Efficacy and Safety of Migraine Surgery

A Systematic Review and Meta-analysis of Outcomes and Complication Rates

Hassan ElHawary, MD, MSc,* Natasha Barone, MSc,† Aslan Baradaran, MD, MSc,* and Jeffrey E. Janis, MD, FACS‡✉

Objective: The objectives of this study are to assess the efficacy and safety of peripheral nerve surgery for migraine headaches and to bibliometrically analyze all anatomical studies relevant to migraine surgery.
Summary Background Data: Migraines rank as the second leading cause of disability worldwide. Despite the availability of conservative management options, individuals suffer from refractive migraines which are associated with poor quality of life. Migraine surgery, defined as the peripheral nerve decompression/trigger site deactivation, is a relatively novel treatment strategy for refractory migraines.
Methods: EMBASE and the National Library of Medicine (PubMed) were systematically searched for relevant articles according to the PRISMA guidelines. Data was extracted from studies which met the inclusion criteria. Pooled analyses were performed to assess complication rates. Meta-analyses were run using the random effects model for overall effects and within subgroup fixed-effect models were used.
Results: A total of 68 studies (38 clinical, 30 anatomical) were included in this review. There was a significant overall reduction in migraine intensity ($P < 0.001$, SE = 0.22, $I^2 = 97.9$), frequency ($P < 0.001$, SE = 0.17, $I^2 = 97.7$), duration ($P < 0.001$, SE = 0.15, $I^2 = 97$), and migraine headache index (MHI, $P < 0.001$, SE = 0.19, $I^2 = 97.2$) at follow-up. A total of 35 studies reported on migraine improvement (range: 68.3%–100% of participants) and migraine elimination (range: 8.3%–86.5% of participants). 32.1% of participants in the clinical studies reported complications for which the most commonly reported complications being paresthesia and numbness, which was mostly transient, (12.11%) and itching (4.89%).
Conclusion: This study demonstrates improved migraine outcomes and an overall decrease in MHI as well as strong evidence for the safety profile and complication rate of migraine surgery.

Keywords: migraine, migraine surgery, peripheral nerve decompression, trigger site deactivation, migraine treatment outcomes, complication rate, safety, efficacy

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From the *Division of Plastic and Reconstructive Surgery McGill University Health Center, Montreal, Canada; †Faculty of Medicine and Health Sciences, McGill University, Montreal, Canada; and ‡Department of Plastic and Reconstructive Surgery, Ohio State University Wexner Medical Center, Columbus, OH.
✉Jeffrey.Janis@osumc.edu.
H.E. and N.B. contributed equally to this work and are considered co-first author.
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Migraines are a common neurovascular disease that affect approximately 1 in 7 individuals worldwide.[1] In the United States alone, >50 million individuals suffer from migraines. Migraines have been traditionally perceived as a central neurovascular disease and medically managed by acute analgesic and abortive medications. However, recent evidence supports peripheral nerve compression as a possible etiology, and thereby, paves the way for surgical management of this condition.[2]

In the early 2000s, surgical approaches were developed to treat medically refractive migraines. These surgeries typically involve peripheral sensory neurolysis, decompression of surrounding potential compressive anatomical structures such as muscle, vessel, fascia, and/or bone, and possible neurectomy.

Since the original article by Guyuron et al in 2000, the number of publications that attempt to assess the efficacy and safety of migraine surgery have been steadily increasing.[3,4] Although the majority of the evidence has demonstrated positive outcomes from migraine surgery, there is still some concern regarding its efficacy.[5,6] Due to the rapidly evolving scientific milieu pertaining to headache surgery, the authors of this article believe an updated systematic review and meta-analysis of evidence is warranted to assess the efficacy and safety of peripheral nerve surgery for migraine headaches.

In addition to a contemporary formal systematic review and meta-analysis, a pooled analysis of complication rates of migraine surgery will be presented which will provide further evidence for the safety profile of this domain of surgery. This can help educate future physicians and patients with regards to the risks associated with these surgeries. The secondary aim is to bibliometrically analyze all anatomical studies relevant to migraine surgery with the goal to demonstrate the close relationship between understanding anatomy and improved clinical outcomes.

METHODS

Search Strategy

A systematic search of both EMBASE and the National Library of Medicine (PubMed) was performed to retrieve all the available literature pertaining to migraine surgery. One of the limitations of previous studies is the general, and often vague term, of migraine surgery. Therefore, for this review, we defined migraine surgery as a surgery that involves trigger site decompression or resection of peripheral sensory nerves with the end goal of addressing headache pain. The search strategy was performed using a combination of keywords and MeSH terms including the terms (''migraine surgery'' OR ''headache surgery'' OR ''OR ''peripheral nerve decompression surgery'' OR ''migraine surgery anatomy'' OR ''extracranial nerve anatomy'').

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was followed.[7] Two authors (N.B. and H.E.) independently reviewed the search entries using strict inclusion and exclusion criteria. Non-duplicate articles were first screened using titles and abstracts for relevance. Relevant articles then underwent a full-text review for inclusion/exclusion. Any discrepancies between reviewers were resolved through consensus.

