JVIN Journal of Vascular and Interventional Neurology
OFFICIAL JOURNAL OF THE ZEENAT QURESHI STROKE INSTITUTE

The Post-Pipeline Headache: New Headaches Following Flow Diversion for Intracranial Aneurysm

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Abstract

Objective—Flow diversion using devices such as the "pipeline" stent is now a common treatment for unruptured intracranial aneurysms. Though much is known about the efficacy of the device, less is reported regarding potential side effects. In this study, we report the frequency and characteristics of the "post-pipeline headache."

Methods—We prospectively enrolled a cohort of 222 patients who underwent pipeline stenting for the treatment of intracranial aneurysm between 2015 and 2018. A follow-up telephone survey was conducted with a mean 21.6 months postprocedure evaluating postprocedure headaches and previous headache history. A post-pipeline headache was defined as a new headache or pain distinct from their prior headache syndrome. Information was collected regarding patient demographics, headache characteristics, headache history, and whether symptoms were ongoing. Logistic regression was used to determine factors associated with post-pipeline headache and the risk of long-term headache persistence.

Results—Eighty-eight individuals were reached by phone for follow-up; 48 (55%) of whom reported a new headache postprocedure. Patients experiencing post-pipeline headache were more likely to be young (OR 0.9; 95% CI: 0.85–0.94) and have a history of prior headaches (OR 2.4, 95% CI: 1.02–5.81). Associated motor (OR 6.1; 95% CI: 1.19–31.47), cognitive (OR 7.0; 95% CI: 081–60.33), visual (OR 5.4; 95% CI: 1.05–27.89), and vestibular (OR 4.8; 95% CI: 1.14–20.23) symptoms were associated with ongoing headache.

Conclusions—Post-pipeline headache is common, particularly in younger individuals with prior headache history, and has distinctive features. Symptoms can remit over time; however, two-thirds experience ongoing headaches, particularly those with associated migrainous features.

Keywords

Stent; migraine; complication

Introduction

The presence of an unruptured intracranial aneurysm is a relatively common condition, occurring in 2%–3% of the general population [1]. Treatments have advanced over time, from early techniques involving craniotomy and wrapping the aneurysm, to clipping, intravascular coiling, and most recently, the use of a flow diverter, often called a "pipeline" stent to redirect blood away from the aneurysm [1,2]. Large studies have been performed demonstrating the safety and efficacy of pipeline stenting with respect to the obliteration of the aneurysm and major procedural complications including stroke [2]. However, other side effects, for example, headache, have not been well studied, but are anecdotally seen in clinical practice. This pain leads to considerable patient anxiety and follow-up imaging (typically normal) to rule out bleeding. There is a paucity of literature describing

Vol. 11, No. 1, pp. 34–39. Published January, 2020.

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the occurrence of headache after this particular procedure [3], and the majority of studies do not make a distinction between pre and postprocedure headache in their estimation of headache frequency associated with pipeline stenting.

We hypothesize that there is a small, but not insignificant rate of new or different headache following flow diversion that is currently poorly described and likely requires alternative management. Better characterization of this headache syndrome, the population at highest risk, natural history, and potential response to treatment will allow for better counseling preprocedure, and potentially future treatment trials that will reduce periprocedural morbidity. In this study, we conduct the largest phone follow-up study to-date evaluating headache status post-pipeline stenting for intracranial aneurysm, characteristics of the pain syndrome, prior headache history, and medical treatments in order to characterize the "post-pipeline headache" phenomenon. Given the relative frequency and disturbing nature of this novel syndrome, we expect results will be important and significantly impact patient care.

Materials and Methods

This study was approved by our Institutional Review Board. Adult patients (18 years of age or greater) who underwent pipeline stenting for the treatment of an unruptured intracranial aneurysm at our institution between January 2015 and June 2018 were identified through the electronic medical record. Individuals were contacted by phone by a member of the study team (DG) and information was collected regarding headaches occurring postprocedure as well as their baseline headache history. Participants provided oral consent over the telephone indicating their willingness to participate. If there was no answer, a message was left containing limited information, along with a call back number. Three attempts at differing times of day were made to reach each patient before they were removed from the dataset. Patients were also excluded if they were found to have a ruptured aneurysm or were unable to participate in answering the questionnaire. Though rare, partial responses were recorded and analyzed up to the point where the patient declined to answer further questions.

