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Marked Circadian Variation in Number and Type of Hyperacute Strokes During the 24 Hour Day-Night Cycle

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Introduction: Circadian variations in stroke onset provide critical information for the allocation of pre-hospital and hospital resources in clinical care. Confining analysis to patients with defined onset in waking and clearly distinguished ischemic and hemorrhagic stroke subtypes, would substantial benefit our understanding of stroke etiology.

Methods: We analyzed patients enrolled in the NIH FAST-MAG phase 3 trial of field-initiated neuroprotective agents in patients with hyperacute stroke within 2h of onset.

Onset times were analyzed in 1h time blocks throughout the 24h day-night cycle.

Patient demographic and clinical features, medical history, imaging characteristics, and stroke deficit severity were correlated with onset times.

Results: Among 1632 patients, final diagnoses were acute cerebral ischemia in 76.2% and intracranial hemorrhage in 23.7%. Acute cerebral ischemia (ACI) had a unimodal distribution with peak onset at midday (12:00-12:59); intracerebral hemorrhage (ICH) a bimodal distribution with peaks at mid-morning (08:00-08:59) and early evening (18:00-18:59). Events were markedly reduced in early morning, with only 3.4% starting in the first 25% of the day. The proportion of hemorrhagic was higher in the first 8h of the day (00:00-07:59) than the remaining 16h, 33.3% vs 22.5%, $p=0.006$. ACI and ICH patients

displayed fairly homogeneous vascular risk factors, presenting deficit severity, and initial brain imaging findings across all time periods.

Discussion: There is marked, more than 10-fold, circadian variation in onset of acute cerebrovascular disease, and circadian variation in the ratio of ischemic to hemorrhagic neurovascular events. These findings can inform resource planning for regional systems of acute stroke care.