Inclusion criteria for this review were any clinical study reporting on the efficacy or safety of migraine surgery (defined above). Studies were only included if they reported on at least one of the following factors: headache intensity, duration, frequency, elimination or improvement rates, or complications. Moreover, anatomy studies with clinically applied relevance to migraine surgery were included and presented as a separate secondary analysis. Biomechanical studies were excluded. Studies reported in a language other than English were excluded.

Data Collection and Extraction

Data extracted included, study title, authors, year of publication, study design, country of publication. For each study, the trigger site addressed for each study was extracted. In addition, patient demographics including number of patients in each study, number of females in each study, mean age, and average follow-up time was also reported. Anatomy studies relevant to migraine surgery were included in a bibliometric analysis.

Patient Outcomes

The main outcomes extracted from each clinical study was migraine intensity (on a scale from 1 to 10), migraine frequency (number of headaches/month), migraine duration (as a proportion of a 24-hour period), and migraine headache index (MHI), defined as the multiplication of migraine intensity, frequency, and duration. Migraine elimination is defined as an MHI score of zero at minimum of three months follow up. For the meta-analyses, means, standards deviations, changes in mean, rates, and P values from each study were extracted.

Quantitative Analysis of Outcomes and Pooled Analysis of Complications

Any complications reported by the included studies were extracted and a pooled analysis of complications was performed.

We performed a subgroup meta-analysis using the Comprehensive Meta-Analysis Version 3 (CMA) software. For effect measurements, we used standardized mean difference with a confidence interval of 95%. The overall effects of all studies were computed with a random-effects model. For studies that reported multiple subgroups, we combined within-study subgroups into 1 entry by the fixed-effect model. The results of the analyses are demonstrated with forest plots. Each study is illustrated with a square that is relative in size to the study's weight and the confidence interval as a line passing through the square. The calculated overall mean and confidence interval for each outcome is demonstrated with a red rhombus.

To measure heterogeneity, we calculated Cochran Q, I^2, and P value of heterogeneity. I^2 values <40%, 60%, 90%, and 100% were considered minimal, moderate, substantial, and considerable, respectively.

RESULTS

Search Outcome

A total of 2435 articles were identified (Fig. 1). Following deduplication of the library, 2137 articles underwent title and abstract screening. Of these, 234 articles were eligible for full-text review. A total of 38 clinical studies,[3,8–44] and 30 anatomical studies[45–74] met our selection criteria and were included in the review.

Clinical Studies

Characteristics of Included Studies and Participants

Six randomized controlled trials (RCTs),[11,14,16,30,33,38] 7 prospective studies,[3,8,26,31,36,40,42] and 25 retrospective studies[9,10,12,13,15,17–25,27–29,32,34,35,37,39,41,43,44] were included in this systematic review. Characteristics of the included studies and participants are presented in Table 1. The trigger sites addressed during surgery included frontal, temporal, greater occipital, nasal, lesser occipital, and auriculotemporal nerves. Single trigger site surgery was performed in 12 studies[3,9–11,15,22,24,27,30–32,37] of which 5 studies[9–11,15,31] addressed only the frontal trigger site, 4 studies[11,27,30,32] addressed only the temporal site, 2 studies[22,24] addressed the occipital trigger site, and 1 study[37] looked at the nasal trigger site. Multiple trigger site surgery alone was reported in five studies[8,13,34,36,40] and a combination of single and multiple trigger site surgery was discussed in twenty studies[12,14,16–21,23,25,26,28,29,33,35,38,39,41–44]. The percentage of females included in the studies ranged from 70% to 100% and the mean age of participants ranged from 16 to 51 years' old. The mean follow-up ranged from 6 months to 60 months (Supplemental Table 1, http://links.lww.com/SLA/D278).

Migraine Intensity

Twenty-three studies[10–12,15,16,18–22,24,25,28–30,33–35,38,39,41,42] reported on migraine intensity among patients who underwent migraine surgery. All studies evaluated migraine intensity on a 10-point scale. The vast majority of the studies (21/23) reported reductions in migraine intensity post-surgery[10–12,15,16,18–22,24,25,28–30,33–35,39,40,42]. Reduction in migraine intensity ranged from 22.4% to 82.3% with a weighted average reduction of 48.9%. Only 1 study reported an increase of 0.7 (9.3%) in migraine intensity post-surgery[38]; however, the change was not statistically significant (Supplemental Table 2, http://links.lww.com/SLA/D278). Eighteen studies met criteria for inclusion in the meta-analysis. The overall reduction in migraine intensity effect was significant ($P < 0.001$, SE $= 0.22$, $I^2 = 97.9$) (Fig. 2).

Migraine Frequency

Twenty-two studies[11,12,14,16–22,24,25,28–30,33,35,38–42] reported on migraine frequency. All 22 studies reported reductions in migraine frequency post-operatively. The reductions varied from as low as 19.3% to as high as 84.9%, with a weighted average reduction of 64.7% (Supplemental Table 3, http://links.lww.com/SLA/D278). Eighteen studies met criteria for inclusion in the meta-analysis. The overall effect was significant ($P < 0.001$, SE $= 0.17$, $I^2 = 97.7$) (Fig. 3).

