Trigger Site Deactivation Surgery for Chronic Headaches: An Investigation Into Postoperative Outcomes

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Trigger Site Deactivation Surgery for Chronic Headaches: An Investigation into Postoperative Outcomes

by

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Abstract

Background

Chronic migraine is a debilitating condition that affects millions of patients. Trigger site deactivation surgery has evolved as an effective treatment for some patients living with refractory chronic headache pain. To improve patient selection and preoperative counseling for surgery, it is critical to understand the expected outcomes of surgery. This study aims to investigate the postoperative outcomes of trigger site deactivation surgery and explore if any preoperative variables, such as history of head injury or pain patterns, are predictive of postoperative results.

Methods

142 patients undergoing trigger site deactivation surgery were prospectively enrolled. Preoperatively, patients were asked to complete a questionnaire on headache history, including the Migraine Headache Index (MHI), information on prior head or neck injury, medication history, and psychiatric comorbidities. Patients were also asked to illustrate their pain using standardized pain pattern forms. Diagrams were analyzed and categorized by two independent, blinded reviewers: 1) Typical- pain over the distribution of a nerve with expected radiation 2) Intermediate- pain over the distribution of the nerve with atypical radiation 3) Atypical- pain outside of normal nerve distribution and atypical radiation. The senior author performed all surgical procedures. Follow up surveys were sent to all patients at twelve months postoperatively.

Results

Of the subjects included in this study, 50% (n=71) reported a history of head or neck injury, and 30% (n=42) classified the injury as the precipitating event leading to their MH. There was no

significant difference in mean preoperative migraine symptoms between patients with an injury versus those without. At twelve months postoperatively, there was a significant decrease in migraine symptoms, medication use, and depressive symptoms. There was no significant difference in postoperative migraine symptoms among patients with head or neck injury versus those without. Patients with atypical pain patterns had significantly poorer postoperative outcomes than patients with typical and intermediate pain patterns.

Conclusions

This study provides several in-depth analyses on the postoperative outcomes of trigger site deactivation surgery and variables which affect postoperative outcomes. We demonstrated that 1) patients with head or neck injury achieve successful postoperative outcomes, 2) atypical pain patterns are associated with inferior outcomes, and 3) surgery is associated with decreased medication use and improved depressive symptoms. It is important for surgeons to be aware of this data as we continue to refine our approach to trigger site deactivation surgery.

Glossary

AT: auriculotemporal

GAD: generalized anxiety disorder

GON: greater occipital nerve

LON: lesser occipital nerve

MDD: major depressive disorder

MH: migraine headache

MHI: migraine headache index

MVA: motor vehicle accident

PE: precipitating event

PHQ-2: patient health questionnaire-2

PSEQ: pain self-efficacy questionnaire

SD: standard deviation

SON: supraorbital nerve

STN: supratrochlear nerve

ZT: zygomaticotemporal nerve

Introduction

Migraine headaches (MH) affect approximately 28 million people in the United States and cost an estimated 11 billion dollars to the healthcare system annually, not including indirect costs from reduced productivity and missed workdays[1,2]. Trigger site deactivation surgery, or "headache surgery", has evolved as an effective method to alleviate pain in some patients suffering from refractory chronic headaches[3-9]. Trigger site deactivation surgery relies on the notion that the development of chronic headaches may involve irritation of craniofacial peripheral nerves. Although the pathophysiologic relationship between extracranial nerves and headache development has not been fully elucidated, current evidence suggests that a subgroup of headache patients may be suffering from neuralgia caused by compression or irritation of extracranial peripheral nerves, which acts as a trigger for migraine headache (MH) and other chronic headaches[4,10-16]. Prior clinical and cadaveric studies have identified several craniofacial nerves and potential points of compression, including the frontal, temporal, occipital, and rhinogenic trigger sites[11,12,16-20]. Trigger site deactivation surgery aims to alleviate headache pain by decompression or avulsion of the involved nerve at these sites.

While not all headache patients may be candidates for surgical treatment, the literature suggests that surgical treatment is effective. In a systematic review of 1253 patients, 86 percent reported at least a 50 percent reduction in the duration, intensity, or frequency of their headaches[21]. Results have been replicated across international groups and have included three randomized controlled trials, including one randomized, blinded, sham-surgery trial[3,4,22]. Studies have also shown that surgery is associated with improvements in the quality of life and activities of daily living[23,24]. Further, surgery is cost effective by reducing both direct and indirect healthcare costs associated with chronic headache[23].

Successful surgery relies heavily on the selection of appropriate candidates, identification of all headache trigger sites, and preoperative counseling. To improve patient selection and preoperative counseling for surgery, it is critical to elucidate the expected outcomes of surgery, both for general headache patients and for specific populations of headache patients.

This study aims to investigate the postoperative outcomes of trigger site deactivation surgery and explore which preoperative variables are associated with outcomes. While previous studies have focused on investigating the efficacy of surgery in improving pain, daily function, quality of life, and reducing costs, this study aims to investigate the following: 1) the effect of head or neck injury on postoperative outcomes, 2) the predictive ability of preoperative pain patterns, 3) the impact of surgery on medication use, and 4) the relationship between psychiatric variables and surgery.

Head or Neck Injury

Patients suffering from chronic headaches report a high prevalence (up to 49%) of prior head or neck injury[25-27]. Epidemiological and prospective studies in patients with head or neck injuries have supported this association, suggesting that the risk of chronic headache increases after suffering a head or neck injury[25,26,28-31]. The International Classification of Headache Disorders edition three (ICHD-3) categorizes posttraumatic headaches as secondary headaches which begin within seven days after an injury or upon regaining consciousness[32]. In this regard, "posttraumatic headache" is an umbrella term that encompasses multiple primary headache subtypes including MH[29].

Patients suffering from posttraumatic MH are traditionally treated with prescription medications. However, standard medical treatment of posttraumatic MH fails to effectively treat the majority of patients, with only 35% of patients achieving greater than a 50% reduction in headache frequency[33,34].

The surgical deactivation of peripheral trigger sites has provided effective relief for select headache patients failing conservative medical therapy[3,4,6,7,10,35]. Preliminary studies suggest that surgery is effective in the posttraumatic headache population[36,37]. However, these studies are limited by their small sample size, retrospective design, lack of validated outcome measures, and no direct comparison to patients without a history of head or neck injury. As such, this study aims to describe the characteristics of headache surgery patients with a history of head or neck injury and compare their postoperative outcomes to patients without a history of head or neck injury.

Predictive Ability of Pain Patterns

Several different screening tools including headache history, physical exam, validated MH questionnaires and imaging studies are available to aid in choosing suitable surgical candidates. However, verbal communication with the patient and written information in the form of questionnaires often does not accurately reflect complex pain patterns. In our experience, pain sketches that depict where the pain starts and to where it radiates are a superior patient-reported method of visualizing pain and identifying nerve trigger sites.

Pain sketches have been used as an easy and inexpensive tool to illustrate pain in different acute and chronic conditions[38,39]. Furthermore, clinical research in patients undergoing spine surgery has demonstrated that pain sketches predict surgical outcomes for lumbar radiculopathy[40,41].

In our MH surgery headache patient population, we have found that there are pathognomonic pain sketch patterns for each trigger site that correspond with the anatomic location of affected nerves. Typically, we do not operate on patients with abnormal pain sketches, because in our experience they are not good candidates for surgery and do not display good outcomes after surgery. Only a small group of patients with abnormal patterns have undergone surgery if there were other strong clinical indications that surgery could be beneficial. This study describes the different pain patterns headache patients present with and investigates whether pain pattern sketches can predict surgical outcomes following trigger site deactivation surgery.

Medication Use

There has been a paucity of studies investigating medication use in MH surgery patients. As physicians caring for MH patients, we must know the disease and its therapies beyond surgery. Pharmaceutical management is an important component of MH and previous data have suggested that the drugs a patient takes can affect surgical outcomes[42].

Broadly speaking, migraine medications can be divided into acute and preventative categories. Acute medications can be further subdivided into abortive, rescue, and anti-emetic. The vast majority of MH patients use medication[43]. However, the response to individual treatments is idiosyncratic and drugs that work well in one patient, may not work in another[44]. The varying effectiveness of medications often leads MH patients to rely on polypharmacy. Overuse of medications, particularly abortive and rescue, can lead to worsening of pain and a separate entity known as medication overuse headache[45]. This can result in endless cycles of pain, medication, and further pain.

To improve preoperative counseling for MH surgery, it is critical to understand expected outcomes, including change in medication use. Thus, another aim of this study is to describe preoperative and postoperative medication use among patients undergoing MH surgery.

Headaches, Surgery, and Psychiatry

Prior studies have shown strong associations between psychiatric conditions and chronic headaches. Patients with chronic migraine are at increased risk for major depressive disorder (MDD), generalized anxiety disorder (GAD), and suicidal behavior when compared to patients without migraine[46-48]. Comorbid depression in patients with migraine is associated with an increased risk of suicide and more frequent and disabling headache episodes[49]. Lastly, migraine patients with MDD or GAD are more likely to suffer from refractory symptoms that respond poorly to available pharmacological management[50-53].

It is unclear which psychiatric comorbidities exist in patients undergoing trigger site deactivation surgery for chronic headache. Additionally, there have been limited studies to investigate the effect of surgery on psychiatric conditions, and vice-versa. Thus, a secondary aim of this study is to describe any psychiatric conditions present in this surgical population and to investigate if surgery is associated with any change in psychiatric variables.

Methods

This study was approved by the Massachusetts General Hospital (Boston, MA) Institutional Review Board. One hundred forty-two patients undergoing trigger site deactivation surgery between 2013 and 2018 were prospectively enrolled in this study. Inclusion criteria were defined as 1) a diagnosis of chronic headache by a neurologist and 2) failure of conservative management, defined as the failure of treatment with three or more different types of prescription medication. Exclusion criteria included an incomplete intake questionnaire at screening.

