# Postoperative Delirium and Short-term Cognitive Dysfunction Occur More Frequently in Patients Undergoing Valve Surgery With or Without Coronary Artery Bypass Graft Surgery Compared With Coronary Artery Bypass Graft Surgery Alone: Results of a Pilot Study

Judith A. Hudetz, PhD, Zafar Iqbal, MD, Sweeta D. Gandhi, MD, Kathleen M. Patterson, PhD, Alison J. Byrne, PhD, and Paul S. Pagel, MD, PhD

***Objective:*** **The authors tested the hypothesis that patients undergoing valve repair or replacement surgery with or without coronary artery bypass graft (CABG) surgery using cardiopulmonary bypass (CPB) had a greater incidence of postoperative delirium and cognitive dysfunction compared with patients undergoing CABG surgery alone.**

***Design:*** **Prospective study.**

***Setting:*** **Veterans Affairs medical center.**

***Participants:*** **Forty-four age- and education-balanced male patients (≥55 years of age) undergoing elective cardiac surgery with CPB (n = 22 valve ± CABG surgery and n = 22 CABG surgery alone) and nonsurgical controls (n = 22) were recruited.**

***Interventions:*** **None.**

***Measurements and Main Results:*** **Delirium was assessed with the Intensive Care Delirium Screening Checklist before and for 5 consecutive days after surgery. Recent verbal and nonverbal memory and executive functions were assessed using a psychometric test battery before and 1 week after cardiac surgery or at 1-week intervals in nonsurgical controls. Intensive care unit stay, hospital stay, and 30-day readmission were significantly ($p = 0.03$, $p = 0.01$, and $p = 0.04$, respectively) longer in patients undergoing valve surgery ± CABG surgery versus CABG surgery alone. Postoperative delirium occurred more frequently ($p = 0.01$) in patients undergoing valve ± CABG surgery versus CABG surgery alone. Overall cognitive performance (composite *z* score) after surgery also was impaired significantly ($p = 0.004$) in patients undergoing valve ± CABG surgery compared with CABG surgery alone. The composite *z* score after surgery decreased by at least 1.5 standard deviations in 11 patients (50%) versus 1 patient (5%) without valve surgery compared with nonsurgical controls ($p = 0.001$, Fisher's exact test). The presence of delirium predicted a composite *z* score decrease of 1.2 points (odds ratio = 0.30; 95% confidence interval, 0.13-0.68).**

***Conclusions:*** **The results indicated that patients undergoing valve surgery with or without CABG surgery have a higher incidence of postoperative delirium and cognitive dysfunction 1 week after surgery compared with those undergoing CABG surgery alone.**



***KEY WORDS: valve repair, valve replacement, coronary artery bypass graft surgery, cardiopulmonary bypass, postoperative delirium, postoperative cognitive dysfunction***

POSTOPERATIVE DELIRIUM and cognitive dysfunction continue to adversely affect patient outcome despite the advances in surgical and anesthetic techniques.[1-3] Delirium occurs in 20% of elderly patients, most commonly within 3 days after surgery. Delirium has a fluctuating clinical course characterized by the acute onset of mental status changes, an altered level of consciousness, and reduced cognition or development of perceptual disturbances.[4] Patients undergoing cardiac surgery are at a particularly high risk for postoperative delirium because of the complexity and duration of the procedure, the use of cardiopulmonary bypass, the presence of macro- or microemboli resulting from aortic and cardiac manipulation, cerebral reperfusion injury, and postoperative complications.[5,6] Postoperative cognitive dysfunction has been linked to the presence of delirium and occurs transiently in the majority of cardiac surgical patients.[7] However, these early changes in cognition may persist or become permanent in a substantial minority of these patients.[3] Difficulty with concentration, reduced short-term memory, and the inability to process information are typical features of postoperative cognitive dysfunction.[8,9] Such deficits may lead to delayed discharge from the hospital, impaired independence, and mortality.[2,10,11] Previous studies suggested that surgery for valvular heart disease may be associated with a greater risk of postoperative cognitive dysfunction compared with coronary artery surgery.[12-14] Whether a similar procedure-based difference in the incidence of postoperative delirium also occurs is unknown. The authors tested the hypothesis that patients undergoing surgical repair or replacement of heart valve(s) with or without coronary artery bypass graft (CABG) surgery using cardiopulmonary bypass (CPB) have a greater incidence of postoperative delirium and cognitive dysfunction than those undergoing CABG surgery alone and whether the link between postoperative delirium and cognitive dysfunction is present after valve surgery. If this hypothesis is confirmed, then postoperative delirium may be a sensitive early indicator of subsequent cognitive dysfunction, particularly in patients undergoing heart valve surgery. This may be significant for a possible future postoperative treatment to prevent later cognitive dysfunction. In fact, as the authors show, a significant relationship between the incidents of postoperative delirium and cognitive dysfunction is present specifically for patients undergoing valve surgery, a finding that has not been shown before.

