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Peripheral Nerve

Assessing the Relationship between Obesity and Trigger Point-specific Outcomes after Headache Surgery

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Background: Trigger point deactivation surgery is a safe and effective treatment for properly selected patients experiencing migraine, with 68.3%–100% experiencing symptom improvement postoperatively. However, it is still unknown why certain patients do not respond. Obesity has been shown to be associated with worsened migraine symptoms and a decreased response to select pharmacotherapies. This study aimed to determine whether obesity may also be associated with an attenuated response to surgery.
Methods: A retrospective chart review was conducted to identify patients who had undergone trigger point deactivation surgery for migraine. Patients were split into obese and nonobese cohorts. Obesity was classified as a body mass index of 30 or higher per Centers for Disease Control and Prevention guidelines. Outcomes and follow-up periods were determined with respect to individual operations. Outcomes included migraine attack frequency, intensity, duration, and the migraine headache index. Differences in demographics, operative characteristics, and operative outcomes were compared.
Results: A total of 62 patients were included in the study. The obese cohort comprised 31 patients who underwent 45 total operations, and the nonobese cohort comprised 31 patients who underwent 34 operations. Results from multivariable analysis showed no impact of obesity on the odds of achieving a more than 90% reduction in any individual outcome. The overall rates of improvement (≥50% reduction in any outcome) and elimination (100% reduction in all symptoms) across both cohorts were 89.9% and 65.8%, respectively.
Conclusion: Obese patients have outcomes comparable to a nonobese cohort after trigger point deactivation surgery for migraine. *(Plast Reconstr Surg Glob Open 2024; 12:e5629; doi: 10.1097/GOX.0000000000005629; Published online 14 March 2024.)*

INTRODUCTION

Migraine is the second leading cause of years lived with disability worldwide.[1] In the United States alone, 21% of women and 10.7% of men are affected, and related expenses cost close to $20 billion annually.[2–4] Moreover, pharmacologic intervention remains insufficient for 5.1% of patients experiencing "refractory migraine attacks," who thus require novel methods to provide symptom relief.[5,6]

The advent of trigger point deactivation surgery has offered migraine patients another option. Originally pioneered by Dr. Bahman Guyuron in 1999, these procedures address focal locations of peripheral nerve compression, known as trigger points, that are thought to cause migraine attacks via extracranial inflammation.[7] Several meta-analyses and literature reviews published over the last decade have corroborated their considerable and reproducible success in addressing migraine symptoms across all established trigger points.[8–13] Recently, a 2022 meta-analysis reviewing 35 studies reported symptom improvement in 68.3%–100% in patients.[14] Despite the significant majority finding benefit, a subset of patients do not respond, and knowledge on factors associated with surgical failure is currently lacking.

The association between obesity and migraine has been previously investigated.[15] Large-scale systematic

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reviews and meta-analyses have collectively suggested an increased risk of developing migraine in obese patients compared with healthy weight individuals.[16–18] Furthermore, obese patients were found to experience increased attack frequency, severity, duration, and resulting disability.[19–21] Of considerable interest, obese patients have previously demonstrated reduced response rates to multiple medical therapeutics for the treatment of migraine, thus raising the question of whether obesity might also be associated with a reduced response to surgical management.[22–24]

In this study, we aimed to evaluate whether obese patients experience differential outcomes compared with nonobese patients following trigger point deactivation surgery for migraine treatment. The results of this study will help to better understand which patient factors might prognosticate an attenuated response to surgical management.

