinal variable by summing the number of individual scores by 3 independent dermatologists in the mild (3-6), moderate (7-10), and severe (11-15) categories. Treatment response was graded as follows by comparing photographs taken before the initial treatment and at the last visit: grade 0, no improvement; grade 1, <20%; grade 2, 20%-39%; grade 3, 40%-59%; grade 4, 60%-79%; and grade 5, 80%-100%. We also collapsed treatment response grades into a single ordinal variable by summing the number of individual grades by 3 dermatologists in the minimal (0-2), fair (3-5), and good (6 or more) responses. There were no missing data in this study because we had started to take photographs of patients with lower eyelid fat bulging at every visit as of January 2017.

The study protocol was approved by the Institutional Review Board of Korean National Institute for Bioethics Policy (P01-201903-21-001), and the requirement for obtaining informed consent was waived.

Intervention

We used the ULTRAFORMER III, SHURINK MFU device (CLASSYS INC., Seoul, Korea) with three different transducers. The EMLA cream (lidocaine 2.5% and prilocaine 2.5%; Astra Pharmaceutical Products Inc., Westborough, MA, USA) was applied to the treatment site 60 minutes before treatment. After the EMLA cream was wiped off, an ultrasound gel was applied to the skin.

In the first step, MFU was performed on the patients in the supine position using the L7-1.5 transducer (7 MHz, 1.5-mm focal depth) and either the L7-3.0 (7 MHz, 3.0-mm focal depth) or the L4-4.5 transducer (4 MHz, 4.5-mm focal depth) to tighten the lower eyelid dermis and orbital septum. Either the L7-3.0 or the L4-4.5 transducer was used depending on the depth of the orbital septum, which was measured before treatment using a handheld ultrasound device (UProbe-L5NC, Sonostar Technology Co., Guangzhou, China). To ensure that the orbital septum could be targeted by each shot, we applied proper pressure toward the infraorbital margin with the transducer during the procedure.

Moreover, in the second step, L7-3.0 and L4-4.5 transducers were used in patients in the sitting position to tighten the orbital septum. While the transducer was being used, patients were instructed to open their eyes and look upwards.

The energy per ultrasound pulse used at the first and second steps ranged from 0.10 to 0.20 J and from 0.3 to 0.5 J, respectively. The 25-mm-long exposure lines of ultrasound pulses were delivered parallel to one another with 3-5-mm spacing. Treatment lines were delivered to the skin located 2 mm below the lower eyelid margin to the inferior orbital rim, parallel to the lower eyelid margin. Patients receiving multiple sessions were treated at 3-week intervals.

F-RAY

To attempt a more precise evaluation of bulging severity and treatment response, additional photographs were taken using the F-RAY (BEYOUNG Co., Seoul, Korea). This device creates contour lines using the moiré phenomenon; thus, it is expected to enable more sensitive volume assessment (Fig. 1). Three dermatologists evaluated baseline bulging severity and treatment response with photographs taken with F-RAY in the same way as when evaluating with conventional digital camera photographs.

Statistical Analysis

Ordinal logistic regression analyses were used to evaluate associations between predictive factors and treatment response. Predictive factors showing univariable associations with treatment response ($P<0.20$) were included in a multivariable ordinal logistic regression model.

Interrater reliability for bulging severity and treatment response scores was assessed using Spearman correlation. Differences in the treatment response evaluation (conventional digital camera vs. F-RAY)

were analyzed with the exact McNemar-Bowker test. All analyses were performed using SPSS statistics software, version 20.0 (SPSS Inc., Chicago, IL, USA). All statistical tests were two-sided and a P-value<0.05 was considered statistically significant.

RESULTS

Patients' Characteristics and Overall Treatment Response

Detailed demographic and clinical characteristics of the patients are presented in Table 1. A total of 191 patients with lower eyelid fat bulging were identified and treated with MFU; of these, 162 (84.8%) were female. Patients' mean age at the time of presentation was 45 (range 20-73) years. The median treatment number per patient was 1 (interquartile range (IQR) 1-2).

The median bulging severity score was 9.0 (IQR 7.0-10.0), and median treatment response score was 4.0 (IQR 3.0-5.0). Overall, when evaluated by photographs taken with the conventional digital camera, 25 (13.1%) have had a minimal response, 119 (62.3%) a fair response, and 47 (24.6%) a good response (Fig. 2). The proportion of patients with good response tended to increase with the number of treatments (Fig. 3).