Migraine Duration

Nineteen studies[11,14,16,17,19–22,24,25,28–30,33,35,38,39,41,42] reported on migraine duration. Migraine durations were reported primarily in days or hours. The percent reduction in migraine duration ranged from 13.1% to 95.6% with a weighted average reduction of 61.9% (Supplemental Table 4, http://links.lww.com/SLA/D278). Sixteen studies met criteria for inclusion in the meta-analysis. The overall effect was significant ($P < 0.001$, SE $= 0.15$, $I^2 = 97$) (Fig. 4).

Migraine Headache Index

Twenty studies[11,14,16,17,19–23,25,28–30,32,33,35,38,39,41,42] reported on MHI. The vast majority (19/20)[11,14,16,17,19–23,25,28–30,32,33,35,39,41,42] reported decreases in MHI post-operatively, whereas only 1 study reported an increase. The percent reductions

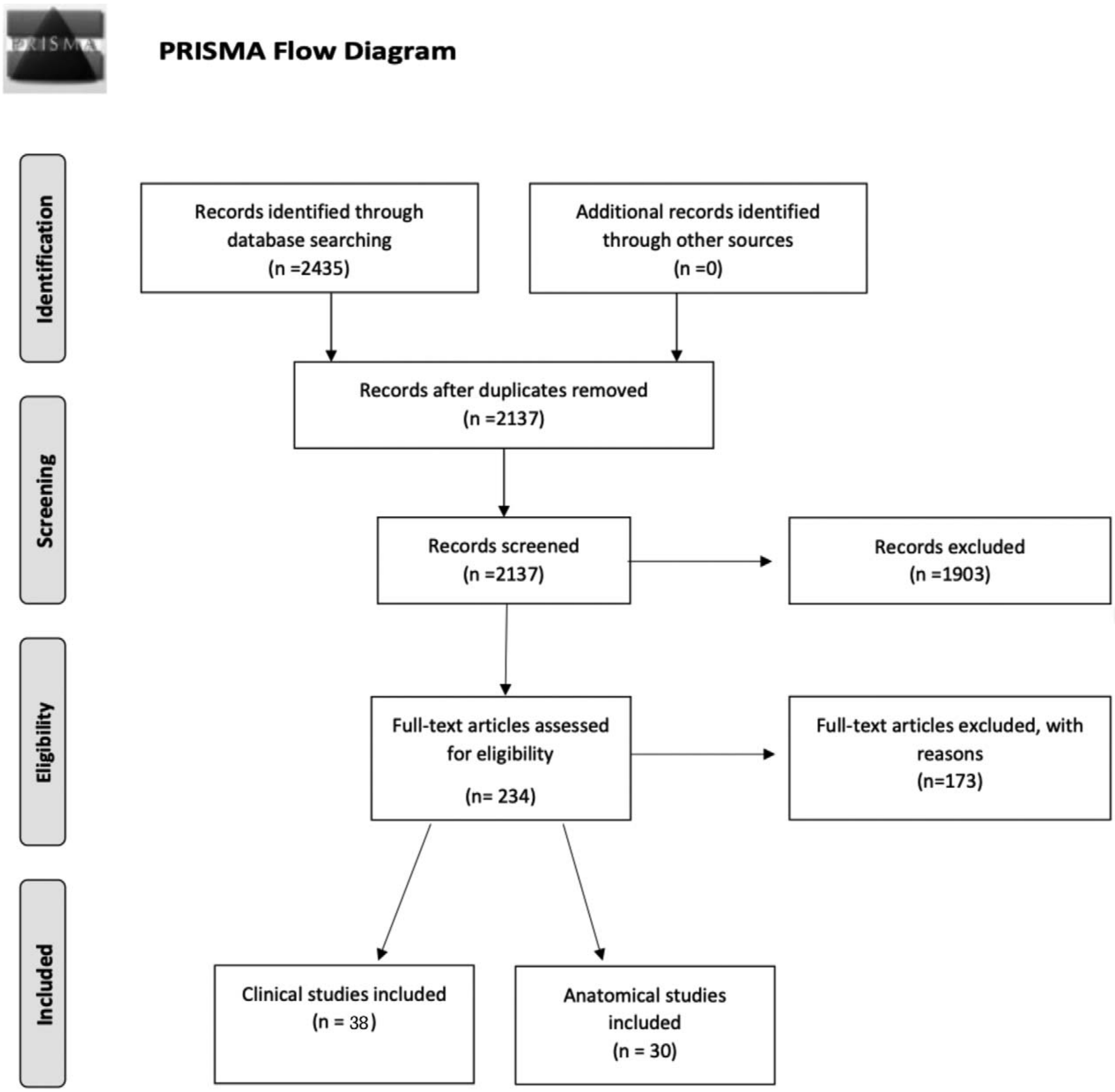

FIGURE 1. PRISMA flowchart.

ranged from as low as 26.3% to as high as 93.1% with an average weighted reduction of 75.5% (Supplemental Table 5, http://links.lww.com/SLA/D278). Fourteen studies met criteria for inclusion in the meta-analysis which demonstrated a significant reduction in migraine headache index ($P < 0.001$, SE = 0.19, $I^2 = 97.2$) (Fig. 5).