Preoperatively, patients were requested to complete a detailed headache history using REDCap (version 8.1.20, Vanderbilt University, Nashville, TN) electronic data capture tools hosted at the Massachusetts General Hospital[54]. Headache severity was quantified using the Migraine Headache Index (MHI), which was defined as the product of headache frequency (days per month), duration (fraction of 24 hours), and pain severity (rated from 0 to 10)[10].

Patients were instructed to draw a pre-operative pain sketch at screening (Supplemental Fig. 1). Patients drew where the pain originates in black or as a cross or dot, and where the pain radiates (if radiating pain present) in a different color, or with lines or arrows. Pain pattern diagrams were analyzed by two independent reviewers who were blinded to the identity of the patient, procedure performed, as well as the outcome of the patient as a result of the surgery. The reviewers had seven years and two years of clinical research experience, respectively. Pain diagrams were analyzed and categorized as: 1) Typical- Pain over nerve distribution, expected radiation pattern along anatomic nerve course 2) Intermediate: Not atypical, but does not follow the exact nerve distribution 3) Atypical-Pain outside of normal nerve distribution, atypical radiation pattern diverting from anatomic nerve course. Pain sketches did not substitute a preoperative visit or exam but were used as an adjunct to evaluate candidacy for surgery. Patients were not questioned about their sketches unless they had atypical features. No patients were excluded from preoperative assessment regardless of atypical pain sketch features. Patients with atypical sketches were only considered candidates for surgery if there was sufficient evidence on preoperative exam that an intervention may help their symptoms (identification of trigger sites on exam, improvement of pain after nerve block, positive Doppler and CT findings).

The Pain Self-Efficacy Questionnaire (PSEQ) was used to determine patients' pain coping abilities and function[55]. PSEQ scores below 30 suggest long-term disability and depression, whereas higher scores indicate better function. The Patient Health Questionnaire-2 (PHQ-2) was used to measure baseline and postoperative depressive symptoms across all patients[56]. Higher PHQ-2 scores suggest more depressive symptoms with a score of three or higher suggesting that major depressive disorder is likely. Information on medication use, including type, dose, and frequency of use was collected.

Information on prior head or neck injury was also collected. This included data specifying: the nature of the injury, timing in relation to headache onset, and a questionnaire assessing whether each patient attributes their headache pain to the specific trauma (precipitating event). No specific temporal relationship such as 7 days from the incident was required. The senior author (W.G.A) performed all surgical procedures using an open approach, as described in prior publications[5]. Patients were requested to complete follow-up surveys at approximately twelve months after the index surgery.

Prior studies suggest that patients who use prescription opioid medications to treat their headache pain have less favorable outcomes following surgery[42]. To evaluate the effect of preoperative opioid use as a confounding variable, additional analyses were performed in which patients who reported preoperative opioid use were excluded across groups.

Statistical Analyses

Data were analyzed with STATA Version 13.0 (StataCorp, College Station, Texas). Categorical variables were described using frequencies and percentages. We described continuous parametric variables using means and standard deviations (SD) and analyzed differences between groups, such as mean MHI of patients with an injury versus those without, using two-tailed T-tests. We expressed continuous non-parametric variables as medians and interquartile ranges (IQR) and analyzed them using the Wilcoxon rank-sum test. Associations between dichotomous variables, such as the presence of injury and achieving a 50% or greater reduction in MHI, were analyzed using the Chi-square and Fisher's Exact tests. Comparisons between paired dichotomous variables, such as the proportion of patients using daily medication preoperatively versus postoperatively, were performed using McNemar's Test. Statistical significance was set at $P<0.05$.

Results

Of the 142 patients who met inclusion criteria, 116 (82%) were female with an average age of 44 years (SD ±14 years). At the time of screening, 70 patients (49%) reported a history of previous head or neck injury. Forty-one (29%) classified the injury as the precipitating event (PE) leading to their headache. Fifty-nine (84%) of the 70 patients with an injury and thirty-two (78%) of the 41 patients with a PE stated that their injury required "medical treatment".

Although injury mechanism varied among patients, the most commonly reported were motor vehicle accident (MVA) with whiplash in 27 patients (39%), fall in 12 (17%), iatrogenic injury in 11 (16%), direct blunt trauma in five (7.1%), traumatic cervical disc herniation in four (5.7%), a diving accident in one (1.4%), and unspecified concussion in ten (14%). For patients who reported the injury as a PE, the injury mechanisms were: MVA in 14 patients (34%), iatrogenic in ten (24%), fall in six (15%), direct blunt trauma in three (7.3%), cervical disc herniation in one (2.4%), diving accident in one (2.4%), and unspecified concussion in six (15%).

Comparison of baseline characteristics between the atraumatic, traumatic, and PE cohorts yielded no significant differences in average age, gender, or PHQ2 score (Table 1). Patients with a PE were significantly less likely to report a family history of MH as compared to patients without a PE (49% versus 71%, P=0.012). Traumatic patients were significantly more likely to be taking prescription opioids preoperatively for their headache pain than atraumatic patients (38% versus 22%, P=0.035).

Among all patients, the average number of days with headaches per month was 19.0 (±9) days. Headaches lasted an average of 16 (±8) hours and were rated 7.7 (±1.4) on average on a ten-point pain scale. There were no significant differences between groups in preoperative MH frequency, severity, duration, MHI, or PSEQ (Table 2).

When asked to describe their pain patterns, 118 patients (83%) reported frontal site pain, 106 (75%) reported occipital site pain, and 95 (67%) reported temporal site pain. Patients reporting isolated occipital only pain were significantly more likely to report a history of injury (77% vs 47%, P=0.037) and PE (62% vs 26%, P=0.0060) as compared to patients reporting pain elsewhere. Patients with temporal pain were significantly less likely to report injury (43% vs 62%, P=0.038) and PE (23% vs 40%, P=0.033) as compared to patients reporting pain elsewhere.

One hundred and thirty-one patients completed a pain sketch at screening. One hundred and six patients (81.5%) had at least one year follow up and were included in the final analysis of pain patterns. Eighty-two patients (77%) were female and 24 (23%) were male. The mean age at surgery was 45 years (18-73). Typical (pain over nerve distribution, expected radiation pattern along anatomic nerve course), and atypical pain patterns (pain outside of normal nerve distribution, atypical radiation pattern diverting from anatomic nerve course) were present for each trigger site. Intermediate pain patterns (pain over nerve distribution, atypical radiation pattern diverting from anatomic nerve course) were present for all triggers except for the lesser occipital nerve site. Both reviewers graded 62 pain sketches as typical (59%), 31 as intermediate (29%) and 13 (12%) as atypical. Inter-rater reliability was 94.3% with a kappa of 0.8984.

For patients with typical and intermediate drawings, the triggers identified in pain drawings correlated with the clinical exam in 84% of cases (n=78). In 10 cases, the pain drawing identified both frontal and occipital trigger sites, but only either the frontal (n=5) or the occipital site (n=5) was confirmed on exam. In three other cases, the rhinogenic trigger site was not marked on the drawings but was confirmed on clinical exam. One patient marked all known trigger sites on the drawing, but only the AT site was confirmed. For patients with abnormal pain sketches, 77% (10/13) of sketches showed either diffuse pain or pain that did not correlate with specific trigger sites. Therefore, trigger site detection was based on clinical exam findings only. Three patient pain sketches displayed specific known trigger sites that correlated with the clinical exam. The drawings were classified as abnormal because patients also drew diffuse facial pain (cheek, jaw, anterior neck) that did not correlate with nerve distributions.

One hundred and one patients (71%) had surgery at the occipital trigger site, 66 (46%) at the frontal, 49 (35%) at the zygomaticotemporal, and 12 (8%) at the auriculotemporal site. All patients who underwent frontal surgery had supraorbital/supratrochlear nerve decompression, while all patients who underwent zygomaticotemporal and auriculotemporal nerve surgery underwent neurectomy. The greater occipital nerve was decompressed in all cases except in three (3%), in which a neurectomy was performed due to poor condition of the nerve. In patients with surgery at the lesser occipital nerve, 28 patients (80%) had neurectomy while seven patients (20%) had a decompression.

Postoperatively, there was a 70% (n=100) response rate to follow-up questionnaires. The median follow-up time was 12.9 months (IQR 11.8-15.2). Among all patients, there was a statistically significant decrease in headache frequency, duration, severity, MHI, and PSEQ (P<0.001 for all four variables). The average reductions in each of these variables were as follows: 12 (±11) headache days per month, 7.6 (±9.9) hours of duration per headache episode, and 2.9 (±3.3) in severity score. The average reduction in MHI was 75 (±93). The average increase in PSEQ score was 19 (±19).

Head/Neck Injury and Postoperative Outcomes

Upon stratifying these analyses by injury cohorts, all groups (atraumatic, traumatic, PE, non-PE) demonstrated a significant decrease in headache frequency, duration, severity, and MHI (P<0.001 across all analyses except duration and MHI for the PE cohort which were significant at P=0.014 and P=0.012, respectively). No significant differences in these four outcomes were found between groups (Tables 3 and 4). There were no significant differences in average PSEQ or PHQ-2 change between groups.

The proportion of patients experiencing a minimum of 50% and 80% improvement in MHI per group, respectively, was: 83% and 67% (atraumatic), 76% and 68% (traumatic), 71% and 63% (PE), and 84% and 70% (non-PE) (Table 5). There were no significant associations found between having an injury or a PE and achieving a 50% or 80% decrease in MHI. Differences in the mechanism of injury such as MVA or fall did not correlate with any significant differences in the proportion of patients who achieved 50% and 80% MHI reduction (P=0.23 and P=0.37, respectively). Additionally, we did not find that surgery at any specific trigger site in patients with a history of injury or PE was superior or inferior to surgery at other sites. The majority of patients with isolated occipital pain and a history of injury achieved a 50% MHI decrease (86%) and an 80% MHI decrease (71%). No significant differences between these outcomes and surgery at other sites were found.

