Migraine Surgery and Determination of Success over Time by Trigger Site: A Systematic Review of the Literature

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OUTCOMES

Prevention

Background: Migraine headache is a debilitating disorder that produces high costs and compromises patient quality of life. This study aimed to evaluate surgery success and the longevity of the surgical benefit by trigger site.

Methods: A systematic literature review was performed by querying the PubMed, Embase, Scopus, and Web of Science databases. The keywords "surgery," "migraine," "outcomes," "headache index," and synonyms in titles and abstracts were used to perform the search.

Results: A total of 17 articles published between 2009 and 2019 met the inclusion criteria. Six studies were prospective and 11 were retrospective. Most of the studies (77.8%, 77.8%, and 80%, respectively) reported success of migraine surgery at 12-month follow-up for trigger sites I, II, and III, respectively. For trigger site IV, the greatest Migraine Headache Index reduction (93.4%) was observed at 12-month follow-up, and the earliest Migraine Headache Index reductions (80.3% and 74.6%) were observed at 6-month follow-up. All studies that evaluated trigger sites V and VI identified surgery success at 12-month follow-up. Migraine surgery was found to remain beneficial at 22 months for trigger sites I, II, III, and IV.

Conclusions: The symptomatic improvement may initially be evident at 6 months for trigger site IV and at 12 months for trigger sites I, II, III, V, and VI. Surgical benefit in trigger sites I, II, III, and IV can persist after 22 months. Further studies are required to evaluate results at longer follow-up. (*Plast. Reconstr. Surg.* 151: 120e, 2023.)

Migraine headache is a debilitating disorder that causes considerable suffering.[1,2] It has an overall prevalence of 15.9% (10.7% in men and 20.6% in women) in the United States.[3] Disability directly related to migraine headache produces costs of more than $13 billion each year in the United States.[4] In addition, admissions to the emergency department for migraine headaches refractory to medical treatment carry a significant economic burden up to a total of $1.2 billion per year.[5]

The definitive pathogenesis of migraine headache remains unclear. It is suspected to be a consequence of the activation and sensitization of first-order trigeminovascular neurons that release vasoactive peptides inducing local inflammation.[6] This supports the use of medical treatment. However, approximately 5% of patients present refractory symptoms.[7] As a result, other therapies such as botulinum toxin injections, selective nerve blocks, and peripheral neurolysis have been tried to improve symptoms with positive results.[7,8] These findings have provided clinical evidence toward a potential peripheral origin of some headaches: the compression of sensory branches of trigeminal and occipital nerves that supply the face and back of the head.[9] Extracranial trigger sites have been identified as site I (frontal), site II (zygomaticotemporal), site III (rhinogenic), site IV (greater occipital), site V (auriculotemporal), site VI (lesser occipital),

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and site VII (nummular).[10,11] Deactivation of these peripheral trigger sites has been shown to improve symptoms.[12–20] Despite significant results after surgery, the differences in success rates and the subjective report of surgical outcomes in some studies have limited evaluation of its efficacy. Many of these patients undergo deactivation of nerves in multiple trigger sites; thus, determination of surgery success by specific trigger site has been difficult to report. In addition, there is no strong evidence yet to determine the time after surgery of significant improvement by trigger site. By evaluating the time in which surgery success occurs, we might predict surgical outcomes more accurately. The purpose of this study was to summarize the current evidence, evaluate migraine surgery success by trigger site, and give an approximation of the surgical benefit over time.

PATIENTS AND METHODS

Study Selection

Our systematic review included all studies evaluating the efficacy of migraine surgery over time by trigger site following the Population, Intervention, Control, Outcome, Study Design/Preferred Reporting Items for Systematic Reviews and Meta-Analyses[21,22] guidelines for article identification and final selection (Table 1 and Fig. 1).

Table 1. Population, Intervention, Control, Outcome, Study Design Inclusion Criteria

Population	Adult patients diagnosed with migraine headache
Intervention	Migraine surgery at one or more trigger points
Control	No need for control group
Outcomes	Surgical outcomes (MHI and/or MH reduction success rate) by trigger site
Study design	All retrospective and prospective studies

MHI, Migraine Headache Index; MH, migraine headache.

Inclusion Criteria

- Adult patients diagnosed with migraine headache.
- Studies reported preoperative and postoperative Migraine Headache Index (MHI) and/or migraine headache (MH)

