

**The Prevalence of Imploding, Exploding and Ocular Headache Types
in a Women's Health Outpatient Practice**

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Abstract

Objectives: (i) Determine the prevalence of imploding, exploding and/or ocular headaches in women with migraine in a primary care practice of women (ii) Investigate the concordance of physician diagnosis with patient self-diagnosis of pain directionality (iii) Assess correlation between the type of headache and severity of migraines, reproductive stage, and response to acute and prophylactic treatments

Background: botulinum toxin A is a drug made from the toxin produced by *Clostridium botulinum* that works by weakening or paralyzing certain muscles or by blocking certain nerves.¹⁷ Recent migraine trials evaluating the efficacy of botulinum toxin A therapy noted differences in the efficacy of botulinum toxin A therapy based on directionality of pain ((imploding exploding and ocular).^{5,6,7} However, the prevalence of these migraine types and their responses to conventional migraine prevention therapies has not yet been assessed.

Methods: 201 patients participated in structured clinician-administered interviews and completed written questionnaires. Directionality of migraines were determined by both patients and physicians. Descriptive statistics, kappa coefficients and Kruskal-Wallis tests were used to assess migraine prevalence, physician-patient diagnosis concordance and association of migraine to severity, treatment and reproductive stage respectively.

Results: 201 patients were enrolled with average age of 46. All patients reported directionality of their migraine and prevalence varied depending upon the method used to assign directionality and were: 33%-42% imploding headaches with or without ocular pain, 18%-44% exploding headaches with or without ocular pain, 7%-39% had ocular pain only, and 8%-13% had imploding and exploding headaches with or without ocular pain. The concordance between physician diagnosis of headache directionality with patient written response, between physician diagnosis and patient diagnosis via selection of representative picture, and between patient diagnosis via written question and via selection of representative pictures were weak to moderate using Kappa coefficient. No correlation between the type of headache and severity of migraines, reproductive stage, and response to acute and prophylactic treatments was found ($p>0.05$).

Conclusion: Improved methods of determining pain directionality and target therapy are needed.

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Introduction/Significance

Background and Impact

Migraine headaches last anywhere from four to seventy two hours and can be debilitating to patients. Most migraine headaches are unilateral, global or bi-frontal, have gradual onset, can be pulsating and/ or crescendo-decrescendo in pattern.¹ They are associated with symptoms such as nausea, vomiting, photophobia, phonophobia.¹ Migraine can occur with or without auras. Auras are neurological symptoms such as visual disturbances that occur just before or at the time of onset of a migraine.² Specific diagnostic criteria have been established for migraine without aura and migraine with aura by the International Headache Society.⁸

From 1980 through 1989, the prevalence of chronic migraine headaches in the United States has increased nearly 60%, from 25.8 per 1000 persons to 41.0 per 1000 persons.³ The prevalence among women less than 45 years of age increased 77%, compared with a 64% increase among men.³ In 2004, the number of people greater or equal to 18 years of age that reported experiencing a severe headache or a migraine in the preceding 3 months in the United States included 18% of people age 18-44 years and 6% in those greater or equal to 75 years.³ In a recent population based study (n= 162,576) by Lipton et al. (2007), the 1 year prevalence of migraines in men was 5.6% and in women was 17.1%.¹⁵ Caucasians, ages 30-39, and those with lower income, had the highest migraine prevalence compared to Black, other age and higher income groups respectively.¹⁵ Most subjects (53.7%) reported severe impairment during migraines.¹⁵ Overall three month disability due to migraine in terms of activity restriction measured using the Migraine Disability Assessment Survey (MIDAS) included little or no disability (68.7%), mild disability (14.3%), moderate disability (10.7%) and severe disability (11.3%).¹⁵

Recent clinical trials have described a correlation between the description of migraines and the efficacy of treatment, specifically in regard to Botulinum Toxin A treatment.^{5,6,7} Jakubowski et al. (2006) noted a trend in the efficacy of migraine treatment with Botulinum Toxin A injections based on how the headache was described by patients in both a prospective and a retrospective trial.⁵ Patient descriptions were related to the directionality of the

migraines and included exploding headaches (build up of pressure inside the head), imploding headaches (clamping by external forces/ crushing) and ocular headaches (eye pain).⁵ In the prospective trial (n = 42), out of the 27 patients (25 female, 2 male) that were clear responders to botulinum toxin A injections, 79% had imploding headaches and 14% had ocular headaches.⁵ While, all 13 non-responders had exploding headaches.⁵ Similar trends were noted in the retrospective trial (n= 36, average age ~ 48 years) where 72% of responders (n= 25) had imploding headaches and 12% had ocular headaches and 82% of the non-responders (n=11) had exploding headaches.⁵

