



Practical Insights on the Identification and Management of Patients with Chronic Migraine

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ABSTRACT

Chronic migraine (CM) is one of the most disabling diseases, and it is commonly misdiagnosed and mistreated. Despite the importance of a timely and accurate diagnosis for the effective management of CM, recent surveys have shown that only 20–25% of individuals with CM receive a correct diagnosis. The obvious consequences of misdiagnosed CM are prolongation of symptoms and their associated effects on disability and health-related quality of life. Additionally, mistreatment of CM can

lead to acute medication overuse headache with escalation of headache and end organ damage. Ideally, a diagnosis of CM should be made in the primary care setting, based on a thorough medical history including detailed descriptions of headaches occurring earlier in life as well as current headaches, and the range of headaches (not just the worst headaches). In our experience, it is often equally informative to ask the patient about the number of headache-free days (HFDs) and no accompanying symptoms (i.e., crystal-clear days) to quantify headache days and accurately estimate headache frequency/impact. Headache frequency is important, as this count is one key means of diagnosing CM, which requires ≥ 15 headache days/month, noting that these do not need to be migraine days. A headache day is defined as more than 4 h a day of headache. Comorbidities are common in CM and may affect the treatment choice and increase disability. Every CM patient should be offered a preventive migraine treatment. In this commentary, we provide practical insights and tips for diagnosing CM and cover issues of medication overuse, patient communication, diagnostic testing, and when to make a referral. Our key message to physicians for a patient who comes to the clinic with frequent disabling headaches having features of migraine is to assume CM until proven otherwise.

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Key Summary Points

Chronic migraine (CM) is a painful, disabling disease that should be identified in primary care but it is often misdiagnosed (most commonly as tension-type headache).

A thorough medical history with detailed descriptions of all headaches (particularly headaches earlier in the lifecycle and including mild as well as severe headaches) is key to diagnosing CM.

Each individual with CM is unique and requires an individualized treatment plan to manage their comorbidities and CM; complex cases may require referrals to specialists.

Providing a patient with an accurate diagnosis of CM can lead to a treatment plan that provides rapid, effective relief from migraine attacks, reductions in attack frequency, improvements in disability and health-related quality of life, and avoids unnecessary emergency department use and opioid exposure.

Migraine is a complex disease but is not difficult to identify: if the essential features of migraine are present, clinicians should consider migraine until proven otherwise.

INTRODUCTION

Migraine is a complex disease that can be subdivided into chronic (CM) and episodic (EM) types, and individuals can shift between EM and CM over time in both directions [1, 2]. The global prevalence of CM varies regionally but is estimated to be 1.4–2.2% [3]. Extrapolating results from the American Migraine Prevalence

and Prevention Study (AMPPS) produces a CM prevalence rate of approximately 1% in the United States, with CM representing 7.7% of all migraine cases [4]. The International Headache Society (IHS) defines CM as headache occurring on ≥ 15 days per month for > 3 months over the previous 12 months with ≥ 8 of those days exhibiting features of a migraine attack, including nonspecific headache associated with aura and nonspecific headache that improves with migraine-specific medications [2]. Diagnosing CM is dynamic, bidirectional, and impacted by numerous internal and external factors (Fig. 1) [1, 5]. An analysis of sequential waves of data collection in the Chronic Migraine Epidemiology and Outcomes (CaMEO) survey study revealed that 73% of individuals with CM at baseline reported headache day frequencies within the range defined for EM at least once during the study, and, conversely, 7.6% of those with EM at baseline reported headache day frequencies within the range defined for CM at least once during the study [6].