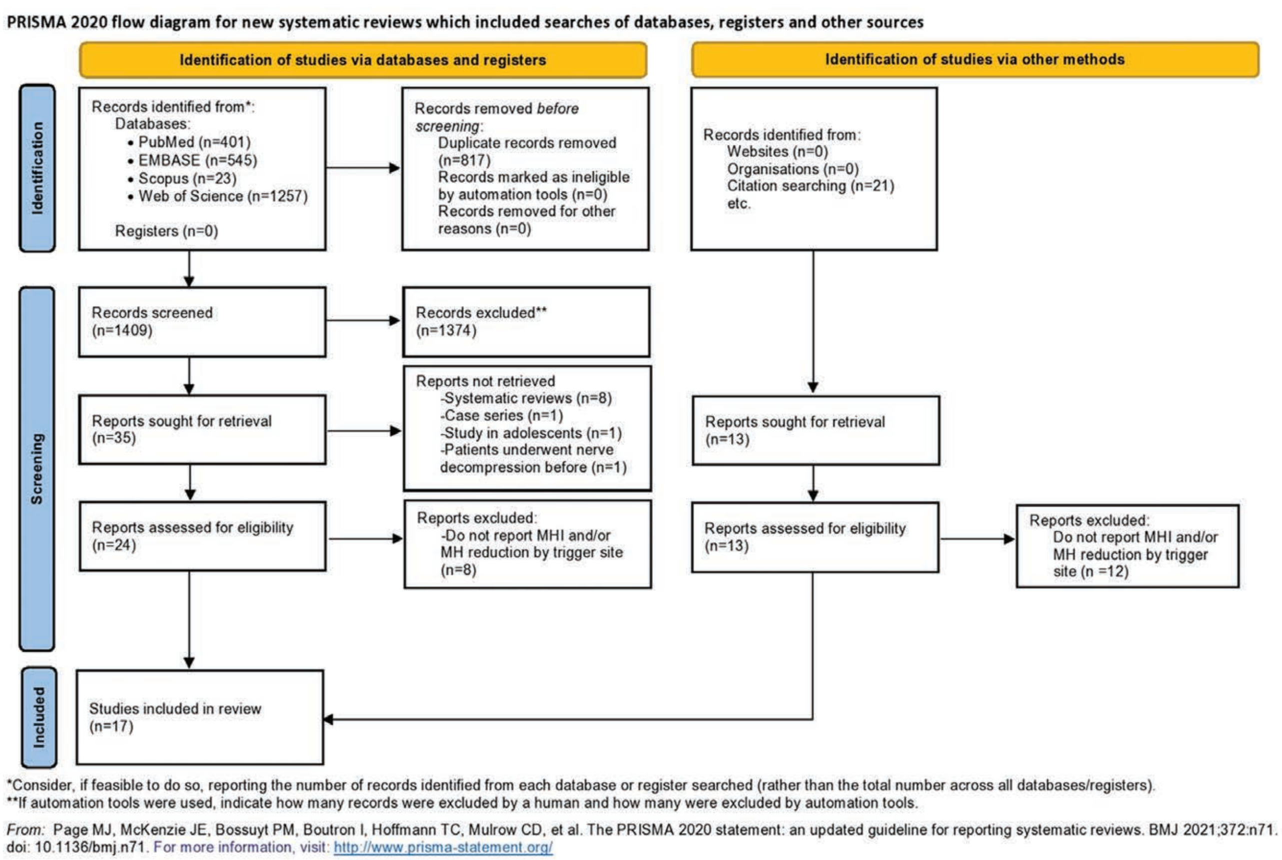

Fig. 1. Inclusion and exclusion criteria following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. *MHI*, Migraine Headache Index; *MH*, migraine headache.

reduction, or success rates by trigger site. MHI was calculated by multiplying frequency (days per month) by intensity (pain visual analogue scale of 0 to 10) by duration (as a fraction of 24 hours). MH reduction was defined as a 50% or greater improvement in migraine headache frequency, duration, or severity. Migraine surgery success was defined as a minimum 50% or more reduction in the frequency, severity, duration, or MHI.
- Studies looked for at least one of the following peripheral trigger points for migraine: sites I, II, III, IV, V, and VI.
- Patients were treated medically without significant improvement of the pain.
- Primary data from prospective/retrospective observational studies and randomized clinical trials.

Exclusion Criteria

- Patients who had undergone any other surgical procedures to treat migraine previously.
- Studies that evaluated the use of botulinum toxin injection without surgery, narcotics before surgery, intraoperative corticosteroids, radiosurgery, or nerve stimulation.
- Studies that did not report surgical outcomes in terms of MHI and/or MH reduction or success rates.
- Review or systematic reviews of the literature, case reports, or case series.

Data Sources and Search Strategy

This systematic review was conducted on June 7, 2021, by querying the PubMed, Embase, Scopus, and Web of Science databases. A search strategy was generated using the following terms: ("surgery"[Title/Abstract] OR "Nerve decompression"[Title/Abstract] OR "Nerve release"[Title/Abstract] OR "Muscle resection"[Title/Abstract]) AND ("Migraine"[Title/Abstract] OR "Migraine Headache"[Title/Abstract] OR "Neuralgia"[Title/Abstract]) AND ("outcomes"[Title/Abstract] OR "headache index" [Title/Abstract]). Identified studies were uploaded into EndNote (Clarivate, London, United Kingdom). References of reviews and systematic review articles on surgical outcomes were further reviewed for eligibility. Articles were first screened manually by one author (M.T.H.) and selected according to inclusion and exclusion criteria. First, studies were reviewed based on the title and abstract. Second, the full texts of the selected studies were screened for the final selection. If there were questionable articles to include, a second reviewer (J.E.J.) reviewed these articles according to selection criteria, and both reviewers came to an agreement for the final decision.

Quality Assessment

The reviewers assessed the level of evidence of the included studies using the Oxford Center for Evidence-Based Medicine. The quality of each study was evaluated with the Newcastle-Ottawa Scale. All articles were cohort studies, and most of them (nine of 17) had a Newcastle-Ottawa Scale score of 5 of 9 (Table 2).[8,11,23–37] These nine studies lost 4 points (1 point in selection, 2 points in comparability, and 1 point in outcome), and the remaining eight lost 3 points (1 point in outcome and 2 points in comparability). The loss of points in selection was attribtutable to the lack of comparative group, whereas the loss of points in comparability was attribtutable to the lack of adjustment for confounders. All the studies were found to be at risk of bias in outcomes given the subjective report of pain improvement after surgery.

Data Pooling and Data Analysis

All the data from the selected studies were pooled. General description of the studies included author, year, study design, number of patients, age, trigger points addressed, type of surgery, and complications (Table 2). Further description considered number of trigger points addressed, preoperative and postoperative MHI, MHI or MH reduction, success rates, and follow-up (Table 3).[8,11,23–37] MHI/MH reduction rates were presented over time by trigger sites (Figs. 2 and 3). This evaluated the time when MHI and/or MH reduction occurred.

