▪ Headache Medicine 2025, 16(4):194-199 ▪ p-ISSN 2178-7468, e-ISSN 2763-6178

Headache Medicine

▪ DOI: 10.48208/HeadacheMed.2025.32

Review

Persistent post-craniotomy headache: a narrative review

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Edited by:
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Introduction
Persistent post-craniotomy headache (PPCH) is a frequent yet underrecognized complication of cranial surgery, often leading to long-term disability and impaired quality of life. Defined as a headache developing within seven days of craniotomy and lasting more than three months, the true PPCH prevalence and incidence remains unclear and varied widely across studies and time windows. Despite its impact, the condition remains poorly understood, and standardized diagnostic and therapeutic protocols are lacking.

Review
PPCH arises from multifactorial mechanisms, including direct nerve injury, muscle adhesion to the dura mater, aseptic inflammation, and central sensitization. Five main phenotypes can be identified: scar-related neuropathic pain, occipital neuralgia–like headache, diffuse tension-type pattern, migraine-like phenotype, and mixed presentations. Risk factors include posterior fossa and suboccipital surgeries, pre-existing migraine, female sex, inadequate perioperative analgesia, and psychological comorbidities such as anxiety or depression. Evaluation must rule out secondary causes through clinical examination and selective imaging. Treatment should follow a multimodal, phenotype-driven approach combining pharmacologic agents with interventional procedures such as peripheral nerve blocks or scar-targeted botulinum toxin A injections. Surgery is reserved for refractory, well-defined cases involving neuromas or hardware irritation.

Conclusions
PPCH represents a complex chronic secondary headache condition that demands systematic identification and personalized, stepwise management. However, evidence remains limited, and prospective multicenter studies with standardized definitions and outcomes are urgently needed to improve prognosis and quality of life for affected patients.

Keywords:
Post-craniotomy headache
Secondary headache
Literature review

Received: October 7, 2025
Revised: October 26, 2025
Accepted: December 22, 2025

Introduction

Persistent headache following craniotomy is increasingly recognized as a clinically meaningful complication of cranial surgery. Although immediate postoperative headache is commonly managed in the perioperative period (1), there is a group of patients that experience a headache that begins short-after surgery and persists for months to years (2). This chronic post-surgical headache not only results in persistent pain but also delays complete rehabilitation, contributes to disability, and negatively impacts long-term quality of life (3). Despite its prevalence and clinical importance, the literature on persistent post-craniotomy headache (PPCH) remains fragmented, consisting largely of narrative reviews, case series, and small interventional reports derived from single centers (4,5).

Consequently, clinicians lack high-quality and generalizable evidence to guide diagnosis, prevention, and treatment. This focused review synthesizes the most relevant bibliographic sources about the subject, and provides a pragmatic, phenotype-directed approach to evaluation and management of PPCH. The goal is to offer an evidence-informed framework that clinicians can apply in neurosurgical follow-up clinics and pain services while highlighting priorities for research and quality improvement.

Methods

Review a search strategy using standardized terms for PPCH: (Headache*[ti] OR Cephal*[ti] OR pain[ti]) AND (Postcraniotom*[ti] OR craniotom*[ti] OR craniectom*[ti] OR Postcraniectom*[ti]). This was used into Pubmed/Medline database on September 22nd, 2025, without timeframe limits. We applied the "Review" and "Systematic Review" filter and retrieved a total of 33 results. We examined all papers individually, as well as their citations, and included them in the present review if they provide relevant information to the subject.

Definition

Terminology used to describe persistent post-surgical cranial pain varies across disciplines like anesthesiology, neurosurgery, and neurology. For the purposes of clinical decision-making and research, the definition from the International Classification of Headache Disorders in its third version is useful: PPCH is defined as new-onset or a clear change in pre-existing headache temporally related to craniotomy within the seven days of the procedure and persisting beyond three months (6).

The three-month threshold aligns with general criteria for chronic postsurgical pain and balances early identification for management with a conservative demarcation that avoids mislabeling a slowly resolving acute pain. Although alternative intervals have been suggested to improve epidemiologic precision, the three-month threshold is frequently used in clinical practice, as it supports timely identification and management of persistent headache (7).