Although migraine has been long recognized as a structured diagnostic entity, individuals with migraine who experience daily or near-daily headaches were not identified as a distinct migraine subpopulation until recently [7]. The nosology of CM has changed substantially over the past 30-plus years (reviewed by Medrea and Christie [7]). The current diagnostic criteria for CM in the International Classification of Headache Disorders, 3rd edition (ICHD-3) are (A) headache (migraine-type or tension-type-like) on ≥ 15 days/month for > 3 months, (B) occurring in a patient who has had ≥ 5 attacks fulfilling criteria for migraine with or without aura, and (C) on ≥ 8 days/month for > 3 months during the previous year fulfilling diagnostic criteria for migraine with or without aura or believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative [2]. Other migraine-specific treatments, such as ditans and gepants, are likely to be included in this definition with the next revision of the classification. The definition based on headache day frequency does not capture the many differences between CM and EM. The diagnosis of EM is not specifically

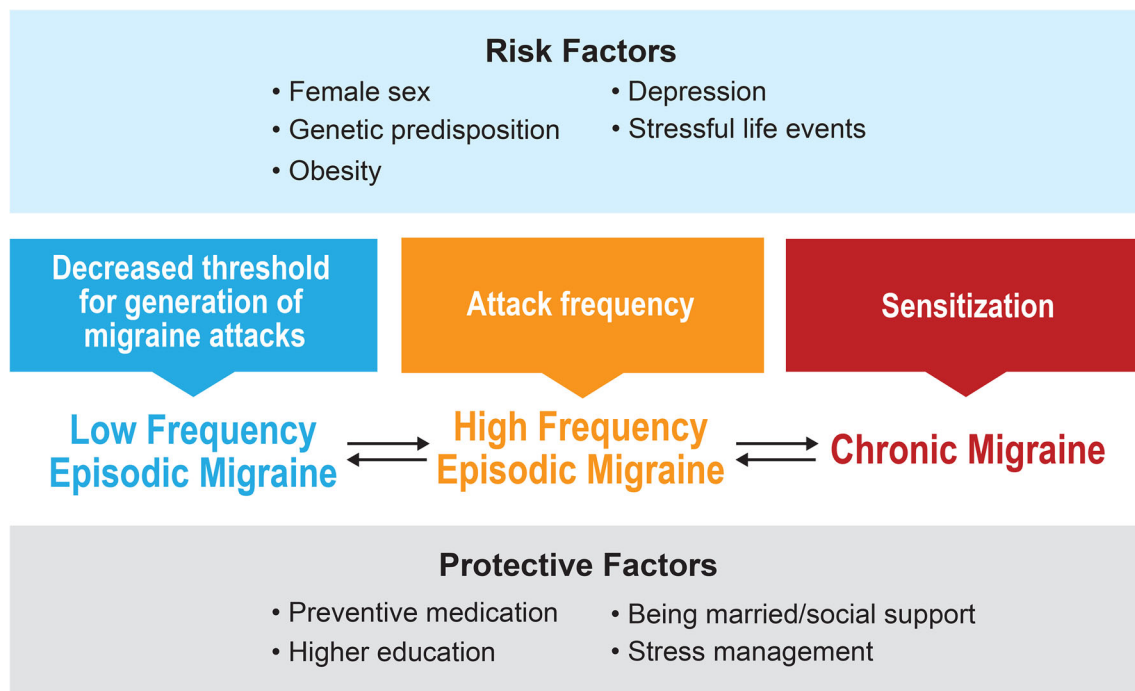


Fig. 1 Transitions between EM and CM. Individuals with migraine can transition from low-frequency EM through an intermediate state of high-frequency EM to CM [1, 5]. *CM* chronic migraine, *EM* episodic migraine

stipulated in the classification, and once the patient has been diagnosed with migraine the breakdown is to stratify by the presence or absence of CM. However, for the purposes of this article, patients with fewer than 15 headache days a month will be referred to as having EM. In 2020, Goadsby et al. [8] suggested criteria for classifying EM.

