Yield of Computed Tomography (CT) Angiography in Patients with Acute Headache, Normal Neurological Examination, and Normal Non Contrast CT: A Meta-Analysis

Imanda M.E. Alons, MD,* Ben F.J. Goudsmit,† Korne Jellema, MD, PhD,* Marianne A.A. van Walderveen, MD, PhD,† Marieke J.H. Wermer, MD, PhD,‡ and Ale Algra, MD, PhD§,‖,¶

Background: Patients with acute severe headache, normal neurological examination, and a normal noncontrast head computed tomography (NCCT) may still have subarachnoid hemorrhage, cerebral venous thrombosis (CVT), cervical arterial dissection, or reversible cerebral vasoconstriction syndrome (RCVS). Computed tomography angiography (CTA) is used increasingly in the emergency department for evaluating this, but its added value remains controversial. *Methods:* We retrospectively collected data on the diagnostic yield of CTA in patients with acute severe headache, normal neurological examination, and normal NCCT who received additional CTA in the acute phase in 2 secondary referral centers for vascular neurology. We combined data of our patients with those from the literature and performed a meta-analysis. *Results:* We included 88 patients from our hospital files and 641 patients after literature search. Of 729 patients 54 had a vascular abnormality on CTA (7.4%; 95% confidence interval [CI] 5.5%-9.3%). Abnormalities consisted of aneurysms (n = 42; 5.4%; 95% CI 3.8%-7.0%), CVT (n = 3, .5%), RCVS (n = 4, .5%), Moyamoya syndrome (n = 2, .3%), arterial dissection (n = 2, .3%), and ischemia (n = 1, .1%). Because most of the aneurysms were probably incidental findings, only 12 (1.6%) patients had a clear relation between the headache and CTA findings. The number needed to scan to find an abnormality was 14 overall, and 61 for an abnormality other than an aneurysm. *Conclusion:* Diagnostic yield of CTA in patients with acute headache, normal neurological examination, and normal NCCT is low, but because of the possible therapeutic consequences, its use might be justified in the emergency setting. Prospective studies

From the *Department of Neurology, MCH Westeinde, The Hague, The Netherlands; †Department of Radiology; ‡Department of Neurology; §Department of Clinical Epidemiology, LUMC, Leiden, The Netherlands; ‖Brain Center Rudolph Magnus, Department of Neurology and Neurosurgery; and ¶Julius Center for Health Sciences and Patient Care, UMC, Utrecht, The Netherlands.

Received April 25, 2017; revision received September 2, 2017; accepted November 14, 2017.

Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest. No funding was received for this study.

Contributor statement: I.M.A. collected the hospital and literature data, performed data-analysis, and wrote the manuscript. B.F.J.G. collected the hospital data, performed data-analysis, and critically reviewed the manuscript. K.J. conceptualized the study, supervised the methodology, and critically reviewed the manuscript. M.J.H.W. conceptualized the study, supervised the methodology, and critically reviewed the manuscript. M.A.A.W. supervised the radiology findings and critically reviewed the manuscript. A.A. conceptualized the study, supervised the methodology and data-analysis, and critically reviewed the manuscript.

Address correspondence to Imanda M.E. Alons, MD, Department of Neurology, MCH Westeinde, The Hague, The Netherlands. E-mail: mandaalons@hotmail.com.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.11.016

confirming these results including cost-effectiveness analyses are needed. **Key Words:** Computed tomography angiography—neuroimaging—acute headache—thunderclap headache—meta-analysis.

Introduction

Acute headache may be the only presenting symptom of life-threatening secondary headache syndromes. Patients with acute severe headache and a normal neurological examination may have not only subarachnoid hemorrhage (SAH), but also cerebral venous thrombosis (CVT), cervical arterial dissection, or reversible cerebral vasoconstriction syndrome (RCVS).[1-8]

Computed tomography angiography (CTA) is increasingly used in the emergency setting for evaluating these important causes of secondary headache. CTA has been proven sensitive in determining the presence of aneurysms and CVT, and, to a lesser extent, RCVS and dissections.[9,10] CTA has higher accessibility than magnetic resonance imaging (MRI) in most hospitals. Also cost and time reductions compared with MRI make it a possible valuable modality in evaluating emergency department (ED) patients, although CTA is more expensive than noncontrast head computed tomography (NCCT) alone. There are other drawbacks of CTA. First, there is an added radiation exposure of approximately 2.5 mSV after the NCCT which is also 2.5 mSV, with a total of 5 mSV.[11] Second, intravenous iodinated contrast media may, rarely, cause allergic reactions and contrast nephropathy, particularly in patients with known nephropathy.[11-13]

The diagnostic yield of CTA in patients with acute headache and normal neurological examination and NCCT is unclear. A pooled analysis of follow-up studies in patients with acute severe headache reported that in the group with normal noncontrast computed tomography (CT) and normal lumbar puncture (LP), none had subsequent SAH. Based on these findings the authors advocated that CTA should not be used on a standard basis in these patients.[14] However, the included studies had a limited follow-up period and in most patients CTA was not performed. Two large series of patients with acute headache concluded that if an NCCT is normal when performed within 6 hours of the start of the headache, an LP is no longer needed due to the highly sensitive nature of third-generation CT scanners.[15,16] This strategy is applicable to the exclusion of SAH, but because CTA was not performed in most patients, other diagnoses such as CVT, RCVS, or cervical arterial dissection might have been missed. Two studies report percentages of vascular abnormalities ranging from 6.6% to 19%, in patients with acute severe headache, normal neurological examination, and normal NCCT.[17,18] This is higher than may be expected in the general population. The first study was a large prospective study of 512 patients, but it was unknown whether LPs had been performed in these patients. In this study a large number of aneurysms were found, but it was not clear whether these were ruptured or unruptured intracranial aneurysms.[17] The second study from our own group had a limited size and patients were selected based on a normal LP. This may have caused selection bias.[18]

The aim of our study was to evaluate the yield of CTA in patients presenting with acute severe headache to the ED in whom neurological examination and NCCT was normal using both our own patient population and a meta-analysis of the literature.

Methods

Own Hospital Data

We retrospectively evaluated data on all patients who underwent a cerebral CTA between 2011 and 2014 in the ED of the Leiden University Medical Center (LUMC), a tertiary vascular neurology referral center and university teaching hospital, and the MC Haaglanden, a secondary vascular referral center and primary teaching hospital. We included all patients who presented with acute headache, defined as headache that developed within 5 minutes and lasted for at least 1 hour.

In the Leiden University Hospital patients were scanned from the aortic arch up using the Aquilion One (Aquilion ONE, Toshiba Medical Systems, Tokyo, Japan) and Aquilion 64 CT scanner (Aquilion 64, Toshiba Medical Systems, Otawara, Japan). In the MC Haaglanden patients were scanned from the aortic arch to the vertex with a GE Lightspeed 64-slice scanner.

We charted patient characteristics (age, sex, patient history and medication, seizures, loss of consciousness before admission, nausea, vomiting) and headache characteristics (location, duration, mode of onset, presence of aura, autonomous symptoms). We recorded results of CTA and other diagnostic procedures including LPs, digital subtraction angiography, and MRI when performed. Patients with focal neurological deficits, abnormalities on standard NCCT and, if performed, abnormal cerebrospinal fluid findings (raised pressure and cerebrospinal fluid chemistry showing hemorrhage or infection) were excluded. We recorded all adverse events that were possibly related to the CTA such as allergic reactions, kidney failure, or infections after intravenous catheter use.