Clinical and Radiological Predictors of Malignant Middle Cerebral Artery Infarction Development and Outcomes

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Background: Optic nerve sheath diameter (ONSD) can predict intracranial hypertension and outcomes in severe traumatic brain injury. Its utility in middle cerebral artery (MCA) stroke is unknown. *Aims:* We reviewed serial radiological measurements, including ONSD, in patients with MCA stroke undergoing decompressive craniectomy (DC) for malignant MCA syndrome and compared demographic, clinical, and radiological data with an age- and gender-matched group of nonmalignant MCA stroke patients. *Methods:* Patients admitted to a large tertiary hospital in London, UK, between April 2012 and October 2016 with MCA infarction were identified through 2 data sources. We quantified ONSD, eyeball transverse diameter (ETD), ONSD/ETD ratio, midline shift (MLS), and infarct volume on computed tomography (CT). *Results:* We identified 19 patients (mean age = 49.8 years [standard deviation = 12.5]) with malignant MCA stroke and 19 patients (47.8 years [16.0]) with nonmalignant MCA stroke. Mean ONSD, ONSD/ETD ratio, MLS, and infarct volume on initial CT all significantly increased after developing malignant MCA syndrome and decreased (except infarct volume, which increased) following DC (all *P*s <.05). ONSD and ONSD/ETD ratios in the malignant group did not correlate with functional outcomes but were significantly higher on initial CT compared with the nonmalignant group (mean ONSD: 5.66 mm [.6] versus 4.97 mm [.5], *P* = .001; mean ONSD/ETD ratio: .25 [.03] versus .22 [.02], *P* = .002). *Conclusions:* ONSD, ONSD/ETD ratio, MLS, and infarct volume change dynamically in patients with malignant MCA infarction who undergo DC. An ONSD of more than 5.25 mm and an ONSD/ETD ratio of more than .232 on initial CT may identify MCA stroke patients at high risk of developing malignant MCA syndrome. **Key Words:** Functional outcomes—intracranial hypertension—intracranial pressure—malignant MCA infarction—middle cerebral artery stroke—optic nerve sheath diameter.

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Introduction

Malignant middle cerebral artery (MCA) infarction is a devastating condition where large MCA territory ischemia can result in space-occupying cerebral edema and rapid neurological deterioration.[1] It affects 10-20 per 100,000 of the population annually[2] and is associated with high morbidity and mortality; without surgery, the mortality rate approaches 80%.[3,4] Clinically, it can manifest as hemiparesis, gaze deviation, higher cortical signs, and with signs and/or symptoms of intracranial hypertension (including headache, vomiting, papilledema, and impaired consciousness). There is class I evidence that decompressive craniectomy (DC) reduces mortality and improves functional outcomes when performed within 48 hours of symptom onset in those aged between 18 and 60.[3]

However, rates of functional disability in survivors following surgery are still high, particularly in older patients, where similar survival but not functional outcome benefits of surgery have been demonstrated.[4]

The ability to reliably predict which patients with MCA stroke will go on to have a malignant course is an area of significant unmet need. Addressing this deficit may facilitate decision-making among clinicians, including decisions about intensive care unit admission.[5,6] At present, infarct volume on cranial imaging is the only widely recognized predictor of a malignant course[2]; a volume greater than 145 cm^3 is considered high risk for malignant progression and has been recommended as an indication for intensive care unit admission.[5] Optic nerve sheath diameter (ONSD), measured on computed tomography (CT) or magnetic resonance imaging, predicts intracranial hypertension[7,8] and mortality[9] in patients with severe traumatic brain injury (TBI). However, its utility in many other pathologies, including ischemic stroke, remains to be evaluated.

Aims

The purpose of this study was to (1) review serial radiological measurements, including ONSD, in patients with MCA stroke undergoing DC for malignant MCA syndrome to evaluate their utility as noninvasive markers of intracranial pressure (ICP), and (2) compare demographic, clinical, and radiological data with a group of nonmalignant MCA stroke patients in order to identify potential associations, predictors, and prognostic indicators.

Methods

Study Design and Population

This was a retrospective study of imaging and prospectively collected demographic and clinical data with a case-control component to the study. Patients aged 18 years or older admitted to a large tertiary hospital (The Royal London Hospital, Barts Health NHS Trust) in London, UK, between April 1, 2012, and October 31, 2016, with a confirmed radiological diagnosis of MCA stroke were identified through 2 sources: a central administrative data set and an electronic neurosurgery referral database. We included in this study all identified patients who were diagnosed with MCA stroke and underwent DC for malignant MCA syndrome. A surgical group of MCA stroke patients were chosen specifically because they would facilitate the serial evaluation of clinical and radiological parameters over several time points, and their prognostic value. For the case-control part of the study, a group of age- and gender-matched patients admitted during the same time period who were diagnosed with MCA stroke but did not develop malignant MCA syndrome were also identified for comparative purposes. The retrospective nature of the study meant that no ethical approval was required.

We used the central administrative data set to identify patients by diagnosis (coded using the International Classification of Diseases-10) and, for the DC group, procedure(s) undertaken (coded using the Office of Population Censuses and Surveys Classification of Interventions and Procedures), using the codes in Appendices 1 and 2. Coding was undertaken by appropriately trained coding staff. A broad range of codes was used to enhance the sensitivity of our search.

Clinical and Demographic Data

Information on the following data were collected: age; gender; clinical signs, symptoms, and National Institutes for Health Stroke Scale (NIHSS) score at presentation; past medical history; stroke laterality; administration of thrombolysis or endovascular treatment; presence of hemorrhagic transformation (on imaging performed at any point during the in-patient stay); length of stay; and mortality at 30 days and last follow-up. Glasgow Coma Scale (GCS) score and pupillary response were documented at admission and, for those who underwent DC for malignant MCA infarction, at the time of clinical deterioration prior to surgery. To evaluate functional outcomes, modified Rankin Score (mRS) was documented pre-morbid, at 30 days, and at last follow-up.

Radiological Data

CT scans with slice thickness of 1 mm were reviewed using the picture archiving and communication system radiology workstation (Centricity Enterprise, GE Medical Systems, Milwaukee, WI). All measurements were performed by a single neurosurgeon (M.A.K.) blinded to all other data of the patient at the time the measurements were taken. ONSD was calculated using electronic calipers, 3 mm behind and in a perpendicular vector with reference to the orbit (Fig 1), as done in most previous

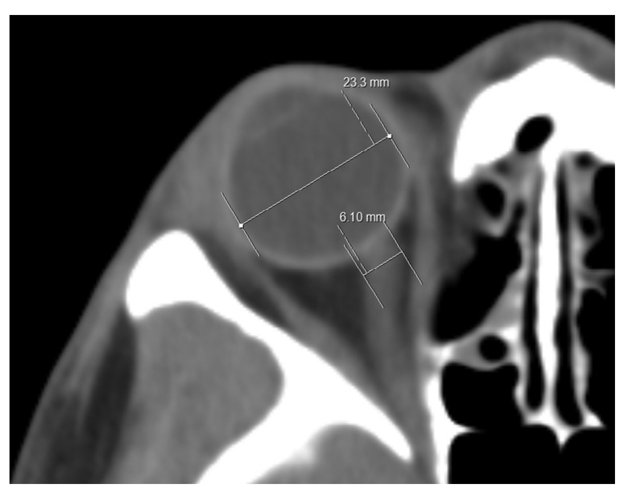

Figure 1. *Axial computed tomography scan showing how optic nerve sheath diameter and eyeball transverse diameter measurements were obtained.*