CM is associated with a high degree of disability, pain and other comorbidities, poor health-related quality of life (HRQoL), and high rates of healthcare resource utilization [9]. Additionally, migraine attacks are severe and last > 6 h among individuals with CM [9]. Based on several studies that administered the Migraine Disability Assessment questionnaire, CM has been shown to be associated with significantly greater headache-associated disability than EM [9–12]. Individuals with CM are more likely to have comorbid diseases than those with EM, including higher rates of depression and anxiety [9, 11, 13]. HRQoL, as measured by the Migraine-Specific Quality of Life Questionnaire (MSQ), is significantly lower among those

with CM compared to EM [9, 14]. Indeed, the differences in mean scores for populations of individuals with CM or EM meet or exceed the minimal important difference for each MSQ domain (role function restrictive, role function preventive, and emotional function) [14]. Compared to those with EM, individuals with CM have more visits to their primary care providers (PCPs) and to neurologists, increased diagnostic testing, more frequent emergency department visits, and a greater number of hospitalizations [9, 15–19]. This increased use of healthcare resources comes with greater costs [15, 16, 18]. As a result, individuals with CM require timely, effective treatment to reduce these burdens. Because the burden of CM may involve the frequent use of analgesics as preventive treatment, we propose to use the term “crystal-clear days” to describe days without headaches and with no associated symptoms.

A timely and accurate diagnosis is important for the management of CM; unfortunately, many patients receive a delayed or incorrect diagnosis (most commonly chronic tension-

type headache [cTTH]), potentially because screening tools have lower sensitivity and specificity compared to direct interviews, which may be most relevant to PCPs who may not have the experience needed to diagnose CM. Among individuals with migraine who participated in the AMPPS and the CaMEO survey, only 20% and 25%, respectively, correctly received a diagnosis of CM [10, 20]. The obvious consequence of undiagnosed CM is the prolongation of symptoms and their associated effects on disability and HRQoL. A recently developed algorithm to identify individuals with undiagnosed CM using healthcare claims [21] showed higher mean annual costs and higher rates of acute medications and, notably, higher rates of opioid prescriptions in individuals with undiagnosed CM than diagnosed CM [22]. An accurate diagnosis is a key step in providing good medical care for individuals with migraine (especially CM), in addition to a consultation with a medical professional and prescription of appropriate medications [20]. A six-item screener has recently been developed that can help to identify CM (i.e., the six-item Identify Chronic Migraine screener [ID-CM(6)] [23], which is also available as a smartphone application [24]. An accurate diagnosis of CM, potentially by increasing PCPs' exposure to and use of new technology, can provide individuals with access to preventive treatments for their migraine.

Individuals with migraine have historically been trivialized and stigmatized, and some patients are reluctant to seek care and may under-report symptoms. The high rates of underdiagnosed CM (and migraine in general) highlight the issues and barriers that many individuals with migraine experience when they seek treatment for their symptoms. Notably, the Landmark Study revealed that 94% of patients with a diagnosis of nonmigraine primary headache actually had IHS-defined migraine or probable migraine [25]. This may be the result of healthcare professionals (HCPs) being unfamiliar with the spectrum of migraine and not adequately understanding patients' symptom burden. A survey of PCPs in a large academic medical center in the United States revealed that only one-third of physicians were

very comfortable diagnosing migraine, whereas two-thirds were only somewhat comfortable [26]. Among the participants of this survey, only 27.8% were aware of American Academy of Neurology guidelines for prescribing preventive medications, and about one-third were unaware of evidence-based guidelines regarding use of nonpharmacologic treatments for migraine. A survey conducted in 2019 at a Primary Health Care Center in Saudi Arabia revealed significant knowledge gaps among general practitioners and family physicians (no specialists participated) regarding CM diagnosis, which improved significantly with years of experience [27]. There is currently a need for global standardized training across medical schools to educate PCPs about diagnosing CM because without an appropriate diagnosis, patients cannot receive appropriate treatment [28, 29]. The most appropriate role of PCPs in diagnosing CM may be to identify patients who are treatment refractory and refer them to a specialist as needed [29, 30]. Providing PCPs with the tools necessary to identify CM patients should be a goal of educational programs.

As headache specialists, we see patients with CM via referrals not only from PCPs, but also from neurologists, university hospitals, and academic researchers, depending upon the local/country healthcare structure. Many of our patients have had headaches for multiple years, most are misdiagnosed with cTTH, and many have had recurrent visits to the emergency department for their headaches. A CM diagnosis should be made in primary care, and appropriate referrals should be made at that time. PCPs often refer patients to neurologists or headache specialists to manage their CM but will still be involved with these patients in the long term [31]. Multiple guidelines and many articles have been written about migraine and diagnosing CM, and most are readily available to physicians who are interested in this topic.