Epidemiology

Accurately estimating the incidence and prevalence of PPCH is challenging due to heterogeneity in case definitions, surgical populations studied, follow-up durations, and measurement methods. Early postoperative pain is closely to 100% across craniotomy cohorts (8). However, estimates of pain persisting at or beyond three months vary substantially. Reports from single-center series and narrative reviews included indicate that a nontrivial minority of patients (ranging from low percentages to more than 90% in some cohorts) continue to experience clinically relevant headache several months after surgery (9). Based on the ICHD-3 criteria, the incidence of PPCH in patients undergoing craniectomy for supratentorial intracranial aneurysms treatment was approximately 30% in one small cohort study (10).

However, the true incidence and prevalence of PPCH remain uncertain across other large and diverse populations. Understanding true population-level incidence requires prospective, multicenter studies with harmonized case definitions, time frames, and consistent use of validated outcome instruments, although such studies are not yet available.

Clinical phenotypes

Persistent post-craniotomy headache is not a single entity but rather a syndrome containing multiple, sometimes overlapping, phenotypes. We can identify five clinical patterns (Figure 1):

1. Scar- or suture-line localized neuropathic pain: Patients describe burning, electric, or lancinating pain localized to the surgical incision, often accompanied by focal hyperesthesia or allodynia. Physical examination may reveal focal tenderness, dysesthesia, or palpable nodules consistent with neuroma formation. These localized presentations point to peripheral nerve injury or entrapment as a dominant mechanism (11).

2. Occipital neuralgia–like pain: Stabbing or shooting paroxysms in the distribution of the greater or lesser occipital nerves are particularly characteristic of posterior fossa or suboccipital surgical approaches. Symptoms may be triggered by neck movement or pressure over the occipital region and are often accompanied by a continuous dull ache between episodes of sharp

pain. Occipital neuralgia features frequently predict responsiveness to occipital nerve blocks or targeted neuromodulation in refractory cases (12,13).

3. Diffuse tension-type pattern: Some patients report pressing, non-pulsatile pain with pericranial tenderness and a less focal distribution, often exacerbated by neck stiffness and postural factors. These features suggest muscular and myofascial contributors amenable to physiotherapy and manual techniques (5).

4. Migraine-like phenotype: A subset of patients experiences migraine-like attacks with unilateral pulsatile pain, photophobia, phonophobia, and sometimes nausea. These presentations may reflect unmasking or exacerbation of pre-existing migraine disorders or central sensitization post-surgery and may respond to migraine-specific therapies in some cases (14).

5. Mixed and evolving phenotypes: Some patients manifest overlapping features or transition from one phenotype to another over time, reflecting dynamic interactions between peripheral nociceptive inputs, central processing, and psychosocial factors. Precising phenotyping form is essential for guiding targeted interventions and predicting clinical outcomes.