METHODS

Patient Selection and Characteristics

After obtaining institutional review board approval, a retrospective chart review was performed on all patients who had undergone trigger point deactivation for the treatment of migraine performed by the senior author (J.E.J.) from October 31, 2014, through November 2, 2022. Patients were selected for surgery based on a neurologist-confirmed migraine diagnosis, previously identified trigger points, migraine symptoms, and the extent of migraine impact on patient quality of life. Patient characteristics were collected at the time of initial presentation, including demographics, tobacco use, history of head or neck injury, and medical comorbidities, including hypertension, hyperlipidemia, diabetes mellitus, cardiovascular disease, depression, and anxiety. Body mass index (BMI) documented within 2 months of initial presentation was also collected. Patient cohorts were defined as nonobese (BMI <30) and obese (BMI ≥30) according to the Centers for Disease Control and Prevention criteria. Before undergoing surgery, baseline headache characteristics were recorded. This included migraine attack frequency (number of migraines per month), migraine attack intensity (1–10), and migraine attack duration (fraction of 24 hours). A baseline migraine headache index (MHI) was calculated by multiplying together frequency, intensity, and duration values. The maximum possible MHI score was 300, representing a 24-hour headache of maximum intensity that occurs every day of the month (predefined as 30 days). If a patient had any additional operation(s), each surgery was included separately. A new set of baseline migraine characteristics specific to each additional operation was recorded. If the patient could not localize baseline migraine characteristics to the specific trigger points targeted in any respective operation, that operation was excluded. Furthermore, any patient who did not have at least 3 months of follow-up or failed to complete all associated questionnaires and forms was excluded from analysis.

Takeaways

Question: Is obesity associated with differential outcomes following headache surgery?

Findings: Obesity was not associated with differential changes in headache frequency, severity, or intensity following surgical intervention when compared with nonobese patients.

Meaning: Despite the biological link between obesity and migraine headaches that increases susceptibility to headache incidence and severity, surgical deactivation of extracranial nerve compression still provides therapeutic relief for properly selected patient regardless of obesity status.

Trigger Point Deactivation Surgery and Postoperative Outcomes

Selected patients underwent trigger point deactivation through local resection or ablation of muscle, fascia, bone, or vessels surrounding the nerve. If a patient had multiple operations, follow-up was tracked according to individual operations. A follow-up of at least 3 months was required for each respective operation. Staged operations, usually no less than 3 months apart, occurred for patients with multiple trigger points diagnosed at frontal, temporal, and occipital locations so that these could be performed as separate outpatient operations not requiring multiple position changes. If pain recurred at a trigger point previously addressed through surgery, any additional operation to address this pain was considered a revision surgery. If postoperative pain developed at a new trigger point that was not previously addressed during the index surgery, this new source of pain was defined as a secondary trigger point after meeting appropriate diagnostic criteria.[25] Postoperative migraine characteristics were recorded for each operation at most recent follow-up. If the patient could not localize postoperative migraine characteristics to the specific trigger points targeted in any respective operation, that operation was excluded.

To determine whether there was a significant difference in surgical outcomes between groups, the percentage change in each individual migraine characteristic (frequency, intensity, duration, and MHI) from baseline to postoperative follow-up was calculated. Regarding overall surgical success, elimination was defined as the complete resolution of symptoms, improvement was defined as a decrease of greater than or equal to 50% in any individual migraine characteristic, and failure was defined as a decrease of less than 50% in all aforementioned migraine characteristics.[26] Additionally, a response of greater than 90% was also tracked in light of previous literature demonstrating that surgical response is an "all or nothing" phenomenon in which patients either achieve a significantly favorable or minimal response to surgery.[27]

Statistical Analysis

Descriptive statistics were used to characterize the overall study population. Demographic, clinical, and operative characteristics along with postoperative migraine outcomes were summarized by cohorts. Means with SDs or medians with interquartile ranges were used for continuous variables, and frequencies and proportions were used for categorical variables. Continuous variables were compared with a two-sample *t* test or Wilcoxon rank sum test, and categorical variables were compared using either a chi-square or Fisher exact test, where appropriate. Mixed-effects logistic regression was used to evaluate the impact of obesity on the odds of achieving a greater than 90% postoperative reduction in outcomes. Four separate models were performed for each postoperative migraine characteristic (frequency, intensity, duration, and MHI). Obesity, sex, and age were included as fixed effects in the model, and patients were included as a random effect to account for the correlation between repeated operations performed on the same patient. Statistical analyses and plots were performed using SAS 9.4 (SAS Institute, Inc.; Cary, N.C.) and R version 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 62 patients who underwent 79 operations were included in the study. The obese cohort comprised 31 patients who underwent 45 operations, and the nonobese cohort comprised 31 patients who underwent 34 operations. The obese cohort had a significantly higher proportion of women (90.3% versus 67.7%, $P = 0.029$) and an earlier average age of presentation (42.0 ± 11.5 versus 49.2 ± 13.4, $P = 0.026$) than the nonobese cohort. No significant differences were found between groups in mean age of migraine onset (25.4 ± 14.6 for nonobese versus 25.7 ± 15.1 for obese, $P = 0.932$), race (93.5% versus 100% White, $P = 0.492$), active tobacco usage at presentation (19.4% versus 16.1%, $P = 0.740$), history of head or neck injury (71.0% versus 58.1%, $P = 0.288$), or any of the tracked comorbidities. Although obese patients had a longer median follow-up, this difference was not significant (16 versus 12 months, $P = 0.136$). These results are summarized in Table 1. Note that all patients who had active nicotine use were required to have complete nicotine abstinence for 30 days before and after any operation, confirmed by objective urine and/or blood tests.