Burstein et al. (2009) also noted similar trends in a migraine prophylaxis trial with Botulinum Toxin A (n= 82, 69 women and 13 men).⁶ Seventy percent of patients with imploding or ocular headaches (n=44) were considered to be responders while 78% of those with exploding headaches (n= 36) were non-responders.⁶ The most recent study in relation to migraine description and botulinum toxin A response was reported by Bogart et al. (2010) where effectiveness of botulinum toxin A was noted for imploding and ocular headaches but not exploding.⁷

Even though the above listed studies report the directionality in migraines impacting botulinum toxin A treatment efficacy, specific studies need to be done to determine the prevalence of imploding, exploding and ocular headaches. Also, their response, if any, to more conventional migraine prevention therapies⁹ such as amitryptiline, timolol, propranolol, topiramate, gabapentin, botulinum toxin A, depakote and verapamil has not yet been assessed. Additionally, since migraine frequency and severity can change with female reproductive stage,¹⁶ the prevalence based on reproductive age also needs to be evaluated.

Aims

The primary aims of this scholarly project were to determine the prevalence of imploding, exploding and/or ocular headaches in women with migraine in a primary care practice of women and to investigate the concordance of physician diagnosis with patient self-diagnosis of pain directionality. The secondary aims were to assess correlation between the type of headache and severity of migraines, reproductive stage, and response to acute and prophylactic treatments

Research Materials and Methods

Internal Review Board (IRB) approval (Appendix A) for the study was received from the Mayo Clinic IRB on 12/4/2007. Patients were identified for participation in the study when they presented at the Women's Health Internal Medicine (WHIM) Clinic at Mayo Clinic Arizona with a migraine or a history of migraines or, if they requested migraine medication refills via the clinic's prescription nurse. Patients presenting to the clinic underwent informed consent and completion of study surveys at presentation while, those requesting migraine medication refills were contacted by the study investigators for recruitment into the study via telephone. A standardized script was used for telephone recruitment (Appendix B) and if the patient telephoned agreed to participate in the study, an appointment with a study investigator was made. The modification for telephone contact was approved by the IRB on 2/25/2011.

Surveys were conducted by study physicians at WHIM and medical students. The surveys included the Migraine Disability Assessment (MIDAS) questionnaire (Appendix C), a Headache Questionnaire (Appendix D) and, Headache Interview Questionnaire (Appendix E). A standardized method of survey administration was implemented. After informed consent, patients were asked to complete the MIDAS questionnaire & Headache Questionnaire (HQ) with the interviewer absent. The Headache Interview Questionnaire (HIQ) was then completed by the interviewer by reading the questions out verbatim to the patient and without looking at the already completed MIDAS and HQ.

The MIDAS questionnaire was used to evaluate migraine disability in the study population. The MIDAS questionnaire's reliability and validity in assessing migraine disability has been verified in multiple studies.¹¹⁻¹⁴ The survey has five questions whose responses are then summed up to grade the amount of disability.¹¹⁻¹⁴ A MIDAS score of 0-5 indicates no disability, 6-10 mild disability, 11-20 moderate disability and 21+ severe disability.¹¹⁻¹⁴ The Headache Questionnaire was used to determine patient description of headache, current and previous migraine treatments and their effectiveness, and reproductive age. In addition to using words to identify patient's directionality of the headache (pushing in, pushing out or within eye socket), pictorial representations of directionality were also utilized.

The pictorial representations in the HQ were adapted from Jakubowski et al.'s⁵ pictorial descriptions of the directionality of patients' migraines. However, in the study by Jakubowski et al. the pictures were not used by patients to describe their own migraines, which, was the case in this study. The pictures were used to evaluate whether there may be a greater correlation of physician diagnosis of directionality from speaking to patients (from HIQ) with the patient completed surveys when comparing the patient responses to the questions in words when compared to pictures. The Stages of Reproductive Aging Workshop (STRAW) Classification system was used to determine reproductive age¹⁰ as part of the HQ. The HIQ re-phrased the migraine directionality questions with words used in the HQ and was used for physician diagnosis of directionality.

Inclusion criteria for participation in the study included a female with a diagnosis of migraine based on the International Classification of Headache Disorders-2nd edition (ICHD-II) criteria for migraine diagnosis. The ICDHD-II diagnostic criteria for migraine diagnosis includes headaches lasting 4-72 hours at least 5 times with at least two typical characteristics (unilateral location, throbbing, moderate- severe pain, aggravated by or avoidance of physical activity) in addition to one associated symptom during the headache (nausea, vomiting, photophobia or phonophobia).⁸

Exclusion criteria include not fulfilling ICHD-II criteria, inability to read English, visual or communication impairment that would lead to inability to complete survey, long term maintenance opioid therapy for headache or another chronic pain condition, patient with medication overuse headaches and patient refusal.