Migraine Improvement and Elimination

Of the 38 studies included in this review, 35 studies[3,8–14,16–18,20–28,30–44] reported on migraine improvement (standardly defined as improvement by >50% in outcome) and 35 studies reported on elimination (standardly defined as MHI of 0 at follow-up). The lowest rate of migraine improvement was 68.3% of participants.[9] In 3 studies,[11,17,20] 100% of patients achieved migraine improvement (Supplemental Table 6, http://links.lww.com/SLA/D278). The trigger sites at which patients reported 100% migraine improvement following nerve decompression surgery were the frontal, occipital, and nasal sites. All other studies reported migraine improvement within the 68.3% to 100%. Among the studies which reported on elimination, the percentage of patients which reported elimination varied from as low as 8.3% to as high as 86.5%[17,43] (Fig. 6).

Complications

Of the included studies, 7 studies reported no complications,[9,29–33,44] 15 studies[3,10,19–27,34,37,38,43] did not discuss complications, and 16 studies[8,11–18,28,35,36,39–42] reported complications following migraine surgery. Among the 23 studies [8,9,11–18,28–33,35,36,39–42,44] which reported on complications (complications or no complications), there was a total of 1635 participants of which 525 (32.1%) experienced complications. The most commonly reported complication was paresthesia and numbness (mostly transient)[8,12,14–16,28,35,40,42] (n = 198), the complication rate was 12.11% (Table 2). Other important complications included

TABLE 1. Overall Complications Associated With Migraine Surgery

Complications	No. of Studies	No. of Participants With Complications	Complication Rate (%)
Numbness or paresthesia[8,12,14–16,28,35,40,42]	9	198	12.11%
Itching[11,12,14,16,28,35,36,39]	8	80	4.89%
Hair loss or thinning [11,12,14,16,17,35]	6	29	1.77%
Hematoma[11,15,42]	3	5	0.31%
Hyposensitivity[16,35,39,40]	4	19	1.16%
Hypersensitivity[16,28,35,39]	4	30	1.83%
Infection (including cellulitis)[11,13,41]	3	6	0.37%
Neck stiffness[11,14,16,39]	4	28	1.71%
Hypertrophic scarring[28,35,39]	3	5	0.31%
Bleeding[9,11]	2	7	0.43%
Dryness[11]	1	12	0.73%
Temporal hollowing[14]	1	10	0.61%
Septal deviation[11]	1	8	0.49%
Rhinorrhea[11]	1	11	0.67%
Ecchymosis[17,40]	2	31	1.90%
Seroma[42]	1	20	1.22%
Wound dehiscence[39,42]	1	2	0.12%
Dry/irritated eyes[35]	1	2	0.12%
Epistaxis[11]	1	3	0.18%
Unilateral airway reduction[11]	1	1	0.06%
Eyelid ptosis[35]	1	13	0.80%
Scar deformity[35]	1	2	0.12%
Strabismus[35]	1	1	0.06%
Uneven brow movement[14]	1	1	0.06%
Temporal nerve injury[16]	1	1	0.06%

