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Does This Patient With Headache Have a Migraine or Need Neuroimaging?

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CLINICAL SCENARIOS

Case 1

A 38-year-old woman presents with pulsatile, unilateral headaches that occur twice a month. The headaches last between 4 and 14 hours and are disabling to the point that she has to lie down and go to sleep. She has no visual auras. The neurologic examination is entirely normal. Does this patient have migraines?

Case 2

A 27-year-old man developed a severe, rapid-onset headache and mild neck stiffness while performing pushups. He reports no prior illness. The neurologic examination identifies no abnormal findings, but the symptoms persist 2 hours after onset. Should you request neuroimaging for this patient?

Case 3

A 45-year-old man tells his family physician, again, about his 10-year history of intermittent unilateral headache of grade 5 (of 10) severity and 4 to 5 hours' duration. An aura does not herald the onset, and no vomiting or photophobia occur. You reassess his physical examination only to find mild weakness (power, grade 4 [of 5]) and increased reflexes in the right leg and

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Context In assessing the patient with headache, clinicians are often faced with 2 important questions: Is this headache a migraine? Does this patient require neuroimaging? The diagnosis of migraine can direct therapy, and information obtained from the history and physical examination is used by physicians to determine which patients require neuroimaging.

Objective To determine the usefulness of the history and physical examination that distinguish patients with migraine from those with other headache types and that identify those patients who should undergo neuroimaging.

Data Sources and Study Selection A systematic review was performed using articles from MEDLINE (1966-November 2005) that assessed the performance characteristics of screening questions in diagnosing migraine (with the International Headache Society diagnostic criteria as a gold standard) and addressed the accuracy of the clinical examination in predicting the presence of underlying intracranial pathology (with computed tomography/magnetic resonance imaging as the reference standard).

Data Extraction Two authors independently reviewed each study to determine eligibility, abstract data, and classify methodological quality using predetermined criteria. Disagreement was resolved by consensus with a third author.

Data Synthesis Four studies of screening questions for migraine (n=1745 patients) and 11 neuroimaging studies (n=3725 patients) met inclusion criteria. All 4 of the migraine studies illustrated high sensitivity and specificity if 3 or 4 criteria were met. The best predictors can be summarized by the mnemonic POUNDing (Pulsating, duration of 4-72 hOurs, Unilateral, Nausea, Disabling). If 4 of the 5 criteria are met, the likelihood ratio (LR) for definite or possible migraine is 24 (95% confidence interval [CI], 1.5-388); if 3 are met, the LR is 3.5 (95% CI, 1.3-9.2), and if 2 or fewer are met, the LR is 0.41 (95% CI, 0.32-0.52). For the neuroimaging question, several clinical features were found on pooled analysis to predict the presence of a serious intracranial abnormality: cluster-type headache (LR, 10.7; 95% CI, 2.2-52); abnormal findings on neurologic examination (LR, 5.3; 95% CI, 2.4-12); undefined headache (ie, not cluster-, migraine-, or tension-type) (LR, 3.8; 95% CI, 2.0-7.1); headache with aura (LR, 3.2; 95% CI, 1.6-6.6); headache aggravated by exertion or a valsalva-like maneuver (LR, 2.3; 95% CI, 1.4-3.8); and headache with vomiting (LR, 1.8; 95% CI, 1.2-2.6). No clinical features were useful in ruling out significant pathologic conditions.

Conclusions The presence of 4 simple historical features can accurately diagnose migraine. Several individual clinical features were found to be associated with a significant intracranial abnormality, and patients with these features should undergo neuroimaging.

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arm. What features distinguish this case from the preceding 2 cases?

WHY ARE THE HISTORY AND PHYSICAL EXAMINATION IMPORTANT?

With a lifetime prevalence of 99% in women and 94% in men, headaches are ubiquitous.[1] Some patients experience headaches frequently enough that they have a primary headache disorder such as cluster-, migraine-, or tension-type headaches. These common clinical conditions have population prevalences of 0.4%, 6% to 17%, and 38.3%, respectively.[2-4] Despite the high prevalence of headaches, physicians often are uncomfortable diagnosing specific headache disorders. Fewer than half of patients with migraine are properly diagnosed, and only one third of affected patients receive migraine-specific prescription drugs.[5,6] The International Headache Society (IHS) developed a formal, comprehensive, and widely cited headache classification system in 1988 that includes diagnostic categories of migraine with and without aura[7]; the system was updated in 2004.[8] However, this classification system may be too cumbersome for most primary care or generalist physicians to use properly. As a result, efforts have been made to produce short, practical, memorable, and effective screening tools.[9-12]

Undifferentiated headache usually is of benign etiology, so neuroimaging rarely reveals significant intracranial pathology. However, central nervous system tumors, abscesses, aneurysms, or hemorrhages may be heralded by headaches, and neuroimaging is required to uncover these diagnoses. Thus, there is a tension between knowing that primary (benign) headache disorders are overwhelmingly common and the urge to order neuroimaging out of fear of missing uncommon serious problems. This fear can lead to an overuse of resources, particularly computed tomography (CT) and magnetic resonance imaging, requiring guidelines to help adjust use of neuroimaging.[13-15]

We performed a systematic review and meta-analysis of published evidence to address 2 important clinical issues pertaining to patients with headaches. We sought to determine the clinical features gleaned from the history and physical examination that distinguish patients with migraine from those who have other types of headaches and that identify those patients who should undergo neuroimaging. Our findings are written primarily for students, generalist physicians, and nonneurologists who encounter patients with headaches. Neurologists may see patients who are more complex and atypical; therefore, this literature review may not apply to them. Neurologists may, however, find this review useful as a teaching tool and as a summary of the evidence that exists to date.