When comparing surgical data between cohorts, a higher proportion of obese patients was found to undergo multiple operations compared with nonobese patients (35% versus 10%, respectively, $P = 0.031$). The overall distribution of the number of trigger points addressed per patient was also significantly different between groups ($P = 0.046$) as seen in Table 1. Additionally, 4.4% of operations on obese patients were revision operations while zero nonobese patients required revisions. Moreover, 13.3% of operations on obese patients were conducted to address secondary trigger points compared with 2.9% of the nonobese cohort, and 13.3% of operations on obese patients were staged operations compared with only 5.9% of the nonobese cohort. An overview of these results is presented in Table 2. The distribution of the specific trigger points addressed across operations was similar between both cohorts, as illustrated in Figure 1. The three most common trigger points addressed in nonobese patients were the auriculotemporal (55.9%), occipital (44.1%), and frontal (29.4%) locations. The three most common trigger points addressed in obese patients were the occipital (51.1%), auriculotemporal (35.6%), and frontal (24.4%) locations.

Migraine characteristics, including frequency, intensity, duration, and MHI, seemed to be similar between both groups both at baseline presentation (Fig. 2) and at postoperative follow-up (Fig. 3). Additionally, the percentage change summaries of all migraine characteristics after operative intervention seemed to be similar across cohorts (Table 3). The overall rates of improvement (≥50% reduction in any migraine characteristic) and elimination (100% reduction) across both cohorts were 89.9% and 65.8%, respectively. Results from the multivariable analysis showed no impact of obesity, sex, or age on the odds of achieving a more than 90% reduction in any individual migraine outcome (Table 4).

Table 1. Patient Demographics and Characteristics by Cohort

	Nonobese n = 31	Obese n = 31	*P*
Age at presentation ± SD, y	49.2 ± 13.4	42.0 ± 11.5	0.026*
Age of migraine onset ± SD, y	25.4 ± 14.6	25.7 ± 15.1	0.932
Female, n (%)	21 (67.7)	28 (90.3)	0.029*
White race, n (%)	29 (93.5)	31 (100)	0.492
BMI ± SD	24.7 ± 3.3	37.9 ± 7.4	<0.001*
Tobacco use at presentation, n (%)	6 (19.4)	5 (16.1)	0.740
History of head or neck injury, n (%)	22 (71.0)	18 (58.1)	0.288
Comorbidities, n (%)			
Hypertension	8 (25.8)	12 (38.7)	0.277
Hyperlipidemia	2 (6.5)	5 (16.1)	0.425
Diabetes mellitus	2 (6.5)	3 (9.7)	0.999
Cardiovascular disease	10 (32.3)	6 (19.4)	0.246
Depression	13 (41.9)	15 (48.4)	0.610
Anxiety	3 (9.7)	9 (29.0)	0.054
No. operations per patient, n (%)			0.031*
1	28 (90%)	20 (65%)	
≥2	3 (10%)	8 (35%)	
No. trigger points per patient, n (%)			
1	14 (45%)	11 (35%)	0.046*
2	8 (26%)	11 (35%)	
3	7 (23%)	1 (3%)	
4	2 (6%)	5 (16%)	
5	0 (0%)	3 (10%)	

*Significant.