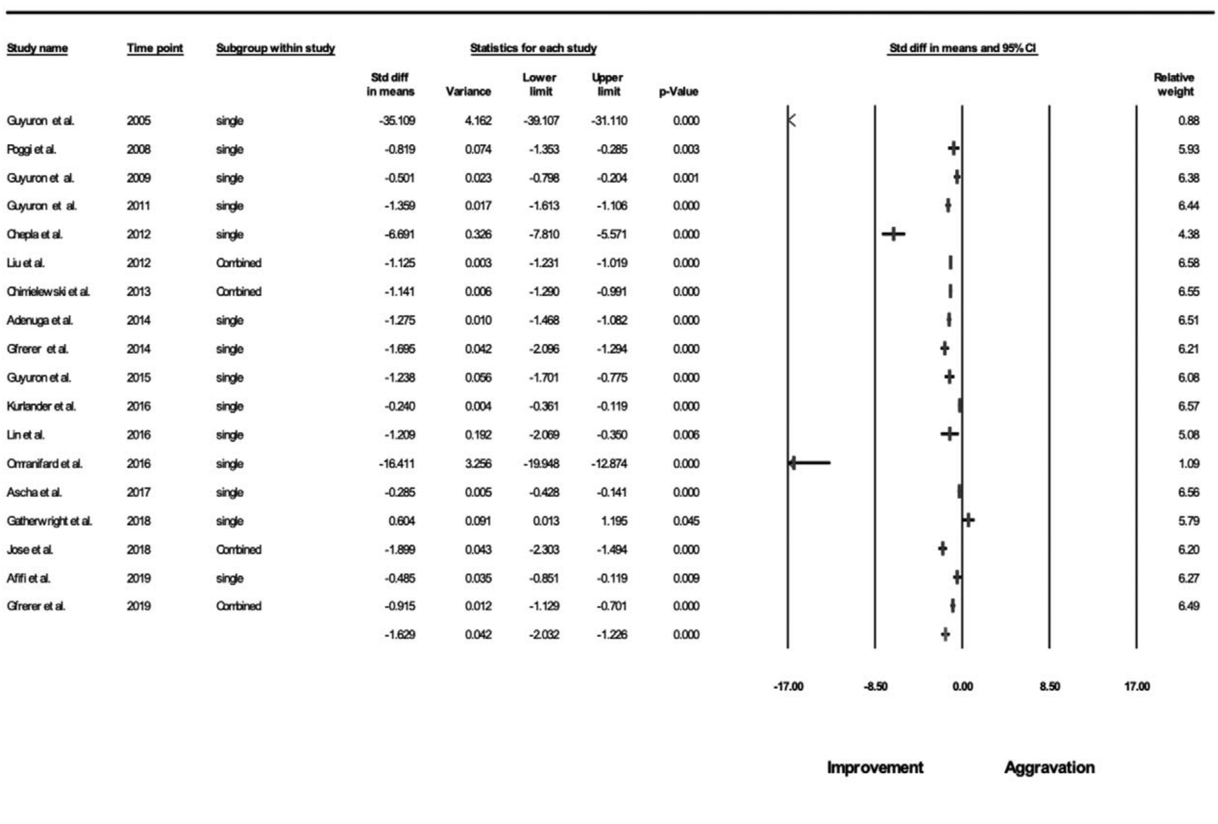

FIGURE 2. Forest plot of migraine intensity using random-effects model. ($Q = 772$, $P < 0.001$, $I^2 = 97.8$).

Study name	Time point	Subgroup within study	Std diff in means	Variance	Lower limit	Upper limit	p-Value	Relative weight
Guyuron et al.	2005	single	-9.270	0.296	-10.337	-8.203	0.000	3.81
Poggi et al.	2008	single	-0.911	0.047	-1.337	-0.486	0.000	5.57
Guyuron et al.	2009	single	-0.423	0.013	-0.650	-0.197	0.000	5.95
Guyuron et al.	2011	single	-0.980	0.013	-1.202	-0.758	0.000	5.95
Janis et al.	2011	single	-1.227	0.044	-1.637	-0.817	0.000	5.61
Chepla et al.	2012	single	-4.806	0.175	-5.626	-3.986	0.000	4.51
Liu et al.	2012	Combined	-1.101	0.003	-1.207	-0.996	0.000	6.07
Chmielewski et al.	2013	Combined	-1.058	0.006	-1.204	-0.913	0.000	6.04
Adenuga et al.	2014	single	-1.058	0.008	-1.237	-0.878	0.000	6.01
Gfrerer et al.	2014	single	-1.521	0.037	-1.898	-1.144	0.000	5.68
Kurlander et al.	2014	single	-0.252	0.004	-0.379	-0.125	0.000	6.06
Guyuron et al.	2015	Combined	-3.261	0.142	-4.001	-2.522	0.000	4.74
Kurlander et al.	2016	single	-0.240	0.004	-0.361	-0.119	0.000	6.06
Omranifard et al.	2016	single	-3.113	0.140	-3.847	-2.379	0.000	4.75
Ascha et al.	2017	single	-0.285	0.005	-0.428	-0.141	0.000	6.04
Jose et al.	2018	Combined	-2.179	0.050	-2.616	-1.743	0.000	5.55
Afifi et al.	2019	single	-0.657	0.038	-1.039	-0.275	0.001	5.67
Gfrerer et al.	2019	Combined	-1.230	0.015	-1.469	-0.991	0.000	5.93
			-1.634	0.030	-1.974	-1.295	0.000	

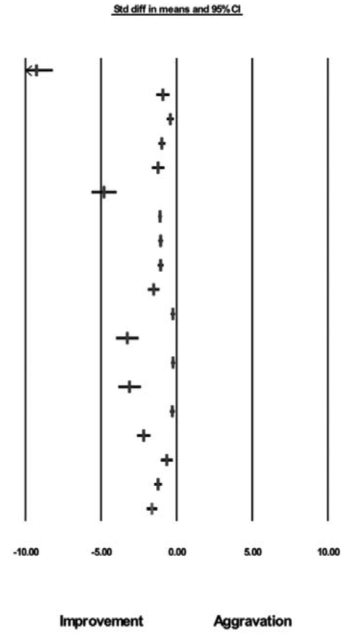

FIGURE 3. Forest plot of migraine frequency using random-effects model. ($Q = 752$, $P < 0.001$, $I^2 = 97.7$).

Study name	Time point	Subgroup within study	Std diff in means	Variance	Lower limit	Upper limit	p-Value	Relative weight
Guyuron et al.	2005	single	-7.334	0.188	-8.183	-6.484	0.000	4.63
Guyuron et al.	2009	single	-0.501	0.023	-0.798	-0.204	0.001	6.77
Guyuron et al.	2011	single	-0.742	0.011	-0.948	-0.535	0.000	7.01
Janis et al.	2011	single	-11.807	1.767	-14.412	-9.201	0.000	1.15
Chepla et al.	2012	single	-3.058	0.079	-3.610	-2.507	0.000	5.85
Liu et al.	2012	Combined	-0.390	0.002	-0.476	-0.304	0.000	7.20
Chmielewski et al.	2013	Combined	-0.526	0.004	-0.650	-0.401	0.000	7.15
Adenuga et al.	2014	single	-0.772	0.007	-0.935	-0.609	0.000	7.09
Gfrerer et al.	2014	single	-1.074	0.027	-1.396	-0.752	0.000	6.70
Guyuron et al.	2015	Combined	-1.506	0.041	-1.903	-1.109	0.000	6.45
Kurlander et al.	2016	single	-0.240	0.004	-0.361	-0.119	0.000	7.16
Omranifard et al.	2016	single	-1.336	0.045	-1.754	-0.918	0.000	6.37
Ascha et al.	2017	single	-0.285	0.005	-0.428	-0.141	0.000	7.13
Gatherwright et al.	2018	single	-0.604	0.091	-1.195	-0.013	0.045	5.69
Afifi et al.	2019	single	-0.300	0.033	-0.654	0.054	0.097	6.60
Gfrerer et al.	2019	Combined	-0.453	0.009	-0.639	-0.267	0.000	7.05
			-1.238	0.024	-1.542	-0.934	0.000	