Pathophysiology

The underlying pathophysiology of headache is complex and remains relatively poorly understood. However, ultimately all forms of headache share a common final link in the perception of pain: nociceptive information from the head is transmitted via the nucleus of the trigeminal nerve.[16] Because the mechanisms activated in secondary headache disorders (ie, those with an identifiable structural or metabolic cause) resemble those activated in primary headache disorders (ie, cluster-, migraine-, and tension-type migraine headaches), diagnosis and differentiation can be particularly difficult.

History and Physical Examination

A thorough history and physical examination is key to the diagnosis of the patient presenting with headache. This includes medical and social histories and use of alcohol and medication, as well as headache-specific questions (onset, location, frequency, character, duration, exacerbating and alleviating factors, radiation, time from onset to maximal intensity, related past history) and other symptoms such as auras (ie, scintillating scotoma or sensory or motor symptoms that precede a migraine headache), hallucinations, nausea or vomiting, rash, and focal neurologic symptoms. The current teaching regarding headache focuses on identification of "red flags," which are thought to increase the likelihood of an adverse etiology. These red flags include headache in patients with cancer or human immunodeficiency virus, sudden onset of symptoms, onset after age 50 years, an accelerating pattern, systemic illness (eg, fever, stiff neck, rash), and focal neurologic signs and symptoms.[17] For example, finding a new cranial nerve palsy, papilledema, sensory abnormality, or focal weakness including hemiparesis on neurologic examination would each be an obvious cause for concern.

METHODS

Search Strategy and Quality Review

We conducted bibliographic searches of the MEDLINE database for the years 1966 to November 2005 and used a search strategy previously published for the Rational Clinical Examination series.[18] For the migraine question, we used the search terms *migraine, diagnosis, medical history taking, physical examination, sensitivity and specificity, professional competence, routine diagnostic tests, diagnostic errors*, and *reproducibility of results*. For the neuroimaging question, the search terms included *headache*, *diagnosis*, *medical history taking*, *physical examination*, *sensitivity and specificity*, *professional competence*, *routine diagnostic tests*, *diagnostic errors*, and *reproducibility of results*. Secondary search strategies included reviewing citations from primary studies, review articles, and bibliographies of standard physical examination and neurology textbooks.

The abstracts found in both literature searches were screened for potential studies of interest. We excluded studies that only assessed patients with a specific underlying chronic disease (ie, cancer or human immunodeficiency virus). Primary studies were independently reviewed by 2 authors (M.E.D., D.R.M); disagreement was resolved by consensus with a third author (C. M. B.). The migraine studies were included if they assessed the usefulness of history and physical examination in predict-

Table 1. Classification of Abnormalities Found on Neuroimaging

Abnormality	Classification
Significant	Related to headache and requiring definite action Examples: acute cerebral infarct, acute cerebral edema, acute cerebral hemorrhage (subarachnoid, intraparenchymal, or extra-axial), neoplastic disease, hydrocephalus, and vascular abnormalities (eg, aneurysm or arteriovenous malformation)
Possibly related to headache	Possibly related to headache; may require definite action Examples: metastases to the calvarium, acute or chronic sinusitis, and abnormalities of the nasal cavity
Insignificant	Unrelated to headache or requiring no action Examples: developmental venous anomaly, cerebral or cerebellar atrophy, subcortical (lacunar) infarction, old cortical infarction, and normal variants (eg, cavum septum pellucidum, physiological calcifications)

From McCrory et al.[20]

ing the diagnosis of a migraine-type headache using IHS criteria as applied by a neurologist as the gold standard. We included studies that examined individual variables and combinations of variables for predicting a migraine diagnosis. The neuroimaging studies were included if they assessed the usefulness of the history and physical examination in predicting the presence of significant intracranial pathology in adults with nontraumatic headache.

The methodological quality of each primary study was assessed in duplicate using criteria previously developed for the Rational Clinical Examination series.[19] Level I studies are independent, blinded comparisons of components of the clinical examination with a gold standard among 100 or more consecutive patients with headache. Level II studies have the same characteristics as level I studies but assess fewer patients (<100). Level III studies are independent, blinded comparisons of components of the clinical examination with a gold standard among nonconsecutive patients with headache. Level IV studies are those that do not meet the criteria for at least level III evidence.

Data Abstraction

For the migraine headache component of the study, 2 authors (M.E.D., D.R.M.) independently assessed each study for both the derivation of screening tools and the assessment of the validity of these tools; disagreement was resolved by consensus with a third author (C.M.B.). For the neuroimaging component of the study, the same authors independently extracted and entered data in duplicate for analysis; disagreement was resolved by consensus with a third author (C. M. B.). Classification of the final neuroimaging diagnosis was based on the system proposed by McCrory et al[20] on behalf of the US Headache Consortium: significant intracranial abnormalities, possibly significant abnormalities, insignificant abnormalities, and normal. The applicable diagnoses for each category are listed in TABLE 1. To create 2×2 evidence tables, we dichotomized "significant abnormalities" as "disease positive" and "abnormalities possibly related to headache" and "insignificant abnormalities" as "disease negative."