The purpose of this article, which is based on previously conducted studies and does not contain new data from studies with human participants or animals performed by any of the authors, is to provide practical insights and tips for diagnosing CM for referring physicians. For PCPs who rely on guidelines to make a

diagnosis, the immediate problem with using the ICHD-3 criteria is traversing a 200-page document to find the multiple sections related to migraine (e.g., migraine with or without aura, and CM) during a clinic visit. The next problem with diagnosing a patient using these criteria is making an accurate determination of headache days versus migraine days, especially during time-constrained clinic visits. Although a frequency of ≥ 15 days per month to classify CM is, frankly, somewhat arbitrary [32], an accurate count of headache days is required for insurance purposes in many countries. Migraine is a complex neurologic disease but is not so difficult to identify. However, an incorrect diagnosis of cTTH is difficult to change, and patients who are sent away with an incorrect diagnosis of cTTH typically do not return to the clinic for migraine treatment. A diagnosis of cTTH also tends to minimize the patient's symptoms and may inaccurately suggest to the patient that the headaches they are presenting with are stress-related. Migraine has been rated by the World Health Organization as the second most disabling disease in terms of days lived with any particular disease [33]. Providing a patient with an accurate diagnosis of CM can lead to a treatment plan that provides rapid, effective relief from migraine attacks, reduces the frequency of attacks, and decreases unnecessary emergency department use and opioid exposure.

DIAGNOSIS OF CHRONIC MIGRAINE

Obtaining a detailed history is important for diagnosing CM. A critical component of the patient's clinical history is a description of headache features, including their duration (untreated headaches lasting 4–72 h are characteristic of migraine attacks) and frequency (to confirm CM vs EM to select appropriate treatment) [34]. Symptoms vary between patients, but throbbing pain, aggravation by physical activity, phonophobia, and photophobia are indicative of migraine even if the attack is mild in severity. Information about headaches occurring earlier in the lifecycle and symptoms

can assist with a migraine diagnosis, as CM usually evolves from low-frequency migraine. In addition, neck pain and stiffness are often early symptoms of migraine and thus the presence of neck pain does not necessarily suggest cervicogenic headache or cTTH. In CM, not all headache days qualify as migraine days, with some headaches having a TTH phenotype, but the diagnosis of CM (rather than cTTH) is made as long as ≥ 8 days/month have features of a migraine attack. A family history of headache (with or without menstruation-associated headache [35]) also supports a migraine diagnosis. When a diagnosis of migraine has been made, the next step is to determine the frequency of the headaches and migraine attacks to facilitate treatment decisions. Diagnostic criteria based on ICHD-3 are helpful in distinguishing between EM and CM, but the purpose of these criteria is to select appropriate patient populations to evaluate migraine treatments in clinical trials [2]. Some patients maintain a headache diary (paper or electronic), which is very helpful for determining headache frequency and severity over time. In lieu of a diary, a brief questionnaire, such as the ID-CM (6), can be sent in advance of the clinic appointment. Having those answers available for discussion will provide the most efficient use of time during visits. For patients with very frequent headaches, it may be easier to ask them how many headache-free days they experience per month. Asking about the number of headache-free days allows for a more accurate understanding of headache impact. A patient who has headache on at least half of the days of each month meets the criteria for CM.

Although each patient is unique, we see some typical patterns of headache history among patients with frequent headaches that are suggestive of CM. Patients often present with 2–3 headache types, with some attacks that are clearly migraine and some that are not. It is important for the patient to describe the milder headaches as well as the more disabling attacks to obtain an accurate count of headache days, which serves to satisfy insurance requirements based on ICHD-3 criteria so the patient can qualify for preventive treatment if needed. When headaches become more frequent, the

features may change; therefore, it is important to always obtain information about patients' lifetime history of headaches, including those occurring in early life. Many patients describe a headache that is constant; however, a thorough history reveals a headache that has variations in intensity and associated symptoms. Each patient is unique with respect to comorbidities, environmental triggers, and willingness or ability to treat their CM. Migraine can be diagnosed only when secondary causes for headache have been ruled out. One method is to use green flags such as typical migraine features to suggest the diagnosis and red flags to exclude secondary causes and then use the combination of green and red flags to make a diagnosis.