RESULTS

A total of 2226 articles were identified from the PubMed, Embase, Scopus, and Web of Science databases, with 21 records from other sources. From all these, only 17 articles met the inclusion criteria (Fig. 1). All included studies were published between 2009 and 2019 (Table 2). Six studies[11,23–27] were prospective and 11[8,28–37] were retrospective. The number of patients included in

Table 2. Published Articles to Date Evaluating Surgical Outcomes of Migraine Surgery by Trigger Point

Reference	Study Design	OCEBM Level of Evidence	Quality (Newcastle-Ottawa Scale)	No. of Patients	Sex	Age of Patients (yr)	Trigger Points Addressed	Surgery	Complications
Gfrerer et al., 2019[11]	Prospective	2	5	83	71 F, 12 M	Mean: 45 (SD: 13, range: 18–73)	Site I: 47 Site II: 36 Site III: 13 Site IV: 51 Site V: 5 Site VI: 13	—	Transient numbness and shooting pain at the surgical site (all patients have this resolved after 3 mo) Persistent numbness at 12 mo (n = 4) Shooting nerve pain at 3 mo resolved with gabapentin (n = 2) Hematoma and wound dehiscence treated conservatively (n = 1) Seroma at the occipital surgical site (n = 2) Neuroma at the occipital site that was resected (n = 1)
Afifi et al., 2019[37]	Retrospective	2	5	71	—	—	Site IV Concomitant LON: 47	Occipital nerve decompression	Infection (n = 1)
Gather-wright et al., 2018[23]	Prospective	2	6	13	13 F	Mean: 41.8 (range: 33–54)	Site I: 13 Concomitant site II: 9 Concomitant site III: 12	Myectomy and foraminotomy/fasciotomy with (n = 4) or without arterectomy (n = 4) Myectomy and arterectomy (n = 5)	Required a site I revision (n = 4) and required an arterectomy as part of the revision
Lee et al., 2017[28]	Retrospective	2	5	98	88 F, 10 M	Mean: 43.6 (range: 18–68)	Site III	—	—
Ascha et al., 2017[24]	Prospective	2	5	195	176 F, 19 M	Median: 47 (range: 16–76)	Site IV: 14 Concomitant: Site I: 148 Site II: 143 Site III: 141 Site V: 8	Occipital nerve decompression	Neck discomfort, tightness or weakness (n = 22) Itching (n = 9) Hypersensitivity (n = 6) Hyposensitivity (n = 2) Hypertrophic scar (n = 1) Reoperation for dehiscence (n = 1)
Peled, 2016[25]	Prospective	2	5	19	17 F, 2 M	ND	Site II: 19 9 Bilateral 10 unilateral	Decompression or neurectomy	None
Kurlander et al., 2016[29]	Retrospective	2	5	270	242 F, 28 M	Median age: 45 (range: 20–70)	Site I: Site I only (n = 34) Concomitant: Site II (n=215) Site III (n = 168) Site IV (n = 125) Site V (n = 2)	Transpalpebral nerve decompression	Numbness (34.5%) and itching (14.8%) Eyelid ptosis (5.8%)

(*Continued*)

Table 2. *Continued*

Reference	Study Design	OCEBM Level of Evidence	Quality (Newcastle-Ottawa Scale)	No. of Patients	Sex	Age of Patients (yr)	Trigger Points Addressed	Surgery	Complications
Guyuron et al., 2015[26]	Prospective	2	6	19	18 F, 1 M	Mean: 38.2 (range: 19–62)	Site (II): Bilateral	Neurectomy (avulsion) and decompression	None
Gfrerer et al., 2014[30]	Retrospective	2	5	35	30 F, 5 M	Mean: 46.1 (SD: 12.7)	43 procedures Site I ($n = 26$) Site II ($n = 27$) Site IV ($n = 21$)	Site I: decompression of the nerves, the glabellar muscle group was removed and a fat pad flap was wrapped around the nerves Site II: decompression of the nerve Site IV: avulsion of the nerves	8 patients underwent a secondary procedure because of unmasking of a latent trigger point
Kurlander et al., 2014[31]	Retrospective	2	5	246	223 F, 23 M	Median: 46	Site II Concomitant with other sites Alone	ZT branch of the trigeminal nerve avulsion and any accompanying vessels were coagulated; the proximal nerve end was allowed to retract into the temporalis muscle	—
Lee et al., 2013[36]	Retrospective	2	6	188 (144: BTA success group, 44: BTA failure group)	—	BTA success group: 44.6 BTA failure group: 44.8	Site I: 109/144 (BTA success), 23/44 (BTA failure) Site II: 100/144 (BTA success), 23/44 (BTA failure) Site III: 72/144 (BTA success), 26/44 (BTA failure) Site IV: 72/144 (BTA success), 22/44 (BTA failure)	Site I: corrugator supercilia, depressor supercilia, and lateral portion of the procerus were removed Site II: 2.5 cm of the ZT branch was removed Site III: septoplasty, turbinectomy, or both Site IV: a portion of the semispinalis capitis muscle was removed to decompress the greater occipital nerve bilaterally	—

(*Continued*)

Table 2. *Continued*

Reference	Study Design	OCEBM Level of Evidence	Quality (Newcastle-Ottawa Scale)	No. of Patients	Sex	Age of Patients (yr)	Trigger Points Addressed	Surgery	Complications
Lee et al., 2013[32]	Retrospective	2	6	229 (TON-R: 111, TON-NR: 118)	TON-R: F 86.5% TON-NR: F 88.1%	TON-R: 44.7 TON-NR: 45.3	Site IV	Occipital nerve decompression. If the third occipital nerve was encountered, it was avulsed and allowed to retract into the proximal portion of the semispinalis capitis muscle	—
Chmielewski et al., 2013[33]	Retrospective	2	6	OAR group: 55 No resection of the occipital artery (control): 115	OAR: 89.1% F Control: 87% F	Mean OAR: 45.9 Mean control: 44.6	Site IV	A small portion of the semispinalis capitis muscle was removed; if there was intimate relationship between the GON and the occipital artery or its branches, the artery was cauterized and removed.	—
Liu et al., 2012[34]	Retrospective	2	6	335 BTA group: 245 Control (patients who either never received BTA or had received multiple-site BTA for therapeutic purposes): 90	ND	ND	1 or combination of trigger sites: Site I Site II Site III Site IV	Site I: removal of the glabellar muscle group to decompress the supraorbital and supratrochlear nerves Site II: avulsion of the ZT branch of the trigeminal nerve Site III: septoplasty and turbinectomy Site IV: removal of small segment of the semispinalis capitis muscle to decompress the GON or remove the occipital artery	—

(*Continued*)