Statistical Methods

Published raw data were used to calculate likelihood ratios (LRs) for the specific clinical variables.[21] Where 2 or more studies examined the same clinical variable, we calculated summary LRs and 95% confidence intervals (CIs) using the Dersimonian and Laird random-effects approach.[22] Estimated variances of LRs were computed using the usual methods for ratios of proportions,[23] with their reciprocals used as study weights. In studies with a zero cell count, the value 0.5 was added to each cell count to permit use of this variance estimation. We also present the LRs and CIs for individual clinical variables.

For neuroimaging studies, differing patient selection strategies led to wide variation in the estimated prevalence of serious underlying intracranial pathology. To account for heterogeneity between prevalence values within these groups, we used a random-effects model to compute summary prevalence estimates. All analyses were performed using R version 2.01 and WinBUGS version 1.4.[24,25]

RESULTS

Does This Patient Have Migraine?

Study Characteristics. This literature search produced 771 abstracts, from which 12 studies were relevant to our review. Seven studies were excluded from the overview for the following reasons: 2 evaluated algorithms that were very similar to the IHS questionnaire and were therefore too long[26,27]; 1 included only migraine patients and therefore had no estimate for specificity[28]; 2 evaluated algorithms that collapsed to only 2 questions (one of which was "have you ever had migraine?")[29,30]; 1 looked at only individual variables[31]; and 1 included no quantitative information from which LRs could be calculated.[32] Our literature search also yielded a high-quality systematic review by Smetana,[33] published in 2000, which highlighted important individual clinical features from the history and physical examination. The precision of the IHS criteria in diagnosing primary headache disorders was assessed in 1 study and found to be substantial ($\kappa = 0.74$).[34]

Individual Findings. Smetana[33] performed a meta-analysis of studies prior to the year 2000 and calculated summary positive and negative LRs for individual clinical features. This study identified 4 individual variables that, when present, were the most predictive of distinguishing migraine from tension-type headache: nausea (LR, 19; 95% CI, 15-25), photophobia (LR, 5.8; 95% CI, 5.1-6.6), phonophobia (LR, 5.2; 95% CI, 4.5-5.9), and exacerbation by physical activity (LR, 3.7; 95% CI, 3.4-4.0). The pooled LRs and their 95% CIs associated with the absence of each of those findings were 0.19 (0.18-0.20), 0.24 (0.23-0.26), 0.38 (0.36-0.40), and 0.24 (0.23-0.26), respectively.

Combinations of Findings. Four studies contained accuracy data for com-

binations of clinical features constituting algorithms or clinical decision rules from which LRs could be calculated.[9-12] Because the algorithms were all different, the data could not be pooled.

TABLE 2 summarizes the data from these 4 studies.[9-12] One study[12] did not clearly state that it used the IHS criteria and lacked a clear description of how the sensitivity and specificity values were calculated. A second study[11] compared known migraine patients with a cohort that had no headaches. The use of patients on opposite ends of the spectrum exaggerates the LRs and CIs found in the study. A third study[10] included 3 variables, but 1 of the variables ("is your headache disabling?") was also part of the entry criteria, thus making it a 2-variable screening tool.

The study by Michel et al[9] had the fewest methodological deficiencies. The authors describe the size of the filters through which the patients moved (1049 screened, 166 evaluable), leaving us with the best idea of the patient population represented. The population in this study is most similar to patients of generalist physicians who might complain of headaches. We transformed the decision rule of Michel et al into a recommended mnemonic (POUNDing [Pulsatile quality; duration of 4-72 hOurs; Unilateral location; Nausea or vomiting; Disabling intensity]) and scoring system based on the data from their report.[35] Headaches were classified as "definite migraine," "possible migraine," or "not migraine."

This study used a screening tool with 5 questions: (1) "Is it a pulsating headache?" (2) "Does it last between 4 and 72 hours without medication?" (3) "Is it unilateral?" (4) "Is there nausea?" and (5) "Is the headache disabling?" Disabling headaches are those that disrupt a patient's daily activities. If the patient answers "yes" to 4 or more of the 5 questions, the LR is 24 (95% CI, 1.5-388) (definite or possible migraine vs not migraine); for 3 criteria, the LR is 3.5 (95% CI, 1.3-9.2); and for 1 or 2 criteria, the LR is 0.41 (95% CI, 0.32-0.52).

Does This Patient Need Neuroimaging?

Study Characteristics. Our search yielded 11 studies that fulfilled inclusion criteria (TABLE 3).[36-46] These studies account for 3725 patients with acute and chronic headache seen in outpatient, inpatient, and emergency department settings. Nineteen other studies were considered for potential inclusion but were excluded for the following reasons: 4 did not present raw data regarding the usefulness of history and physical examination[47-50]; 4 included children[51-54]; 4 did not distinguish "significant" from "possibly significant" or "insignificant" abnormalities on neuroimaging[55-58]; 2 were restricted to patients with a specific medical condition[59,60]; and 5 had 2 or more of the aforementioned reasons.[61-65] No studies specifically addressed precision of the clinical examination in assessing patients with headache.

Prevalence of Significant Intracranial Pathology. Pooling data to estimate the prevalence of significant intracranial pathology requires that we compare similar groups of patients. We classified each study's patient population into 1 of 6 categories.