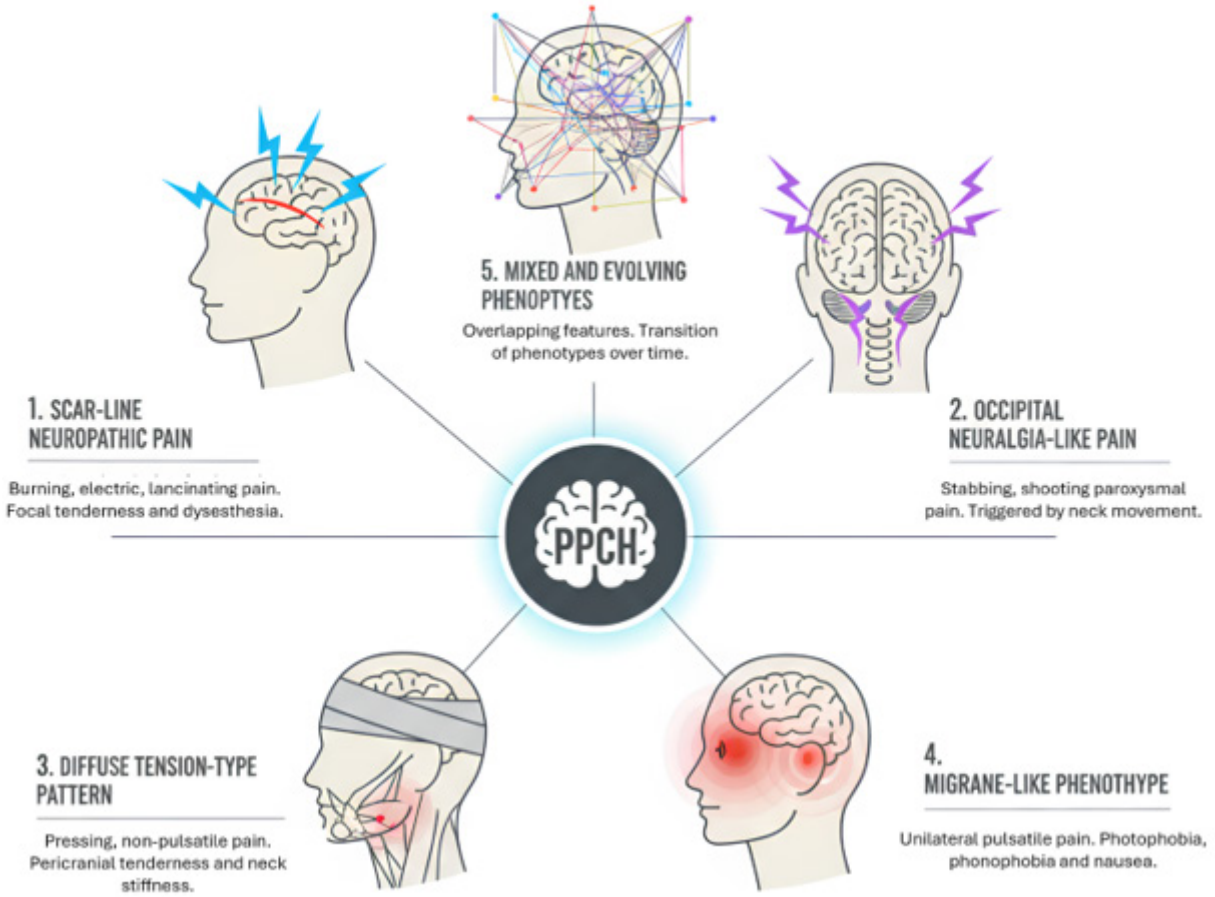

Figure 1. Clinical phenotypes of persistent post-craniotomy headache (PPCH).

Risk factors

Observational data and expert syntheses point to several factors that increase the likelihood of PPCH. Surgical approach and incision techniques might be the most important factors. Posterior fossa and suboccipital craniotomies have been reported in observational studies with higher rates of PPCH, compared with supratentorial procedures (15–17). In surgeries involving the posterior fossa, some studies reported that patients who had techniques that minimize bone loss or repair the craniotomy site (craniotomy with bone flap replacement and use of adipose grafts) reported lower headache prevalence (18,19). Postoperative pain can also be influenced by how much temporalis and neck muscles are removed during surgery. Thus, the use of a less invasive incision and craniotomy instead of craniectomy could reduce the chronic pain for patients with vestibular schwannoma (20).

Pre-existing primary headache disorders, particularly migraine, appear to predispose patients to postoperative uncontrolled pain after craniotomy for neoplasm or epilepsy surgery, likely through pre-existing central sensitization or genetic susceptibility to pain amplification (14). While, female sex has also been observed as a risk factor in the same sample, mirroring sex differences in primary headache epidemiology (14). Among patients with PPCH, psychological comorbidities are notably more common. Higher prevalence of depressive symptoms is significantly associated with increased frequency of PPCH in patients after acoustic neuroma surgery (21). Moreover, greater anxiety intensity correlates with more severe headaches and a heightened negative impact on patients' quality of life in patients with patients operated for treatment of supratentorial intracranial aneurysms (10).

Clinical evaluation and investigations

The evaluation of suspected PPCH should balance the need to exclude secondary causes with a focused assessment of peripheral pain generators amenable to targeted therapy. History should precisely document timing of onset relative to the cranial surgery, the spatial distribution of pain (scar, occipital region, diffuse), quality, temporal pattern, and the response to prior interventions. Neurological examination should assess scalp sensory abnormalities, occipital trigger points, and any new focal deficits that would prompt urgent neuroimaging or neurosurgical review.

Neuroimaging (MRI with and without contrast or CT when indicated) is reserved for atypical presentations or red flags (fever, progressive neurological signs, new seizures, suspected CSF leak, or concern for lesion recurrence). In uncomplicated PPCH, imaging is typically not necessary.