All survey data were entered into a study specific database. Descriptive statistics were used to determine the prevalence of each headache direction. Kappa coefficients were calculated to determine the concordance between the clinician diagnosis of directionality, patient self-diagnosis via the written question, and patient self-diagnosis via selection of the most representative pictures. The Kruskal-Wallis test, a non parametric test, was used to assess the correlation between the type of headache and severity of migraines, reproductive stage, response to acute treatments and response to prophylactic treatments.

Results

Demographics

One hundred and seventy six out of the 201 patients (88.4%) were Caucasian, 5 were African-American (2.5%), 8 (4%) were Asian/Pacific Islanders, 10 (5%) were other and 2 patients did not list their race. The average age was 46 (SD 13.1, range 11.7-77.2). Four patients (2%) had completed grade 11 or less, 7 (3.5%) graduated high school, 60 (30%) had some college or technical school training, 65 (32.5%) had graduated college, 16 (8%) had done some graduate work and 48 (25%) had a graduate degree. The average age of the first migraine was 22.3 (SD 10.9). Sixty five (34.2%) were of reproductive age. Thirty two (16.8%) were in menopausal transition. Fifty nine (31.1%) were post-menopausal. Thirty four (17.9%) had a hysterectomy with ovaries removed before the age of 50. Eleven females (5.5%) did not list their menopausal status. The summary of the demographics and menopausal status are presented in Table 1 below.

Table 1: Demographics summary and menopausal status

Age	Average Range	46 11.7- 77.2
Race	Caucasian Asian/Pacific Islanders African-American Other No response	176 (88.4%) 8 (4%) 5 (2.5%) 10 (5%) 2 (0.99%)
Education	Missing 1 = Grade 11 or Less 2 = Graduated High School 3 = Some college or technical school 4 = Graduated College 5 = Some graduate work 6 = A graduate degree	1 (0.5%) 4 (2.0%) 7 (3.5%) 60 (30.0%) 65 (32.5%) 16 (8.0%) 48 (24.0%)
Menopausal status	1 = Reproductive Stage 2 = Menopausal transition 3 = Postmenopausal 4 = Hysterectomy with ovaries removed before age 50 No response	65 (34.2%) 32 (16.8%) 59 (31.1%) 34 (17.9%) 11 (5.5%)

Prevalence

All patients reported directionality of their migraines in the patient completed survey (HQ) and the physician completed survey (HIQ). The patients' responses to the directionality of the migraine resulted in different prevalence based on whether they were responding to the pictorial representation (Question 1, HQ), written words (Question 3 HQ) or being asked by the physician (Questions 1-2, HIQ).

The prevalence of imploding headaches (with and without ocular migraines) based on the pictorial representation was 32.7% (n = 65) when compared to words which, was 41.9% (n=83). While, 35.8% (n=72) were identified by the physician or medical student to have an imploding headache. The prevalence of exploding headaches (with and without ocular migraines) based on the pictorial representation was 18.1% (n=36) when compared to words which, was 26.7% (n= 53). While, 44.3% (n=89) were identified by the physician or medical student to have an exploding headache.

The prevalence of combined exploding and imploding headaches (with and without ocular migraines) based on the pictorial representation was 10.1% (n = 20) when compared to words which, was 8.1% (n=16). While, 12.9% (n=26) were identified by the physician or medical student to have a combined exploding and imploding headache. The ocular only migraines based on the pictorial representation was 39.2% (n = 78) when compared to words which, was 23.2% (n=46). While, 6.8% (n=14) were identified by the physician or medical student to have an ocular only headache. Table 2 below lists these findings.

The concordance rate between the physician's diagnosis and the patient self report using the pictorial representation of the migraine type is 49.75% (99/199). Since the concordance rate does not account for the agreement between responses by chance only, the Kappa coefficient was calculated. The Kappa coefficient is 0.34, indicating weak agreement ($p < 0.0001$) between physician diagnosis and patient self report using the pictures. The concordance rate between physician's diagnosis and patients' self report based on words is 54.44% (108/198) and The Kappa coefficient is 0.36, indicating weak agreement ($p < 0.0001$). Additionally, when patient responses to the pictorial (question 1, HQ) are compared to their responses to the written questions (question 3, HQ), the concordance rate is 54.08% (106/196) and the Kappa

coefficient is 0.35, indicating week agreement ($p=0.0005$).