Category I included 1 prospective study of patients seeking a neurologist's evaluation of chronic headache.[36]

Table 2. Results of Clinical Prediction Rules for Migraine Diagnosis by International Headache Society Criteria as Applied by a Neurologist

Source	Level of Evidence	Study Population and Setting	Mean Age, y	No. of Patients	Migraine Prevalence, No. (%)	Question Panel	Result	LR (95% CI)
Michel et al,[9] 1993	I	Primary care, France*	40	166	125 (75)	POUNDing criteria*	≥4 features†	24 (1.5-388)
							3 features†	3.5 (1.3-9.2)
							≤2 features†	0.41 (0.32-0.52)
							≥4 features‡	5.8 (2.7-12)
							3 features‡	1.0 (0.64-1.7)
							≤2 features‡	0.45 (0.3-0.66)
Lipton et al,[10] 2003	III	Primary care, United States§	39	443	332 (75)	Disability headache Nausea Sensitivity to light	≥2 features	LR+ 3.2 (2.7-3.9) LR– 0.25 (0.22-0.28)
Lainez et al,[11] 2005	IV	Patients referred to headache specialists, Spain	39	140	70 (50)	Frequent or intense Lasts >4 h Nausea Photophobia or phonophobia Limits activities	≥4 features	LR+ 5.0 (3.0-8.2) LR– 0.08 (0.04-0.21)
Pryse-Phillips et al,[12] 2002	IV	Patients referred to headache specialists, Canada	40	461	412 (89)	Daily headaches Unilateral Stops you from doing things	1 = "not" 2 or 3 = "yes"	3.1‖
							1 = "yes" 2 and 3 = "no"	0.19‖

Abbreviations: CI, confidence interval; LR, likelihood ratio.
*Pulsatile quality; duration 4-72 hOurs; Unilateral location; Nausea/vomiting; Disabling intensity.
†For definite or possible migraine diagnosis by International Headache Society criteria as applied by a neurologist.
‡For definite migraine diagnosis by International Headache Society criteria as applied by a neurologist.
§Participants were derived from a primary care setting but evaluated by a neurologist to determine the diagnosis of migraine.
‖Confidence interval could not be calculated because raw data were not available.

This is therefore referred to as a "chronic headache" study. Neuroimaging was performed in 1876 consecutive patients. The prevalence of significant intracranial pathology in this category was 1.2% (95% CI, 0.77%-1.8%).

Category II studies involved patients with new or changed headaches. There were 2 types of new headaches: adult-onset migraine headaches (patients older than 40 years), known as category IIa,[37] and new-onset or changed headaches (within the last 12 months), known as category IIb.[38] These patients were evaluated in a neurology clinic. The prevalence of significant intracranial pathology in Category IIa was 0% (95% CI, 0.0%-5.3%) and in IIb was 32% (95% CI, 24%-42%).

Category III included studies that enrolled patients with acute thunderclap headache and looked only for subarachnoid hemorrhage as the significant abnormality.[39,40] Thunderclap headache is severe and of sudden onset. These headaches typically result in a patient seeking urgent care.[66] All category III studies came from emergency department visits. The combined prevalence of significant intracranial pathology for category III was 43% (95% CI, 20%-68%). Although neuroimaging can be useful in assessing patients with subarachnoid hemorrhage, it is important to recognize that lumbar puncture (not CT scan) is the reference standard for diagnosis of this clinical entity.

Category IV studies reviewed all patients who had undergone CT scans at their institution and identified those patients whose indication for neuroimaging was headache.[41-43] These studies were retrospective and can be labeled "reverse-cohort studies" (ie, they go in the reverse direction from CT to symptom). The combined prevalence of disease in category IV was 7.2% (95% CI, 1.5%-18%).

Category V studies included patients who were at high risk of an abnormality because either the studies were conducted at a time when CT scans were not readily used and were thus highly selected, or they consisted of a cohort that only included patients with at least 1 high-risk clinical finding. The clinical findings included increase in intensity or frequency of headache, abrupt onset of headache signs and symptoms, persistence of headache despite analgesia, altered characteristics of headache, and/or presence of focal neurologic finding.[44-46] Patients in these studies could be labeled as "high-risk." The combined prevalence of significant intracranial pathology in category V was 18% (95% CI, 6.8%-35%).

The first 4 categories (I, IIa, IIb, and III) represent distinct patient groups that allow us to derive pretest probabilities based on clinical presentation.[36-40] Categories IV and V do not reflect distinct patient subtypes but rather the manner in which patients were enrolled (ie, study methodology) and therefore do not give useful prevalence values for patients based on clinical presentation.[41-46] We used all categories to derive operating characteristics (ie, LRs) of specific clinical variables but used only categories I, II, and III for patient pretest probability of significant intracranial pathology.