Variable	All patients (n=191)
Age, mean (range), y	45.3(20.0-73.0)
Sex, n (%)	
Male	29 (15.2)
Female	162 (84.8)
Number of treatment, median (IQR)	1.0 (1.0-2.0)
Bulging severity score*, median (IQR)	9.0 (7.0-10.0)
Treatment response score†, median (IQR)	4.0 (3.0-5.0)
Mild (3-6), moderate (7-10), severe (≥ 11)	
†Minimal (0-2), fair (3-5), good (≥ 6)	
IQR, interquartile range	

TABLE 1 Demographic and clinical characteristics of patients

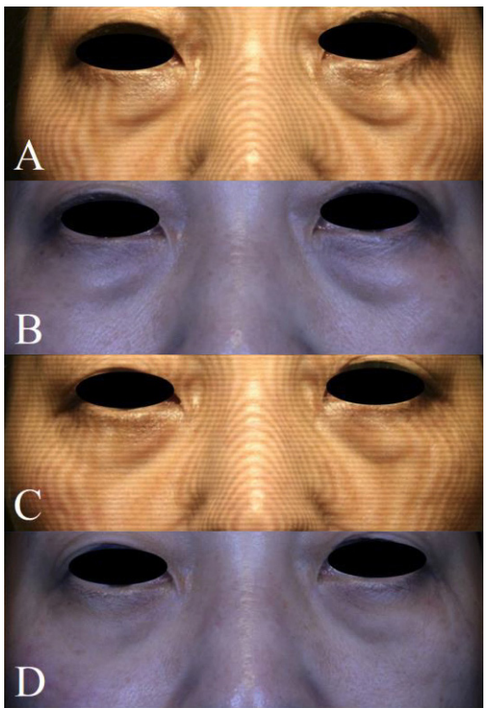

FIGURE 1 Preoperative (A, B) and postoperative (C, D) photographs. (A, C) Photographs taken with F-RAY. Contour lines on skin surface assist volume assessment.

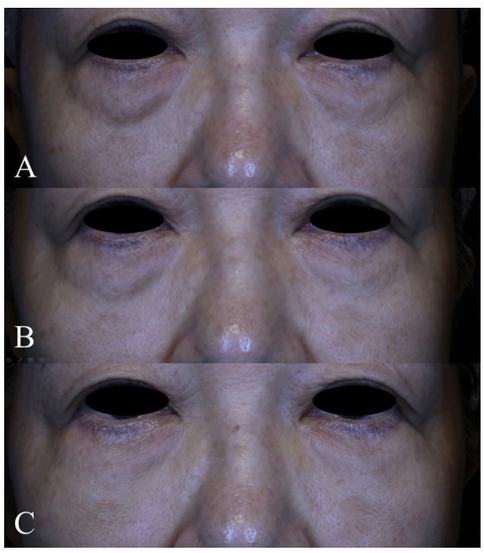

FIGURE2 Preoperative and postoperative photographs using a conventional digital camera in a patient with a good response. Compared with pretreatment (A), photographs after the third treatment (B) and the seventh treatment (C) show gradual improvement.

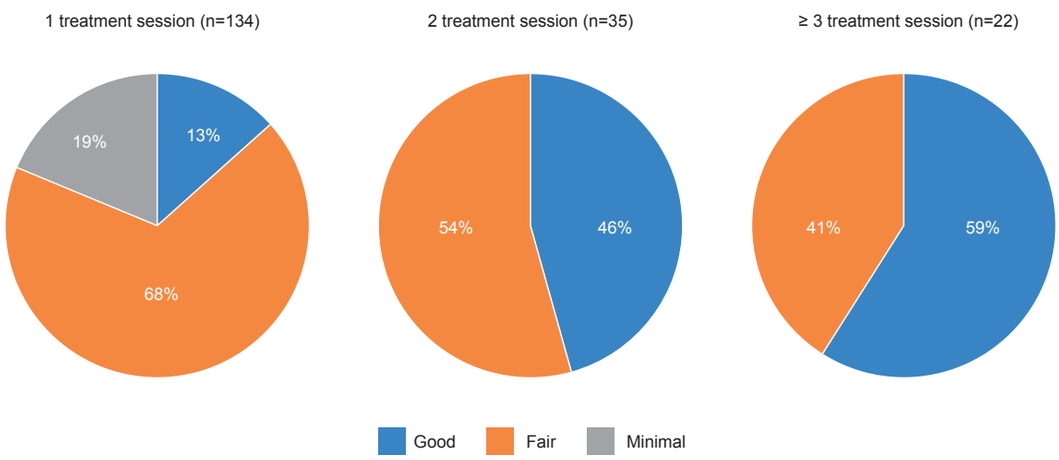

FIGURE 3 Frequency of treatment response depending on the number of treatment sessions.

Association Between Predictive Factors and Treatment Response

As shown in Table 2, the univariable ordinal logistic regression analysis revealed multiple treatment sessions, and more severe lesions were associated with greater treatment response (Table 2). There were no significant differences in the treatment response according to age and sex.