Defining post-pipeline headache

In collaboration with our Headache Center, a questionnaire was developed based on the International Classification of Headache Disorders (ICHD-3) criteria [4] in an effort to capture different types of headache characteristics in this patient population. Data were gathered regarding the presence of a new headache, how long it occurred following procedure, frequency, severity, history of prior headache, whether this headache was different from that of previous headaches, the natural history of the new headache (abated vs. still present), location of the pain (behind the eye, side of the head, back of the head, forehead, neck), quality (stabbing, drilling, dull, electric, sharp, throbbing, crushing, pressure like, zapping, thunderclap), intensity (scale 1–5), associated features (visual symptoms, sensitivity to light, sound, noise; nausea/vomiting, nasal congestion, flushing, motor weakness, cognitive difficulties, imbalance, ringing in the ears, dizziness, confusion, fainting), medications tried [anticonvulsant, beta blocker, calcium channel blocker, tricyclic antidepressant, triptan, nonsteroidal antiinflammatory drug (NSAID), Tylenol, serotonin and norepinephrine reuptake inhibitor (SNRI)], and triggers (rising to stand, bending over).

Patient demographics and characteristics regarding their aneurysm and procedure were also collected in order to account for possible confounding factors. All data were stored in a secure RedCap database and used for further analysis.

Statistical analysis

Statistical analyses were performed using Stata v 14. Our primary outcome was defined as the frequency of a "post-pipeline headache"—a new or different headache occurring following pipeline stenting. Student's *t*-tests and chi-square analyses were used to determine factors associated with a higher risk of post-pipeline headache and ongoing headache. Variables significant in univariate analyses ($p < 0.05$) were included in multivariable logistic regression models and receiver operating characteristic (ROC) analyses were conducted to determine the model that best predicted post-pipeline headaches.

Results

Two hundred twenty-two patients underwent pipeline stenting for intracranial aneurysm over the study period. Eighty-eight (40%) were able to be reached by phone, a mean 21.6 months following treatment and completed the follow-up survey. There were no differences in demographics or aneurysm characteristics between those who participated and those unable to be reached. The average age of the follow-up cohort was 60.4 years. Eighty-five percent were women; 26% were black. Most had aneurysm repair of the distal internal carotid artery (ICA) ($n = 72$). Approximately half of the patients reported a history of headaches prior to treatment of their aneurysm; however, of the 88 patients reached for

Table 1. Post-pipeline headache characteristics

Characteristics	Patients with new headache No. (%) (*n* = 48)	Characteristics	Patients with new headache No. (%) (*n* = 48)
Age, mean years (SD)	55.3 (11.0)	*Motor*	18 (38%)
Race, black	17 (35%)	Eyelid droop	4 (8%)
Sex, male	5 (10%)	Leg weakness	2 (4%)
History of prior headaches	29 (60%)	Arm weakness	6 (13%)
History of symptoms with pain*	24 (50%)	Leg numbness	5 (10%)
Family history of headache	21 (44%)	Arm numbness	7 (15%)
Current pain different from prior headaches	19 (40%)	Slurred speech	7 (15%)
Headaches still occurring	33 (69%)	Difficulty getting out words	8 (17%)
Can Identify a trigger	14 (29%)	*Cognitive*	12 (25%)
Rising to stand	3 (6%)	Confusion	7 (15%)
Bending over	2 (4%)	Memory problems	8 (17%)
Pain		*Physical*	32 (67%)
Location		Tender scalp	14 (29%)
Forehead	4 (8%)	Nausea	16 (33%)
Behind eye	10 (21%)	Vomiting	7 (15%)
Front of head	1 (2%)	Stuffy nose	6 (13%)
Middle of head	1 (2%)	Nasal congestion	7 (15%)
Side of head	12 (25%)	Nasal drainage	5 (10%)
Back of head	9 (19%)	Watery eyes	11 (23%)
All over head	6 (13%)	Face pain	8 (17%)
Neck	1 (2%)	*Visual*	17 (35%)
Same side as aneurysm	33 (69%)	Blurred vision	9 (19%)
Quality		Double vision	2 (4%)
Stabbing	4 (8%)	Zigzag lines	1 (2%)
Drilling	1 (2%)	Clouds	1 (2%)
Dull	15 (40%)	Checkerboard patterns	0 (0%)
Electric	0 (0%)	Kaleidoscopes	0 (0%)
Sharp	13 (27%)	Arc shapes	0 (0%)
Throbbing	16 (33%)	Tunnel vision	1 (2%)
Crushing	0 (0%)	Blind spots	1 (2%)
Pressure	6 (13%)	Other	6 (13%)
Zapping	1 (2%)	*Other*	14 (29%)
Thunderclap	0 (0%)	Fainting	2 (4%)
Associated symptoms		Seizure	0 (0%)
Sensitivities	29 (60%)	Pacing/restlessness	13 (27%)
Light	27 (56%)	Face flushing	2 (4%)
Sound	13 (27%)	**Medications**	35 (73%)
Smell	6 (13%)	Anticonvulsant	3 (6%)
Vestibular	21 (44%)	Beta blocker	1 (2%)
Motion sickness	7 (15%)	Calcium channel blocker	1 (2%)
Vertigo	8 (17%)	Tricyclic	0 (0%)
Dizziness	9 (19%)	5-HT agonist	1 (2%)
Imbalance	10 (21%)	NSAID	5 (10%)
Ringing in ears	9 (19%)	Tylenol	23 (48%)
		SNRI	0 (0%)