Positive LRs. There were several clinical findings with pooled positive LRs that were statistically significantly greater than 1.0 (TABLE 4). The following variables had clinically important LRs: cluster-type headache (LR, 11; 95% CI, 2.2-52); abnormal findings on neurologic examination (LR, 5.3; 95% CI, 2.4-12); undefined headache (ie, not cluster-, migraine-, or tension-type) (LR, 3.8; 95% CI, 2.0-7.1); headache with aura

Table 3. Studies of the Accuracy of the Clinical Examination in Predicting Significant Intracranial Abnormality

Source	Level of Evidence	Study Population and Setting	Location	Mean Age, y	No. of Patients	Prevalence, No. (%) [95% CI]*
		Category I†				
Sempere et al,[36] 2005	I	Chronic headache, neurology clinic	Spain	38	1876	22 (1.2) [0.77-1.8]
		Category II				
Cull,[37] 1995	IV	Migraine headache after age 40 y, neurology clinic	Scotland	52	69	0 [0.0-5.3]
Duarte et al,[38] 1996	IV	New/changed headache, neurology clinic	Spain	46	100	32 (32) [24-42]
		Category III				
Landtblom et al,[39] 2002	IV	Thunderclap, ED	Sweden	42‡	137	30 (22) [16-30]
Linn et al,[40] 1998	IV	Thunderclap, ED	Netherlands	46	102	65 (64) [54-72]
		Category IV				
Carrera et al,[41] 1977	IV	Reverse-cohort, in-patient and out-patient	Boston	35	85	6 (7.0) [3-15]
Kahn et al,[42] 1993	IV	Reverse-cohort, in-patient, out-patient, and ED	Chicago, Ill; Winnipeg	47	1111	120 (11) [9-13]
Weingarten et al,[43] 1992	IV	Reverse-cohort, out-patient	California	48	89	0 [0-4]
		Category V				
Aygun and Bildik,[44] 2003	IV	High-risk, ED	Turkey	47‡	70	22 (31) [22-43]
Cala and Mastaglia,[45] 1976	IV	High-risk, NA§	Australia	NA§	46	8 (17) [9-31]
Larson et al,[46] 1980	IV	High-risk, outpatient	Washington State	NA§	40	1 (2.5) [0-13]

Abbreviation: CI, confidence interval; ED, emergency department; NA, not available (see below).
*Prevalence values refer to the number of patients with a significant abnormality identified in computed tomography scan as defined in Table 1.
†Study category definitions are fully described in the Methods section.
‡Values reflect median age.
§Data not provided.

Table 4. Likelihood Ratio (LR) Combined Results That Predict an Increased (LR+), or Decreased (LR–) Likelihood of Significant Abnormality on Neuroimaging

Clinical Feature	Source	LR+ (95% CI)	LR– (95% CI)
Cluster-type headache*	Sempere et al,[36] 2005	5.7 (0.81-40)	0.95 (0.84-1.1)
	Weingarten et al,[43] 1992	30 (2.4-374)	0.51 (0.07-3.6)
	Summary LR	11 (2.2-52)	0.95 (0.84-1.1)
Abnormal findings on neurologic examination*	Cala and Mastaglia,[45] 1976	2.6 (1.2-5.8)	0.49 (0.20-1.2)
	Carrera et al,[41] 1977	2.8 (1.9-4.1)	0.11 (0.01-1.6)
	Cull,[37] 1995	7.8 (0.95-67.0)	0.53 (0.07-3.8)
	Duarte et al,[38] 1996	3.9 (1.7-8.9)	0.66 (0.49-0.89)
	Larson et al,[46] 1980	3.5 (1.3-9.6)	0.32 (0.03-3.5)
	Sempere et al,[36] 2005	42 (16-113)	0.78 (0.62-1.0)
	Summary LR	5.3 (2.4-12)	0.71 (0.60-0.85)
"Undefined" headache*†	Sempere et al,[36] 2005	4.2 (2.3-7.5)	0.65 (0.44-0.97)
	Weingarten et al,[43] 1992	1.4 (0.20-10.3)	0.77 (0.11-5.5)
	Summary LR	3.8 (2.0-7.1)	0.66 (0.44-0.97)
Headache with aura*	Cala and Mastaglia,[45] 1976	3.0 (1.3-6.7)	0.47 (0.19-1.2)
	Cull,[37] 1995	1.7 (0.23-12)	0.71 (0.10-5.0)
	Weingarten et al,[43] 1992	12.9 (1.4-117)	0.52 (0.07-3.7)
	Summary LR	3.2 (1.6-6.6)	0.51 (0.24-1.1)
Headache with focal symptoms	Aygun and Bildik,[44] 2003	9.8 (2.3-42)	0.62 (0.43-0.88)
	Linn et al,[40] 1998	1.1 (0.54-2.4)	0.96 (0.77-1.2)
	Summary LR	3.1 (0.37-25)	0.79 (0.51-1.2)
Headache aggravated by exertion or valsalva*	Duarte et al,[38] 1996	2.5 (1.1-5.6)	0.73 (0.51-1.0)
	Linn et al,[40] 1998	2.1 (1.1-4.2)	0.69 (0.52-0.91)
	Summary LR	2.3 (1.4-3.8)	0.70 (0.56-0.88)
Headache with vomiting*	Linn et al,[40] 1998	1.7 (1.2-2.5)	0.46 (0.28-0.76)
	Weingarten et al,[43] 1992	3.9 (0.51-30)	0.57 (0.08-4.1)
	Summary LR	1.8 (1.2-2.6)	0.47 (0.29-0.76)
Worsening headache	Aygun and Bildik,[44] 2003	4.4 (0.86-22)	0.9 (0.70-1.0)
	Sempere et al,[36] 2005	0.62 (0.16-2.3)	1.1 (0.93-1.2)
	Summary LR	1.6 (0.23-10)	1.0 (0.78-1.2)
Male sex	Cull,[37] 1995	1.5 (0.20-11)	0.75 (0.11-5.4)
	Linn et al,[40] 1998	1.3 (0.79-2.2)	0.83 (0.60-1.2)
	Sempere et al,[36] 2005	1.2 (0.73-2.0)	0.89 (0.63-1.3)
	Summary LR	1.3 (0.89-1.8)	0.86 (0.68-1.1)
Quick-onset headache	Aygun and Bildik,[44] 2003	2.7 (1.6-4.4)	0.32 (0.15-0.71)
	Linn et al,[40] 1998	0.65 (0.47-0.92)	1.9 (1.0-3.3)
	Summary LR	1.3 (0.33-5.1)	0.79 (0.14-4.4)
New-onset headache	Sempere et al,[36] 2005	1.2 (0.74-2.0)	0.89 (0.63-1.3)
	Weingarten et al,[43] 1992	0.90 (0.13-6.5)	1.11 (0.15-8.0)
	Summary LR	1.2 (0.74-2.0)	0.89 (0.63-1.3)
Headache with nausea	Cull,[37] 1995	0.82 (0.11-5.9)	1.3 (0.18-9.2)
	Duarte et al,[38] 1996	1.4 (0.71-2.8)	0.85 (0.59-1.2)
	Linn et al,[40] 1998	1.0 (0.83-1.3)	0.89 (0.43-1.8)
	Weingarten et al,[43] 1992	1.6 (0.22-11.5)	0.73 (0.10-5.2)
	Summary LR	1.1 (0.87-1.3)	0.86 (0.63-1.2)
Increased headache severity	Duarte et al,[38] 1996	1.0 (0.52-1.8)	1.0 (0.69-1.5)
	Sempere et al,[36] 2005	0.72 (0.39-1.3)	1.2 (0.92-1.6)
	Summary LR	0.83 (0.54-1.3)	1.2 (0.91-1.4)
Migraine-type headache	Kahn et al,[42] 1993	0.52 (0.13-2.1)	1.0 (1.0-1.1)
	Sempere et al,[36] 2005	0.47 (0.20-1.1)	1.5 (1.2-2.0)
	Weingarten et al,[43] 1992	1.4 (0.19-10)	0.78 (0.11-5.6)
	Summary LR	0.55 (0.28-1.1)	1.2 (0.84-1.7)

