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The importance of surgical maneuvers during treatment of frontal migraines (site I): A prospective, randomized cohort study evaluating foraminotomy/fasciotomy, myectomy, and arterectomy

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Summary *Background:* The current prospective, blinded, randomized cohort study aims to delineate the relative contribution of different surgical treatments for frontal migraines.
Methods: Patients undergoing migraine surgery in the frontal region (site I) were prospectively enrolled and blindly randomized into one of the following four groups: (1) myectomy alone, (2) myectomy and foraminotomy/fasciotomy, (3) myectomy and arterectomy, and (4) foraminotomy/fasciotomy alone. Pre- and post-surgical migraine headache severity, duration, Migraine Headache Index (MHI) score, and migraine-free days (MFDs) were obtained.
Results: Thirteen patients agreed to participate in the study. For all patients, the mean pre- and post-operative MHI scores demonstrated a significant improvement from 52.6 (3.8–85) to 4.7 (0–21.3) ($p = 0.0001$). Thirty-one percent of patients required a site I revision that included an arterectomy. Patients who had an arterectomy at their initial surgery demonstrated statistically significant improvement in both frequency (12 vs. 6.11; $p = 0.02$) and MHI scores (51.71 vs. 5.55; $p < 0.01$). Arterectomy patients also demonstrated a significant improvement in the number of MFDs following surgery, from 18 to 24 MFDs ($p = 0.021$). Those patients not undergoing arterectomy demonstrated statistically significant improvements in the number of MFDs after their initial surgery (13.25 MFDs, $p = 0.01$), but the improvement was significantly less when compared to the arterectomy group (13.25 vs. 24 MFDs; $p = 0.026$). Following revision arterectomy, both groups had statistically equivalent improvement in MFDs (20.75 vs. 24 MFDs; $p = 0.178$).

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Conclusions: These findings suggest that arterectomy is necessary for successful treatment of frontal migraines (site I).

Background

Migraine is a common and debilitating primary headache disorder affecting approximately 12% of American adults, with 22% of those suffering moderate or severe disability and resulting in a total of 112 million bedridden days and close to $14 billion in direct and indirect costs in the United States annually.[1–3] The "gold standards" of migraine treatment continue to be pharmaceutical and behavioral. However, 5.1% of patients in a headache clinic population have symptoms that meet criteria for "refractory migraines," which are unresponsive to optimal medical management.[4] Additionally, there are patients who are unable to tolerate medical treatment and may even prefer surgery over the negative side effects associated with pharmacologic therapies.

There is a mounting body of evidence demonstrating superior outcomes following migraine surgery when compared to traditional management. Our research has shown that 80–90% of appropriately selected patients, despite previously failed non-surgical treatment, will achieve at least a 50% improvement in frequency, severity, duration, and migraine-free days (MFDs). Despite these promising results, there is a significant portion of the scientific community that is critical of the surgical treatment of migraine headaches, and they dismiss it as either controversial or experimental.[5–9] These claims are largely unfounded and are inconsistent with published studies to the contrary, which include retrospective,[5] prospective,[8] comprehensive prospective randomized,[6] prospective randomized with sham surgery,[10] and 5-year follow-up[7] studies. These studies have been unfairly criticized for flaws in design and arguments that patients were not appropriately selected. These unjustified claims are made in direct contradiction to peer-reviewed, published studies that were designed and analyzed by reputable biostatisticians. In addition, patients were selected by respected, board-certified, fellowship-trained neurologists. Previous study results were collected and analyzed independently by a nurse coordinator and dedicated biostatistician, respectively. Another common and unsubstantiated claim is that these results represent a placebo effect, which has been extensively addressed on a study-by-study basis by the senior author.[9] Therefore, the claim that an over 50% improvement in 80–90% of the patients sustained over 5 years can be attributed solely to a placebo effect is scientifically unfounded.

Modern migraine surgery is the product of an observation by patients who underwent forehead rejuvenation and noticed improvement and sometimes complete elimination of their migraine headaches. Similarly, patients have observed these same effects following injection of botulinum toxin-A in the forehead; however, it was not clear which component of surgery had the most important role in the elimination of headaches. Frontal migraine headaches, believed to originate from compression or irritation of the supraorbital and supratrochlear nerves in the brow area (migraine site I),[8] represent the most commonly reported trigger site in the senior author's surgical patient population.[7] This area can be treated in several different ways: (1) resection of the glabellar muscle group, consisting of corrugator supercilii, depressor supercilii, and lateral procerus (myectomy), (2) removal of any arteries in close proximity to the nerves (arterectomy), and/or (3) decompression of the nerves at their exit from the skull through bony foramina or notches (foraminotomy/fasciotomy). Each of these decompression techniques can be performed alone or in combination. The current prospective, randomized cohort study aims to delineate the relative efficacies of each of these previously described surgical techniques at the frontal headache trigger site.