Table 2. Surgical Data with Reasons for Additional Operations on Patients Who Received Multiple Operations

	Nonobese (n = 34)	Obese (n = 45)
Revision surgery, n (%)	0 (0)	2 (4.4)
Additional staged surgery, n (%)	2 (5.9)	6 (13.3)
Surgery to address secondary trigger point, n (%)	1 (2.9)	6 (13.3)
Follow-up (mo), median (IQR) [range]	12 (8–21) [3–66]	16 (9–32) [3–92]

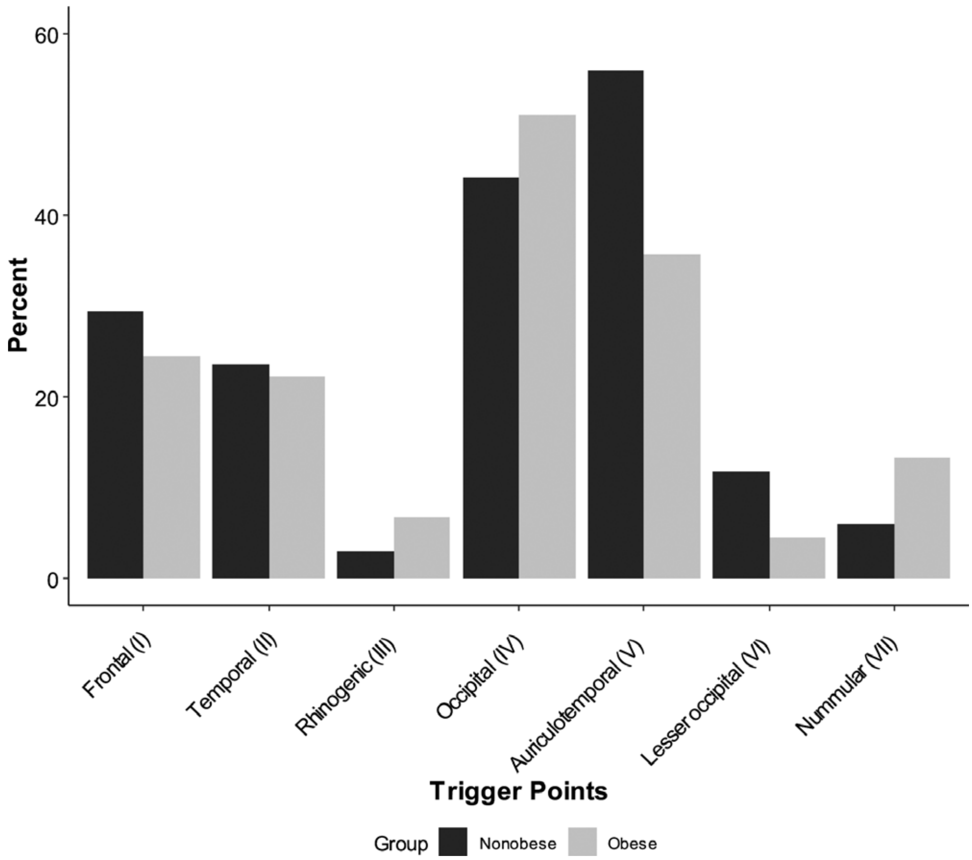

Fig. 1. Percentage of operations that addressed each respective trigger point by cohort.

DISCUSSION

The aim of this study was to investigate the association between obesity and surgical outcomes following trigger point deactivation for the treatment of migraine. The key result was that obesity status did not impact the odds of achieving a more than 90% reduction in any individual outcome. Additionally, 78% of all patients experienced a more than 90% postoperative reduction in MHI; 13% of patients, a reduction ranging from 10% to 90%; and 9% of patients, a reduction of less than 10%. These results resemble those from a previous study by Gfrerer et al, in which 69% of patients who underwent trigger point deactivation surgery experienced an 80% reduction or more in MHI; 17%, a reduction ranging from 5.1% to 79.9%; and 14%, a reduction of 5% or less (total n = 83).

