Section Editor: **Gregory J. Crosby**

# Outcomes of Early Delirium Diagnosis After General Anesthesia in the Elderly

Karin J. Neufeld, MD, MPH,* Jeannie-Marie S. Leoutsakos, PhD, MHS,* Frederick E. Sieber, MD,† Brett L. Wanamaker,† Jennifer J. Gibson Chambers, MS,§ Veena Rao,‖ David J. Schretlen, PhD,*¶ and Dale M. Needham, MD, PhD#

**BACKGROUND:** Postoperative delirium in the elderly, measured days after surgery, is associated with significant negative clinical outcomes. In this study, we evaluated the prevalence and in-hospital outcomes of delirium diagnosed immediately after general anesthesia and surgery in elderly patients.

**METHODS:** Consecutive English-speaking surgical candidates, aged 70 years or older, were prospectively enrolled during July to August 2010. After surgery, each participant was evaluated for a Diagnostic and Statistical Manual of Mental Disorders IV diagnosis of delirium in the postanesthesia care unit (PACU) and repeatedly thereafter while hospitalized. Delirium in the PACU was evaluated for an independent association with change in cognitive function from preoperative baseline testing and discharge disposition.

**RESULTS:** Ninety-one (58% female) patients, 78% of whom were living independently before surgery, were found to have a prevalence of delirium in the PACU of 45% (41/91); 74% (14/19) of all delirium episodes detected during subsequent hospitalization started in the PACU. Early delirium was independently associated with impaired cognition (i.e., decreased category word fluency) relative to presurgery baseline testing (adjusted difference [95% confidence interval] for change in T-score: −6.02 [−10.58 to −1.45]; $P = 0.01$). Patients whose delirium had resolved by postoperative day 1 showed negative outcomes that were intermediate in severity between those who were never delirious during hospitalization and those whose delirium in the PACU persisted after transfer to hospital wards (adjusted probability [95% confidence interval] of discharge to institution: 3% [0%–10%], 26% [1%–51%], 39% [0%–81%] for the 3 groups, respectively).

**CONCLUSIONS:** Delirium in the PACU is common, but not universal. It is associated with subsequent delirium on the ward, and potentially with a decline in cognitive function and increased institutionalization at hospital discharge. (Anesth Analg 2013;117:471–8)

Delirium, characterized by an acute change in level of consciousness, inattention, and disturbed cognitive function,[1] is an important and common medical condition, particularly in hospitalized patients. Delirium during hospitalization is associated with postdischarge morbidity,[2,3] institutionalization,[4] and mortality.[5] Older patients are at high risk for delirium especially in the postoperative setting,[6] with up to 50% of postoperative patients ≥65 years of age developing postoperative delirium.[7–10]

Studies frequently assess delirium on postoperative day 2 or later.[7,9,10] Reasons for delaying evaluation include: (1) concern that delirium in the postanesthesia care unit (PACU) will be obscured by a nearly universal occurrence of cognitive impairment during emergence from anesthesia and (2) impression that the natural history of postoperative delirium involves an initial period of lucidity immediately after surgery.[11] Sharma et al.[12] evaluated delirium in the PACU using the Confusion Assessment Method (CAM) diagnostic algorithm in hip fracture surgery patients ≥55 years of age and reported a prevalence of 45%, with PACU delirium being highly predictive of delirium during the postoperative hospitalization period. The generalizability of this study is limited because only 50 patients of 1 surgical type were included, and delirium assessments were based on the CAM diagnostic algorithm without direct cognitive examination of the patients in the PACU. Because there was no examination of related outcomes such as change in cognitive function or health care resource utilization, the clinical importance of PACU delirium was not fully delineated in this prior study.

From the Departments of *Psychiatry and Behavioral Sciences and †Anesthesiology, Johns Hopkins University School of Medicine; ‡Johns Hopkins University School of Medicine, Baltimore, Maryland; §College of Osteopathic Medicine, University of New England, Biddeford, Maine; ‖School of Medicine American University of Antigua, Coolidge, Antigua; and ¶Russell H. Morgan Department of Radiology and Radiological Science and #Division of Pulmonary and Critical Care Medicine, and Department of Physical Medicine and Rehabilitation, School of Medicine, Johns Hopkins University, Baltimore, Maryland.