Table 2: The prevalence of imploding, exploding and ocular headaches based on physician diagnosis and patient self report

	Physicians' Diagnosis		Patient self report (Q1/ picture)		Patient self report (Q3/ words)	
	n	%	n	%	n	%
Imploding (with and without ocular)	72	35.82	65	32.66	83	41.92
Exploding (with and without ocular)	89	44.28	36	18.09	83	26.77
Imploding and exploding (With and without ocular)	26	12.94	20	10.05	16	8.08
Ocular only	14	6.97	78	39.20	46	23.23

Severity

The average number of days of missed work or school was 0.8 (standard deviation 2.3, range 0-18). The average number of days in the last three months productivity at work or school was reduced by at least half was 2.9 (standard deviation 8.2, range 0-90). The average number of days in the last three months housework was not done was 3.4 (standard deviation 6.7, range 0-45). The average number of days in the last three months housework productivity was reduced by at least half was 3.6 (standard deviation 8, range 0-90). The number of days in the last three months family social or leisure activities were missed because of migraines were missed was 2.1 (standard deviation 3.9, range 0-30).

The average for the total number of days affected by migraines (sum total questions 1-5 in MIDAS) in the last three months were 12.5 (standard deviation 23.2, range 0-255) which indicates moderate disability. However, there was a broad range with mild, moderate and severe disability included in the sample. The average number of days in the last 3 months that the patients experienced a migraine was 17.2 (SD 22.5, range 0-90). The average severity of headaches on a scale of 0-10 with 0 being no pain and 10 being the worst pain was 5.7 (SD 2.5, range 0-10). Table 3 below summarizes the results of the MIDAS questionnaire.

Table 3: Summary of responses to Migraine Disability Assessment (MIDAS) questionnaire

Question	Mean (SD)	Median	Range
1. Days in last 3 months missed work or school	0.8 (2.3)	0.0	0.0-18.0
2. Days in last 3 months productivity at work or school was reduced by at least half	2.9 (8.2)	0.0	0.0-90.0
3. Number of days in the last three months housework was not done	3.4 (6.7)	1.0	0.0-45.0
4. Number of days in the last three months housework productivity was reduced by at least half	3.6 (8.0)	1.0	0.0-90.0
5. Number of days in the last three months family social or leisure activities were missed because of migraines	2.1 (3.9)	1.0	0.0-30.0
Total number of days affected by migraines (sum questions 1-5)	12.5 (23.2)	6.0	0.0-255.0

Medication use

Thirty nine percent of the patients (n= 71) were taking pain medicine on a regular basis for symptoms other than headaches. These symptoms mostly included pain in muscles or joints (back and neck most common) and cramps. The medication classes used to treat these symptoms included NSAIDS (most common), muscle relaxants, narcotics, gabapentin, serotonin and norepinephrine reuptake inhibitors, anti-emetics, tricyclic antidepressants, anti-epileptic medication and topical patches. Sixty one percent (n= 111) of the sample were not taking pain medicines for anything other than their migraines.

One hundred twenty three patients (61.5%) had never tried any of the listed prophylactic medicines. Those that had tried migraine prophylactic medications had used amitriptyline (n=24 (11.9%), effective for 7 (11.9%)), nortriptyline (n= 19 (9.5%), effective for 8 (42.1%)), propranolol (n= 33 (16.4%), effective for 13 (39.4%)), topiramate (n = 32 (15.9%), effective for 17 (53.1%)), valproic acid (n= 6 (3%), effective for 6 (100%)), neurontin (n=17 (8.5%), effective for 5 (29.4%)), botulinum toxin A (n=23 (11.4%), effective for 10(43.5%)), verapamil (n=9 (4.5%), effective for 4 (44.4%)), sumatriptan (n=105 (52.2%), effective for 73 (69.5%)), naratriptan (n=13 (6.5%), effective for 9 (69.2%)), almotriptan (n= 9 (4.5%), effective for 4 (44.4%)), frovatriptan (n=8 (4%), effective for 5 (62.5%)), eletriptan (n=18 (9%), effective for 10 (55.6%)), rizatriptan (n=49 (24.4%), effective for 37 (75.7%)), zolmitriptan (n= 26 (12.9%), effective for 17 (65.4%)).

Correlation between headache type and menstrual cycle

Seventy eight females (39.2%) reported that the headaches were associated with their menstrual cycle while, 121 (60.8%) reported no correlation. Twenty seven (38.57%) of females with imploding headaches reported the headache to be associated with their menstrual cycle. Thirty four (38.2%) women with exploding headaches reported an association with their menstrual cycle. Five females (35.71%) with ocular only migraines reported an association with their menstrual cycle. While, 12 patients (46.15%) with combined imploding and exploding migraines reported an association of their headache with their menstrual cycle. The correlation between migraine type and association with menstrual cycle was not statistically significant ($p=0.8996$). Table 2 below summarizes the prevalence of menstrual cycle associations with each migraine type.