Patients frequently report only their very worst headaches. Open-ended questions followed by directed questions may be needed to elicit information about all headaches instead of just the worst attacks. Discussions should include the pattern, nature, and severity of the pain associated with each headache type. It is necessary to inquire about associated symptoms (e.g., aura, nausea, or other symptoms that accompany attacks). It is also important to discuss any prior and current treatments for headache pain, including both prescription and over-the-counter (OTC) medications. Many patients who present with frequent headaches have already been taking acute prescription and/or OTC medications for their migraine attacks. As many as half of patients with CM who are referred to us have medication overuse, with or without medication overuse headache (MOH) [36–39]. However, the real-world regional situation varies, where self-medication managed in pharmacies can produce different levels of the risk of usual or borderline abusers. Acute medication intake (number of days used per month) should be determined to estimate the risk of medication overuse [40].

Patients are often uncomfortable admitting to frequent OTC medication use and may need to be asked specifically about use of non-steroidal anti-inflammatory drugs and other OTC analgesics. Patients should be cautioned about using OTC or acute prescription medications for more than 10 days per month, regardless of the dose. It is also helpful to ask

about caffeine consumption, as this can be a migraine trigger and increase the frequency of migraine attacks [41]. Similarly, tobacco use (both smoked and smokeless) is associated with migraine [42].

Comorbidities do not change the diagnosis of CM but they do affect the choice of treatment and should be thoroughly evaluated. Many comorbidities are common among individuals with CM, most notably mood disorders (including depression, anxiety, and bipolar disease), hypertension, asthma, epilepsy, and fibromyalgia (reviewed by Burch, et al. [43]). CM has historically been treated with medications that were originally designed to treat diseases other than migraine, such as antiepileptic medications or beta-adrenergic blocking agents. A benefit of these drugs is that they can provide symptomatic improvement for multiple diseases with a single medication. However, this method of choosing medications often fails as patients have multiple comorbidities. For example, although an antidepressant can help treat depression and prevent migraine, it may worsen other comorbidities such as obesity. Another example would be the choice of a beta blocker in a patient who had comorbid hypertension, but if that patient also has asthma, it would be a poor choice.

A thorough understanding of an individual patient's comorbidities is therefore important so that treatment can be tailored to address all diseases. Patients should be queried in particular about any depressive, anxiety, and/or sleep disorders. Depression and anxiety can improve when patients receive effective treatment for their CM. Patients who report poor sleep should be offered medications to treat their sleep disorders. These patients should also be aware of caffeine overuse issues, as caffeine might help their daytime fatigue but caffeine withdrawal will worsen their headaches.

Patients with CM who also have multiple comorbidities may need to be referred to specialists for the treatment of these diseases. Unfortunately, drug–drug interactions occur between many medications used to treat migraine attacks and prevent migraine and medications that are used to treat comorbidities [44]. The challenge of selecting an optimal

treatment should not deter a physician from making the critical diagnosis of CM; instead, referrals to specialists who can assist with treating comorbidities should be considered.

Patients who present to PCPs with recurrent disabling headaches nearly always have migraine, so the presumptive diagnosis should be migraine until other types of headache diagnoses have been eliminated. The other primary headaches that need to be eliminated are cTTH and new daily persistent headache (NDPH). Patients who meet the ICHD 3 criteria for CM should be diagnosed with CM whether or not they experience tension-like headaches or other milder headaches during this period [2]. MOH is defined as headaches occurring on ≥ 15 days per month in a patient with pre-existing primary headache that develops as a consequence of overuse of acute headache medication for > 3 months [2]. While traditionally MOH is treated by withdrawing the overused medication, in our experience, starting the patient on preventive medications to reduce the monthly headache burden may help the patient withdraw from these acute medications, which is why we use the term crystal-clear days to quantify days with no headache and/or associated symptoms. NDPH involves a daily headache from the onset, and the onset is invariably recalled by the patient. Patients with NDPH generally have no prior headache history, and the headaches have no characteristic features but may resemble either migraine or cTTH [2].