Methods

After obtaining Institutional Review Board approval, patients undergoing migraine site I surgery at the senior author's practice, following informed, written consent, were prospectively enrolled to undergo randomization into one of the following four groups: (1) myectomy alone, (2) myectomy and foraminotomy/fasciotomy with or without arterectomy, (3) myectomy and arterectomy, and (4) foraminotomy/fasciotomy alone. Surgeries were performed as previously described.[11,12]

To randomize patients, a biostatistician prepared serially numbered, opaque, sealed envelopes containing randomly ordered instruction cards, which were drawn by the senior author in the operating room immediately preceding surgery. Patient enrollment and data collection were performed by a clinic nurse who was blinded to the patients' study conditions. Furthermore, patients themselves remained blinded to their own study conditions until the follow-up period was completed. All patients were evaluated for migraine headache frequency (number of headaches per month), severity (on a scale from 0 to 10), duration of headaches (hours per day), and Migraine Headache Index (MHI) score (calculated by multiplying frequency, duration, and severity) preoperatively and at post-operative follow-up. Self-reported MFDs were also recorded according to the normal postoperative follow-up of the senior author's practice. Patients who did not achieve a clinically significant reduction in their MHI scores were offered a revision surgery to address any remaining sites of potential nerve compression. Post-revision frequency, severity, duration, and MHI scores were also collected for patients requiring revision.

Statistical analysis was performed using SPSS (SPSS Inc.; Chicago, IL, USA) using paired Student's t-test and Fischer's exact for parametric and non-parametric continuous variables.

Results

A total of 13 patients agreed to participate in the study, with a mean age of 41.8 years (age range, 33–54 years). All patients were female. Mean follow-up was 21.6 months (7.6–34.1 months). Five patients underwent myectomy and arterectomy, four patients underwent myectomy and fasciotomy/foraminotomy without arterectomy, and four patients underwent myectomy and fasciotomy/foraminotomy with arterectomy. This resulted in nine patients who had an arterectomy at their initial surgery and four who did not. For all patients, mean pre- and post-operative MHI scores demonstrated a significant improvement from 52.6 (3.8–85) to 4.7 (0–21.3) ($p = 0.0001$). Four out of 13 patients underwent an endoscopic primary release (31%). Four patients (31%) required a site I revision – 50% were endoscopic primaries. The majority of patients underwent concomitant migraine site II and III surgeries at the time of the primary migraine I surgery (site II = 9/69%; site III = 12/92%). Six patients (46%) underwent subsequent migraine site V surgeries. One patient (8%) also underwent migraine site VI surgery later. The mean pre- and post-operative MHI scores between patients who subsequently underwent a revision and those who did not were not significantly different between the arterectomy and non-arterectomy groups ($p > 0.05$). All four patients who subsequently underwent a revision migraine site I procedure had an arterectomy performed as part of the revision. One patient had a bilateral neurectomy performed in addition to bilateral arterectomies. All nine patients who did not require a revision had an arterectomy performed at their initial surgery.

Migraine headache index

The average pre-operative frequency, severity, duration, and MHI values between the group undergoing an arterectomy and the group not having an arterectomy can be found in Figures 1–4. There was no statistically significant difference between the two groups pre-operatively (all $p > 0.05$). The group that had an arterectomy at their initial surgery demonstrated improvement in all four measurements, and this was statistically significant for both frequency (12 vs. 6.11; $p = 0.02$) and MHI scores (51.71 vs. 2.83; $p < 0.01$). The group that did not have an arterectomy demonstrated a large but not statistically significant increase in their MHI scores (54.74 vs. 103.85). Severity and duration values increased (7.47 vs. 8.2 and 0.34 vs. 0.66, respectively; all $p > 0.05$) while frequency remained grossly unchanged (20.75 vs. 16.75). The group that had a subsequent revision including arterectomy demonstrated improvement in all migraine indices, with a statistically significant improvement in their MHI from their pre-operative and post-revision values (54.74 vs. 2.83; $p = 0.029$). All average values are summarized in Figures 1, 2, 3, and 4 for frequency, severity, duration, and MHI, respectively.