Correlation between headache type and menopausal status

In patients with imploding migraines, 30 (45.45%) were reported to be in a reproductive stage, 5 (7.58%) were in menopausal transition, 19 (28.79%) were postmenopausal, and 12 (18.18%) had a hysterectomy with ovaries removed before the age of 50. For those with exploding migraines, 25 (28.74%) were reported to be in a reproductive stage, 18 (20.69%) were in menopausal transition, 27 (31.03%) were postmenopausal, and 17 (19.54%) had a hysterectomy with ovaries removed before the age of 50. In patients with ocular only migraines, 4 (36.36%) were reported to be in a reproductive stage, 3 (27.27%) were in menopausal transition, 3 (27.27%) were postmenopausal, and 1 (9.09%) had a hysterectomy with ovaries removed before the age of 50. While, in patients with combined imploding and exploding migraines, 6 (23.08%) were reported to be in a reproductive stage, 6 (23.08%) were in menopausal transition, 10 (38.46%) were postmenopausal, and 4 (15.38%) had a hysterectomy with ovaries removed before the age of 50. When comparing menopausal status with different types of headache, the association was not statistically ($p=0.2812$). Table 2 below summarizes the prevalence of the different reproductive statuses for each migraine type.

Table 4: The prevalence of menstrual cycle association and reproductive status for each migraine type

	Imploding n (%)	Exploding n (%)	Ocular only n (%)	Imploding and exploding n (%)
Migraine associated with menstrual cycle	27 (38.57)	34 (38.2)	5 (35.71)	12 (46.15)
Reproductive stage	30 (45.45)	25 (28.74)	4 (36.36)	6 (23.08)
Menopausal transition	5 (7.58)	18 (20.69)	3 (27.27)	6 (23.08)
Postmenopausal	19 (28.79)	27 (31.03)	3 (27.27)	10 (38.46)
Hysterectomy with ovaries removed before age 50	12 (18.18)	17 (19.54)	1 (9.09)	4 (15.38)

Correlation between headache type and Severity

The average total number of days and standard deviations (SD) affected by each of the headache types: imploding, exploding, ocular only and combined imploding and exploding were 10.65 (SD 16.26), 13.07 (SD 29.55), 9.43 (SD 9.8) and 17.62 (19.91) respectively. There was no difference in the total number of days affected by each of the headache types with $p=0.1136$ based on the Kruskal-Wallis test.

The average number of days in the last three months with SD for imploding, exploding, ocular only and combined imploding and exploding headache types were 12.5 (14.2), 17.48 (24.62), 9.79 (14.61), 33.00 (29.94) respectively. The differences in the number of days last 3 months between each type of headache was statistically significant ($p=0.0008$, Kruskal-Wallis test). The differences occurred when comparing imploding with combined imploding and exploding, exploding and combined imploding and exploding and ocular only with combined imploding and exploding.

The severity of the headaches (on a 0-10 scale, 10 being the worst) for imploding, exploding, ocular only and combined imploding and exploding headache types were 6.10 (2.24), 5.76 (SD 2.51), 4.14 (SD 3.55), and 5.4 (SD 2.35) respectively. There was no difference in the severity of headache between the different headache types ($p=0.0914$, Kruskal-Wallis test). Table 3 summarizes the severity and frequency of headaches based on the headache types.

The mean and median MIDAS score for imploding migraines ($n=72$) was 10.65 (SD 16.26) and 5 respectively. While, the mean and median MIDAS score for exploding migraines ($n=89$) was 13.07 (SD 29.55) and 5 respectively. The mean and median MIDAS score for ocular only ($n=14$) was 9.43 (SD 9.80) and 7 respectively. While those with combined imploding and exploding migraines ($n=26$) had a mean and median MIDAS score of 17.62 (19.91) and 12.50 respectively. Since the sample size for some of the migraine types are small, the median is more reflective of the MIDAS score than is the mean. The Kruskal-Wallis test showed no difference in MIDAS severity scores among different types of headache ($p=0.1136$). Table 4 below summarizes the frequency and severity of migraines based on migraine typ