Table 2. *Continued*

Reference	Study Design	OCEBM Level of Evidence	Quality (Newcastle-Ottawa Scale)	No. of Patients	Sex	Age of Patients (yr)	Trigger Points Addressed	Surgery	Complications
Chepla et al., 2012[35]	Retrospective	2	6	43 (group 1: foraminotomy and myomectomy) 43 (group 2: only myomectomy)	Group 1: 42 F, 1 M Group 2: 42 F, 1 M	Group 1: 46.47 (SD: 1.92) Group 2: 42.51 (SD: 1.46)	Site I and concomitant sites: I, II, III, and IV: group 1 (n = 19), group 2 (n = 21) Sites I, II, and III: group 1 (n = 10), group 2 (n = 9) Sites I, II, and IV: group 1 (n = 5), group 2 (n = 6) Sites I, III, and IV: group 1 (n = 1), group 2 (n = 0) Sites I and II: group 1 (n = 5), group 2 (n = 6) Sites I and III: group 1 (n = 1), group 2 (n = 0) Sites I and IV: group 1 (n = 1), group 2 (n = 0) Site I: group 1 (n = 1), group 2 (n = 1)	Group 1: supraorbital foraminotomy and myectomy Group 2: only glabellar myectomy	—
Janis et al., 2011[8]	Retrospective	2	5	24	23 F, 1 M	Mean: 44.4 (range: 23.2–66.5)	Multiple trigger sites: SON/STN alone: n = 1 SON/STN/ZTN alone: n = 4 GON alone: 4 SON/STN/ZTN plus GON: n = 7 SON/STN/ZTN plus septoplasty: n = 3 SON/STN/ZTN plus GON plus septoplasty: n = 5	63 surgical trigger point decompressions	Immediate postoperative migraine headache (n = 11) Paresthesias lasted 163 days on average, 1 patent experienced it over 1 yr Mild incisional alopecia (n = 11), which resolved in 5 patients for the last follow-up

(*Continued*)

Table 2. *Continued*

Reference	Study Design	OCEBM Level of Evidence	Quality (Newcastle-Ottawa Scale)	No. of Patients	Sex	Age of Patients (yr)	Trigger Points Addressed	Surgery	Complications
Guyuron et al. 2009[27]	Prospective	2	6	75 (surgery: 49, sham surgery: 26)		Surgery: 45.1 range: (SD: 9.5) Sham surgery: 44.6 (SD: 8.3)	Multiple sites Site I: Surgery: 19 Sham: 10 Site II: Surgery: 19 Sham: 9 Site IV: Surgery: 11 Sham: 7	Site I: removal of the glabellar muscles Site II: endoscopic removal of a segment of the ZT branch of the fifth nerve Site IV: Segment of the semispinalis capitis muscle medial to the GON was removed	All experienced paresthesia in the immediate postoperative period Numbness 1 yr postoperatively (n = 1) Temporal hollowing (n = 10) Temporary intense itching (n = 1) Uneven brow movement (n = 1) Temporary hair loss or thinning (n = 1) Residual corrugator supercilii muscle function (n = 1) Neck stiffness 1 yr postoperatively (n = 1)

OCEBM, Oxford Center for Evidence-Based Medicine; F, female; M, male; LON, lesser occipital nerve; ND, not determined; ZT, zygomaticotemporal; BTA, botulinum toxin type A; TON-R, third occipital nerve resected; TON-NR, third occipital nerve not resected; OAR, occipital artery resection; GON, greater occipital nerve; SON, supraorbital nerve; STN, supratrochlear nerve; ZTN, zygomaticotemporal nerve.

each study ranged from 13[23] to 335,[34] with a mean age ranging from 38.2[26] to 47[24] years. Nine studies[8,11,23,27,29,30,34–36] evaluated surgical outcomes for trigger site I; nine,[8,11,25–27,30,31,34,36] for trigger site II; five,[8,11,28,34,36] for trigger site III; 10,[8,11,24,27,30,32–34,36,37] for trigger site IV; two,[11,30] for trigger site V; and two,[11,30] for trigger site VI (Table 3).

Trigger Site I

For trigger site I, all studies identified that migraine surgery was successful (had ≥50% of MHI/MH reduction) (Fig. 2, *above*). Seven studies (77.8%) reported a MHI/MH reduction at 12-month follow-up.[11,27,29,30,34–36] When outcomes were assessed in a long-term study, Gatherwright et al.[23] observed the greatest MHI reduction of 91% at a mean follow-up of 21.6 months, and Janis et al.[8] reported a MH reduction of 50% or more at a mean follow-up of 22 months.

Trigger Site II

Seven studies (77.8%)[11,26,27,30,31,34,36] observed a greater than or equal to 50% MHI/MH reduction in trigger site II at 12 months after surgery (Fig. 2, *center*). At long-term follow-up (mean, 22 and 23 months), two studies[8,25] identified a 50% or greater MHI/MH reduction in site II.

Trigger Site III

All studies evaluating trigger site III reported a successful operation at 12 months or more of follow-up (Fig. 2, *below*). Gfrerer et al.[11] observed the greatest benefit (MHI reduction, 63.4%) at 12 months after surgery.

Trigger Site IV

At 12-month follow-up, Guyuron et al.[27] observed the greatest MHI reduction (93.4%). The earliest MHI reductions (80.3% and 74.6%) after deactivation of trigger site IV were reported at 6-month follow-up[32] (Fig. 3, *above*). All studies reported 50% or more MHI/MH reduction at 6-,[32] 8-,[37] 12-,[11,24,27,30,32,34] 18-,[33] and 22-month[8] follow-up.

Trigger Site V

The two studies that evaluated trigger site V found that migraine surgery was successful at 12-month follow-up (Fig. 3, *center*). Gfrerer et al.[11] reported a MHI reduction of 68.6% at 12-month follow-up.