There was no significant difference in preoperative MHI found between patients reporting opioid use and those not taking opioid medications (98±81 versus 118±98 points, P=0.20). Postoperatively, patients who reported opioid use had higher MHI scores (more severe symptoms) as compared to non-opioid users (53±78 versus 29±46 points, P=0.037). After excluding patients reporting preoperative opioid use, the proportions of patients experiencing at least a 50% and 80% improvement in MHI, respectively, were more similar across groups: 80% and 63% (atraumatic), 80% and 72% (traumatic), 80% and 73% (precipitating event), 80% and 65% (no precipitating event).

Pain sketch patterns

Occipital pain sketches

Greater occipital nerve (GON)

A typical pain sketch depicts the origin of pain at the occiput around 3cm below the occipital protuberance and 1.5cm lateral to the midline, which marks the point where the GON pierces the semispinalis muscle[57]. Pain usually radiates towards the forehead (Fig. 1, A) or to the eye (Fig.1, B).

Intermediate pain sketches show pain that originates at the exit point of the GON from the semispinalis muscle but does not radiate along the anatomic nerve distribution, or only partially radiates along the anatomic course of the nerve (Fig. 1, C).

Atypical GON pain patterns can be variable. Oftentimes, pain sketches depict pain over the posterior neck that is lower than expected and may radiate towards the spine, shoulders, or arms. Another atypical pattern is pain that does not start at a specific location but spreads diffusely across the occiput (See Fig. 1, D).

Lesser Occipital Nerve (LON)

Typically, lesser occipital pain is drawn further lateral and inferior as compared to the GON pattern with radiation towards the ear and temple (Fig. 1, E1). No intermediate sketches were identified for this trigger site. Atypical LON pain sketches show either diffuse pain in the back of the head or pain radiating towards the jaw or arms (Fig. 1, E2).

Greater and Lesser Occipital Nerve

The above pain patterns may be combined if both nerves are affected. Examples of typical (Fig. 1, F) and atypical (Fig. 1, G) GON/LON pain are demonstrated in Fig. 1.

Frontal/ temporal pain sketches

Frontal- Supraorbital and Supratrochlear nerve (SON, STN)

Typical frontal pain sketches demonstrate pain originating at or above the eyebrow radiating along the forehead (Fig. 2, A). Intermediate pain patterns start at the site of the nerve but may radiate in a large radius across the front of the head and/or around the eye (Fig. 2, B).

Atypical pain is drawn as broad pain across the forehead radiating across the face or in an atypical location (facial pain that is not located at or above the eyebrows, forehead or temples, around the eye) (Fig. 2, C).

Temporal- Zygomaticotemporal (ZT) and Auriculotemporal (AT) nerves

Both ZT and AT pain is typically drawn at the temple. AT pain usually occurs superolateral to ZT pain in the hair-bearing area of the scalp, but patients oftentimes consider both types of pain to occur at the temple (Fig. 2, D). Intermediate pain patterns originate at the temple and radiate to an unusual location such as the vertex (Fig. 2, E).

Atypical pain is drawn at the temple, with no distinct starting point and is drawn diffusely (Fig. 2, F).

Frontal and temporal pain

Oftentimes, frontal (SON/ STN) and temporal pain occurs simultaneously. Typical combined pain is drawn as starting at both frontal and temporal sites and radiating across the forehead (Fig. 2, G).

Intermediate pain patterns originate at the site of both nerves but radiate in a large radius across the front of the head or to an abnormal location (Fig. 2, H). Atypical combined patterns have no distinct starting point, but instead multiple starting points across the face with diffuse radiation (Fig. 2, I).

Multi- Trigger Pain Sketches

Multi trigger pain sketches display the pain origin at typical trigger locations with radiation along the expected anatomic nerve distribution (Fig. 3, A). Atypical patterns show pain starting in non-trigger locations that is diffuse across the head and face (Fig. 3, B).

Effect of Pain Sketches on Postoperative Outcomes

The mean MHI improvement for patients within each pain sketch group was as follows: 73±38% for typical pain patterns, 78±30% for intermediate pain patterns, and 30±40% for atypical pain patterns. There was no significant difference in percent MHI improvement between typical and intermediate pain sketch patients ($p=0.43$). There was, however, a significant difference in MHI % improvement between the typical and atypical group ($p=0.03$), as well as the intermediate and atypical groups ($p <0.01$) (Fig. 4). The chance of having MHI improvement of more than 30% in the atypical group was 20%. The chance of having MHI improvement of less than 50% in the typical and intermediate group combined was 20%.

Atypical pain patterns were analyzed as a group to establish more detailed and easier to understand criteria that define atypical sketches. The criteria for atypical sketches are:

1) Facial pain that is not located at or above the eyebrows/ forehead, temples, or around the eye (for example cheek, jaw, anterior neck).
2) Pain that starts in an atypical location that does not correspond to a trigger site.
3) Diffuse pain that is not localized

Medication Use Among Patients

One hundred and nine patients provided information on their medication use preoperatively. Ninety patients (82%) were female with an average age of 44 years (SD ±13 years).

At the time of screening, 103 patients (95%) described taking prescription medication for their MH pain. When asked, “how many days in the last month did you take prescription medication?”, the median number of days reported was 30 (IQR 17-30). Sixty-three (61%) reported using daily migraine medication. Sixty-four patients (59%) reported using over the counter medications. These patients reported using over the counter medications at a median frequency of 3.3 days (IQR 0.7-8.7) in the previous month. The type of prescription medication varied among patients but included abortive in 46% (n=47), preventative in 54% (n=56), rescue in 62% (n=64), and antiemetic in 18% (n=19) (Fig. 5). Forty patients (37%) who underwent surgery reported using prescription opioid medication to treat their MH pain at the time of screening.

Sixty-five patients (65%) responded to follow up medication surveys at twelve months. Postoperatively, patients reported using prescription medications at a median frequency of ten days (IQR 3-25) per month, a significant decrease compared to pre-operative values of 30 days (IQR 17-30) per month (P<0.001; Fig. 6). Twenty-three percent (n=14) were using daily medication at twelve months, also a significant decrease from 61% at screening (P<0.001, Fig. 7). Fourteen patients (22%) reported no prescription medication use at twelve months. When asked, “Does your migraine medication help more compared to before surgery?”, 32 patients (52%) stated yes.

Psychiatric Conditions in Patients Undergoing Surgery

Preoperatively, 48 patients (34%) reported a diagnosis of depression, while 45% of patients met PHQ-2 criteria for likely major depressive disorder (PHQ-2 score of three or greater). Patients with depression reported significantly more severe preoperative headache symptoms as compared to patients without depression (MHI of 134±90 vs. 89±81, P=0.003). Similarly, patients who met PHQ-2 criteria for likely major depressive disorder reported significantly more severe preoperative migraine symptoms as compared to patients without likely major depressive disorder (MHI of 120±92 vs. 87±77, P=0.027).

Thirty-eight patients (27%) reported a diagnosis of anxiety. Patients with anxiety reported significantly more severe preoperative migraine symptoms as compared to patients without anxiety (MHI of 131±91 vs. 95±83, P=0.025).

At one year postoperatively, patients reported a significant decrease in their PHQ-2 score (P=0.02, Fig. 8), with 22% of patients meeting PHQ-2 criteria for likely major depressive disorder, as compared to 45% preoperatively.

Postoperatively, patients with depression or anxiety achieved successful outcomes not significantly different from patients without depression or anxiety: 82% of patients who self-reported a diagnosis of depression achieved a successful surgical outcome (>50% MHI reduction), as compared to 71% of patients who did not self-report a diagnosis of depression (P=0.22). Seventy-one percent of patients who self-reported a diagnosis of anxiety achieved a successful surgical outcome (>50% MHI reduction), as compared to 78% of patients who did not self-report a diagnosis of anxiety (P=0.50).

Discussion

Trigger site deactivation surgery has previously been established as an effective method for treating pain in patients suffering from chronic migraine and other types of chronic headache. This study further investigates postsurgical outcomes and their associations with some preoperative variables. We demonstrated that 1) the surgical outcomes of traumatic headache sufferers are comparable to those without injury, 2) patient pain sketches can help predict outcomes, and 3) surgery is associated with decreased medication use and improved mental health.

Head or Neck Injury

Patients with posttraumatic headache are clinically challenging to treat with conservative medical therapy alone[33,34]. This study describes the characteristics of patients with posttraumatic headache undergoing trigger site deactivation surgery and compares their surgical outcomes to those without a history of trauma. We demonstrated that 1) there is a high prevalence of head or neck injury in patients undergoing trigger site deactivation surgery, 2) the baseline characteristics of traumatic headache sufferers are largely similar to those without trauma, except that traumatic headache sufferers are significantly less likely to report a family history of MH and are more likely to report opioid use, and 3) the surgical outcomes of traumatic headache sufferers are comparable to those without injury.

In our cohort, 50% of patients report a history of head or neck injury, with motor vehicle accident being the most common injury mechanism (in 38%). Thirty percent of patients reported their traumatic injury to be the precipitating event leading to their headaches. These figures are similar to those reported in previous studies. Couch et al. reported in a series of general MH patients that 49% had a history of injury while 14% had a potential precipitating injury. Huang et al. analyzed 102 occipital neuralgia patients receiving radiofrequency treatment, and demonstrated that just over one-third of patients described an inciting traumatic event[27]. In a series of twenty-four MH patients undergoing surgery, Janis et al. reported that nine (37%) had a history of head or neck injury[10].

The association between head or neck injury and MH has been studied. Lipton et al. proposed that specific brain states that result from head injury, such as neuronal hyperexcitability, may increase the probability of developing MH[1]. Neurochemical analyses of traumatic head injury and MH have revealed similarities in the mechanisms underlying both conditions, suggesting a common pathway[58]. A shared pathomechanism could elucidate why some patients with preexisting MH report exacerbation of symptoms following traumatic head or neck injury. Based on the high prevalence of posttraumatic headache patients in our cohort, we speculate that trauma and microtrauma may also be associated with migraines triggered at extracranial sites.