*From the Department of Anesthesiology, Medical College of Wisconsin and Clement J. Zablocki Veterans Administration Medical Center, Milwaukee, WI.*

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*Address reprint requests to Judith A. Hudetz, PhD, Department of Anesthesiology, Clement J. Zablocki Veterans Administration Medical Center, 5000 W National Avenue, Milwaukee, WI 53295. E-mail: judith.hudetz@va.gov*



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## MATERIALS AND METHODS

The study was approved by the Institutional Review Board of the Clement J. Zablocki VA Medical Center, Milwaukee, WI. All subjects provided written informed consent.

Forty-four age- and education-balanced male patients (≥55 years of age) were enrolled (valve surgery with or without CABG surgery [n = 22] or CABG surgery alone [n = 22]) from a consecutive series of 96 patients undergoing elective cardiac surgery. In the first group, 12 patients undergoing a valve procedure alone (6 mitral valve repair, 1 mitral valve replacement, and 5 aortic valve replacement) and 10 patients undergoing valve surgery plus CABG surgery (1 mitral valve repair and 9 aortic valve replacement) were included. Twenty-two patients with coronary artery disease who were not undergoing surgery were recruited from other hospital clinics. The inclusion of these patients was important to account for practice effects of repeated cognitive testing.[15] Exclusion criteria included a history of a cerebrovascular accident, permanent ventricular pacing, previously documented cognitive deficits, or vascular dementia (Hatchinski score[16] >4). Patients with hepatic impairment (aspartate aminotransferase or alanine aminotransferase more than twice the upper normal limit) and chronic renal insufficiency (creatinine >2 mg/dL) also were excluded.

Delirium and cognitive functions were evaluated within 1 week before surgery. The CAGE (Cut, Annoyed, Guilty, Eye-opener) questionnaire was used as a screening instrument for detecting a history of alcohol abuse.[17] Recent verbal and nonverbal memory and executive functions were assessed as indices of cognitive function. The anesthetic technique was standardized as previously described.[18] All patients underwent a median sternotomy. Heparin (400 U/kg) was used for systemic anticoagulation to maintain an activated coagulation time >500 seconds. Myocardial protection during cardiopulmonary bypass consisted of antegrade and retrograde cold blood cardioplegia administered at regular intervals (15 minutes), topical hypothermia (slushed 0.9% saline), and systemic hypothermia (30°-32°C). A dose of continuous warm blood cardioplegia was administered during rewarming before the removal of the aortic cross-clamp. Arterial blood flow and mean arterial pressure during cardiopulmonary bypass were maintained between 2.4 and 2.5 L/min/m$^2$and between 55 and 70 mmHg, respectively. Delirium repeatedly was reassessed for as many as 5 days after surgery by 2 independent psychologists. If these psychologists had disagreed, then a third psychologist's rating would have determined whether or not the diagnosis of delirium could be established. Scores were averaged if a patient received different delirium scores on any postoperative day from the separate observers. The 2 psychologists agreed with the diagnosis of delirium 100% of the time; therefore, the interrater consistency between them was 100%. Neurocognitive functions were reassessed 1 week after surgery or at hospital discharge (whichever occurred first) or at 1-week intervals in patients who did not have surgery (controls).