Management

General principles

Management of PPCH is multimodal and should be individualized according to the dominant phenotype. General principles includes: a) Confirm the diagnosis and exclude treatable secondary causes; b) phenotype the headache into dominant mechanistic categories (peripheral neuropathic/scar-related, occipital neuralgia–like, migraine-like, or tension-type) because the phenotype may guide the therapy selection; c) apply pharmacological interventions; and d) reserve invasive or surgical interventions for well-selected patients after multidisciplinary evaluation and demonstration of peripheral generator via diagnostic blocks. Additionally, practitioners should consider avoiding or control known risk factors for PPCH like incisions close to sensory nerves, pre-existing primary headache disorders, psychological comorbidities, and inadequate acute postoperative analgesia.

Pharmacologic therapies

Medication strategies should be individualized according to the patient's headache phenotype. Analgesics such as acetaminophen and NSAIDs may help with acute pain but are typically insufficient as monotherapy for chronic presentations. Sumatriptan, which targets 5HT1 receptors, have proven beneficial for patients experiencing ongoing headache following acoustic neuroma surgery (22). For PPCH with neuropathic features and scar-related pain, first-line agents include gabapentin, pregabalin, tricyclic antidepressants, and SNRIs, titrated to effectiveness and tolerability (4,12). For the other side, preventive therapies used in chronic migraine and for migraine-like phenotypes of persistent post-traumatic headache (beta-blockers, topiramate, valproate, and CGRP-targeted agents) (23,24), may be beneficial for PPCH migraine-like phenotypes. However, direct evidence for acute and chronic management in patients with any PPCH phenotype is very limited, and all these choices should be individualized.

Peripheral nerves blocks

Diagnostic local anesthetic blocks targeting specific scalp nerves or suture lines are valuable tools. A robust, temporally related reduction in pain following a well-executed targeted block supports a peripheral generator and can predict responsiveness to repeated blocks, corticosteroid-added injections, or procedural interventions such as botulinum toxin or neuromodulation. The diagnostic block also aids surgical decision-making by identifying patients who may benefit from scar revision (25).

Therapeutic peripheral nerve blocks are central to the interventional approach of PPCH. Targeted blocks of the greater and lesser occipital nerves, supraorbital and supratrochlear nerves, or suture-line field blocks can be performed using local anesthetics. Addition of corticosteroids to local anesthetic can extend duration of benefit for inflammatory-mediated processes in selected cases (25,26).

Botulinum toxin A

Onabotulinumtoxin A injected into the craniotomy scar and along adjacent suture lines has emerged as a promising targeted therapy for refractory localized scar-related PPCH in recent case series. Mechanisms may include decreased peripheral nociceptive input through modulation of neuromuscular transmission and local neurotransmitter dynamics. The available evidence is preliminary and consists primarily of small open-label series. So, rigorous randomized controlled trials are needed to confirm efficacy, optimal dosing, and injection paradigms (27).

Surgical options

Surgical revision—such as excision of symptomatic neuromas, hardware removal when implicated in focal irritation, or scar revision—is reserved for carefully selected patients. Candidate selection should include positive diagnostic block response, clear structural correlation (e.g., palpable neuroma or hardware prominence), and multidisciplinary review given the risk of new sensory deficits and limited evidentiary support. Outcomes are variable across small case series, therefore, surgery should be considered only after exhaustive conservative and interventional measures have been trialed (28).

Prognosis and outcomes

The clinical course of PPCH is heterogeneous. Some patients experience gradual improvement with multimodal approach and targeted interventions, whereas others endure persistent and disabling pain despite comprehensive treatment. Predictors of poorer outcome include neuropathic scar-related phenotype, delayed initiation of targeted therapies, and psychiatric comorbidity (5,11). The lack of standardized outcome reporting and limited long-term follow-up in existing series complicate definitive prognostication. Prospective registries with standardized outcome sets would greatly aid in defining trajectories and informing prognosis.

Conclusion

Persistent post-craniotomy headache is a multifaceted complication that requires systematic identification, careful phenotyping, and a staged multimodal management strategy. Diagnostic peripheral blocks are uniquely informative and should be used to confirm peripheral generators when suspected. Emerging procedural options such as scar-targeted onabotulinumtoxinA show promise for refractory localized pain but require robust randomized data. In the interim, clinicians should prioritize conservative, low-risk therapies, coupled with thoughtful escalation to targeted interventions for well-selected patients. Improved consensus definitions, standardized outcomes, and prospective trials are vital to advancing care for patients with PPCH.

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Authors Contributions: CAAR: Investigation, data curation, writing – original draft; MTG: Conceptualization, validation, investigation, resources, writing – review & editing, supervision.
Conflict of interest: None.
Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.