Migraine-free days

Patients not having an arterectomy had, on average, fewer pre-operative MFDs than the arterectomy group (9.25 vs. 18 MFDs), but this was not statistically significant. Patients that did have an arterectomy demonstrated a significant improvement in the number of MFDs following surgery, from 18 to 24 MFDs ($p = 0.021$; Figure 5A). Those patients not undergoing arterectomy demonstrated statistically significant improvements in the number of MFDs both after their initial surgery (13.25 MFDs, $p = 0.01$) and after their revision surgery including arterectomy (20.75 MFDs, $p < 0.001$; Figure 5B). However, the number of MFDs was significantly better in the arterectomy group than in the non-arterectomy group following their initial surgery (13.25 vs. 24 MFDs; $p = 0.026$). Following revision arterectomy, both groups had statistically equivalent improvement in MFDs (20.75 vs. 24 MFDs; $p = 0.178$). These comparisons are seen in Figure 5C.

Revision experience

When examining the senior author's entire experience with migraine site I surgery patients, the revision rate for site I for all patients in the database is currently 8.7% (85 out of 978 total patients including the four in the study), which is significantly lower than the revision rate for the current study (31%).

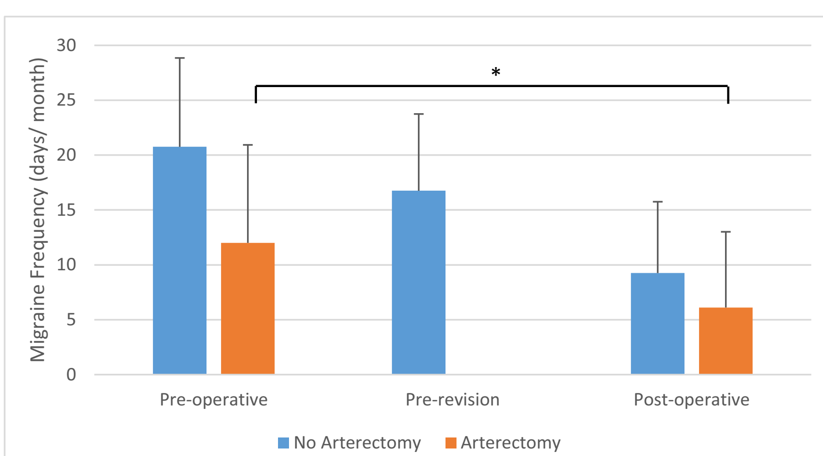

Figure 1 Average migraine frequency (days/month). Error bars represent SD. * represents $p < 0.05$.

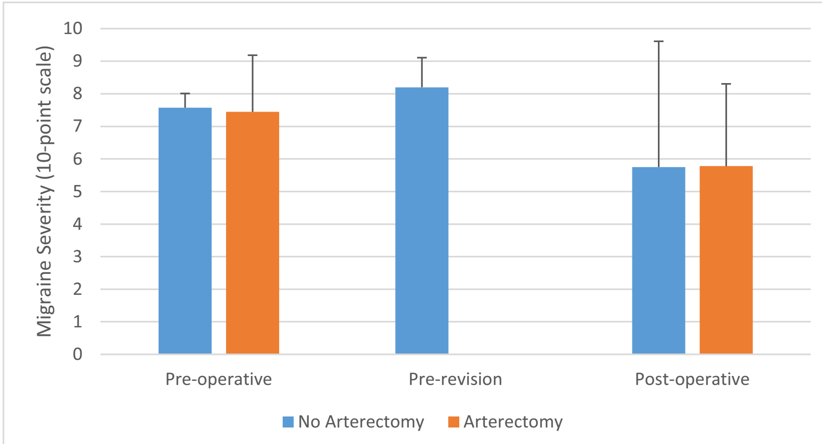

Figure 2 Average migraine severity scores (10-point scale). Error bars represent SD.