One year postoperatively, patients with head or neck injury had comparable outcomes to those without injury. In contrast, standard conservative therapy with medications results in unsatisfactory results in most posttraumatic MH patients[33,34]. Our results validate the theory that posttraumatic patients tend to fail standard MH medication therapy but respond to targeted anatomical interventions like steroidal nerve blocks and total neurectomy[27,35,59-61]. Blume et al. performed radiofrequency electrocoagulation of the occipital nerve in 450 cases and reported positive outcomes in 85% of patients with equal success in patients with or without trauma[59]. These findings have been replicated by other investigators performing nerve block and neurectomy[35,61]. Some studies using interventional therapy have reported superior outcomes in patients with trauma as compared to those without trauma[27,60]. Gawel et al. performed occipital nerve block and reported a 72% response rate in traumatic patients as compared to 54% of the nontraumatic patients. Huang et al. reported a similar result using radiofrequency, in which 65% of traumatic patients reported a positive outcome as compared to 43% of non-traumatic patients.

Our study found that a relatively high proportion of patients reported opioid use preoperatively and that posttraumatic patients were more likely to use opioids for headaches as compared to patients without a history of injury (38% versus 22%). Despite there being no significant differences in headache characteristics preoperatively, patients reporting opioid use experienced significantly poorer headache symptoms postoperatively. This data supports the findings of a prior study by Adenuga et al., which reported that patients who used narcotics preoperatively had worse outcomes following trigger site deactivation surgery[42].

Although the mechanisms explaining why posttraumatic headache patients have superior outcomes with invasive treatment as compared with medication alone have not been elucidated, several studies have attempted to investigate the mechanisms. Anthony et al. found that 30% of patients with primary headaches have evidence of greater occipital nerve irritation and proposed that this may be a confounding variable in trials of MH medication trials[62]. Because patients with nerve irritation tend to fail standard medication but respond to invasive therapy, he coined the diagnosis "headache due to irritation of the greater occipital nerve".

We caution the readers of this study to interpret its results with an understanding of its limitations. We relied on patients' subjective accounts of head or neck injury and this may have introduced recall bias. This limitation is important to consider since some patients' injuries and headache onset may have occurred many years ago. Patients may have overreported head injuries as precipitating events leading to their headache or underreported minor head traumas. This reliance on historical accounts also limited our ability to assign a temporal relationship between injury and headache among patients. While some patients did report the time difference between their injury and headache onset, most others could not reliably produce this information. We therefore do not have this data for the majority of our patients and this data was not included. Additionally, we did not base the presence of all injuries on clinical diagnoses. This is an important distinction since clinically diagnosed head injuries are more likely to represent severe trauma. However, prior studies showing an association between headache onset and injury have shown that it is not only severe injuries that are associated with headache but minor ones as well[25,28,30]. As such, we believe that it is important to consider all injuries. Lastly, we cannot distinguish between head and neck injury as we asked about them collectively. If head injury is a more predictive risk factor than neck injury, the decision to combine them may have resulted in an underestimation of the effect of head as opposed to neck injury.

While further research is needed to investigate the pathophysiology of patients who suffer posttraumatic headache, this study describes a subset of these patients who underwent surgical decompression. We report that outcomes in headache surgery patients with a history of head or neck injury are comparable to those without injury. Trigger site deactivation surgery candidates with a history of injury can therefore expect similar outcomes as reported for surgery patients overall.

Pain Sketches

Pain sketches are an important tool for chronic pain patients to visually express complex pain conditions, and communicate their symptoms to health care providers[38,39]. Pain diagrams have previously been used as a screening tool to predict surgical outcomes in patients undergoing spine surgery for lumbar radiculopathy[63]. To our knowledge, this is the first time that this concept has been applied to trigger site deactivation surgery for headaches. Advantages of pain drawings include the ability for patients to independently perform this task free of the bias that can occur at office visits. Furthermore, drawings are inexpensive, readily available, and easy to interpret by practitioners with limited experience. They are a useful supplement, but not a substitute for the trigger site detection algorithm pioneered by Guyuron et al[17-19,64,65]. This algorithm varies per site but consists of identifying the headache origin with one finger, an arterial Doppler signal, and chemodenervation using nerve block of the trigger site. We have developed and published the

PAINS diagram to summarize the Guyuron trigger site algorithm and amend the preoperative algorithm to include the use of pain sketches to identify trigger sites[65,66] (Fig. 9).

In this study, we demonstrate that three different types of pain sketches exist in patients undergoing trigger site deactivation surgery, and we provide definitions and examples for each trigger site (Fig. 1-3):

1) Typical: Pain origin at the anatomic trigger site with radiation pattern along the anatomic nerve course

2) Intermediate: Not atypical, but does not follow the exact nerve distribution

3) Atypical:

  a) Facial pain that is not located at or above the eyebrows/ forehead or temples (for example cheek, jaw, anterior neck)

  b) Pain that originates in an atypical location that does not correspond to a trigger site.

  c) Diffuse pain that is not localized

Although there are distinct differences between typical and intermediate pain sketches, surgical outcomes do not differ between groups (MHI improvement of 73±38% in the typical, versus 78±30 %, in the atypical group; p= 0.43). Therefore, there is no need to distinguish between the two upon screening. However, it is important to detect atypical pain sketches, as surgical outcomes are significantly worse in this group (30±40 %) as compared to the typical (p=0.03), and intermediate (p=0.01) groups (Fig. 4). Pain sketch red flags such as facial pain, pain starting at an atypical location and diffuse pain should alert surgeons to consider patient classification as "atypical". One limitation of this concept is the subjective nature of evaluating sketches. However, inter-rater reliability was high in our study and specific criteria for atypical sketches were developed to help clearly define atypical pain patterns. Only 20% of patients in the atypical group had a mean MHI improvement of over 30%. Therefore, in general, we do not operate on patients with atypical pain sketches in our practice, as we have always suspected and have now demonstrated that they are poor candidates for surgery. However, patients with atypical sketches should not be excluded from preoperative assessment by a physician. If there is a compelling reason to operate regardless of an atypical sketch, it is important to counsel the patient about lower chances of a positive outcome.

Medication Use

Prior studies investigating headache surgery have utilized headache symptoms, pain coping abilities, quality of life, and socioeconomic factors as outcome measures. In this study, we show that medication use offers another method by which to measure outcomes in headache surgery. We demonstrated that surgery is associated with a significant decrease in medication use postoperatively.

There were limitations to this aspect of the study. First, we did not investigate which medication types a patient took at follow up as these questions were not included as part of the postoperative survey. It is possible that some patients switched to more effective long-term medication or other interventions, like botulinum toxin injections. Secondly, we did not have a control group of patients without surgery to compare outcomes to and this could have revealed other confounding variables.

Psychiatric Conditions

Chronic headache patients with comorbid psychiatric conditions tend to have more severe headache symptoms that are more challenging to treat with pharmacological treatment alone[50-53]. This study describes the psychiatric comorbidities in patients undergoing trigger site deactivation surgery for chronic headache and investigates the effect of surgery on depressive symptoms. We demonstrated that 1) there is a high prevalence of psychiatric ailment in patients undergoing headache surgery, 2) comorbid psychiatric conditions do not appear to affect postsurgical outcomes, and 3) surgery is associated with a significant decrease in depressive symptoms.

Our study found a high prevalence of psychiatric comorbidities in patients undergoing trigger site deactivation surgery, with 34% and 27% of patients reporting a diagnosis of depression or anxiety, respectively. The relationship between headache and psychiatric comorbidities has been previously studied. Most current literature suggests that it is likely a bidirectional relationship, with one condition affecting the other and vice-versa. A study investigating depression and headache by Breslau et al. found that the presence of each disorder enhanced the risk for a first onset of the other disorder[67]. Other studies have demonstrated shared environmental and genetic factors between both conditions[68]. In an effort to elucidate the pathophysiologic links between both diseases, some studies have focused on the point that serotonin plays a key role in both disorders. Chronic migraine patients have increased ictal serotonin levels but decreased interictal levels, suggesting that decreased levels in interictal periods can predispose to depression[69]. Genetic polymorphisms in serotonin receptors have been linked to both depression and migraine[70]. Proponents of this association have also commented on the effectiveness of antidepressive agents in preventing and treating some migraine pain[71].

In this study, we demonstrate that patients with comorbid depression or anxiety undergoing headache surgery achieve successful improvements in their headache symptoms and these are comparable to those without these comorbid conditions. Postoperatively, depressed patients did well with over half of patients no longer meeting PHQ-2 criteria for likely major depressive disorder. While the bidirectional influence and shared mechanisms between headaches and depression may lead to a higher risk of one condition when afflicted by the other, some authors suggest that this relationship allows some treatments to work effectively for both disorders. Prior studies have demonstrated that depressed migraine patients who receive botulinum toxin injections have significantly improved headache symptoms as well as reduced depression and anxiety[72,73]. Similarly, cognitive behavioral therapy has been shown to reduce symptoms of headache, anxiety, depression, and improve the quality of life in patients with both conditions[74]. While not all headache sufferers with comorbid psychiatric conditions are candidates for surgical intervention, it is important for surgeons to be aware that it is an option for some who have failed more conservative therapies.

Summary

Successful trigger site deactivation surgery for chronic headache relies heavily on the selection of appropriate candidates, identification of all headache trigger sites, and preoperative counseling. This study provides several in-depth analyses on the postoperative outcomes of trigger site deactivation surgery and variables that affect postoperative outcomes. We demonstrated that 1) patients with head or neck injury achieve successful postoperative outcomes, 2) atypical pain patterns are associated with inferior outcomes, and 3) surgery is associated with decreased medication use and improved depressive symptoms. It is important for surgeons to be aware of this data as we continue to refine patient selection and preoperative counseling for trigger site deactivation surgery.