The overall rates of improvement (≥50% reduction in any migraine characteristic) and elimination (100% reduction in all symptoms) in this study were 89.9% and 65.8%, respectively. According to a 2022 meta-analysis of trigger point deactivation outcomes by ElHawary et al, rates of improvement from 35 studies in the literature have ranged from 68.3% to 100%, and rates of elimination have ranged from 8.3% to 86.5%, thus placing our outcomes near the higher ends of both spectrums.[14] This could, in part, be due to our novel approach in tracking outcomes and follow-up periods with respect to individual trigger point operations rather than individual patients. This was conducted in consideration that patients may require multiple operations over time, and the evaluation of outcomes in total without context on clinical history or pain localization may obscure the true efficacy of individual operations. The development of secondary trigger points is a key topic of discussion in this regard. Punjabi et al previously reported that, after trigger point deactivation surgery performed on 185 patients, 17.8% developed trigger points at new locations during follow-up.[28] Further authors have acknowledged that tracking outcomes for a given surgery without appropriately accounting for this secondary trigger point pain may lead to reductions in reported surgical improvements.[27,29] Additionally, in our practice, select patients presenting with multiple trigger points spanning the occipital, temporal, and frontal regions are approached through staged operations performed three months apart. Thus, to comprehensively evaluate treatment efficacy with regard to specific trigger points, we have aimed to separate the outcomes of each surgery for a given patient.

Regarding past investigations on the relationship between trigger point deactivation surgery and obesity, the literature is sparse. Larson et al previously found no significant differences in BMI among three cohorts split by symptom elimination, improvement, and failure when they attempted to identify patient factors predictive of response to headache surgery.[30] Although our results corroborate these findings, there is limited other