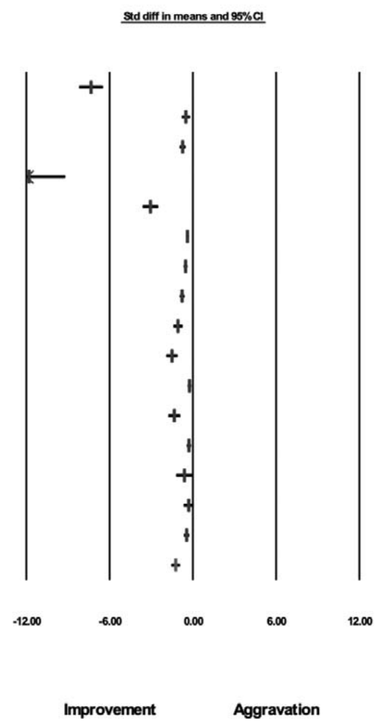

FIGURE 4. Forest plot of migraine duration using random-effects model. ($Q = 505$, $P < 0.001$, $I^2 = 97$).

Study name	Time point	Subgroup within study	Std diff in means	Standard error	Variance	Lower limit	Upper limit	p-Value	Relative weight
Guyuron et al.	2005	single	-7.825	0.462	0.213	-8.730	-6.920	0.000	5.40
Guyuron et al.	2009	single	-0.255	0.112	0.013	-0.475	-0.034	0.024	7.65
Guyuron et al.	2011	single	-0.890	0.110	0.012	-1.106	-0.674	0.000	7.66
Janis et al.	2011	single	-1.024	0.195	0.038	-1.407	-0.642	0.000	7.26
Chepla et al.	2012	single	-4.062	0.359	0.129	-4.766	-3.358	0.000	6.16
Liu et al.	2012	Combined	-0.588	0.046	0.002	-0.678	-0.498	0.000	7.82
Adenuga et al.	2014	single	-0.884	0.086	0.007	-1.054	-0.715	0.000	7.73
Gfrerer et al.	2014	single	-0.823	0.151	0.023	-1.119	-0.526	0.000	7.49
Guyuron et al.	2015	Combined	-1.817	0.231	0.053	-2.270	-1.364	0.000	7.05
Omranifard et al.	2016	single	-2.632	0.327	0.107	-3.273	-1.990	0.000	6.39
Peled et al.	2016	single	-1.139	0.295	0.087	-1.717	-0.562	0.000	6.63
Ascha et al.	2017	single	-0.239	0.073	0.005	-0.382	-0.097	0.001	7.77
Afifi et al.	2019	single	-0.550	0.190	0.036	-0.921	-0.178	0.004	7.30
Gfrerer et al.	2019	Combined	-0.794	0.100	0.010	-0.991	-0.597	0.000	7.69
			-1.502	0.192	0.037	-1.878	-1.126	0.000	

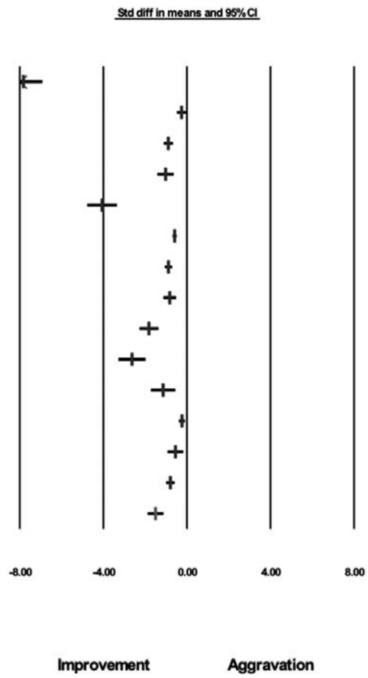

FIGURE 5. Forest plot of migraine headache index using random-effects model ($Q = 460$, $P < 0.001$, $I^2 = 97$).