Delirium was assessed with the Intensive Care Delirium Screening Checklist.[19] This is an 8-item (altered level of consciousness, inattention, disorientation, hallucination-delusion psychosis, psychomotor agitation or retardation, inappropriate speech or mood, sleep/wake cycle disturbance, and symptom fluctuation) checklist based on the *Diagnostic and Statistical Manual of Mental Disorders*, *4th edition*[4] criteria and features of delirium. Raters completed the checklist based on data from the previous day. Routinely collected data (such as orientation) were combined with short observations of obvious manifestations of described features. The 8 items are scored 1 (present) or 0 (absent) for a total of 8 points. A score of 4 or greater is a positive indicator of delirium.[19]

The test battery from several neuropsychologic tests was comprised of standard clinical measures that were appropriate for use with subjects in the age group studied, making minimal sensory or motor demands. The tests covered 3 cognitive modalities: verbal recent memory, nonverbal recent memory, and executive functions. The total test administration time was less than 1 hour. Two alternate forms were used to reduce practice effects between sessions. The order of presentation was counterbalanced with half of the subjects receiving 1 form in the first session and the other half receiving the other form. Story Memory and Word List Memory subtests from the Repeatable Battery for the Assessment of Neuropsychological Status[20] were used to test verbal recent memory. Story Memory measures the ability to learn and recall a narrative story in 2 trials (maximum score of 20) and delayed free recall (maximum score of 10). Word List Memory assesses the ability to learn and remember a list of 10 unrelated words across 4 sequential learning trials (maximum score of 40) and delayed free recall (maximum score of 10). The Brief Visual Memory Test Revised[21] was used to test nonverbal recent memory. A card showing 6 simple geometric designs was shown for 10 seconds on 3 sequential trials to test nonverbal recent memory. When the card was removed, the examinee drew the designs in the locations remembered (2 points per design, a maximum score of 36). A free recall trial was administered 20 minutes later (maximum score of 12). Backward Digit Span,[22] Semantic Fluency[20] (ie, "name all the fruits and vegetables" [form A] and "all the animals in the zoo" [form B] that you can think of in 1 minute), and Phonemic Fluency[23] (ie, name all the words that you can think of that start with the letter "S" [form A] and "P" [form B] in 1 minute) were used to test executive functions. The test scores are the numbers of correct responses produced in the allotted time.

Depression was assessed with the Geriatric Depression Scale 15-item version.[24] The obtained score was the number of symptoms endorsed. Scores range from 0 to 15, with higher scores indicating greater depression.

To test for between-group differences in demographic and medical data, chi-square or Fisher's exact tests were used for proportions and the Student *t* test was used for continuous variables. Postoperative delirium rates between groups of patients were compared using the Fisher's exact test. Moller's *z* scores were used to assess cognitive change from baseline to 1 week or discharge after surgery.[25] The *z* score for the change in each neuropsychological assessment was calculated by using the following formula:

$$z\ \text{score} = ([\text{change score}] - [\text{mean change score}_{\text{control}}])/(\text{standard deviation change score}_{\text{control}}).$$

The use of a suitable normative population was used to correct for practice effects and variability between sessions (control).[15] The authors obtained composite *z* scores for the individual surgical patients by averaging all their *z* scores. Cognitive performance between groups, based on composite *z* scores or the degree of deterioration measured by standard deviation, was compared using the Student *t* test and Fisher's exact test, respectively. Finally, logistic regression analysis was performed to examine if postoperative delirium predicted cognitive dysfunction and was expressed as an odds ratio. All comparisons were made using 2-sided tests. The null hypothesis was rejected when $p < 0.05$. All errors were reported as standard deviations. Statistical calculations were performed using NCSS 2001 (NCSS, Kaysville, UT) and STATA/IC 10.0 (StataCorp LP College Station, TX) software.

## RESULTS

Demographic and medical data were similar between groups (Table 1). Aortic cross-clamp and CPB times were significantly ($p = 0.02$ and $p = 0.03$, respectively) longer in patients undergoing valve surgery with or without CABG surgery compared with CABG alone (Table 2). The duration of intensive care unit stay, hospital stay, and the 30-day readmission rate also were significantly ($p = 0.03$, $p = 0.01$, and $p = 0.04$,