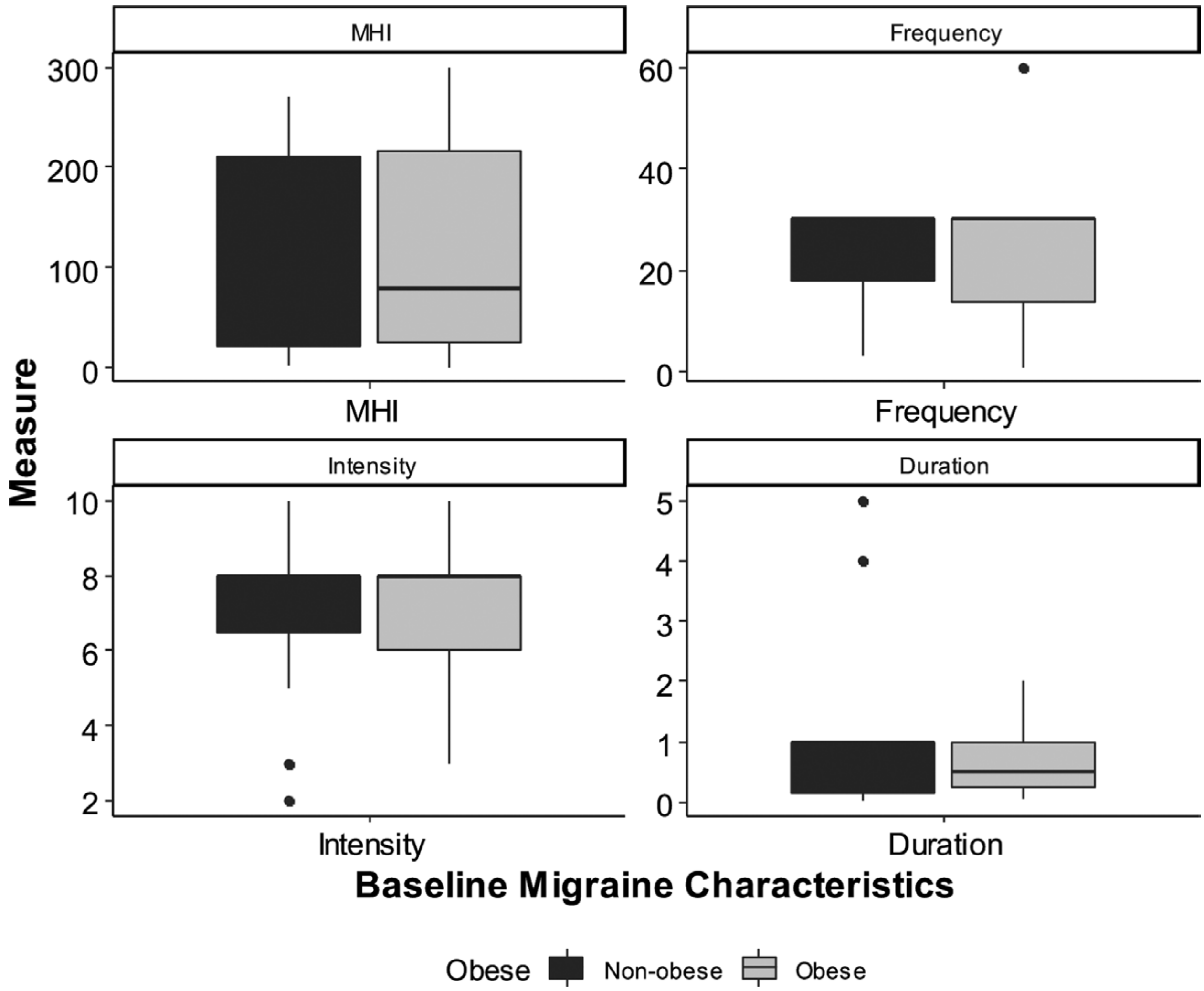

Fig. 2. Distribution of migraine characteristics at baseline compared across cohorts.

surgical literature to provide more context. When considering further perspective from the neurology literature, Afshinmajd et al previously found that obese patients experienced an attenuated response to nortriptyline and propranolol following an eight-week study period.[22] Similarly, in a large prospective study, obesity was found to be associated with lower response rates to monoclonal antibodies targeting the calcitonin gene related peptide, a salient player in the development of migraine pathology.[23] Even in the setting of episodic migraine, obese patients have been shown to have decreased pain relief after abortive triptan intake compared with nonobese counterparts.[24] Thus, these studies collectively underscore an association between obesity and the degree of patient response to select medical therapeutics for migraine.

Several biological links between obesity and migraine may explain this observed phenomenon. Previous investigations have revealed a common dysfunction of the hypothalamus and its associated neurotransmitters,[31] and both conditions have been noted to share key proinflammatory mediators, such as interleukin-6, tumor necrosis factor-alpha, and leptin.[32–34] Furthermore, obesity has also been shown to alter dural levels of calcitonin gene related peptide and modulate estrogen metabolism, both of which have been linked to migraine pathology.[35–38] Interestingly, however, the results of our study do not reflect an influence of this shared pathology. Compared with the differential responses reported after medication use, the present inconsistency begs the question whether a unique relationship between obesity and trigger point deactivation surgery exists, and if so, why?

In a recent 2022 study, Chen et al reported that patients with menstrual-related migraine had no difference in surgical outcomes compared with those with migraine unrelated to menstruation.[29] The authors speculated that while estrogen may biologically prime extracranial nerve inflammation, extrinsic compression of these susceptible nerves was a necessary complement to elicit symptom manifestation. This explanation aligns with the working theory that migraine pathology exists on a spectrum of both central and peripheral instigators.[10] Considering that patients from both cohorts were equally likely to respond to surgery, the diagnostic algorithm for surgical candidacy