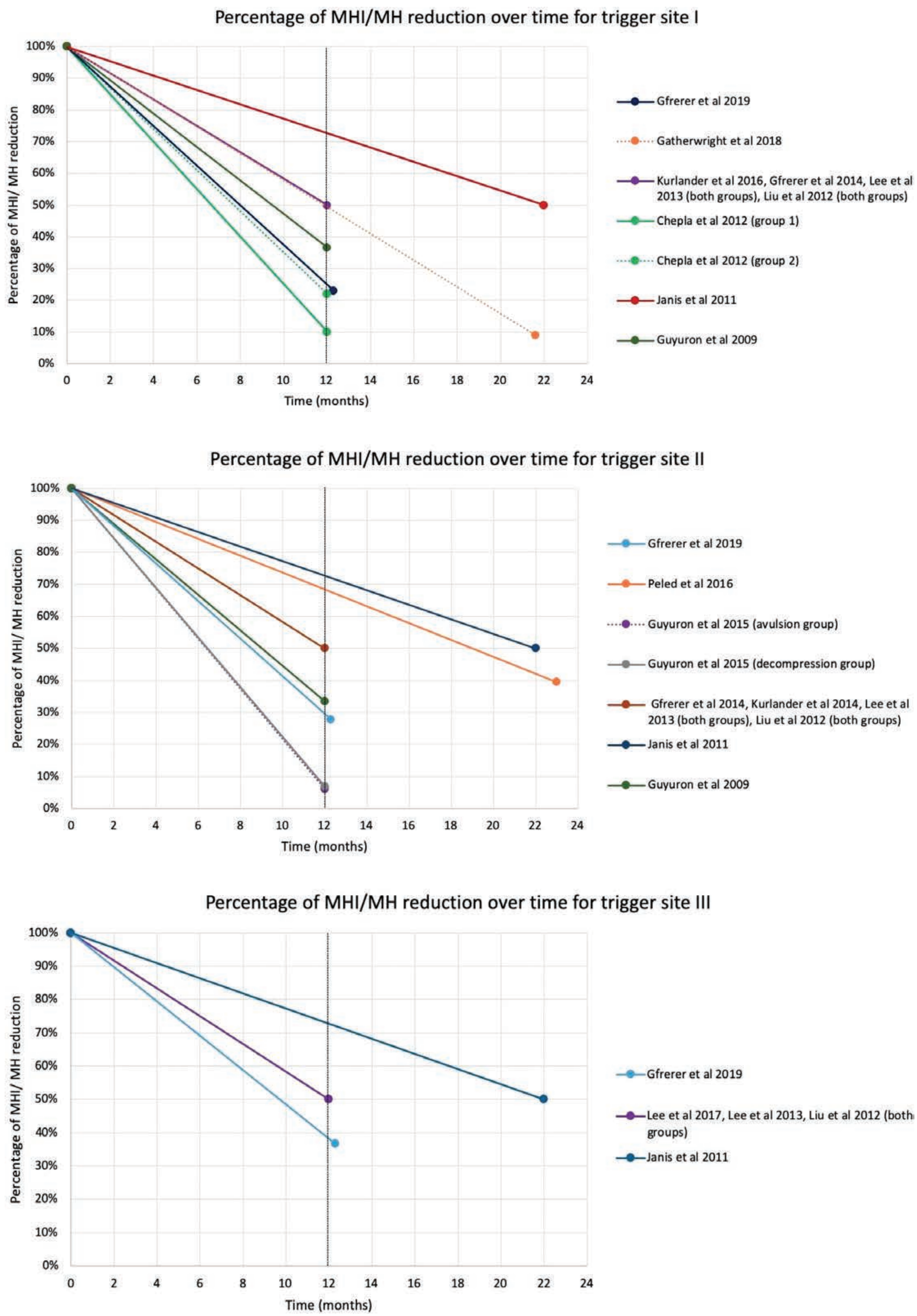

Fig. 2. Percentages of MHI or MH reduction over time for trigger points I, II, and III.

Trigger Site VI

Similar to trigger site V, surgery success was identified at 12-month follow-up (Fig. 3, *below*). Gfrerer et al.[11] observed a MHI reduction of 84% at 12 months when evaluating surgery on trigger site VI.

DISCUSSION

Migraine surgery resembles any peripheral nerve decompression. For instance, in carpal tunnel syndrome release, immediate symptomatic relief is often achieved. However, failure has been