Table 5: Summary of frequency and severity of migraines based on migraine type

	Imploding Mean (SD)	Exploding Mean (SD)	Ocular only Mean (SD)	Combined imploding and exploding (without ocular) Mean (SD)	Significance
Total number of days affected by headache	10.65 (16.26)	13.07 (29.55)	9.43 (9.80)	17.62 (19.91)	P = 0.1136
Number of days in the last three months with headache	12.5 (14.20)	17.48 (24.62)	9.79 (14.61)	33.00 (29.94)	P = 0.0008
Severity of headache in the last three months	6.10 (2.24)	5.76 (2.51)	4.14 (3.55)	5.40 (2.35)	P = 0.0914
MIDAS	10.65 (16.26)	13.07 (29.55)	9.43 (9.80)	17.62 (19.91)	P = 0.1136

Correlation between migraine type and efficacy of medication

Twenty one (29.17%) patients with imploding migraines had taken prophylactic medications, out of which 13 (61.9%) thought they were effective. Thirty seven (41.57%) patients with exploding migraines had taken prophylactic medications, out of which 27 (72.97%) thought they were effective. Six (42.86%) patients with ocular only migraines had taken prophylactic medications, out of which 4 (66.67%) thought they were effective. While, 13 (50%) patients with combined exploding and imploding migraines had taken prophylactic medications, out of which 7(53.85%) thought they were effective. The number of patients per headache type considering prophylactic agents to be effective were not statistically significant ($p=0.7393$).

A total of 135 patients (67.16%) had attempted triptan medications out of whom, 46 patients (63.89%) had imploding migraines and 42 (91.3%) had thought they were effective. Sixty one (68.54%) patients with exploding migraines had attempted a triptan medication and 50 (81.97%) had thought these were effective. Eight (57.14%) patients with ocular migraines had attempted triptan medications and 6 (75%) thought they were effective. While 20 (76.92%) patients with combined imploding and exploding agents had attempted triptans and 14 (70%) thought they were effective. The number of patients per migraine type considering triptan agents to be effective were not statistically ($p=0.1686$).

Discussion

The study highlights the widespread prevalence of directionality in migraines among a sample of mostly Caucasian females, as hypothesized. All patients in the study reported directionality of their migraine which included imploding, exploding, ocular and combined imploding/exploding headaches. However, the prevalence of each of these headache types varied based on whether the patients were self-reporting in response to words or pictorial representations, and physician diagnosis. Subjects were females between with mean age 46 years. The prevalence of the migraine based on physician diagnosis were: imploding 35.82%, exploding 44.28%, combined imploding and exploding 12.94% and ocular only 6.97%. The concordance (Kappa coefficient) between physician diagnosis of headache directionality with patient response to the written question was 0.36 (weak to moderate), between physician diagnosis and patient diagnosis via selection of representative pictures was 0.34 (weak to moderate), and between patient diagnosis via written question and via selection of representative pictures was 0.35 (weak to moderate).

There may be many reasons for the low concordance rates between physician and patient diagnosis including physician/ medical student variability in diagnosis, patient incomprehension of questions, and inadequate correlation of the written and spoken words with the pictures. Attempting to use the pictures to assess migraine direction can therefore not currently be recommended. There was no correlation between the type of headache and severity of migraines, reproductive stage, and response to acute and prophylactic treatments was found ($p > 0.05$). This may have been due to an inadequate sample size as a larger sample size may have demonstrated a statistically significant p-value.

Migraines did cause patients moderate disability on average in the last three months. The majority of the patients had not tried many of the common prophylactic medications even among the few who did take migraine prophylactic medications, even fewer found them to be effective. The barriers of prescribing prophylactic medications in the women's health primary practice setting are likely multifactorial and may include physician lack of knowledge/ experience prescribing the prophylactic medication and patient reluctance to be on frequent

medication. It is likely prophylactic medication prescriptions are much liberally handed out in migraine specialty practices. This may be a setting where education of primary care physicians may be indicated. Larger studies need to be done to evaluate the barriers for primary care physicians to prescribing migraine prophylactic medications.

There was no difference in the total number of days affected by each of the headache types. The difference in the number of migraine days in the last 3 months between each type of headache was statistically significant. There was no difference in the severity of headache between the different headache types. The response to treatment based on headache type was unremarkable, unlike hypothesized by the authors based on results from published botulinum toxin A trials.^{5,6,7} However, more research needs to be done on this topic to further delineate differences among treatment options and responses of the migraine types.

The strengths of the study included a large sample size (n=201), evaluation in a primary care setting to evaluate actual prevalence (unlike skewed data obtained from a migraine specialty clinic), and a standardized method to survey patients. Also, the validity of the sample is supported by the fact that the population most affected is captured (Caucasians with mild-severe MIDAS scores).¹⁵ The weakness of the study includes a mostly homogenous sample with decreased generalizability to the general public.