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Table 1. Comparison of Demographic Variables Among Groups

	All Patients	Atraumatic	Traumatic	Precipitating Event	No Precipitating Event
No. of patients, %	142	72, 51%	70, 49%	41, 29%	101, 71%
Average age	44 ± 14	45 ± 12	43 ± 15	42 ± 16	44 ± 12
p vs. AT (PE)			0.37	0.38	(0.46)
No. of female patients, %	116, 82%	59, 82%	57, 81%	35, 85%	81, 80%
p vs. AT (PE)			0.94	0.80	(0.47)
Average PHQ2 Score	2.5 ± 2.1	2.5 ± 2.1	2.6 ± 2.2	2.4 ± 1.9	2.6 ± 2.2

Table 2. Comparison of Baseline MH Characteristics among Groups

	Atraumatic	Traumatic	Precipitating Event	No Precipitating Event
Average MH frequency	19 ± 8.9	19 ± 9.9	18 ± 9.8	20 ± 9.2
p vs. AT (PE)		0.778	0.44	(0.337)
Average MH severity	7.6 ± 1.4	7.7 ± 1.4	7.6 ± 1.4	7.7 ± 1.4
p vs. AT (PE)		0.63	0.889	(0.916)
Average MH duration, days	17 ± 8.0	15 ± 8.4	14 ± 8.6	17 ± 8.0
p vs. AT (PE)		0.139	0.069	(0.075)
Average MH index	110 ± 80	100 ± 93	91 ± 90	110 ± 85
p vs. AT (PE)		0.541	0.271	(0.225)
Average PSEQ	18 ± 12	18 ± 13	20 ± 13	17 ± 12
p vs. AT (PE)		0.88	0.37	(0.14)

Table 3. Comparison of Postoperative MH Characteristics among Groups

	Atraumatic	Traumatic	Precipitating Event	No Precipitating Event
Average MH frequency	6.3 ± 7.9	7.0 ± 9.3	7.8 ± 10.2	6.2 ± 7.8
p vs. AT (PE)		0.73	0.51	(0.44)
Average MH severity	4.7 ± 3.0	4.9 ± 3.3	5.3 ± 3.7	4.6 ± 2.9
p vs. AT (PE)		0.79	0.51	(0.40)
Average MH duration, days	8.1 ± 8.9	8.8 ± 9.5	8.3 ± 9.3	8.5 ± 9.2
p vs. AT (PE)		0.74	0.96	(0.92)
Average MH index	20 ± 37	35 ± 63	39 ± 72	22 ± 39
p vs. AT (PE)		0.18	0.15	(0.17)
Average PSEQ	38 ± 19	35 ± 19	34 ± 20	38 ± 19
p vs. AT (PE)		0.61	0.53	(0.53)

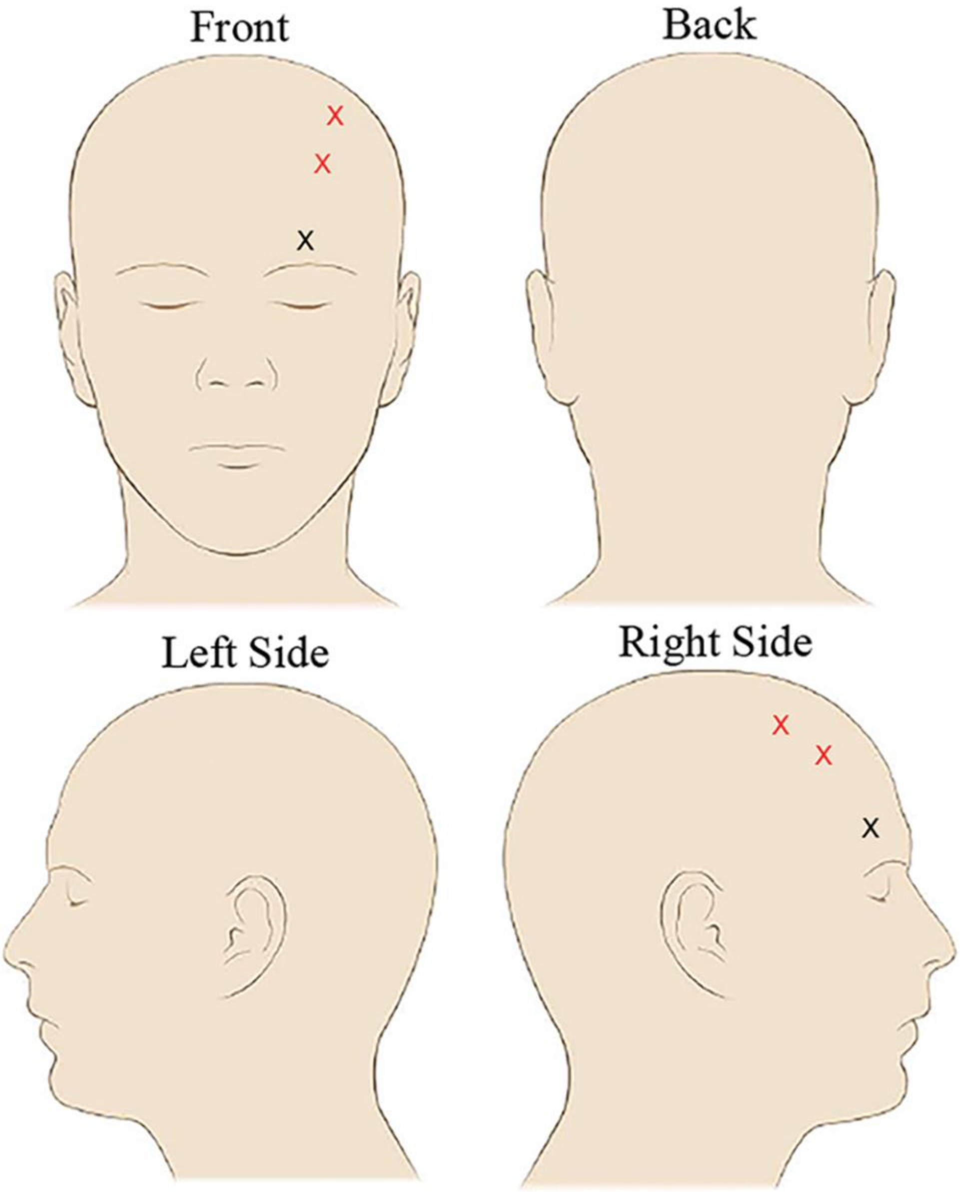
Table 4. Comparison of Change in MH Characteristics among Injury Groups

	Atraumatic	Traumatic	Precipitating Event	No Precipitating Event
Average MH frequency reduction	11 ± 10	13 ± 13	11 ± 15	12 ± 9.9
p vs. AT (PE)		0.65	0.97	(0.85)
Average MH severity reduction	2.9 ± 3.3	2.9 ± 3.4	2.6 ± 3.9	3.1 ± 3.1
p vs. AT (PE)		0.94	0.70	(0.54)
Average MH duration reduction, days	8.5 ± 10	6.5 ± 9.6	5.9 ± 11	8.3 ± 9.6
p vs. AT (PE)		0.35	0.32	(0.32)
Average MH index reduction	78 ± 71	72 ± 120	59 ± 130	81 ± 73
p vs. AT (PE)		0.76	0.43	(0.31)
Average PSEQ increase	20 ± 19	17 ± 19	13 ± 17	21 ± 20
p vs. AT (PE)		0.51	0.19	(0.13)

Table 5. Comparisons of MH Outcomes Among Injury Groups

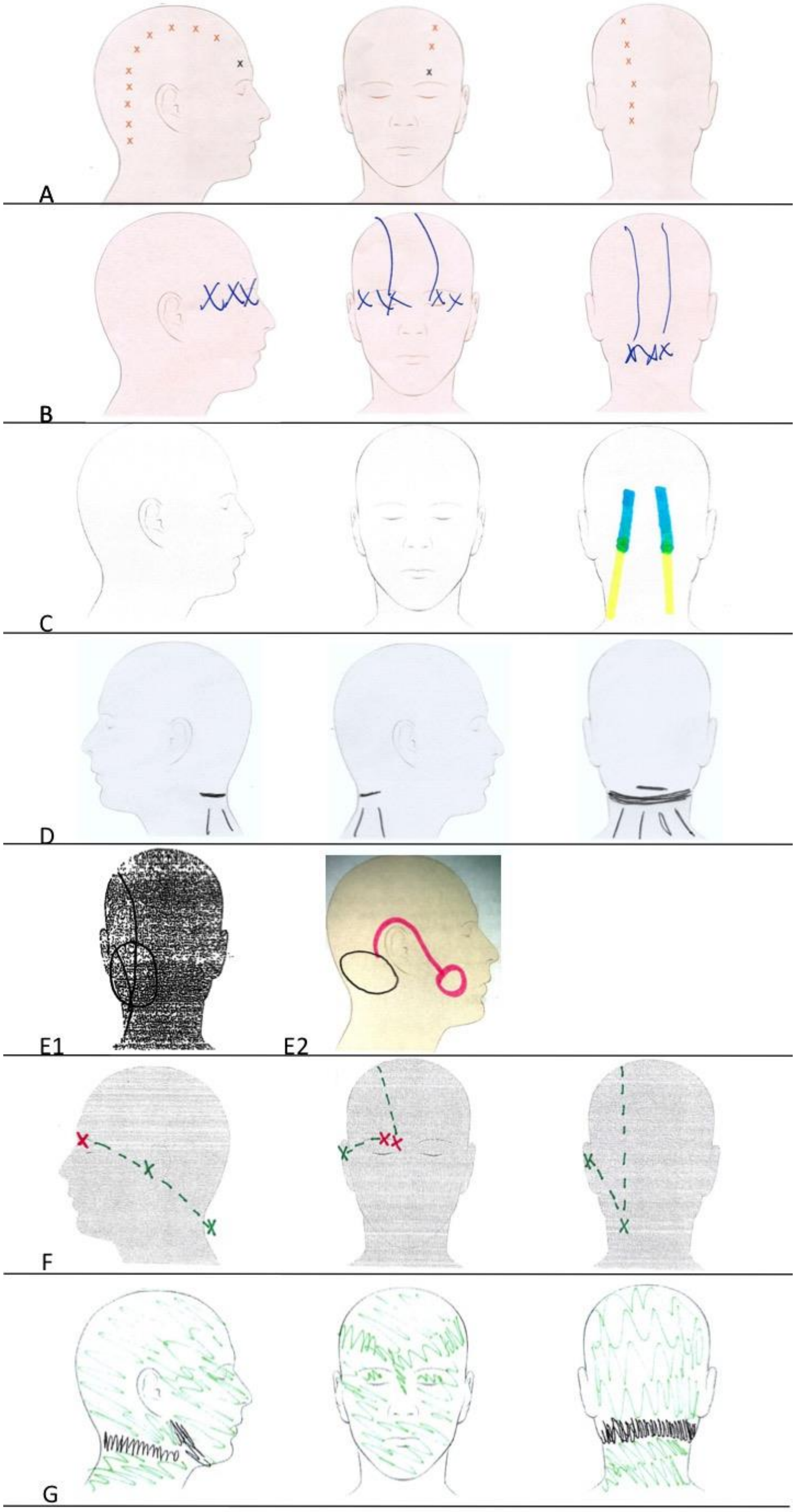
	All patients	Atraumatic	Traumatic	Precipitating Event	No Precipitating Event
% with frequency improvement	83	84	82	71	87
p vs. AT (PE)			0.80	0.20	(0.069)
% with severity improvement	69	67	71	54	75
p vs. AT (PE)			0.71	0.27	(0.066)
% with duration improvement	72	74	71	71	73
p vs. AT (PE)			0.80	0.81	(0.84)
% with MHI reduction	87	88	87	79	91
p vs. AT (PE)			0.90	0.34	(0.16)
% with 50% MHI Reduction	81	83	76	71	84
p vs. AT (PE)			0.39	0.20	(0.16)
% with 80% MHI Reduction	68	67	68	63	70
p vs. AT (PE)			0.92	0.68	(0.51)