Abbreviation: CI, confidence interval.
*Clinically significant combined LR+ result with a 95% CI excluding 1.0.
†Refers to headaches that were difficult to classify and were not recognized as primary headache disorders (cluster-, migraine-, tension-type).

(LR, 3.2; 95% CI, 1.6-6.6); headache aggravated by exertion or a valsalva-like maneuver (LR, 2.3; 95% CI, 1.4-3.8); and headache with vomiting (LR, 1.8; 95% CI, 1.2-2.6).

Clinical features associated with LRs that were not found to be useful in predicting significant intracranial abnormalities in patients with headache were headache with focal symptoms; worsening headache; male sex; quick-onset headache; new-onset headache; headache with nausea; increased headache severity; and migraine-type headache.

Negative LRs. Four pooled clinical variables were found to have pooled negative LRs with upper confidence limits less than 1: normal neurologic examination (LR, 0.71; 95% CI, 0.60-0.85); headache not aggravated by valsalva-like maneuver (LR, 0.70; 95% CI, 0.56-0.88); absence of vomiting (LR, 0.47; 95% CI, 0.29-0.76); and headache of defined type (ie, cluster-, migraine-, or tension-type) (LR, 0.66; 95% CI, 0.44-0.97). All other variables had upper confidence limits greater than 1.

SCENARIO RESOLUTION

Case 1

This woman has 4 features of the POUNDing mnemonic, and therefore the positive LR for having a definite migraine or possible migraine-type syndrome is 24. She should therefore be diagnosed as having migraine headache, and proper migraine therapy should be initiated. In the absence of any other findings, neuroimaging is not indicated.

Case 2

The young man with a thunderclap headache has a very high pretest probability (≈43%) of serious pathology (ie, subarachnoid hemorrhage). Despite not having any features that significantly increase his posttest probability, he is clearly at significant risk and merits urgent CT scanning and lumbar puncture.

Case 3

The history suggests some features of migraine headache, but only 2 features (unilateral headaches that last more than 4 hours) of the POUNDing mnemonic are present (LR for "definite" migraine, 0.45). The absence of nausea and photophobia can be assessed in combination with the lack of disability, also suggesting that migraines are less likely (LR by the Lipton criteria, 0.25). Thus, the clinician should be considering other diagnoses. This patient has chronic headaches, and the pretest probability of having a significant intracranial abnormality is ≈1%. However, he has abnormal findings on neurologic examination (positive LR, ≈5) and therefore a posttest probability of ≈5%. The difference between this case and the preceding 2 cases is that there is an important neurologic finding on the physical examination. Since this is a chronic headache scenario, the pretest probability of a finding is low. However, the finding on examination increases the suspicion of intracranial pathology, and most physicians would obtain neuroimaging.

THE BOTTOM LINE

Does This Patient Have Migraine?