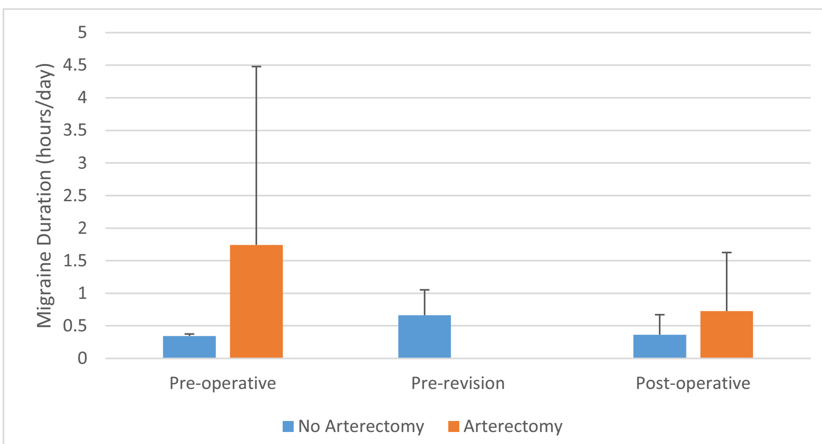

Figure 3 Average migraine length (hours/day). Error bars represent SD.

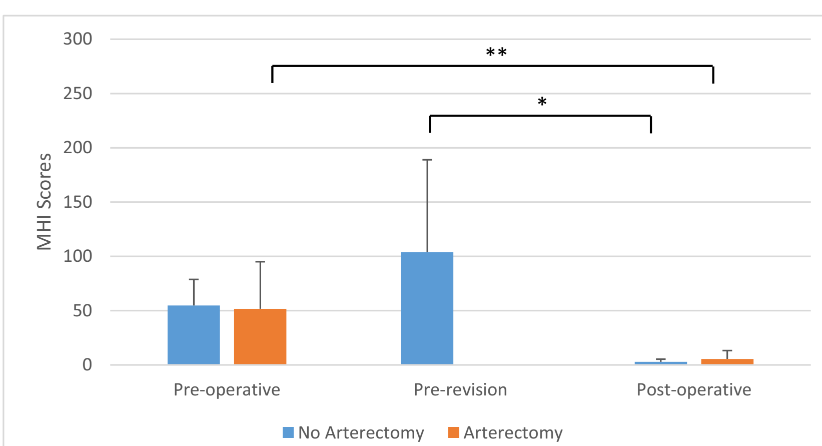

Figure 4 Average Migraine Headache Index (MHI) scores (calculated as the product of frequency, severity, and length). Error bars represent SD. * represents $p < 0.05$. ** represents $p < 0.01$.