Study name	Time point	Subgroup within study	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Guyuron et al.	2000	single	0.385	0.247	0.544	-1.428	0.153	3.30
Guyuron et al.	2002	single	0.455	0.265	0.659	-0.426	0.670	2.81
Dirnberger & Becker	2004	single	0.283	0.184	0.409	-3.239	0.001	3.52
Bearden & Anderson	2005	single	0.583	0.308	0.815	0.575	0.566	2.13
Guyuron et al.	2005	single	0.348	0.257	0.453	-2.816	0.005	3.83
Poggi et al.	2008	single	0.167	0.055	0.409	-2.545	0.011	1.96
Ducic et al.	2009	single	0.350	0.287	0.417	-4.251	0.000	4.15
Guyuron et al.	2009	single	0.571	0.431	0.701	0.997	0.319	3.51
Guyuron et al.	2011	single	0.290	0.195	0.407	-3.377	0.001	3.63
Janis et al.	2011	single	0.083	0.021	0.279	-3.247	0.001	1.63
Larson et al.	2011	single	0.391	0.320	0.466	-2.823	0.005	4.11
Li et al.	2012	single	0.764	0.665	0.841	4.707	0.000	3.70
Liu et al.	2012	Combined	0.473	0.433	0.513	-1.319	0.187	4.34
Chmielewski et al.	2013	single	0.559	0.483	0.632	1.530	0.126	4.12
Lee et al.	2013	Combined	0.307	0.265	0.353	-7.670	0.000	4.28
Adenuga et al.	2014	single	0.366	0.282	0.459	-2.799	0.005	3.95
Caruana et al.	2014	single	0.400	0.214	0.620	-0.888	0.374	2.67
Gfrerer et al.	2014	single	0.465	0.323	0.613	-0.457	0.648	3.42
Kurlander et al.	2014	single	0.545	0.447	0.641	0.903	0.366	3.93
Guyuron et al.	2015	Combined	0.500	0.367	0.633	0.000	1.000	3.57
Raposio & Caruana	2015	single	0.395	0.262	0.546	-1.362	0.173	3.39
Kurlander et al.	2016	single	0.567	0.482	0.648	1.550	0.121	4.04
Lin et al.	2016	single	0.222	0.056	0.579	-1.562	0.118	1.46
Omranifard et al.	2016	single	0.360	0.199	0.560	-1.381	0.167	2.86
Peled et al.	2016	single	0.368	0.187	0.597	-1.133	0.257	2.59
Ascha et al.	2017	single	0.518	0.448	0.587	0.501	0.616	4.16
Raposio & Caruana	2017	single	0.692	0.409	0.880	1.349	0.177	2.07
Jose et al.	2018	Combined	0.415	0.276	0.569	-1.088	0.277	3.36
Raposio & Bertozzi	2019	single	0.865	0.802	0.911	7.932	0.000	3.78
Raposio & Simonacci	2020	single	0.620	0.502	0.726	1.988	0.047	3.72
			0.455	0.399	0.513	-1.513	0.130	

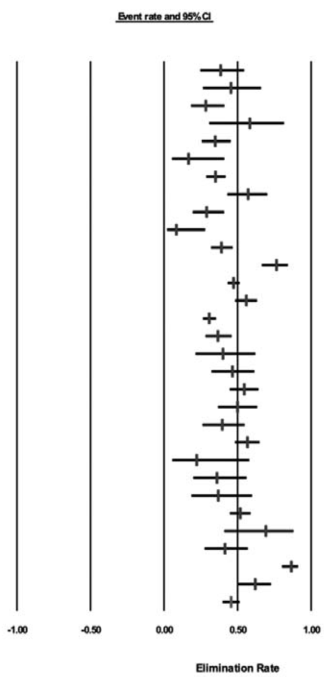

FIGURE 6. Forest plot of elimination rates using random-effects model. ($Q = 278$, $P < 0.001$, $I^2 = 87$).

itching[11,12,14,16,28,35,36,39] (n = 80, 4.89%), hyposensitivity[16,35,39,40] (n = 19, 1.16%), hair loss or thinning[11,12,14,16,17,35] (n = 29, 1.77%), hypersensitivity[16,28,35,39] (n = 30, 1.83%), neck stiffness[11,14,16,39] (n = 28, 1.71%), ecchymosis[17,40] (n = 31, 1.90%), and seroma[42] (n = 20, 1.22%) (Table 1). Several other complications were reported including; hematoma,[11,15,42] infection (including cellulitis),[11,13,41] eyelid ptosis,[35] scar deformity,[35] strabismus,[35] hypertrophic scarring,[28,35,39] dryness,[11] bleeding,[9,11] temporal hollowing,[14] septal deviation,[11] rhinorrhea,[11] wound dehiscence,[42] dry/irritated eyes,[35] epistaxis[11] and unilateral airway reduction,[11] uneven brow movement,[14] nerve injury to the temporal branch of the facial nerve[16] of which the complication rates were all under 1% (Table 1).

Anatomical Studies

A total of 30 anatomical studies were included and published in this bibliometric analysis.[45–74] The vast majority of these papers (n = 24; 77.4%) are published in plastic surgery journals. Approximately half (n = 14; 45.2%) of the anatomical studies addressed the occipital nerve (including the greater and lesser occipital nerve)[45,46,48,50,54,56,58,60–62,65,69,73,75] followed by the frontal[47,51,52,55,64,66,71] and temporal (includes auriculotemporal and zygomaticotemporal)[49,53,57,70,74] trigger sites (Supplemental Table 7, http://links.lww.com/SLA/D278).

DISCUSSION

The results of this systematic review and meta-analysis highlight several interesting findings. Our results are in line with previous reviews showing that migraine surgery is associated with significantly improved migraine outcomes (duration, intensity, and frequency) and an overall decrease in migraine headache index. However, our systematic review is the first to demonstrate strong evidence regarding the safety profile and complication rate of migraine surgery.