Accepted for publication April 4, 2013.

Funding: This study was funded by (1) Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, School of Medicine; (2) Johns Hopkins Predoctoral Clinical Research Training Program Grant Number 1TL1RR-025007 from the National Center for Research Resources (NCRR) for support of BLW; (3) The Walker Award for Research in Psychiatry and Behavioral Sciences, Johns Hopkins University, School of Medicine for support of BLW; and (4) American Federation on Aging Research, Medical Student Training in Aging Research Program for support of JJGC.

Conflict of Interest: See Disclosures at the end of the article.

This report was previously presented, in part, at the American Delirium Society June 2012, Academy of Psychosomatic Medicine November 2011

Reprints will not be available from the authors.

Address correspondence to Karin J Neufeld, MD MPH, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Johns Hopkins Hospital, Osler 320 General Hospital Psychiatry, 600 North Wolfe St., Baltimore, MD 21287-5371. Address e-mail to kneufel2@jhmi.edu.


DOI: 10.1213/ANE.0b013e3182973650

The objectives of the current study were: (1) to evaluate the prevalence of delirium in the PACU and during subsequent inpatient hospital stay for elderly surgical patients undergoing general anesthesia for a wide variety of surgical procedures using direct neuropsychiatric examination and (2) to assess independent associations of delirium in the PACU with patient outcomes including change in cognition from preoperative baseline and health care resource utilization including discharge disposition.

## METHODS

### Patients

This study was approved by the Johns Hopkins IRB; the requirement for written informed consent was waived. Verbal informed consent was obtained from all participants.

All consecutive English-speaking patients, aged 70 years and older, scheduled to undergo elective or emergent surgery with general anesthesia at a teaching hospital on weekdays for 8 weeks from July to August 2010 were eligible for participation. Patients were excluded if they were cognitively incapable of providing informed consent before surgery using an IRB-approved structured evaluation of their decision-making capacity.[13]

### Baseline Physical and Cognitive Status Before Surgery

The baseline physical and cognitive status of patients was obtained by a research assistant via either phone interview (if undergoing elective surgery) or in-person interview (if undergoing emergent surgery, or in the event that a phone interview could not be completed). The following instruments were used: (1) Activities of Daily Living,[14] which assesses basic physical function (e.g., bathing, dressing); (2) Instrumental Activities of Daily Living,[15] which assesses higher level physical function (e.g., ability to prepare meals and perform housekeeping); (3) Forward and Backward Digit Span tests, which evaluate immediate memory, frontal lobe, and executive function, respectively;[16,17] (4) Letter ("s" and "p") and Category (animals) Word Fluency tests from the Calibrated Ideational Fluency Assessment were used to assess working memory, attention, and executive function[18]; and (5) the Mini-Mental State Exam (MMSE),[19] for in-person interviews or the 26-item version for telephone interviews[20] (converted to the standard 30-item MMSE score). For digit span and verbal fluency tests, raw scores were converted to T-scores (mean = 50, SD = 10), based on population norms controlling for age, sex, and education.[21]

### Other Covariates

The following were obtained preoperatively from the patient interview: demographics; residence and living arrangements; alcohol, tobacco and sedative use; and self-reported memory problems. The following additional data were obtained from the medical record: Charlson comorbidity index,[22] preoperative laboratory values (serum sodium, potassium, bicarbonate, total calcium, albumin, creatinine, blood urea nitrogen, hematocrit, white blood cell count), type and dose of IV anesthetics, total IV fluids received during surgery, and surgery duration (time between patient entry and exit from surgical suite). Hospital charges and length of stay data were also collected.