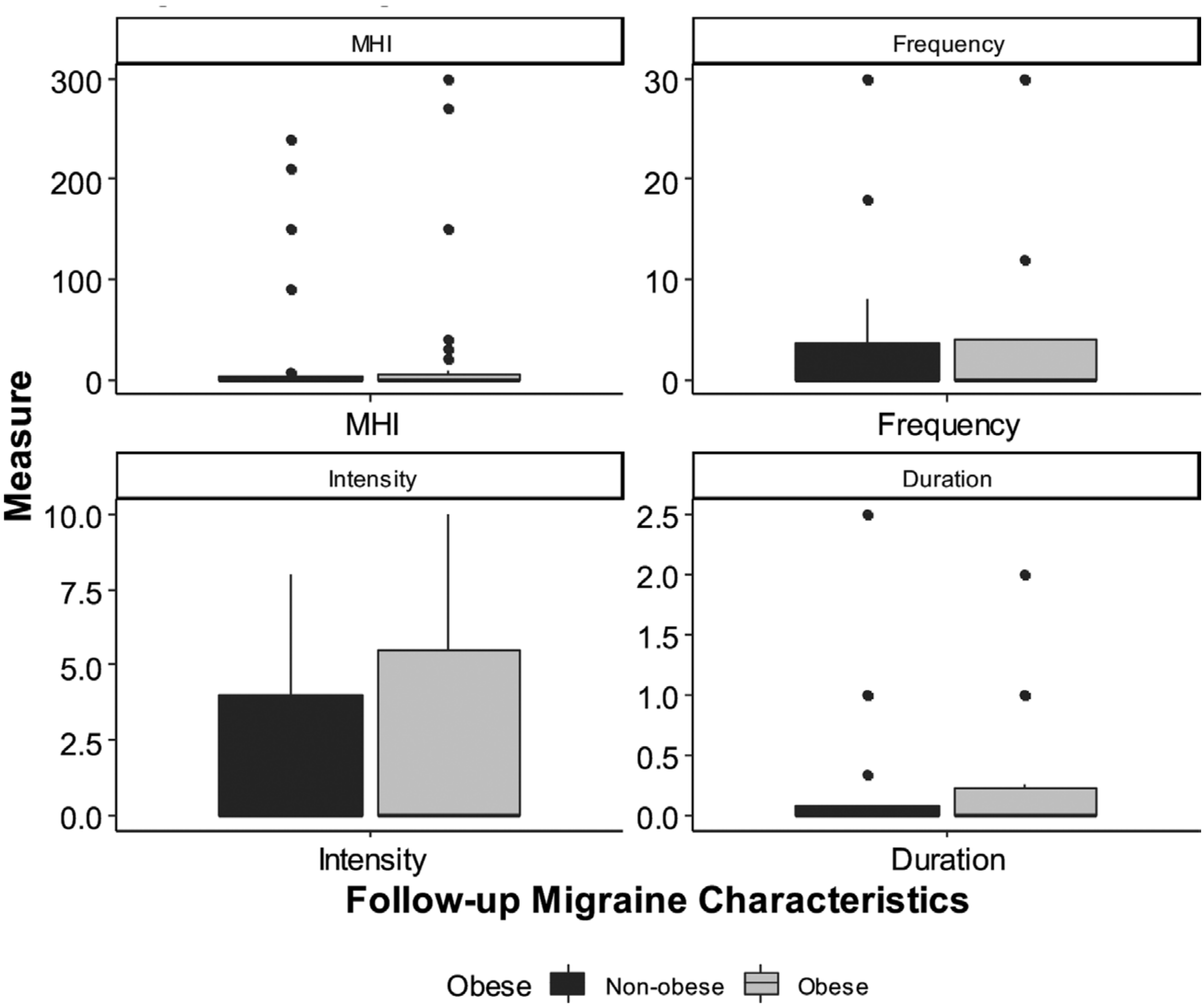

Fig. 3. Distribution of migraine characteristics at most recent follow-up compared across cohorts.

may ultimately select for patients with peripheral pathology that is amenable to surgical deactivation regardless of further migraine contributors.[39] By this logic, we hypothesize that in our study, while the proinflammatory mechanisms upregulated in obesity may have predisposed patients to developing migraine, trigger point deactivation surgery was equally sufficient to provide relief across cohorts because it neutralized the common peripheral insult required for symptomatic provocation.

This hypothesis is further supported by the current finding that sex also had no impact on the odds of achieving a more than 90% reduction in any surgical outcome. Similar to the context of obesity, previous neurological studies have demonstrated sexually dimorphic differences in migraine symptoms and medical treatment responses.[40,41] Similarly as well, biological links have been identified that may explain these observations, including baseline differences in sex hormone concentrations between men and women,[42,43] underlying epigenetic signatures susceptible to environmental modulation,[44,45] and psychosocial differences in coping strategies and pain perception.[46] Nonetheless, neither our study nor previous surgical investigations have found an association between sex and operative outcomes,[26,30,47–49] and this could again be plausibly explained by the presence of extracranial pathology in patients, regardless of sex, that is both necessary for symptom onset and amenable to surgical deactivation. Although this remains evidenced-based theorization, our current results ultimately indicate that neither sex nor obesity is associated with outcomes after trigger point deactivation surgery. Of note, there was still an appreciable subset of patients (10.1%) who either failed operative management or improved only marginally, and further research is necessary to better identify predictive variables.