Prior symptoms include: sensitivity to light, sensitivity to sound, sensitivity to smell, nausea, vomiting, worse with physical activity, throbbing pain

follow-up, 48 (55%) reported that following the procedure they experienced a "new headache"; with either no prior headache history, or symptoms inconsistent with their prior headache syndrome.

Post-pipeline headache characteristics

Patients who endorsed new or different headaches following placement of their pipeline stent reported a fairly consistent pain syndrome. Full results are reported in Table 1. On average, the headache began 20 days following the procedure and was described as either a sharp (28%), dull (32%), or throbbing (35%) sensation located behind the eye (22%), or over the side (27%) or back (20%) of the head on the same side as the aneurysm (69%). Headaches occurred 2–3 times per week lasting for hours (mean 9.7 hours), with an intensity of 3.6 of 10 on the pain rating scale. About one-third of patients could identify triggers such as bending over. For nearly two-thirds, the pain was ongoing at the time of follow-up, though many reported improvement in frequency and severity after several months. Over 90% reported corresponding photophobia, and many reported other associated vestibular, motor, or cognitive symptoms. Many (76%) tried medication, most commonly Tylenol, to relieve symptoms. Very few were placed on prophylactic medications.

Likelihood of post-pipeline headache

Factors associated with a higher likelihood of post-pipeline headache are outlined in Table 2. Patients experiencing a post-pipeline headache were significantly more likely to be young (OR 0.9; 95% CI: 0.85–0.94) and have a history of prior headaches (OR 2.4, 95% CI: 1.02–5.81). Considering prior headache history increased the likelihood of new headache for each age point (Figure 1). In ROC analyses, combining age and

Table 2. Factors associated with post-pipeline headache

Variables	Total population*n* = 88	Post-pipeline headache*n* = 48	No new headache*N* = 40	*P*-value
Age, mean years (SD)	60.4 (11.6)	55.3 (11.0)	66.8 (8.9)	**<0.001**
Race, n (%) black	23 (26%)	16 (33%)	7 (18%)	0.106
Sex, n (%) women	75 (85%)	43 (90%)	32 (80%)	0.311
Location of aneurysm, *n* (%) ICA	72 (82%)	37 (77%)	35 (88%)	0.370
Family history of headaches, *n* (%)	37 (42%)	21 (44%)	16 (40%)	0.733
Prior headache history, *n* (%)	44 (50%)	29 (60%)	15 (38%)	**0.042**
Prior symptoms,* *n* (%)	37 (42%)	24 (50%)	13 (33%)	0.371

ICA = internal carotid artery; prior symptoms include: sensitivity to light, sensitivity to sound, sensitivity to smell, nausea, vomiting, worse with physical activity, throbbing pain