Migraine surgery, consisting of extracranial peripheral nerve decompression and trigger site deactivation, has reemerged as a potential method to treat refractory migraines 2 decades ago. Guyuron et al's seminal article in 2000 demonstrated that corrugator muscle excision leads to significant improvement and a high rate of elimination of migraine headaches.[3] This was followed by a plethora of publications and research efforts to better understand migraine surgery and how we can improve outcomes. Although clinical studies are extremely important in assessing the efficacy of migraine surgery, anatomical studies played a critical role in improving our understanding of anatomy and cementing the knowledge needed to improve outcomes. This is evident in our analysis that shows >30 anatomical studies dedicated to improving our knowledge of anatomy of peripheral extracranial nerves associated with nerve migraine trigger sites.

Although both our qualitative systematic review and the quantitative meta-analysis show overall improved outcomes post migraine surgery, there is a wide variability in the results. The first factor that is probably contributing to this wide variability in outcomes is the fact that we included different trigger site decompression/deactivation surgeries. It is quite possible that some surgeries are more effective than others which would contribute to this wide variability. Furthermore, although some studies only included patients who received 1 trigger site deactivation, others included those who underwent all trigger site releases. This evidently increased the results' heterogeneity. Moreover, it is important to understand that since migraine surgery is a young and rapidly evolving field, different surgeries have been performed with different variations, which may contribute to this wide variability in outcomes. For example, the greater occipital nerve has been identified as a trigger site for patients suffering from occipital neuralgia. Although this surgery usually entails a 6-point decompression of the greater occipital nerve that includes segmental muscle resection and nerve release to free any associated entrapment, the effects of concurrent occipital artery resection has been debated. Although some preliminary evidence shows that the dissection and ligation of occipital artery (OA) has no effect on migraine outcomes,[24] there is still wide variability in practice mainly due to the lack of consensus coupled with our anatomical and pathophysiological understanding of this disease that support OA resection.[54,69,75]

Migraine surgery, a once denounced field, which has even been called a pure placebo,[5] has been able to proliferate, backed up by the present existing literature supporting its efficacy (as summarized in this systematic review). However, there is still some concern regarding its safety profile. In fact, the American Headache Society, published a statement expressing their concern on the lack of evidence supporting its safety.[6] Although many individual studies have reported on their complications since then, no systematic review has reported on a pooled analysis of complication rates to date. Our study is the first to compile all published complication rates and perform a pooled analysis to show the safety profile of this surgery. We conservatively included all complications to demonstrate any safety concerns, if they exist. Of 1645patients, over one-third experienced some sort of complication. However, the vast majority of these complications were quite minor such as transient numbness and hyposensitivity. Major complications such as bleeding and nerve damage were very rare (<1%). Moreover, although the former overall number might seem high at first glance, we believe it is an overestimate of the real complication rate as a considerable number of articles have the same author groups and therefore patients might have been counted more than once, hence overexaggerating the pooled complication rate.

Thus far we have been able to show that migraine decompression surgery works and is safe, however what remains to be discussed is the impact of these procedures on patients' lives. As previously mentioned, migraines rank second among the world's causes of disability.[76] When a patient experiences a migraine, a plethora of events can occur starting with a premonitory phase (prodrome) or an aura.[77] Patients can then experience pulsating, throbbing or pounding head pain, which can be further aggravated by movement and is associated with symptoms such as photophobia, sonophobia, osmophobia, nausea, and vomiting.[78] If left untreated the symptoms can remain for hours and even days.[78] Although medical management is effective in managing a lot of these symptoms, there remains a significant number of patients that are refractory to medical treatment, and thereby constantly suffering.[79] For this subset of patients, migraine surgery offers an opportunity to ameliorate their symptoms, improve their function, and increase their quality of life.

This review has several limitations. The first of which is that we included varying levels of evidence (1–4) in our analysis. Although we acknowledge that this introduces a limitation to our analysis, due to the relative novelty of the field and in an attempt to be as exhaustive as possible, we believe the benefit in including all the outcome studies outweighs the limitation introduced due to the varying levels of evidence. As mentioned earlier, several of the included studies have the same senior authors and so, it is possible that the same database was used several times. Therefore, we need to interpret the meta-analyses with caution given the fact that some participants could have been included in several studies and this may overexaggerate the actual number of participants. Nevertheless, we believe a meta-analysis provides higher level evidence that is important for physicians and patients to base their clinical decisions. In addition, as was discussed earlier, many of the studies addressed multiple trigger sites in the same surgery which limits our ability to assess the effectiveness of a specific trigger site deactivation. As more evidence gets published on individual trigger sites, we believe future reviews of specific trigger site deactivations will be warranted to further improve our understanding of this promising domain.

CONCLUSIONS

Migraine surgery is a rapidly evolving field supported by a plethora of clinical and anatomical research. The present systematic review and meta-analysis demonstrates the overall effectiveness of migraine surgery, defined as trigger site deactivation/decompression. Although previous reviews on this topic have been published, this is the first to perform a pooled analysis of complication rates, demonstrating the overall safety of this procedure. Moreover, in addition to reviewing clinical studies, this is the first review to encompass a bibliometric analysis of anatomical studies that serves as a reference for surgeons in training/junior surgeons in the field. In the absence of large robust clinical, we believe meta-analyses such as this one can inform clinical guidelines and provide practitioners with an evidence-based reference to improve informed consent.

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