In the multivariable ordinal logistic regression analysis, two variables (treatment number and bulging severity) remained significantly associated with treatment response (Table 2). Multiple treatment sessions were significantly associated with greater treatment response (odds ratio [OR], 6.618; 95% confidence interval [CI] 3.242-13.513; P<0.001). Additionally, patients with moderate or severe lesions showed greater treatment response than patients with mild lesions (OR 4.328; 95% CI 1.755-10.671; P=0.001, and OR 7.570; 95% CI 2.537-22.585; P<0.001, respectively) (Table 2).

The study protocol was approved by the Institutional Review Board of Korean National Institute for Bioethics Policy (P01-201903-21-001), and the requirement for obtaining informed consent was waived.

Comparison of Evaluation by Digital Camera and F-RAY

Average interrater reliability (Spearman) of bulging severity score and treatment response score evaluated by the conventional digital camera was 0.40 and 0.33, respectively. When evaluating using F-RAY, the average interrater reliability increased to 0.52 (P=0.139) and 0.39 (P=0.504), respectively, which was not significantly different. Figure 4 compares the treatment responses evaluated by a conventional digital camera and F-RAY. There were significantly more fair and good responses evaluated by the F-RAY than by the conventional digital camera (P=0.003). This suggests that a more sensitive and reproducible evaluation has been done when evaluating with F-RAY.

Safety Assessment

The most common adverse events were pain and swelling (reported by approximately half of the patients), which were mild in severity. Other adverse events observed were bruising (reported by 5 patients), nodules (reported by 2 patients), ectropion (reported by 1 patient), and unilateral dacryorrhea (reported by 1 patient). All adverse effects were mild and resolved within 2 weeks. No serious adverse events were reported.

Variable	Univariable analysis					Multivariable analysis	
	Minimal response (n=25)	Fair response (n=119)	Good response (n=47)	OR (95% CI)	P-(Value)	OR (95% CI)	P-(Value)
Age,y, median(IQR)	44.0 (39.0-48.0)	47.0 (36.0-53.0)	49.0 (39.0-54.0)	1.011 (0.984-1.039)	0.418	-	
Sex, n(%)							
Female	22(88.0)	100(84.0)	40(85.1)	Reference 1.081 (0.489-2.390)	0.8	-	
Male	3(12.0)	19(16.0)	7(14.9)		48		
Treatment number, n(%)							
1	25(100.0)	91(76.5)	18(38.3)	Reference 7.720 (3.827-15.571)	<0.001	Reference 6.618 (3.242-13.513)	<0.001
≥2	0(0)	28(23.5)	29(61.7)				
Bulging severity, n(%)							
Mild	9(36.0)	18(15.1)	0(0)				
Moderate	15(60.0)	77(64.7)	32(68.1)	Reference 5.266 (2.160-12.840)	<0.001	Reference 4.328 (1.755-10.671)	0.001
Severe	1(4.0)	24(20.2)	15(31.9)	10.711 (3.736-30.734)	<0.001	7.570 (2.537-22.585)	<0.001

CI, confidence interval; IQR, interquartile range; OR, odds ratio.

TABLE 2 Univariable and multivariable analysis of treatment response to MFU in lower eyelid laxity (n=191)

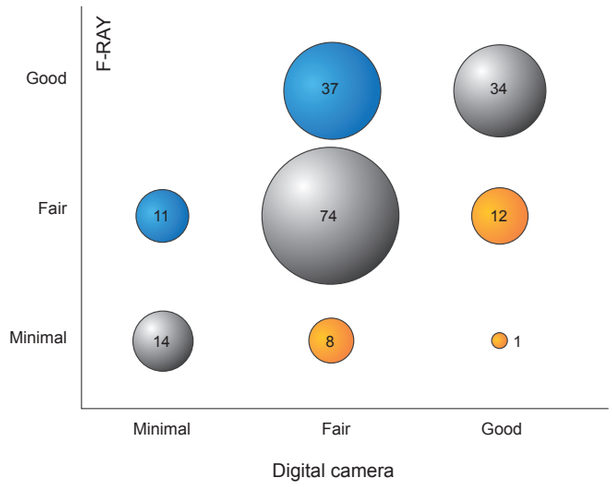

FIGURE 4 Comparison of treatment responses evaluated by conventional digital camera and F-RAY (n=191). Significant asymmetry (P=0.003, Bowker test), i.e. significantly more fair and good responses evaluated by the F-RAY than by the conventional digital camera.