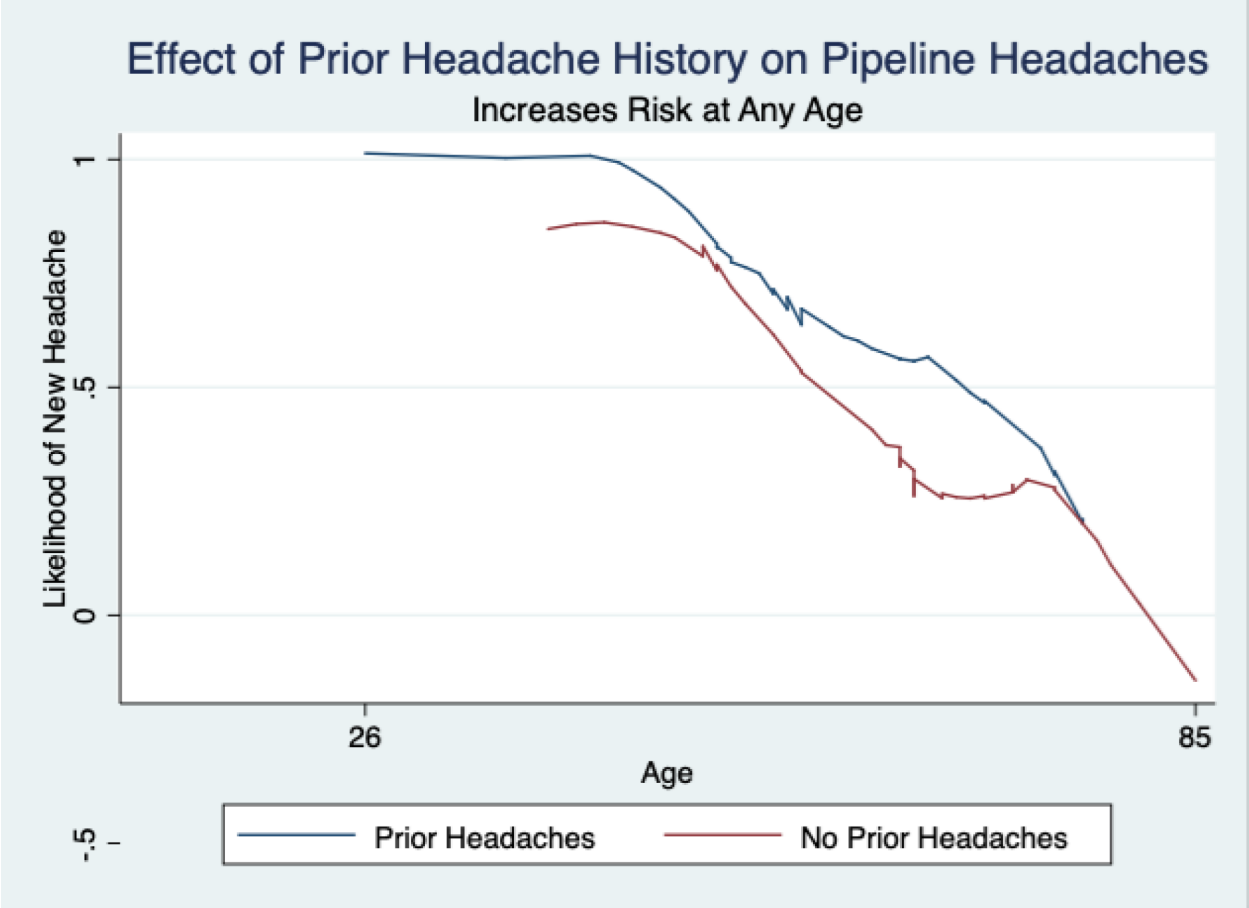

Figure 1. Prior headache history increases the likelihood of post-pipeline headache at any age.

headache history to predict new headache resulted in an area under the curve of 0.80.

Likelihood of ongoing headache

Thirty-three (69%) patients reported that at the time of their follow-up phone call, they continued to experience a post-pipeline headache. Headache persistence was more likely for patients who were young (OR 0.9; 95% CI: 0.89–1.00), and who had accompanying motor (OR 6.1; 95% CI: 1.19-31.47), cognitive (OR 7.0; 95% CI: 081–60.33), visual (OR 5.4; 95% CI: 1.05–27.89), or vestibular (OR 4.8; 95% CI: 1.14–20.23) symptoms (Table 3).

Discussion

Flow diversion is rivaling coiling and clipping as the favored treatment for nonruptured intracranial aneurysms [2]. Studies have shown the efficacy of aneurysm thrombosis with low complication rates [2]. However, as it remains a relatively new procedure, much remains to

