Original Research

The Association of Brain MRI Characteristics and Postoperative Delirium in Cardiac Surgery Patients

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ABSTRACT

Purpose: Delirium is common after cardiac surgery and is associated with adverse consequences, including cognitive decline. Identification of vulnerable older adults might allow for early implementation of delirium-prevention strategies. Brain MRI findings provide insight into structural brain changes that may identify vulnerable patients. The purpose of this study was to examine the association between brain MRI characteristics potentially associated with delirium vulnerability and the development of postoperative delirium in a nested cohort of patients undergoing cardiac surgery.

Methods: We identified 79 cardiac surgery patients who had brain MRI imaging after cardiac surgery, as part of an ongoing randomized trial evaluating the efficacy of blood pressure management based on cerebral autoregulation monitoring versus standard management for improving neurological outcomes. Cerebral lateral ventricular size, cortical sulcal width, and white matter hyperintensities (WMH) on brain MRI scans were graded on a validated 0 to 9 scale, and categorized into tertiles. New ischemic lesions were characterized as present or absent. Delirium was assessed using a validated chart-review. Neuropsychological testing performed before surgery was used to establish preoperative cognitive baseline. Multivariable logistic regression was used to assess the independent association between MRI characteristics and postoperative delirium.

Findings: The average age of patients was 70.1 ± 7.8 years old, and 72% were male. Twenty-eight of 79 (35.4%) patients developed postoperative delirium. Patients with delirium had higher unadjusted ventricular size (median 4 vs. 3, $P = 0.003$), and there was a trend towards higher sulcal sizes and WMH grades. Increasing tertiles of ventricular size (Odds Ratio [OR] 3.59; 95% Confidence Interval [CI] 1.59-8.12; $P = 0.002$) and sulcal size (OR 2.15; 95%CI 1.13-4.12; $P = 0.02$) were associated with postoperative delirium, with a trend for tertiles of WMH grade (OR 1.91; 95%CI 0.99-3.68; $P = 0.05$). In multivariable models adjusted for logistic EuroSCORE, baseline cognitive status, bypass time, and any postoperative complication, each tertile of ventricular size was associated with increased odds of postoperative

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delirium (OR 3.23 per tertile increase in ventricular size; 95%CI 1.21-8.60; $P = 0.02$). There were no differences in odds of delirium by tertiles of sulcal grade, tertiles of white matter grade, or presence of new ischemic lesions, in adjusted models.

Implications: Increased brain ventricular size was independently associated with delirium after cardiac surgery. These results suggest that cerebral atrophy may contribute to increased vulnerability for postoperative delirium. Baseline brain MRIs may be useful in identifying cardiac surgery patients at high risk for postoperative delirium, who might benefit from targeted perioperative approaches to prevent delirium. ClinicalTrials.gov identifier: NCT00981474. (*Clin Ther*. 2015;37:2686–2699)

Key words: cardiac surgery, postoperative delirium, sulcal width, ventricular size, white matter hyperintensities.

INTRODUCTION

Delirium is an acute confusional state that is common in hospitalized older adults.[1] The incidence of delirium after surgery is reportedly between 4% and 65%,[2] with the highest incidences generally reported after hip fracture surgery[3] and cardiac surgery.[4,5] Although once thought to be transient and self-limiting, postoperative delirium is now recognized as being associated with increased morbidity,[6] mortality,[7] institutionalization,[8] and cognitive decline.[9,10] Thus, increasing efforts have focused on characterizing the pathophysiology of postoperative delirium and, in particular, identifying vulnerable older adults who might benefit from targeted delirium prevention strategies.

In patients undergoing cardiac surgery, the characteristics most strongly associated with postoperative delirium reflect cerebral pathology, including prior stroke,[11] baseline cognitive impairment,[5,12] and depression.[5] Because these brain measures are somewhat nonspecific, better characterization of brain structure and function, through modalities such as brain magnetic resonance imaging (MRI), may yield insights into the pathophysiology of delirium and also identify vulnerable patients at highest risk for postoperative delirium so that anesthetic approaches could be modified.[13]

Despite the potential of MRI findings as biomarkers, the reports of an association between brain MRI findings and risk for postoperative delirium have not been consistent.[14] Multiple cerebral infarcts[15] and white matter hyperintensities (WMH)[16–18] have been associated with postoperative delirium in some studies. Similarly, cerebral atrophy has been associated with postoperative delirium in heterogeneous patient populations.[19,20] However, weaknesses of previous studies include the use of poorly validated delirium assessments, imprecise characterization of MRI findings, lack of accounting for potentially confounding variables, and heterogeneous patient populations. Recently, a prospective, well-conducted study in noncardiac surgery patients addressed many limitations of the earlier studies, and it found no difference in cerebral atrophy or WMH according to delirium status after surgery.[21] However, it is unclear if these findings would be generalizable to patients undergoing cardiac surgery, because the pathophysiology of delirium in cardiac surgery patients may be different because of underlying patient characteristics (eg, high prevalence of cerebrovascular disease) and different surgical insults (eg, cardiopulmonary bypass and associated inflammatory burden).

In the present study, we hypothesized that specific brain MRI characteristics (ventricular and sulcal size, WMH, and new ischemic lesions) would be associated with postoperative delirium in patients undergoing cardiac surgery.

PATIENTS AND METHODS

The study procedures met with the approval of the institutional review board and were performed after receiving individual written informed consent.

Patients

This study was a prospective observational trial, nested in an ongoing multiyear randomized controlled study evaluating the association between cerebral blood flow autoregulation[22] and brain injury after cardiac surgery. The objectives of this study were not the primary outcome of the original trial, and thus the present study is a secondary data analysis.

Patients underwent surgery between October 2009 and August 2012. The primary inclusion criterion was primary or re-operative coronary artery bypass graft (CABG) and/or valve or aortic surgery that required cardiopulmonary bypass bypass, as well as having an elevated risk of stroke or encephalopathy, based on a