### Delirium Assessment

Reference raters for the delirium assessment included 2 physician experts who evaluated each patient for delirium using the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV criteria[1]: (1) a board-certified psychiatrist and director of the inpatient psychiatry consultation service with >20 years of clinical experience (KJN) and (2) a 4th year psychiatry resident. The resident psychiatrist performed >25 neuropsychiatric examinations under supervision of the board-certified psychiatrist before starting this study, and then performed DSM-IV–based delirium evaluations on 15 patients in the PACU throughout the study under the direct observation of the board-certified psychiatrist who made her own independent ratings of delirium with excellent inter-rater agreement ($\kappa = 0.93$).

The DSM-IV delirium assessment was based on a neuropsychiatric evaluation of the patient (including MMSE) and all available information gathered in the PACU, including interview of the nurses responsible for the patient. Timing of the PACU delirium assessment was standardized, occurring once the patient reached an Aldrete score[23] ≥9 indicating an appropriate level of wakefulness, hemodynamic and respiratory stability for discharge to phase 2 recovery as an outpatient or transfer to an inpatient unit. This same neuropsychiatric assessment for delirium was repeated daily 5 days per week after surgery for those patients admitted to hospital. The psychiatrists performing all delirium evaluations were blind to preoperative cognitive testing results.

### Outcome Measures

At hospital discharge, digit span and verbal fluency cognitive tests performed preoperatively were repeated by research assistants who were blind to the DSM-IV delirium assessment results. Outcome measures evaluated in this study were: (1) change in cognitive test scores at hospital discharge versus preoperative baseline and (2) disposition at hospital discharge. Since MMSE was used as part of the daily neuropsychiatric assessment,[24] it was not included as an outcome measure. Assessment of Activities of Daily Living and Instrumental Activities of Daily Living were not repeated at hospital discharge due to the confounding effects of hospitalization, rather than delirium, on these measures.

### Statistical Analysis

Fisher exact or Wilcoxon rank-sum tests were used to assess univariate (such as time to evaluation in the PACU) as well as bivariate associations of each of the baseline and demographic covariates in patients with versus without delirium in the PACU. The set of candidate covariates evaluated in this study was determined based on previous literature and knowledge of expected exposure–outcome associations. Not all covariates could be included in the multivariable regression model due to concern for overfitting.[25,26] Hence, a standard multivariable regression model building technique of choosing covariates based on strength of bivariable association with delirium was used. This was operationalized as the covariate having $P < 0.10$ in bivariable analyses of the covariate and the outcome, with the goal of avoiding overfitting by aiming for a ratio of covariates to outcomes of approximately 1 to 10.[25,26] All $P$ values were 2-sided with $P < 0.05$ indicating

statistical significance. Data analyses were performed using STATA v.11(StataCorp, College Station, TX).[27]

To estimate the association of delirium in the PACU (exposure), with the change in cognitive test scores from preoperative baseline to hospital discharge (outcome), linear regression models with random intercepts[28] were used, adjusting for the following covariates: (1) baseline MMSE and (2) surgery duration. There are 4 standard assumptions of any linear regression model: (1) linear relationship between the independent and dependent variables, (2) constant variance of residuals over time and as a function of each covariate, (3) residuals are normally distributed, and (4) residuals are independent. Our linear mixed effects model is an extension to the standard linear regression model, which allows for residuals to be correlated within individuals over time. Appropriateness of assumptions and model fit was assessed via graphical methods, including plots of adjusted versus observed outcomes and adjusted values versus residuals at each time point.

For evaluating the effect of PACU delirium (exposure) on discharge location, logistic multivariable regression models were used, adjusting for the following covariates: (1) baseline MMSE, (2) surgery duration, and (3) preoperative residence (e.g., home, nursing home).

As a secondary analysis to evaluate for a dose–response relationship of delirium duration,[29] associations with each of the above outcome measures were evaluated for the following discrete subgroups of admitted patients: (1) patients who were never delirious during the hospitalization, (2) patients with delirium only in the PACU (i.e., resolution on postoperative day 1), and (3) patients with delirium that started in the PACU and extended into the postoperative hospitalization on the inpatient ward.

## RESULTS

Figure 1 outlines the consort flow diagram. The participants had a mean age of 79 years, 58% were females, 89% were Caucasian, and 45% reported at least some college education (Table 1). Most (82%) were retired, 78% were living in their own homes, and 23% were living alone before surgery. Anesthetic technique was comparable among subjects and for >90% of the sample, consisted of propofol induction followed by maintenance with isoflurane, narcotic, and muscle relaxation as needed. Forty-six percent ($n$ = 42) of patients received midazolam.