For the most part, the use of imaging and other types of tests/investigations are not necessary to make a diagnosis of CM. Imaging should be used only in cases when clinical assessment suggests the probability of a change in cerebrospinal fluid pressure (raised or lowered), an underlying tumor, or other secondary diseases. If the onset of migraine occurred after the age of 40 or the pattern/symptoms of migraine clearly changed, then the risk of an underlying cause should be excluded. Magnetic resonance imaging is recommended in cases requiring imaging, but electroencephalograms are no longer recommended for headaches. Some simple blood tests, including tests for hemoglobin, erythrocyte sedimentation rate,

C-reactive protein, nutrient deficiencies, and thyroid function, may be helpful to gain a broader understanding of the possible causes for the headache.

Although many patients with CM can be effectively managed in primary care settings, there are times when a referral to a specialist becomes necessary. Every patient with CM should be offered a preventive treatment for migraine, which can be initiated while waiting for a referral if needed [31]. After a failure to tolerate or respond to first- or second-line preventives, a referral to a headache specialist is warranted. Notably, a patient who is indicated for treatment with onabotulinumtoxinA should be referred to an HCP who is experienced in administering those specific injections. Patients with too many headaches to treat effectively with acute medications without a risk of secondary MOH should be referred to a specialist or headache clinic for re-evaluation.

It is important to develop a trustful relationship and cultivate open communication, which can assist with obtaining an accurate diagnosis and choosing the most effective management plan [45]. It is also important to promote shared decision-making [45]. The visit at which a diagnosis is made is a good time to emphasize the chronicity of CM and the possibility of transformation from EM to CM, as well as the need for preventive treatment to reduce the frequency of headache days and the need for acute medications. The goal is to reduce the overall time the patient's brain is exposed to migraine. Medication overuse should be discussed with non-judgmental and validating language explaining that physiological dependence on the medication may be an exacerbating factor, rather than labeling this subgroup as addicts. It may be helpful to encourage the use of a headache diary, to assure both clinicians and patients that a treatment is or is not working. Finally, practical treatment expectations should be set, including realistic time frames for response to preventive treatments. A CM diagnosis can be upsetting to receive and deliver, but newer migraine treatments now offer the clinician the ability to deliver hope along with the diagnosis. There are now treatments that can improve HRQoL, which occurs

disproportionally to the rate of reduction in headache frequency.

KEY MESSAGES TO PRIMARY CARE PHYSICIANS

As headache specialists who treat patients with CM, we understand the difficulties physicians face when evaluating a patient with frequent, painful headaches. As mentioned previously, CM is a complex disease but diagnosing a patient with CM does not need to be difficult. We find that patients with CM are often misdiagnosed with cTTH. However, in patients with CM the patient history reveals that the present headaches have often gradually changed from previous EM. Future avenues for controlling headache disorders, including new technology, are being explored [46]. Additionally, non-pharmacologic interventions, such as nutraceuticals and neuromodulation and behavioral treatments, have been shown to be effective and of interest to patients [19, 47].

CONCLUSIONS

It is important to make a diagnosis of CM based on the patient's history and clinical presentation. Reassurance and education are important to help patients understand that there is not a grave, life-threatening underlying cause. Only patients with an accurate diagnosis can have access to some available treatments. CM is associated with significant burden, pain, and disability and requires an individualized treatment approach that is not solely based on medication. Patients reap the clinical and HRQoL rewards of an accurate CM diagnosis and effective treatment, and the physicians who provide the diagnosis and treatment are rewarded with the satisfaction of relieving the significant burden experienced by patients with migraine.

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