Diagnostics in patients presenting to the emergency room with headache

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Chapter 1

INTRODUCTION

Headache in general is a common problem and accounts for up to 4.5% of the visits to the emergency department [1]. For the treating physician the challenge lies in differentiating patients with primary headaches, such as migraine, tension type headache, or cluster headache, from patients with possible life threatening secondary headache. The causes of secondary headaches can be divided into three main groups: vascular causes, infectious and trauma. A suspicion of secondary headache may arise in patients who present with first ever headache, in acute or worst ever headache, in the presence of neurological deficit on examination or in patients with fever, systemic illness, pregnancy or immune deficiency.

Acute headache is defined as a severe headache that peaks within five minutes [2]. A subarachnoid hemorrhage (SAH) is the cause of isolated acute headache in approximately 11-25% of patients [3,4]. This is a diagnosis should not be missed as SAH has a high mortality and morbidity [4-7]. Other secondary headaches of vascular origin may be suspected in acute headache. Reversible cerebral vasoconstriction syndrome (RCVS) may be a cause of 'benign' thunderclap headache in which non-contrast head CT and LP are normal. It has been reported to be present in one out of eleven (8.8%) of patients with acute headache in whom signs of SAH are absent [8]. While some cases occur spontaneously or in the post-partum period, the majority of cases (60%) is caused by vaso-active substances (nasal decongestants, cannabis or XTC). It may have a benign course, but also ultimately cause SAH, cerebral hemorrhage or ischemia. Diagnosis can be made with angiography or MR angiography but imaging needs to be repeated over time [9]. Sometimes headache is the only symptom of vascular disease. Cervical artery dissection (CAD) may present with acute headache alone in 8% of cases[10,11], cerebral venous thrombosis (CVT) present with isolated headache in one in seven patients (14%) [12,13]. Cerebral ischemia may present with isolated headache in 2 to 25% of patient cases [14].

These causes of headache may still be present when neurological examination is normal. Herein lies a challenge: selecting the patients who benefit from CT angiography (CTA). In the current medical practice there is more focus on diagnostic sensitivity than specificity and the danger of too many diagnostic procedures is increasingly present, fuelled by the fear of missing an important diagnosis.

Another challenge is the selection of the correct imaging modality. In patients with a clear neurological deficit or altered consciousness after headache, either acute or not, it is clear that at least a non-contrast head CT or MRI should be performed. The imaging of the cervical and intracranial arteries with CT angiography (CTA) or MR angiography (MRA) may give additional information on the presence of RCVS, dissection or CVT. However, the choice for either CTA or MRI/MRA is also determined by the availability of each imaging modality and cost and duration of the scan. In the emergency department setting the high pressure on resources and time make MRI/MRA a less attractive imaging option. However the diagnostic yield of CTA may be insufficient. Furthermore, a CTA causes added radiation exposure and iodine contrast may cause allergic reactions and nephropathy.

What could be the consequence of a missed diagnosis in patients with acute headache? A pooled analysis of follow up studies with normal neurological examination and normal CT found no SAH after six months to one year follow up [15]. The authors advocated that no additional imaging is necessary. Unfortunately follow up time was relatively short and not all patients received additional CTA or MRI. The authors suggest that the natural course in these patients is benign even if other diagnoses such as RCVS, dissections, CVT or meningitis are missed.

Patients presenting to the emergency room may have a wide range of secondary headaches or non-threatening, albeit painful, primary headache. In this thesis a variety of diagnostic tests and their diagnostic yield are evaluated in patients with both vascular and infectious secondary headache. In each case the question is addressed whether expansion or reduction of diagnostic testing is necessary. Apart from identifying patients who benefit from cranial imaging we also searched for methods to avoid unnecessary scanning. We evaluated the yield of CTA in patients with acute headache in a retrospective study and a meta-analysis in **chapter 2 and 3**. Secondly we evaluated possible clinical criteria for a more purposeful selection of headache patients for CTA in **chapter 4.**

In the past few years lumbar puncture after acute headache is performed less frequently. The turning point has been the publication of an article which showed that when a CT is made within 6 hours after the start of the acute headache a lumbar puncture is no longer necessary to rule out SAH due to high sensitivity of current CT techniques [16]. If CT is performed more than six hours after acute headache a lumbar puncture is still mandatory to exclude hemorrhage. If other diagnoses necessitating cerebrospinal fluid testing are suspected a lumbar puncture is of course also needed. Also, if on imaging an aneurysm is detected a lumbar puncture is still necessary to evaluate whether this aneurysm has bled or whether it is an unruptured intracranial aneurysm (UIA) and a coincidental finding. The lumbar puncture is needed to evaluate intrathecal bilirubin, a blood breakdown product. Visual inspection lacks sensitivity and photospectometry is used to determine bilirubin based on an absorbance of 450-460 nm. We compared two methods of photospectometry evaluation in order to evaluate sensitivity and specificity in **chapter 5**.

To further investigate the value of cerebrospinal fluid (CSF) analysis we also performed a prospective study concerning the determination of procalcitonin in CSF in the diagnosis of bacterial meningitis. Viral or bacterial meningitis may present with headache alone and may be difficult to differentiate based on classic CSF findings [17]. Patients with an external ventricular drain after SAH have an increased risk of contracting bacterial meningitis due to a foreign body. Clinical signs and symptoms may be unclear as patients with SAH also may have nuchal rigidity and lowered consciousness. A diagnostic marker to differentiate between bacterial infection and aseptic meningitis would be valuable.

Procalcitonin is an acute phase protein and may become such a marker. There is evidence suggesting it is produced intrathecally by glia cells [18]. In serum it is produced in response to

bacterial infection. We studied procalcitonin formation in a varied group of patients suspected of viral or bacterial meningitis in **chapter 6**.

In patients with acute or worst ever headache cerebral venous thrombosis is often considered. Patients with a normal neurological examination may have CVT and are at risk for secondary deterioration [19]. In patients suspected of pulmonary embolism or deep venous thrombosis Wells criteria are employed in combination with D-dimer to determine which patients are at low risk. Patients in the low risk category do not require further imaging. In **chapter 7** we performed a meta-analysis to determine whether D-dimer may play a similar role in the work up of patients with suspected CVT and a normal neurological examination and normal non-contrast head CT.

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