Supplemental Figure 1. Pain sketch blank form



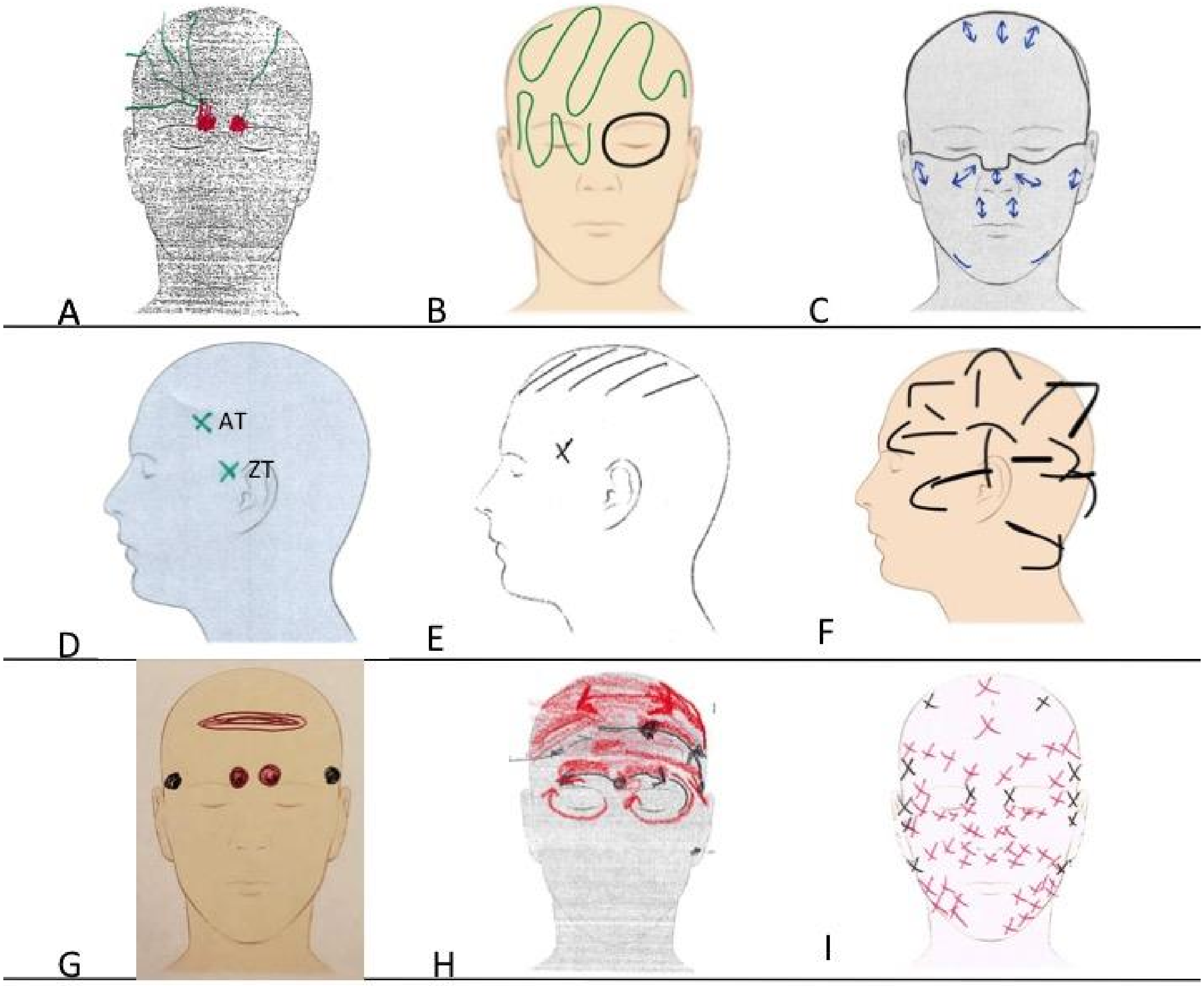
An example of a pain pattern form that a patient was asked to complete preoperatively to describe where their pain starts (black x) and where it radiates to (red x). This pattern is typical for isolated frontal trigger site pain.

Figure 1. Occipital pain sketches.



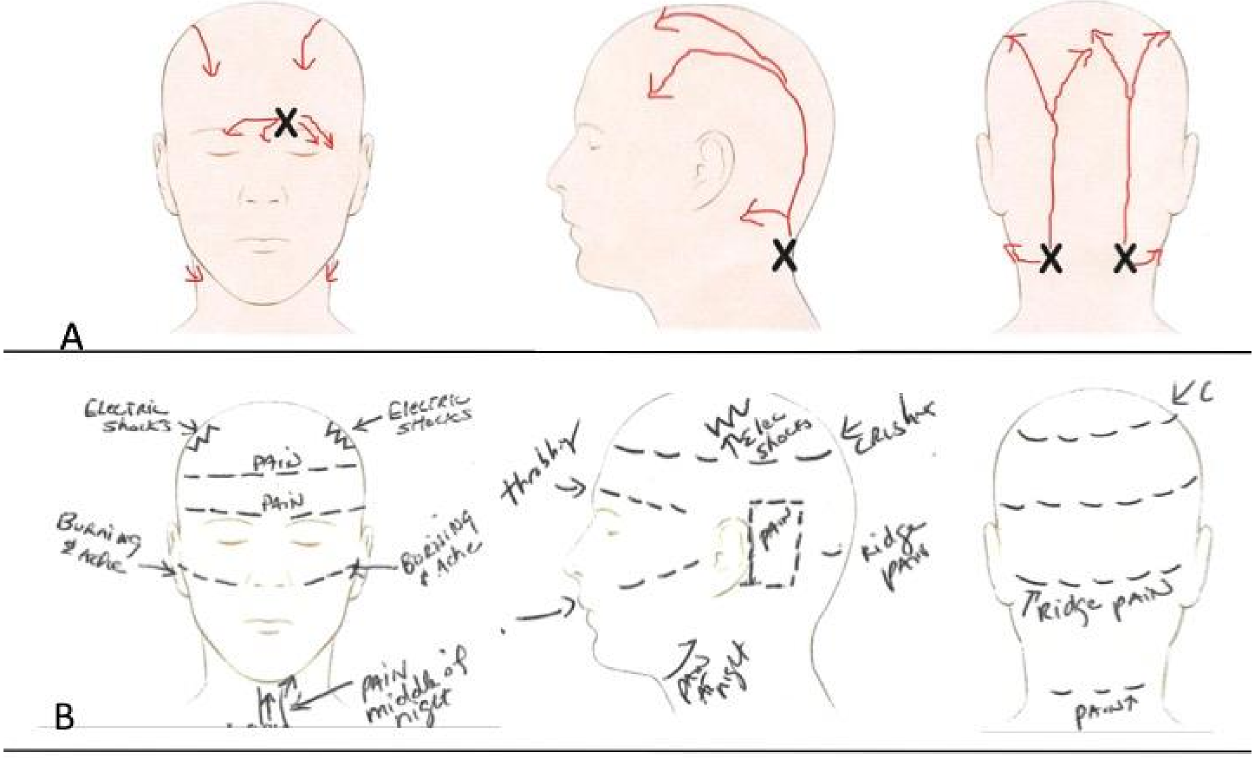
(A) Typical pain pattern with pain origin at GON exit from semispinalis muscle and radiating pain towards the forehead and (B) behind the eye. (C) Intermediate pain pattern with pain that originates at the GON exit site with partial radiation along nerve course, but also radiation towards the neck. (D) Atypical pain pattern with pain in atypical anatomic position. (E1) Typical LON pain sketch drawn more lateral than GON pain. (E2) Atypical LON pain radiating to the cheek. (F) Typical pain sketch for combined GON and LON. (G) Atypical GON and LON pain sketch.