Future Directions

Directionality of migraines is an area that needs to be explored in future research studies. The effects of conventional preventive and prophylactic medicines on specific migraine directionalities needs to be further explored in larger prospective trials in order to evaluate for a correlation that was not noted in this study but was suggested by prior studies.^{5,6,7} Also, since insufficient migraine prophylactic medications were being prescribed by primary care physicians, this can be a topic that can be targeted for continuing medical education (CME).

Conclusion

This study highlights the widespread prevalence of directionality in migraines among a sample of mostly Caucasian females, as hypothesized. Concordance rate between physician and patient diagnosis was low. No correlation between the type of headache and severity of migraines, reproductive stage, and response to acute and prophylactic treatments was found.

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Appendix A

Principal Investigator Notification:

From: IRB

To: [Julia Files](#)

CC: StudyTeam Members that are marked as wishing to receive correspondence regarding the protocol/grant application

Re: Application # 07-007163

Click the link below to access the protocol/grant application information in your IRBe workspace, as well as the approved consent document(s)/Rough Word consent document(s) that need to be used when submitting consent changes as part of a modification request (if applicable) under the Documents tab:

[07-007163](#)

Title: The Prevalence of Imploding vs. Exploding headache types in a Women's Health Outpatient practice.

IRB#: 07-007163

Please note that all correspondence (modifications, continuing reviews, reportable events) related to this study/grant application must be submitted electronically in the IRBe system.

The following is an excerpt from the minutes of the Expedited Review B of the Mayo Clinic Institutional Review Boards meeting dated 12/4/2007:

The Committee reviewed and approved for human studies the protocol entitled "The Prevalence of Imploding vs. Exploding headache types in a Women's Health Outpatient practice." from Dr. Julia Anne Files and colleagues. The Committee noted that the human studies aspects involve conducting a survey of female subjects whom suffer from migraine headaches, to determine the prevalence of imploding and exploding headaches. A maximum of 200 adult female participants with migraine headaches is approved for enrollment in this protocol at Mayo Clinic Arizona. The Midas and Headache questionnaire were approved as written. The consent form was approved with minor edits. The IRB office will provide the final approved consent form on the IRBe workspace for this item. The Committee determined that this constitutes minimal risk research, and therefore was eligible for expedited review in accordance with 45 CFR 46.110(b)(1) and 63 FR 60364, items 5 and 7. This approval is valid for exactly one year unless during the year the IRB determines that it is appropriate to halt or suspend the study earlier. 07-007163

[Rubin, Joseph M.D., Chair](#)

[Gina Dahleren](#), Specialist

Mayo Clinic Institutional Review Boards

Expedited Review B

Appendix B

Telephone Script (approved 2/25/2011)

Telephone Script [Template IRB 10139.001]

Effective 12/19/2008

Mayo Clinic: Office for Human Research Protection
Telephone Script

Protocol Title: The Prevalence of Imploding vs. Exploding headache types in a Women's Health Outpatient practice.

IRB #: 07-007163

Principal Investigator: Julia Files

Introduction:

Hello, this is _____ calling from the Women's Health Internal Medicine Clinic at Mayo Clinic in Phoenix, Arizona. May I please speak to _____?

***If the participant is there continue with the script.

***If the participant is not there, ask when it would be a good time to speak with _____?

Describe the Reason for the Call:

(Example of phone call to potential participant)

We are conducting a research study to learn about the prevalence of certain types of headaches types in a primary care setting. You were identified as someone that has a history of headaches/ migraines.

Would you be willing to come to the Women's Health Internal Medicine (WHIM) Clinic to complete study related surveys? The visit will be of no cost to you and you will see either a WHIM physician or one of the medical student investigators to complete study surveys. There will be two short surveys for you to complete describing your headaches. Thereafter, the medical students or physician will complete the third (and last) survey with you. Your participation in the study is voluntary. Please understand that your current or future medical care at the Mayo Clinic will not be jeopardized if you choose not to participate.

If no: Thank them for their time and stop the recruitment process.

If yes: Describe the purpose of the study, time involved, contacts, and location. Thereafter, schedule the subject for informed consent and survey completion appointment at WHIM.

Closing

Thank you for considering participation in our research study. Give them some follow-up contact information (name and telephone number) in case they think of any more questions afterwards.

Appendix C

MIGRAINE DISABILITY ASSESSMENT QUESTIONNAIRE

Patient Number _____ Exam Date _____/_____/_____

Please indicate the number of days over the previous 3 month period that your migraine headaches affected the following activities described in questions 1 through 5 below. For questions A and B, indicate the number of days you had a headache over this time and their average severity, respectively.