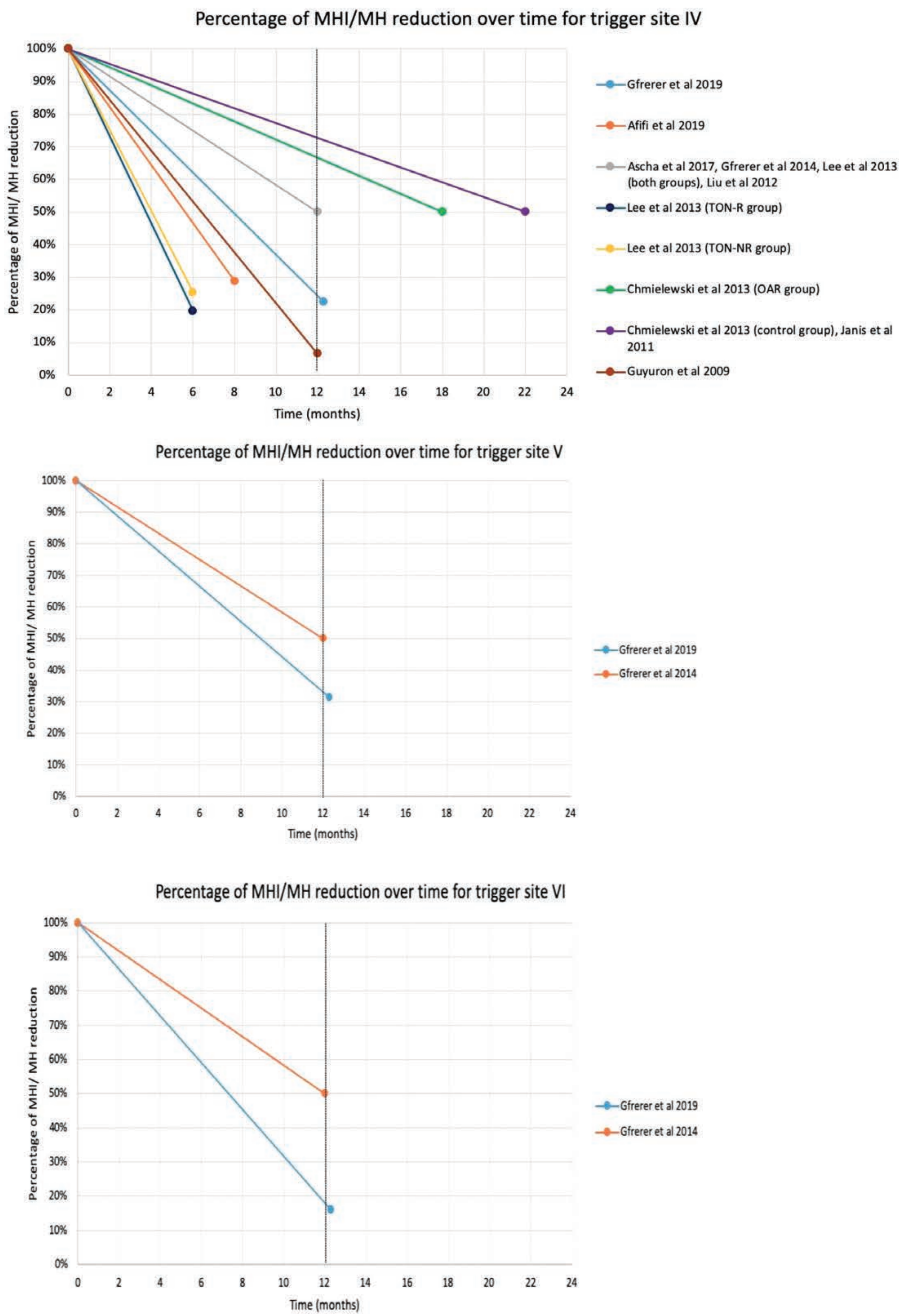

Fig. 3. Percentages of MHI or MH reduction over time for trigger points IV, V, and VI.

reported in 7% to 25% of patients in cases where the median nerve has been compressed for many years.[38] The possible causes of this treatment failure include incomplete release, recurrent compression because of new scar tissue formation or edema, and incorrect diagnosis.[38,39] Similarly, these causes may explain the different rates of success after migraine surgery.

Table 3. Studies by Migraine Trigger Site with MHI and/or MH Reduction and Success Rates at Last Follow-Up

Trigger Site and Reference	No. of Trigger Sites	Preoperative MHI	Postoperative MHI	MHI Reduction	MHI and/or MH Reduction (%)	Success Rate	Follow-Up (mo)
Site I: frontal site							
Gfrerer et al., 2019[11]	47	126.6 (SD: 97)	29.1 (SD: 12.2)	97.5 (SD: 97.7)	77%	—	Mean: 12.3
Gather-wright et al., 2018[23]	13	52.6 (range: 3.8–85)	4.7 (range: 0–21.3)	47.9	91%	—	Mean: 21.6 (range: 7.6–34.1)
Kurlander et al., 2016[29]	34	—	—	—	≥50%	88%	At least 12
Gfrerer et al., 2014[30]	26	—	—	—	≥50%	92%	12
Lee et al., 2013[36]	93	—	—	—	BTA success group: ≥50% BTA failure group: ≥50%	BTA success group: 92% BTA failure group: 69%	12
Chepla et al., 2012[35]	43 (group 1: foraminotomy and myomectomy) 43 (group 2: only myomectomy)	Group 1: 107.80 (SD: 15.51) Group 2: 120.30 (SD: 21.84)	Group 1: 11.13 (SD: 2.95) Group 2: 26.45 (SD: 6.51)	Group 1: 96.67 (SD: 15.79) Group 2: 93.85 (SD: 22.79)	Group 1: 90% Group 2: 78%	—	12
Liu et al., 2012[34]	186 (BTA group), 67 (control group)	—	—	—	BTA group: ≥50% Control group: ≥50%	BTA group: 87% Control group: 90%	12
Janis et al., 2011[8]	20	—	—	—	≥50%	85%	Mean: 22 (range: 5–54)
Guyuron et al., 2009[27]	19	24.3 (SD: 25.9)	8.9 (SD: 32.2)	15.4 (SD: 19.1)	63.4%	—	12
Site II: zygomaticotemporal site							
Gfrerer et al., 2019[11]	36	127.6 (SD: 92.8)	32.9 (SD: 13.1)	94.7 (SD: 93.72)	74.2%	—	Mean: 12.3
Peled, 2016[25]	19	131.7	52	79.7	60.5%	—	Mean: 23
Guyuron et al., 2015[26]	19	Avulsion group: 41 (SD: 9.6) Decompression group: 42 (SD: 9.5)	Avulsion group: 2.5 (SD: 0.9) Decompression group: 2.9 (SD: 0.9)	Avulsion group: 38.5 (SD: 9.64) Decompression group: 39.1 (SD: 9.54)	Avulsion group: 93.9% Decompression group: 93%	—	12
Gfrerer et al., 2014[30]	27	—	—	—	≥50%	93%	12
Kurlander et al., 2014[31]	246	—	—	—	≥50%	85%	At least 12 (range: 12–120)
Lee et al., 2013[36]	82	—	—	—	BTA success: ≥50% BTA failure: ≥50%	BTA success group: 95% BTA failure: 73%	12
Liu et al., 2012[34]	164 (BTA group), 70 (control group)	—		—	BTA success: ≥50% BTA failure: ≥50%	BTA group: 87% Control group: 86%	12

(*Continued*)