Figure 2. Frontotemporal pain sketches.



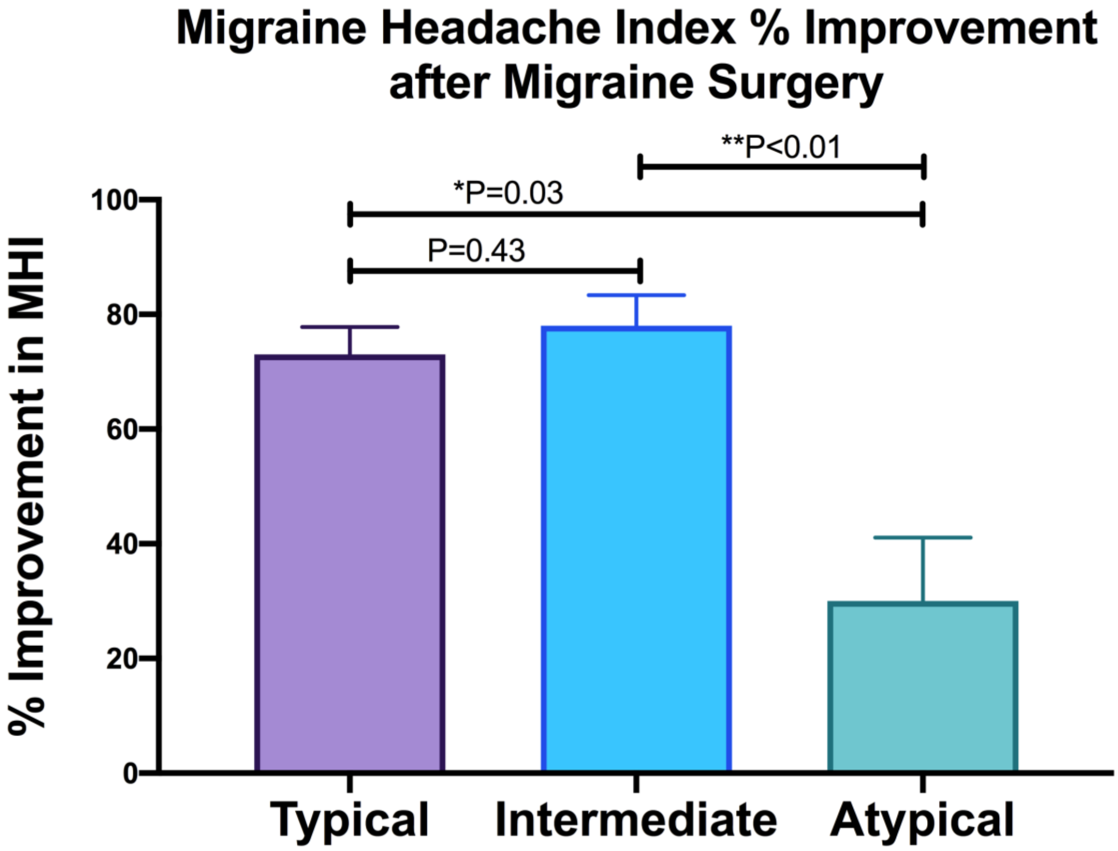
(A) Typical frontal pain pattern with pain origin at eyebrow radiating across forehead (B) Intermediate pain pattern with pain that originates at/ around the eye with broad radiation pattern (C) Atypical pain pattern with pain starting broadly and radiating across the face. (D) Typical ZT and AT pain patterns are drawn at the temple. Intermediate patterns start in the right location but radiate to an unusual location such as the vertex of the scalp. (E) Abnormal patterns have no clear point of onset and no clear radiation pattern. Frontal and temporal pain often occurs together (G-I). Typical pain patterns start over the frontal and temporal trigger site (G). Intermediate patterns start in the correct location with broad radiation pattern (H) and abnormal patterns encompass the entire face with no clear onset and radiation pattern (I).

Figure 3. Multiple trigger pain sketches.



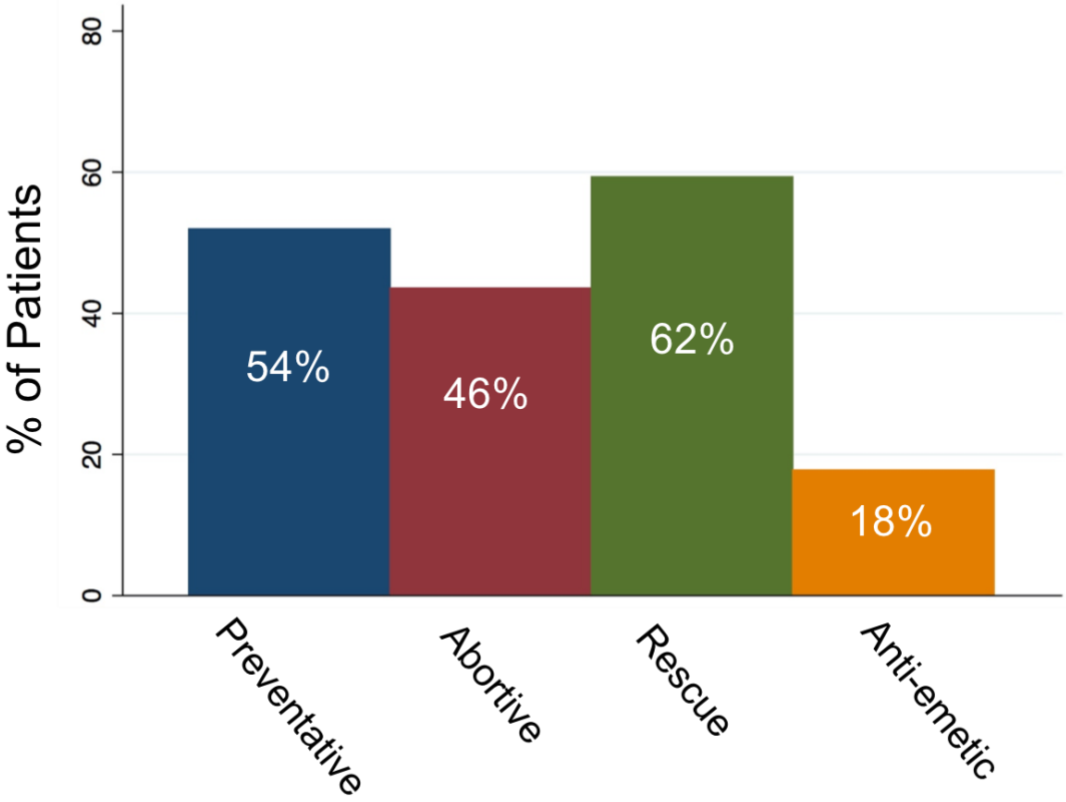
(A) Typical pain sketches show pain at different trigger sites with typical radiation patterns. (B) Atypical sketches depict pain all across the head and neck in non anatomic locations and radiation patterns.

Figure 4: MHI Improvement after migraine surgery between different pain sketch groups.



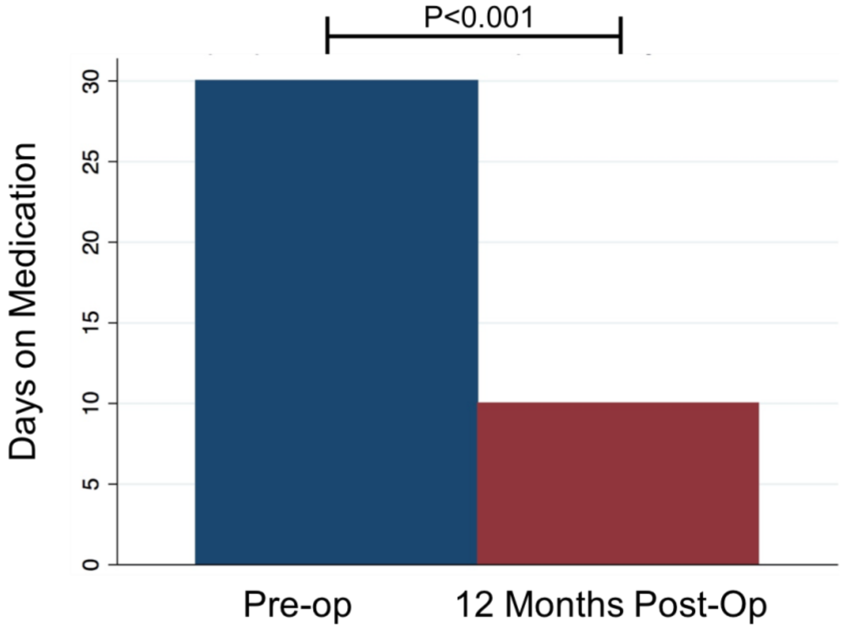
There was no significant difference between MHI in the typical and intermediate pain sketch group (p=0.43). There was a significant difference between the typical and atypical (p= 0.03), as well as the intermediate and atypical group (p= <0.01).

Figure 5: Preoperative Medication Type



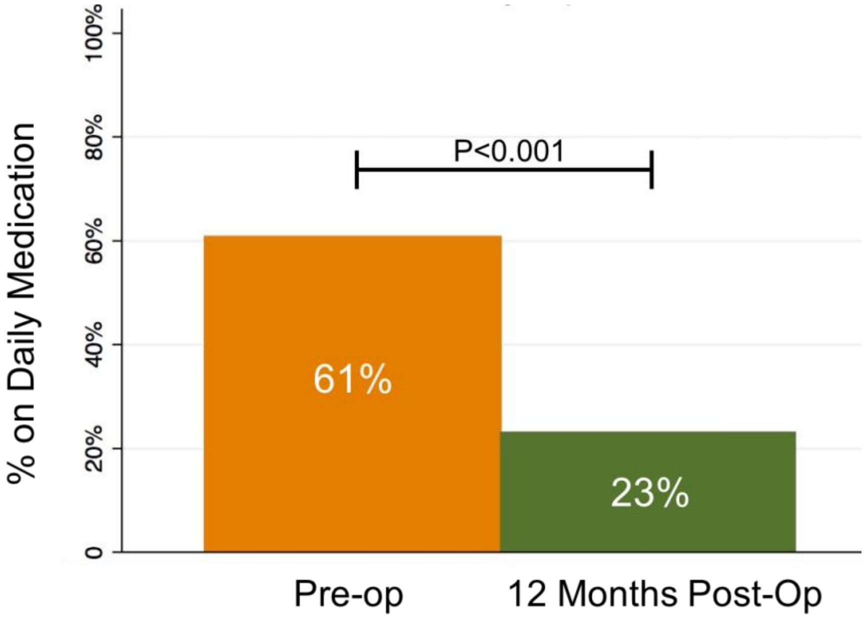
The various medications that patients were taking for their MH at the preoperative visit.