Table 3. Factors associated with ongoing headache at follow-up

Variables	All pipeline headaches*n* = 48	Still occurring*n* = 33	Abated*n* = 15	*P*-value
Age, mean years (SD)	55.3 (11.0)	53.3 (10.4)	59.9 (11.8)	0.056
Race, *n* (%) black	16 (33%)	11 (33%)	5 (18%)	1.000
Sex, *n* (%) women	43 (90%)	28 (85%)	15 (100%)	0.111
Location of aneurysm, *n* (%) ICA	37 (77%)	23 (70%)	14 (93%)	0.469
Family history of headaches, *n* (%)	21 (44%)	16 (48%)	5 (33%)	0.284
Prior headache history, *n* (%)	29 (60%)	21 (64%)	8 (53%)	0.499
Prior symptoms*, *n* (%)	24 (50%)	18 (55%)	6 (40%)	0.495
Medication use, *n* (%)	35 (73%)	25 (76%)	10 (67%)	0.624
Triggers, *n* (%)	14 (29%)	33 (100%)	15 (100%)	0.669
Intensity, mean score (SD)	3.6 (1.1)	3.6 (1.1)	3.6 (1.1)	0.880
Sensitivities, *n* (%)	29(60%)	22 (67%)	7 (47%)	0.189
Associated symptoms, *n* (%)	35 (73%)	27 (82%)	8 (53%)	**0.040**
Location**				0.462
Frequency, mean times per week (SD)	2.8 (2.4)	2.7 (2.4)	3.0 (2.4)	0.715
Duration, mean hours (SD)	9.7 (11.0)	9.0 (11.0)	11.5 (11.3)	0.503
Pain type**				0.206

*ICA = internal carotid artery; prior symptoms include: sensitivity to light, sensitivity to sound, sensitivity to smell, nausea, vomiting, worse with physical activity, throbbing pain; associated symptoms include: motor, cognitive, visual, and vestibular

**See Table 2 for pain types and locations

be learned. Anecdotally, it is not uncommon for patients to experience a headache following the procedure. This phenomenon is patient-reported but has yet to be well-described in the literature. Previous studies have evaluated the frequency of headaches following pipeline stenting, but studies were small and the majority of included patients had headache syndromes (e.g., migraine) prior to the procedure [3]. In this cohort, the frequency of postprocedural pipeline headaches was high at just over 50%. Pain was typically deep and over the same side of the head as the aneurysm repair.

Our data suggest that both age and prior headache history can help to predict the likelihood of post-pipeline headache. Older individuals were less likely to develop the syndrome, though prior headache history increased risk at any age. This may reveal an underlying headache predisposition and indicate that if one has made it to their later years without frequent headaches they may be more resistant. Sex was not a predictor of headache in our cohort, though the majority of our population was younger women. This may indicate a bias—younger women had headaches which led to imaging and detection of their aneurysm and then were more likely to develop a new or different type of pain postprocedure, though we did not find an association with sex in older patients either.

For some individuals, the pain was temporary, and the syndrome seemed to resolve after several months. These headaches are no less important, given that periprocedural headache can provoke significant anxiety for both the patient and physician—potentially indicating stent misalignment or intracranial bleeding. Pain may be explained due to the innervation of the intracranial vessels, similar to pain resulting from dissection [5,6]. By characterizing this phenomenon, associated qualities, predisposing risk factors, natural history, and potential treatments will be useful first steps in allowing physicians to better counsel and treat patients postprocedure. Interestingly, patients who had ongoing headaches tended to experience one or more associated visual, cognitive, motor, or vestibular factors. These factors also tend to be more common with migraine syndromes, again suggesting that the predisposition to migraine may make patients more likely to experience new and ongoing headaches following the procedure. Exacerbation of migraines has been reported following other neurovascular procedures as well as due to periprocedural anesthesia [7,8]. It also suggests that perhaps medications useful for preventing migraine in the general population may be efficacious in this postprocedure cohort, especially younger patients with prior headache histories. Further trials are needed to determine the most appropriate therapy.

Our study is not without limitations. Ours is data from a single center with a significantly higher number of younger women treated. In addition, though collected prospectively, phone calls were made after several months had elapsed, introducing the issue of recall bias. However, despite these limitations, this is one of the largest reported cohorts of patients undergoing pipeline stenting for treatment of intracranial aneurysm and the first to report new periprocedural headaches distinct from prior diagnoses. We feel that this is particularly important as we have illustrated that the phenomenon is quite common and both doctors and patients need to be aware so that when headaches occur they do not immediately think the patient has a subarachnoid hemorrhage, so patients can be counseled as to the risk, and to consider abortive and prophylactic medications early, particularly in those at highest risk.

Conclusions

Post-pipeline headache is common and can occur in up to 50% of individuals undergoing the procedure. It is more common in younger individuals with prior headache history, and has distinctive features. While symptoms can remit over time, up to two-thirds endorse ongoing headaches. Associated features such as co-existing visual, cognitive, motor, or vestibular disturbances make ongoing headache more likely and suggest that the lingering headache syndrome may fall along the migraine spectrum. Further studies are needed to determine the most appropriate treatment regimen and should be considered given its prevalence.

Acknowledgments:

None.

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