Table 3. *Continued*

Trigger Site and Reference	No. of Trigger Sites	Preoperative MHI	Postoperative MHI	MHI Reduction	MHI and/or MH Reduction (%)	Success Rate	Follow-Up (mo)
Janis et al., 2011[8]	19	—		—	≥50%	89%	Mean: 22 (range: 5–54)
Guyuron et al., 2009[27]	19	28.4 (SD: 22.7)	9.5 (SD: 31.5)	18.9 (SD: 21.8)	66.5%	—	12
Site III: rhinogenic site							
Gfrerer et al., 2019[11]	13	103.7 (SD: 108.5)	37.9 (SD: 82.6)	65.8 (SD: 25.9)	63.4%	—	Mean: 12.3
Lee et al., 2017[28]	98	—	—	—	≥50%	74%	Mean: 14 (range: 1–30)
Lee et al., 2013[36]	6	—	—	—	≥50%	50%	12
Liu et al., 2012[34]	BTA group: 124 Control group: 68	—	—	—	BTA success: ≥50% BTA control: ≥50%	BTA group: 85% Control group: 81%	12
Janis et al., 2011[8]	8			—	≥50%	100%	Mean: 22 (range: 5–54)
Site IV: greater occipital nerve site							
Gfrerer et al., 2019[11]	51	128.3 (SD: 97.5)	28.7 (SD: 48.2)	99.6 (SD: 108.76)	77.6%	—	Mean: 12.3
Afifi et al., 2019[37]	71	191	55	136	71.2%	—	Mean: 8
Ascha et al., 2017[24]	195	111.8	45.5	—	≥50%	82%	At least 12
Gfrerer et al., 2014[30]	21			—	≥50%	90%	12
Lee et al., 2013[32]	TON-R: 111 TON-NR: 118	TON-R: 130.3 TON-NR: 107.7	TON-R: 25.6 TON-NR: 27.4	TON-R: 104.7 TON-NR: 80.3	TON-R: 80.3% TON-NR: 74.6%	—	At least 6
Chmielewski etal.,2013[33]	OAR group: 55 No resection of the occipital artery (control): 115	OAR: 8 (SD: 2.9) Control: 8.2 (SD: 1.9)	OAR: 4.7 (SD: 3.1) Control: 4.1 (SD: 3.7)	—	OAR: ≥50% Control: ≥50%	OAR: 80% Control: 91.3%	Mean: 18 (range: 12–87) Control group: 22
Lee et al., 2013[36]	72/144 (BTA success), 22/44 (BTA failure)	—	—	—	BTA success group: ≥50% BTA failure group: ≥50%	BTA success group: 96% BTA failure group: 62.5%	12
Liu et al., 2012[34]	86 (BTA group) 57 (control group)	—	—	—	BTA group: ≥50% Control group: ≥50%	BTA group: 90% Control group: 81%	12
Janis et al., 2011[8]	16	—	—	—	≥50%	94%	Mean: 22 (range: 5–54)
Guyuron et al., 2009[27]	11	39.7 (SD: 47.4)	2.6 (SD: 67.7)	37.1 (SD: 48.4)	93.4%	—	12
Site V: auriculotemporal site							

(*Continued*)

Table 3. *Continued*

Trigger Site and Reference	No. of Trigger Sites	Preoperative MHI	Postoperative MHI	MHI Reduction	MHI and/or MH Reduction (%)	Success Rate	Follow-Up (mo)
Gfrerer et al., 2019[11]	5	148.9 (SD: 102.8)	46.8 (SD: 76.9)	102.1 (SD: 128.38)	68.6%	—	Mean: 12.3
Gfrerer et al., 2014[30]	5	—	—	—	≥50%	80%	12
Site VI: lesser occipital nerve							
Gfrerer et al., 2019[11]	13	159.5 (SD: 110.2)	27.1 (SD: 35.5)	132.4 (SD: 115.78)	84%	—	Mean: 12.3
Gfrerer et al., 2014[30]	12			—	≥50%	100%	12

BTA, botulinum toxin type A; TON-R, third occipital nerve resected; TON-NR, third occipital nerve not resected; OAR, occipital artery resection.

Despite the efforts to determine the trigger site before surgery,[20,40–45] the rates of migraine surgery success vary between studies.[8] Possible reasons for incomplete headache migraine elimination are the unmasking of untreated trigger sites, the incorrect selection of the trigger site, the clinical presentation of multiple trigger sites at the same time and, as a consequence, the lack of specificity of outcomes for each trigger site and the time when these outcomes were evaluated. We discuss below the differences on MHI/MH reduction and surgery success by trigger site and over time.

Trigger site I

Chepla et al.[35] observed the greatest MHI reduction of 90% in the frontal site at 12 months after surgery. They reported this MHI reduction in patients who underwent glabellar myectomy and supraorbital foraminotomy. In contrast, they observed a lower but significant MHI reduction of 78% in patients who underwent traditional resection of the glabellar myectomy without foraminotomy at 12 months.[35]

The longest follow-up at which migraine surgery outcomes were evaluated was 5 years.[46] Although outcomes by trigger site were not reported, 88% of the patients who underwent migraine surgery expressed 50% or more reduction of frequency, intensity, or duration of migraine.[46] Gatherwright et al.[23] and Janis et al.[8] reported the longest mean follow-up (21.6 months and 22 months, respectively) at which surgery has been proven to be successful for site I. Gatherwright et al.[23] found a higher MHI reduction compared with the other studies. This study included patients who underwent myectomy and arterectomy, fasciotomy/foraminotomy in addition to myectomy and arterectomy, and myectomy and fasciotomy/foraminotomy but no arterectomy.[23] Most of these patients had a concomitant migraine operation on sites II ($n = 9$) and III ($n = 12$) at the time of surgery.

We believe that the surgical approach (type of surgery and trigger sites operated on) may likely be the origin of the differences in surgical outcomes between studies. For instance, the study by Chepla et al. did not include patients who underwent arterectomy. Moreover, the smaller sample size and the number of trigger sites per patient in the study by Gatherwright et al. may be another factor that could explain the differences in MHI reduction compared with the study by Chepla et al.