Figure 6: Days on Medication per Month



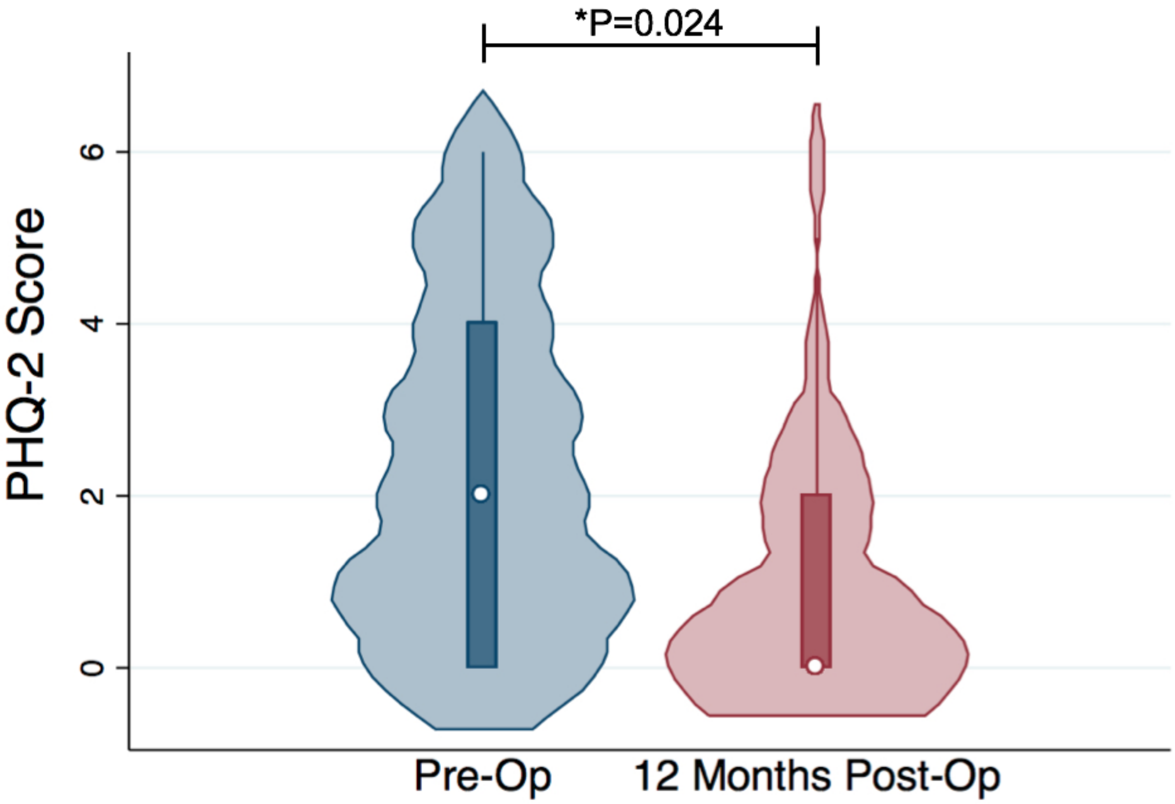
When patients were asked about the number of days they used prescription medication in the previous month, there was a significant decrease at 3 months and twelve months postoperatively.

Figure 7: Patients on Daily Medication



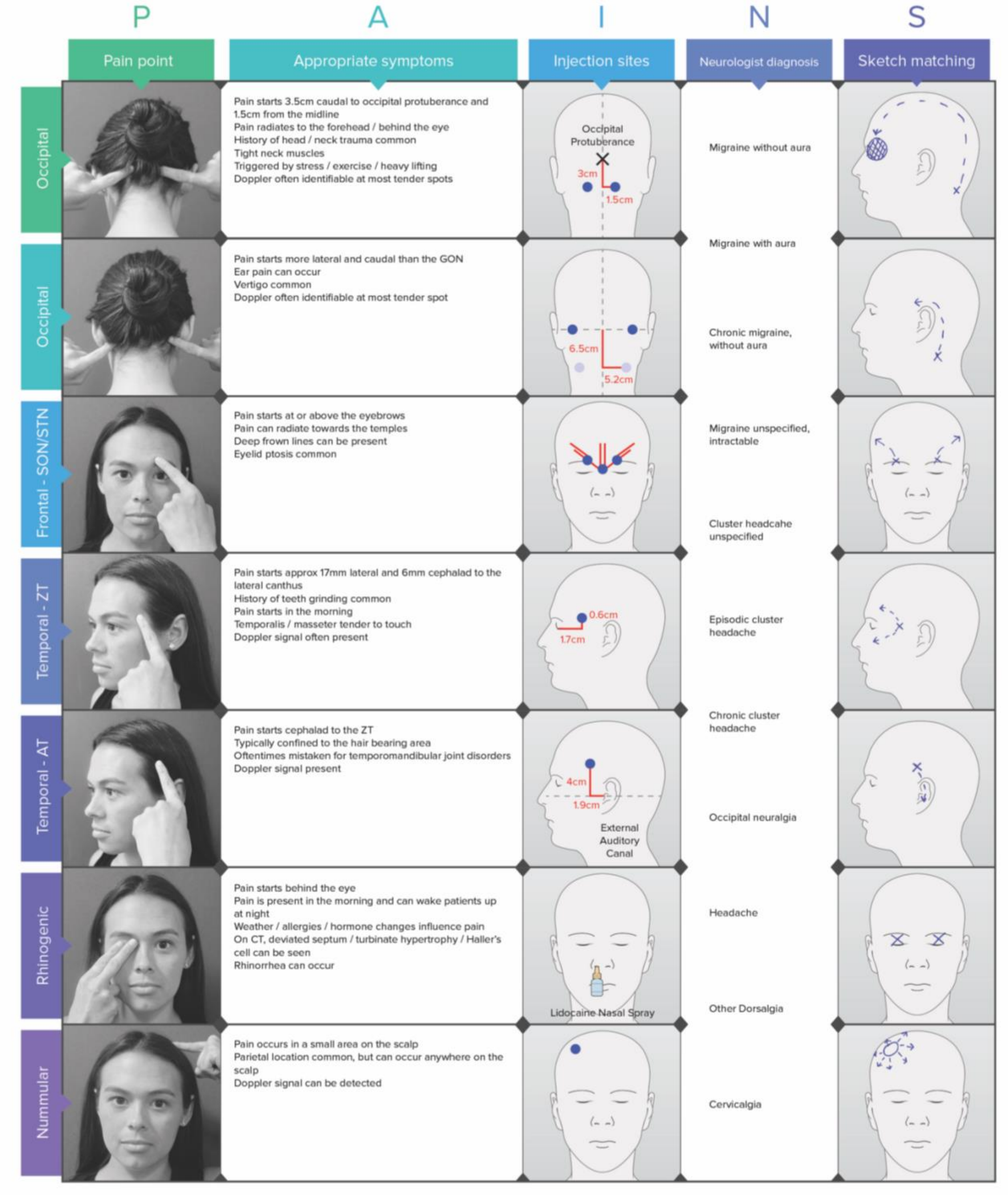
The percentage of patients reporting daily MH medication use at twelve months postoperatively significantly decreased compared to preoperatively.

Figure 8: Change in depressive symptoms postoperatively.



Postoperatively, there was a significant decrease in depressive symptoms, as measured by PHQ-2.

Figure 9: PAINS diagram



Pain point	Appropriate symptoms
Occipital	Pain starts 3.5cm caudal to occipital protuberance and 1.5cm from the midline Pain radiates to the forehead / behind the eye History of head / neck trauma common Tight neck muscles Triggered by stress / exercise / heavy lifting Doppler often identifiable at most tender spots
Occipital	Pain starts more lateral and caudal than the GON Ear pain can occur Vertigo common Doppler often identifiable at most tender spot
Frontal - SON/STN	Pain starts at or above the eyebrows Pain can radiate towards the temples Deep frown lines can be present Eyelid ptosis common
Temporal - ZT	Pain starts approx 17mm lateral and 6mm cephalad to the lateral canthus History of teeth grinding common Pain starts in the morning Temporalis / masseter tender to touch Doppler signal often present
Temporal - AT	Pain starts cephalad to the ZT Typically confined to the hair bearing area Oftentimes mistaken for temporomandibular joint disorders Doppler signal present
Rhinogenic	Pain starts behind the eye Pain is present in the morning and can wake patients up at night Weather / allergies / hormone changes influence pain On CT, deviated septum / turbinate hypertrophy / Haller's cell can be seen Rhinorrhea can occur
Nummular	Pain occurs in a small area on the scalp Parietal location common, but can occur anywhere on the scalp Doppler signal can be detected

Neurologist diagnosis:

Migraine without aura
Migraine with aura
Chronic migraine, without aura
Migraine unspecified, intractable
Cluster headcahe unspecified
Episodic cluster headache
Chronic cluster headache
Occipital neuralgia
Headache
Other Dorsalgia
Cervicalgia

The PAINS diagram summarizes the Guyron trigger site algorithm and considers symptoms, injection sites, diagnosis, and pain illustration during the preoperative evaluation of patients.