Interestingly, the obese cohort presented significantly earlier for evaluation compared with the nonobese cohort despite having a similar mean age of onset and similar symptom severity at baseline. Previous literature has shown that general populations of obese patients have higher health care utilization rates than nonobese patients, including a higher number of primary care physician visits.[50] One explanation for the earlier age of presentation witnessed in this study could thus be higher exposure to medical providers that would offer more opportunity to vocalize

Table 3. Distribution of Operations according to Percentage Change from Baseline to Follow-up

	Nonobese (n = 34)	Obese (n = 45)	Total (n = 79)
MHI			
<10%	2 (6%)	5 (11%)	7 (9%)
10–49.9%	3 (9%)	0 (0%)	3 (4%)
50–90%	3 (9%)	4 (9%)	7 (9%)
>90%	26 (76%)	36 (80%)	62 (78%)
Frequency			
<10%	6 (18%)	6 (13%)	12 (15%)
10–49.9%	1 (3%)	0 (0%)	1 (1%)
50–90%	1 (3%)	7 (16%)	8 (10%)
>90%	26 (76%)	32 (71%)	58 (73%)
Intensity			
<10%	6 (18%)	12 (45%)	18 (23%)
10–49.9%	3 (9%)	0 (0%)	3 (4%)
50%–90%	2 (6%)	4 (9%)	6 (8%)
>90%	23 (68%)	29 (64%)	52 (66%)
Duration			
<10%	6 (18%)	8 (18%)	14 (18%)
10–49.9%	1 (3%)	2 (4%)	3 (4%)
50%–90%	3 (9%)	4 (9%)	7 (9%)
>90%	24 (71%)	31 (69%)	55 (70%)

Table 4. Multivariable Analysis Assessing the Impact of Obesity, Sex, and Age on the Odds of Achieving a >90% Postoperative Reduction in Each Migraine Characteristic

	OR (95% CI)	*P*
MHI		
Obese versus nonobese (ref)	0.90 (0.2–4.4)	0.888
Age	0.99 (0.9–1.1)	0.785
Female versus male (ref)	2.10 (0.4–11.4)	0.369
Frequency		
Obese versus nonobese (ref)	0.55 (0.1–2.3)	0.392
Age	1.00 (1.0–1.1)	0.872
Female versus male (ref)	1.67 (0.3–8.4)	0.510
Intensity		
Obese versus nonobese (ref)	0.62 (0.2–2.4)	0.455
Age	1.00 (0.9–1.0)	0.892
Female versus male (ref)	0.93 (0.2–4.4)	0.924
Duration		
Obese versus nonobese (ref)	0.63 (0.2–2.5)	0.488
Age	0.99 (0.9–1.0)	0.711
Female versus male (ref)	1.18 (0.2–5.8)	0.831

their headache symptoms. Ultimately, this process is likely multifactorial and may include a higher general awareness of medical symptoms and a difference in threshold to seek medical assistance for obese patients; however, a definitive explanation is currently inconclusive.

One primary limitation is that we included any operation with at least three months of follow-up, which is recognized as the initial period necessary to evaluate surgical efficacy. However, it is not until the 1-year time point that surgical response stabilizes and reflects long-term outcomes at 5 years.[51] Additionally, the current study is limited by the number of operations excluded because either pre- or postoperative trigger point-specific migraine characteristics could not be determined. This was most frequently due to either absences in documentation or overlapping pain distributions that precluded patient ability to attribute symptoms to specific trigger points. Also, our analytical power was limited by the sample size and the necessity to account for multiple operations performed on the same patient. Thus, additional comparisons of significance across patient characteristics were restricted. In addition, further confounding variables, such as seasonal changes experienced during follow-up that may trigger migraine attacks for some patients, were not controlled for. Finally, this study represents a single surgeon's experience on a predominantly White, female population, which reduces external generalizability. Future studies should aim to have larger sample sizes, longer follow-up, prospective patient enrollment, and outcome evaluation with respect to individual operations to further build upon the preliminary findings presented in this study.

CONCLUSIONS

This retrospective study is the first to demonstrate that obesity status is not associated with outcomes after trigger point deactivation surgery for the treatment of migraine. Furthermore, tracking outcomes with respect to individual operations for patients undergoing multiple operations allows for a more nuanced and complete accounting of surgical efficacy. Future studies should utilize a similar approach with follow-up past 1 year to further investigate obesity and other potential prognosticators of a null response following surgery.

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DISCLOSURES

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