The literature we reviewed primarily addresses the diagnosis of migraine without aura. Patients who present with classic visual aura (ie, a slowly evolving scintillating scotoma that moves or passes through the visual field over roughly 30 minutes, then disappears and is followed by the onset of headache) followed by unilateral disabling headaches constitute an easy diagnosis for the clinician. However, for those patients without aura, there is much evidence that the diagnosis is frequently missed.[5] The IHS classification system is too cumbersome to be useful as a screening test. Because migraine is a symptom complex, it is unlikely that any single feature of the clinical examination (except, perhaps, for classic visual auras) will be sufficient to rule in or rule out the condition. Clinicians, however, are fortunate in having 4 studies that estimated the accuracy of combinations of variables.[9-12] In our opinion, the data from Smetana[33] and these 4 studies indicate that virtually any combination of 3 or 4 of the clinical features would be sufficient to diagnose migraine, and 2 or fewer features makes migraine somewhat less likely. Our modification of the Michel algorithm into the POUNDing mnemonic is a useful screening tool for distinguishing patients with migraine from those without. While the presence of photophobia, phonophobia, and exacerbation with exertion were important independent variables quantified in the systematic review by Smetana,[33] when included with the POUNDing criteria the addition of these symptoms to the other 5 did not statistically significantly improve the diagnostic accuracy of the algorithm in the study by Michel et al[9] (Michel et al considered photophobia and phonophobia together). On the other hand, both of the algorithms derived by Lipton et al[10] and Lainez et al[11] included photophobia as an independent predictor (and in the case of Lainez et al, phonophobia). In these 2 algorithms, it appears that the absence of photophobia (along with the absence of other features of those algorithms) is useful for ruling out migraine (ie, the negative LRs for the algorithms of Lainez et al[11] and Lipton et al[10] are lower than the negative LR for POUNDing). However, the presence of photophobia is less helpful for ruling in migraine, because the positive LR for POUNDing is much higher than the positive LRs for the other algorithms (Table 2). These results illustrate the importance of looking at a combination of features in the diagnosis of migraine and not using individual signs or symptoms.

Does This Patient Need Neuroimaging?

For the purposes of this review, we categorized primary articles based on the type of patient and headache included. Prevalence of intracranial pathology is highly variable, depending on the initial presentation. This ranges from 1% in chronic headache to 43% in thunderclap headache.

Although 4 clinical features were found to have negative LRs with CIs less than 1, none are sufficiently low enough

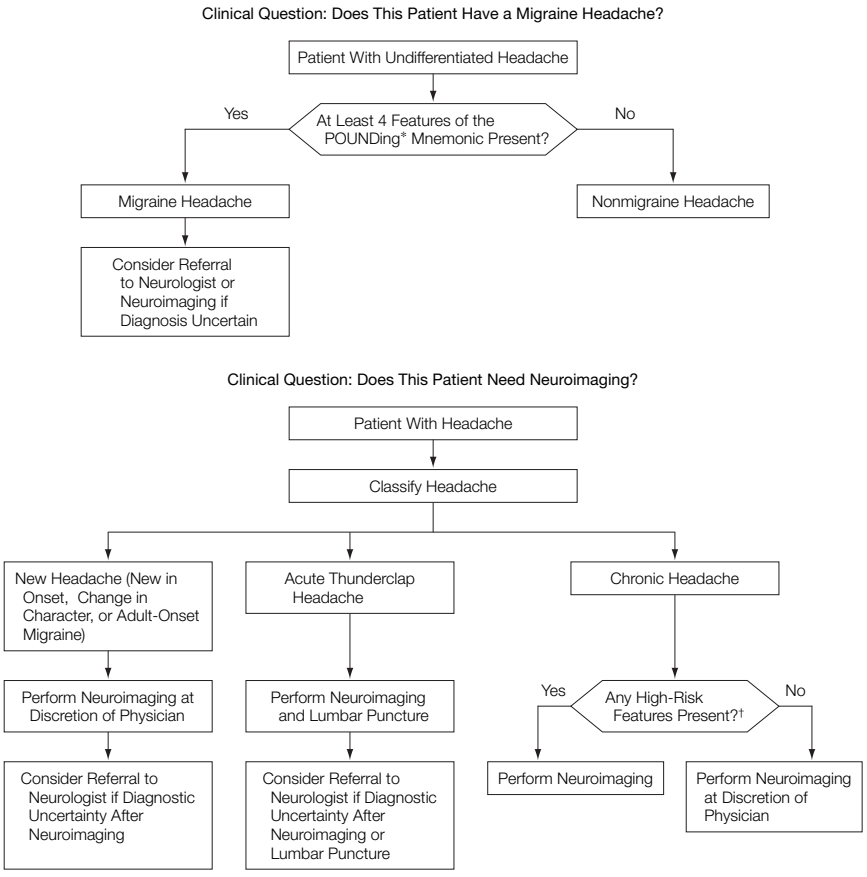
(ie, LR<0.1) to decrease the posttest probability in a clinically important manner. However, because the pretest probability of intracranial abnormality in the population with chronic headache is so low (1%), a further decrease in probability would not likely change clinical management. Does it truly help a clinician to know that a particular feature on history or physical examination lowers the pretest probability from 1% to 0.5%? Furthermore, for patients with thunderclap headache, the pretest probability of having significant pathology is high enough (43%) that the absence of abnormal findings is unlikely to provide enough reassurance to forego further investigations.