DISCUSSION

This study investigated the efficacy and prognostic factors of a new two-step MFU protocol to tighten the lower eyelid dermis and orbital septum in patients with lower eyelid fat bulging. More than 80% of patients showed a fair or good response after undergoing the treatment with the new MFU protocol. Moreover, we showed that the clinical factors associated with the greater treatment response were multiple treatment sessions and moderate or severe bulging. Age and sex were not associated with the treatment response. In the first step, we employed a relatively lower energy (0.1-0.2 J) than 0.2-0.45 J from conventional protocols to reduce the risk of untoward side effects, and added the second step using a higher energy (0.3-0.5 J) with a 3.0 mm- or 4.5 mm-focal depth probe for effectively targeting the orbital septum as well as tightening the lower eyelid dermis. Also, looking upwards in the sitting position allows the orbital fat to bulge out so that physicians can treat it more precisely. In studies using conventional protocols of MFU for lower eyelid fat bulging, Suh et al.[9]

reported that 86.7% of patients were considered to have much improved or improved lower eyelid, and Pak et al.[5] reported an average improvement score of 3.45 and 3.25 on a scale of 0 (no involvement) to 4 (severe). It is difficult to compare the efficacy of the conventional and new treatment protocols directly because the evaluation was carried out 6 months after the single treatment session in previous studies, and the grading scale was different.

When treating the lower eyelid fat bulging with MFU, careful treatment is needed because the therapeutic response varies greatly depending on how precise the orbital septum is targeted.[5] Firstly, the target depth assessment through diagnostic ultrasound should be preceded to select probes for the appropriate treatment depth. During the procedure, the orbital septum becomes shallower as pressure increases; thus, proper pressure should be applied to adjust the target depth. Moreover, the probe should be placed parallel to the lower eyelid margin. If the probe is placed perpendicular to the lower eyelid margin, as Pak et al.[5] reported, the orbital septum would become deeper. To keep the depth change constant during the procedure on the orbital septum, it would be better to target the part that originates from the orbital rim.

It is also important to stay on the bone when treating the periorbital area, because the ultrasound waves will bypass any protective eye shield and can cause corneal damage.[10, 11] If the MFU is performed toward the inferior orbital rim, eye damage can be avoided without the need for an eye shield. In the second step, corneal damage was prevented by instructing patients to look upwards. Although one additional treatment step has been added, it was well tolerated with an adverse event profile similar to those in previous studies. Meanwhile, high-intensity focused ultrasound in bone metastasis is known to increase skeletal remodeling,[12] and a similar mechanism may contribute to improving lower eyelid fat bulging through the 'hammock effect'.[1]

Diagnostic ultrasound can also be used to distinguish other conditions that can be confused with fat bulging.[13] In dark circles with which the causes other than fat bulging are predominant, the effect of MFU is reduced and it may be better to perform other treatments. For example, treatment with a polynucleotide or hyaluronic acid can yield satisfactory results in dark circles due to the thin, translucent skin.[14]

We found that the number of treatment sessions was associated with treatment response. Improvement can be more pronounced with a longer observation period because the lipolysis and tightening process can last more than three months after a single session of MFU.[15] However, since the proliferative phase lasts for approximately 21 days in the wound healing process,[16] frequent treatments at 3-week intervals may lead to a rapid improvement.

In this study, more severe bulging led to better clinical outcomes. Although the severe group tended to receive more treatment sessions, the significance was still maintained in the multivariable analysis. In general, mild-to-moderate laxity is considered to be an ideal indication for MFU,[10, 17] but the satisfactory outcome can also be expected in severe cases.

We found that age was not associated with treatment response to MFU. This is consistent with two retrospective chart reviews showing that age was not associated with patient satisfaction after MFU.[18, 19] Although previous studies have reported that younger patients are more likely to have a good outcome, no statistical analysis was performed in these studies.[17, 20]

The evaluation using F-RAY was more sensitive, because the fluctuations of the skin surface can be evaluated more delicately with the aid of contour lines.[21] In addition, this device minimizes ambient light interference by using a blackout curtain and takes standardized photographs at a consistent angle by using cephalostats for the forehead and chin. It is also non-invasive; thus, it will be useful for the precise evaluation without any inconvenience. Our study had several limitations. Similar to other retrospective chart review studies, it is possible that there were unmeasured confounding factors, such as patient compliance. In addition, extent of fat bulging was not quantitatively measured. However, for more reliable results, we combined the scores of three independent dermatologists and also evaluated using F-RAY.

In conclusion, our results suggest that the new treatment protocol of MFU is effective and safe for lower eyelid fat bulging regardless of age and sex. Clinicians could consider additional MFU is effective and safe for

lower eyelid fat bulging regardless of age and sex. Clinicians could consider additional MFU sessions if the improvement is not apparent after the first treatment.

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