- 1. How many days in the last 3 months did you miss work or school because of your headaches? (If you did not attend work or school enter zero in the box.).....
- 2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (If you did not attend work or school enter zero in the box, but if you did, do not include the days counted in question 1.).....
- 3. How many days in the last 3 months did you not do housework because of your headaches?.....
- 4. How many days in the last 3 months was your housework productivity reduced by half or more because of your headaches?.....
- 5. How many days in the last 3 months did you miss family, social or leisure activities because of your headaches?.....

Total Number of Days for Questions 1 – 5

Total number of days = 0 - 5, patient has little or no disability.
Total number of days = 6 - 10, patient has mild disability.
Total number of days = 11 - 20, patient has moderate disability.
Total number of days = 21+, patient has severe disability.

- A. How many days in the last 3 months did you have a headache?
- B. On a scale of 0 to 10, with 0 = no pain and 10 = pain as bad as it can get, what was the average severity of your headaches over the last 3 months?.....

Appendix D

Headache Questionnaire



1. Please choose the picture that most accurately represents your migraine headache.



2. Describe your **typical** migraine headache pain.

Severity: Mild Moderate Severe

Duration: 4-12 hrs. 12 – 24 hrs. > 24 hours

Throbbing: Yes No

3. Is your headache pain **pushing in** or **pushing out** of your head or is it located **within your eye socket (ocular)**? (Check all that apply)

In Out Ocular

4. How many days of the month do you have **NO** head pain of any type? _____

5. How many days in a month are you taking an analgesic to treat a headache of any type? _____

6. Do you take a pain medication on a regular basis for anything other than headaches? If so what do you take and for what symptom?

Medication:

1. _____

2. _____

3. _____

Symptom:

1. _____

2. _____

3. _____

7. Which migraine prophylactic medication(s) do you use or have you tried?

	<u>Used</u>	<u>Effective</u>	<u>Not Effective</u>
Elavil® (amitriptyline)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pamelor® (nortriptyline)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Inderal® (other Beta Blockers)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Topamax®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Depakote®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Neurontin®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Botox®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Calan® (Verapamil)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

List the medications that reduced the **frequency** of your migraine headaches.

1. _____
2. _____
3. _____

8. Do you now or have you used a triptan medication for your migraine?

	<u>Used</u>	<u>Effective</u>	<u>Not Effective</u>
Imitrex ®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Amerge®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Axert ®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Frova ®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Relpax ®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Maxalt ®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Zomig ®	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9. Are your headaches associated with your menstrual cycle?

Yes No

If yes, do you have migraines:

Only with your menses?

With Menses and ~~at~~ at other times of the month?

10. Menopausal status:

Reproductive stage _____

Menopausal transition _____

Postmenopausal _____

Hysterectomy with ovaries removed before age 50 _____

About You

11. Age of first migraine _____
12. What race best describes your racial/cultural background? Mark all that apply:
- | | |
|--|--|
| <input type="checkbox"/> American Indian or Alaska Native | <input type="checkbox"/> Asian |
| <input type="checkbox"/> Native Hawaiian or Other Pacific Islander | <input type="checkbox"/> White |
| <input type="checkbox"/> Black or African American | <input type="checkbox"/> Other: Please specify _____ |
13. What is the highest level of education you have completed?
- | | |
|---|--|
| <input type="checkbox"/> Grade 11 or Less | <input type="checkbox"/> Graduated college |
| <input type="checkbox"/> Graduated high school | <input type="checkbox"/> Some graduate work |
| <input type="checkbox"/> Some college or technical school | <input type="checkbox"/> A graduate degree
(master's degree or doctorate Ph.D.) |

Appendix E

Headache Interview Questionnaire

1a. Does your headache pain involve your eye?

No Yes

1b. If yes- In addition to pain in your eye do you have pain anywhere else?

No (stop patient has ocular headache) Yes (proceed to 1c)

1c. Do you ever have headache pain that only involves your eye without pain anywhere else? No Yes

(Proceed to 2)

2. How would you describe your headache:

- a. a stabbing, piercing, and/or squeezing sensation that is coming from outside to inside
- b. A sensation of pain or pressure that builds from within and feels as if your head is expanding
- c. Neither

(Patients can choose A, B, C, or A & B)

(If patients chose A & B, ask Question 3 below)

2. If you have more than one type of headache, do you have different headaches at different times (inter-attack variability), or do you have a change in the type of headache during one episode (intra-attack variability)?

3. If you have different headaches at different times (inter-attack variability), what percentage do you have of each headache?

Physician identified headache type (please circle one or more)

Imploding

Exploding

Ocular

Mixed Describe _____