Finally, we found that several clinical signs and symptoms do increase in a meaningful way the likelihood of the patient having serious intracranial pathology. These include abnormal findings on neurologic examination; cluster-type headache; headache with aura; headache that could not be clearly defined by a clinician as a common primary headache disorder (ie, not a cluster-, migraine-, or tension-type headache); headache with vomiting; and headache aggravated by exertion or valsalva-like maneuver. The most robust of these findings is the presence of any abnormal finding on neurologic examination: it is supported by more studies than the other findings, the studies were nearly uniform in finding statistical significance of the positive LR, and the highest-quality (and largest) study showed the strongest effect.[36] If a patient presents with a chronic headache and abnormal findings on neurologic examination, then the probability of a significant abnormality is high enough to warrant a neuroimaging study. The findings and recommendations of this report are consistent with the results of a previous analysis[67] but are based on data that include substantially more total patients (3725 vs 2272) and new, higher-quality data.[36]

The other features with clinically significant LRs are associated with fewer studies (cluster-type headache), smaller effects (undefined headache type, headache with aura, headache aggravated by exertion or valsalva, and headache with vomiting), or no high-quality study (headache with aura, headache aggravated by valsalva, and headache with vomiting). Because these features have less reliability and smaller effects, their influence on clinical decision making is less certain. Cluster-type headaches are those that present as excruciating pain around the eye and temple and come and go in a "cluster"-like pattern. This type of headache may have potential usefulness in identifying patients with significant abnormalities; however, more data are required to narrow the CI around the true point estimate.[36] Finally, because some auras may be difficult to distinguish from visual manifestations of transient ischemic attacks, and because most studies did not provide information regarding the type of aura, it is difficult to interpret the fact that aura was found to be predictive of intracranial abnormalities in this overview.

The results of our meta-analysis should be interpreted in the context of study limitations. We discuss 5 limitations here. The first limitation is the significant heterogeneity in the type of headache and patient population that limits the generalizability of our findings. For the neuroimaging section, only 1 study used patients from a primary care setting, likely resulting in

Figure. Suggested Algorithm for the Approach to Headache



*POUNDing: Pulsatile quality; duration 4-72 hOurs; Unilateral location; Nausea and vomiting; Disabling intensity.
†Cluster-type headache, abnormal findings on neurologic examination, undefined headache (ie, not cluster-, migraine-, or tension-type), headache with aura, headache aggravated by exertion or valsalva-like maneuver, headache with vomiting.

higher estimates of prevalence of serious pathology. The second limitation concerns the fact that these studies span several decades and there have been marked changes in imaging technology over that period. The use of magnetic resonance imaging and CT with contrast has improved the sensitivity of imaging in detecting intracranial abnormalities.

The third potential limitation is that of possible missed studies and missed significant pathologic conditions. There may be unpublished data which are not included in this overview. Within the thunderclap studies, the only significant pathology studied was subarachnoid hemorrhage. Other pathologic conditions (eg, tumors) were excluded.[39,40]

A fourth limitation concerns the use of a classification system developed by the US Headache Consortium to define significant intracranial pathology. Diagnoses such as calvarial metastases and nasal cavity abnormalities were considered "possibly related to the headache" and lumped with the "insignificant abnormality" and "normal imaging" group. These diagnoses may be of interest to some clinicians.

Finally, we do not have information about variables that were not evaluated in the studies we included in this systematic review. Obvious findings such as altered mental status, human immunodeficiency virus disease, and cancer should raise the suspicion of serious intracranial pathology in patients with new-onset headaches.

Despite these limitations, we believe our results support the following approach (FIGURE). When assessing a patient with headache it is useful to rule in or rule out migraine as a diagnosis, as this clearly has important therapeutic implications. To determine whether imaging is indicated, the clinician should then classify the headache presentation to derive a pretest probability of serious intracranial pathology. The next step is to look for 1 of the several features that have clinically useful LRs. Patients presenting with thunderclap headache are at sufficient risk of subarachnoid hemorrhage and therefore should undergo investigations irrespective of associated clinical features. Because of a paucity of published data in the evaluation of a "new headache," it is difficult to make recommendations about the need for imaging in these patients. This population should be the focus of future research efforts. In the patient with chronic headache, the presence of the high-risk clinical features (Table 4) can raise the probability of serious pathology from less than 1% to approximately 5% to 10% among patients referred to a neurologist for headache. In a primary care clinic, the prevalence of serious intracranial abnormalities for patients with headache should be much less than the 1% prevalence in neurology clinics. Accordingly, if none of the features in Table 4 are present, the probability of a serious disorder should be much less than 1%, and these patients do not need neuroimaging. Finally, further research (through prospective study) is required to validate the algorithm (Figure) and the POUNDing mnemonic.

The patient with aura and headache deserves special consideration. In the patient with recurrent episodes of classic visual aura followed by headache, the diagnosis of migraine is relatively straightforward and the patient does not require neuroimaging. However, patients with other types of aura (sensory or motor), an aura that has changed in character, or one that cannot be clearly described as typical of migraine aura should undergo imaging, as they may in fact have a nonmigraine diagnosis that is associated with an intracranial lesion. Patients who present to an emergency department with an aura and headache for the first time are often most problematic. Although the study of patients who presented with migraine at a late age indicated a 0% rate of significant intracranial abnormalities,[37] many physicians would order neuroimaging if the patient presents with a clear neurologic abnormality during this first episode.

In summary, when evaluating a patient with headache, it is important to perform a focused history and physical examination with the aim of confirming a diagnosis of migraine or underlying intracranial pathology. The POUNDing mnemonic is both easy to remember and very effective at ruling in or ruling out the diagnosis of migraine. The decision to proceed with neuroimaging should take into account the type of headache (ie, the pretest probability of intracranial pathology) and the presence of any clinical features that significantly increase this probability.

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