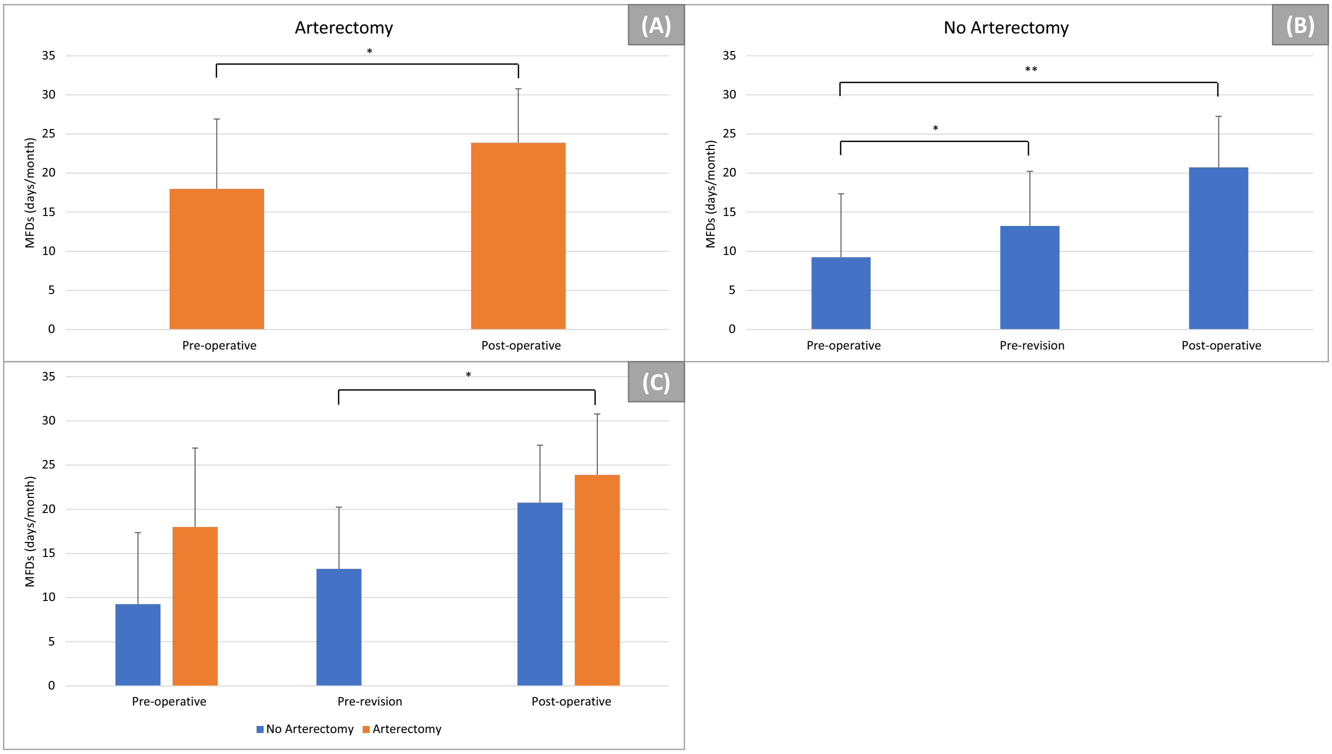

Figure 5 Average number of migraine-free days (MFDs) before and after surgery (days/month). Error bars represent SD. * represents $p < 0.05$. ** represents $p < 0.01$.

Discussion

This is the first study of its kind to compare the relative efficacy of varying surgical maneuvers in the treatment of migraine headaches at a single site. Despite the small sample size of our prospective cohort, the nearly 350% increase in the revision rate compared to our retrospective control cohort makes further study unethical.

Of note, none of the patients in our study cohort who underwent primary arterectomy required revision surgery, and this closely corresponds with the senior author's 15-year experience in 978 patients. In addition, decompression of the supraorbital and supratrochlear nerves without arterectomy was associated with an overall increase in the MHI, although this was not statistically significant. There was statistical improvement in the number of MFDs in both groups following the first surgery. However, the non-arterectomy group did not achieve similar MFD values until after an arterectomy was performed (Figure 5C). To further evaluate the role of arterial flow in the evolution of migraine symptomatology, we are currently using thermography to track migraine activity. Preliminary thermographic data demonstrates a steady increase in "heat signatures" corresponding to worsening pain at the frontal (migraine site I) location and a subsequent decrease and eventual return to baseline heat levels associated with concurrent migraine resolution (unpublished data). Taken together, these data lend support to the idea of a predominantly vascular etiology in the development of migraine headaches, an idea that has long been supported in the neurological literature.[13] Clinically, this also correlates with anecdotal patient reports of headache improvement with placing pressure at the site of pain. This mollifying effect may result from limiting blood flow through the vessel adjacent to a nerve, thereby partially relieving compression. From this experience, the senior author has changed his pre-operative evaluation to include the use of a hand-held ultrasound Doppler to confirm the locations of migraine trigger sites, and he has demonstrated that a Doppler signal over the location of most intense pain consistently predicted the presence of an artery at this location intra-operatively.[14]

This study is not without limitations, most notably the small sample size and potential selection bias. This has been an ongoing study for 6 years, and enrollment has been difficult. Surgery is often a last resort for patients who have exhausted all other treatment options, and as a result, the majority of patients were reluctant to participate in a study in which certain aspects of treatment may be withheld. While some may argue that the study population is so small that it is not possible to properly interpret these results, the statistically significant findings and the overwhelmingly high revision rate in the study group, in the background of the senior author's experience poses an ethical dilemma that, in our opinion, precludes further research. It appears from our limited data, that non-arterectomy study groups had sub-standard treatment outcomes, with associated prolongation of migraine symptoms and exposure to multiple procedures. Similarly, enrolling a sham surgery control group would also be fraught with the same ethical and logistical issues. This has also been addressed to some extent in a previous study.[10] While an argument could be made that these findings are related to a placebo response, this would be unlikely given the blinded nature of the study. The only potential confounding factor would be if the patient were able to identify which procedure he/she had undergone. The only outward change that would be noticeable to the patient would be continued animation if the muscles were not removed, or if there were contour irregularities. As all patients underwent myectomy and contour replacement with fat in a similar fashion, the possibility that a patient could discern his/her treatment group is nearly impossible. Similarly, the nurse study coordinator that collected and input the data was blinded to the treatment arm and would have been unable to influence the patient response directly or indirectly.

Conclusions

The current study is the first of its kind to compare different surgical approaches in the treatment of frontal (supra-orbital/trochlear) migraine headaches in a randomized, prospective cohort. While there appears to be a multi-factorial anatomic etiology to the development of migraine headaches in the supra-orbital/trochlear area, our study suggests that arterectomy is necessary for successful surgical treatment at this site.

Conflict of interest and funding

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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