Trigger Site II

The greatest MHI reduction (93.9%) was reported at 12 months after surgery for trigger site

II.[26] At this follow-up, the study by Guyuron et al. in 2009 observed a significant MHI reduction of 66.5% after surgery of site II.[27] In this study, participants underwent surgery of a single predominant trigger site, which means that other trigger sites may have also been present at the time of surgery.[27] This may have limited their surgical outcomes. In a more recent prospective study, Guyuron et al.[26] found the greatest MHI reductions (93.9% and 93%) for trigger site II at 12 months after surgery. In this recent study, the authors compared the MHI reduction in 20 patients who underwent avulsion of the zygomaticotemporal branch of the trigeminal nerve on one side (avulsion group), and decompression by means of fasciotomy and removal of the zygomaticotemporal artery on the other side (decompression group). They did not find any statistical difference between groups in terms of MHI reduction, suggesting that both procedures were appropriate to deactivate the temporal trigger site.[26]

When evaluating the surgery success in the long term, Janis et al.[8] observed that the surgery success remained after 22 months. Similarly, Peled[25] observed a 60.5% reduction in MHI at 23-month follow-up.

Trigger Site III

Other studies have documented surgical success for trigger site III. At almost 10 years after surgery, Welge-Luessen et al.[47] reported that from 20 patients who were followed up, 30% remained free of pain, 35% had significant improvement of symptoms, and 35% did not have any benefit from surgery. Furthermore, Novak and Makek[48] evaluated 229 patients with migraines, cluster headaches, and idiopathic headaches with nasal pathology who underwent surgery of trigger site III. They found that 78.5% of these patients remained asymptomatic postoperatively, whereas 11.5% had a sensation of pressure in the head on rare occasions but no migraines.[48] Even though these studies suggest a long-term benefit of migraine surgery in this trigger site, these studies lack a more specific instrument to measure surgical outcomes such as the MHI and did not use a standard definition for surgery success.

This systematic review found that all studies reported a significant MHI/MH reduction (≥50%) at 12 months. Lee et al.[36] evaluated patients who underwent migraine surgery in multiple trigger sites. Only six patients who underwent surgery exclusively of trigger site III were included in this review. The surgery success of this study accounted for 50%, which means that only three of six patients had a greater than or equal to 50% MHI reduction after surgery at 12 months.[36] Likewise, Lee et al.[28] performed a more recent study evaluating the intranasal abnormality in migraine surgery. Interestingly, they found that patients who failed surgery (<50% MHI reduction) had significantly higher contact points compared with successful patients. This highlighted the correlation of the nasal abnormality with migraine episodes.

Trigger Site IV

Our results agree with previous systematic reviews that support the effectiveness of migraine surgery for site IV.[14,19] In particular, our study observed that migraine surgery can be successful as early as 6 months compared to other trigger sites. Lee et al.[32] conducted a retrospective study to evaluate whether removing the third occipital nerve, which is often encountered during the dissection for greater occipital nerve decompression, offers any additional benefit in surgical outcomes. Results of this study did not find any statistical difference in overall MH reduction and elimination between those in which the third occipital nerve was removed and those in which this nerve was not removed. However, both groups demonstrated to have the greatest MHI reduction at 6-month follow-up, considered the earliest when compared with the other studies included in this systematic review.

Similarly, Ducic et al.[49] reported the surgical outcomes of 206 patients who underwent neurolysis of the greater or excision of the greater and/or lesser occipital nerves. This study was not included in our systematic review, given that the MHI change was not specific for trigger sites IV and VI. However, it is important to mention that a significant MHI reduction of 91.6% was identified after surgery at 12 or more months. In addition, a total of 35% of participants experienced complete relief at the same follow-up.[49]

Trigger Site V

Even though site V has been historically considered a minor site, compression of the auriculotemporal nerve can cause significant pain.[50] Our study reported a significant and specific MHI reduction for this specific trigger site at 12-month follow-up. These results are supported by Baldelli et al.,[13] who performed a systematic review evaluating the effectiveness of site V nerve surgical decompression. Success rates (>50% improvement) ranged between 79% and 97%.

Trigger Site VI

The lesser occipital nerve is the ventral ramus of C2 and sometimes C3, and goes from the extradural segment of C2 to its terminal branches in the skin.[51] Compression or stretching in multiple segments along this nerve or from its relationship with the superior cervical ganglion or the ophthalmic branch of the trigeminal nerve may trigger this site.[52] In the same manner of trigger site IV, our results observed success after trigger site VI deactivation only at 12-month follow-up. There were no other studies that evaluated surgical outcomes of this trigger site alone.

Strengths and Limitations

This study is not without limitations. The heterogeneity and the surgical approach of the studies limited the combination of results to report a unique MHI change by trigger site over time. The report of studies that analyze outcomes at different follow-ups would have been more accurate to compare success rate by trigger site over time; however, all studies reported outcomes only at the last follow-up. Regardless, we were able to identify the surgery success for each study over time and provided evidence at different follow-ups by trigger site. This systematic review included only studies that reported MHI/MH reduction or surgery success to have a uniform unit of measurement to evaluate surgical outcomes. Migraine surgery is sometimes performed in more than one trigger site, limiting the accuracy of surgical outcomes by trigger site. To address this limitation, we included the studies that reported trigger site–specific outcomes. In future studies, we recommend using the trigger site–specific MHI and other surgical outcomes to ensure there is no influence of other concomitant sites. This might have led to a selection bias. Nevertheless, we compared our findings with the results from the studies that were relevant but not included in this systematic review. In addition, inherent limitations of the review methodology attributable to search and publication biases were present. Migraine surgery has proven to be not only therapeutically effective, but also cost-effective. Its cost-effectiveness has been reported at longer follow-up, such as at 5 years after surgery,[53] and in patients who require nonsurgical/medical treatment for more than 6.75 years[54] and 8.25 years.[55] Even though this systematic review confirmed its efficacy in each trigger site with at least 12-month follow-up, based on the evidence, this procedure will likely remain cost-effective when each trigger site is independently evaluated at longer follow-up. We believe these reported data are valuable, as they give a first approximation to the longevity of surgery success for each trigger site.

CONCLUSIONS

Migraine surgery can be effective as early as at 6-month follow-up on trigger site IV and at 12-month follow-up on trigger sites I, II, III, V, and VI. In addition, we observed that the benefit of migraine surgery remains at 22 months after surgery for trigger sites I, II, III, and IV. Further studies should be conducted to evaluate surgery success by trigger site at longer follow-up.

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