On reaching an Aldrete score ≥9, the prevalence of delirium in the PACU was 45%. The median interquartile range (IQR) time from operating room exit to start of neuropsychiatric examination in the PACU for those patients determined to be delirious versus not delirious was 48 (33–62) vs 42 (28–53) minutes ($P$ = 0.70). Table 1 includes the bivariate analyses of preoperative factors associated with delirium in the PACU. Other covariates collected in this study but not reported in Table 1 were not associated with delirium, including the doses of narcotic (administered both intraoperatively and in the recovery room), propofol, and midazolam.

After PACU delirium assessment, 24 patients (of whom 38% were delirious) were discharged home the same day (Fig. 1). Of the 67 admitted patients, 58 had at least 1 delirium assessment on subsequent hospital days, for a total of 224 days of observation, with delirium identified on 32% of those days. Of admitted patients who did not have delirium in the PACU, 23 of 28 (82%) had no delirium on any assessment during their hospitalization, whereas the remaining 5 (18%) developed new onset delirium in subsequent days at a median (IQR) of 1 (1–3) days of observation after surgery. Of the 30 admitted patients who had delirium in the PACU, 16 (53%) resolved on our next day of observation on the hospital ward, whereas the remaining 14 (47%) patients continued to have subsequent days of delirium. The median (IQR) number of consecutive positive delirium assessments was 3 (2–6). Six patients (10% of all admitted patients) were delirious on the day of hospital discharge (3 discharged to an institution and 3 discharged to home).

Of the 67 inpatients, 55 (82%) completed repeat cognitive testing at hospital discharge. Twelve were not tested due to being discharged over the weekend (9), unavailability of patient to complete cognitive testing on day of discharge (2), and patient declining to complete (1). Another 5 patients who were delirious in the PACU lacked cognitive testing at baseline due to lack of time before surgery or patient declining testing. Table 2 presents the unadjusted outcomes for these patients. In adjusted analyses, including baseline MMSE and surgery duration, PACU delirium was significantly associated with decline in the verbal fluency cognitive test (for categories) from baseline testing (Table 3—adjusted difference [95% CI] for change in T-score: 6.02 [−10.58 to −1.45]; $P$ = 0.01). This association remained statistically significant after excluding patients found to be delirious at hospital discharge. After adjusting for MMSE, surgery duration and residence before admission, the effect of delirium in the PACU remained large in magnitude but no longer reached statistical significance in association with discharge to an institution (versus home) (Table 3—adjusted odds ratio [95% confidence interval]: 4.2 [0.9–19.7]; $P$ = 0.07).

In secondary analyses of only those patients admitted after surgery, a multivariable regression model compared the outcomes of patients (1) who had no delirium at any time during their hospital stay ($n$ = 23; Fig. 1) with (2) those patients who had delirium only in the PACU and did not have delirium on the hospital ward, ($n$ = 16) versus (3) those with delirium both in the PACU and on subsequent hospital days ($n$ = 14). This analysis (Table 4) demonstrated that delirium only in the PACU was associated with worse verbal fluency (category) ($P$ = 0.07) and with a greater probability of discharge to an institution (26% vs 3%; $P$ = 0.05) when compared with patients who had no delirium diagnosis at any time. Pairwise comparison among the 3 patient groups with different durations of delirium ("never" versus "PACU only" versus "both PACU and hospital ward" delirium) revealed outcomes for the "PACU only" group were intermediate between the other 2 groups for the following outcomes (Table 4): (1) verbal category fluency change from baseline (adjusted T-score: 2.74 vs −2.00 vs −8.40), (2) digit span backward change from baseline (adjusted T-score: −1.17 vs −2.60 vs −7.90), and (3) probability of discharge to institution (3% vs 26% vs 39%).

## DISCUSSION

This study demonstrates that elderly postoperative patients can be successfully evaluated for delirium in the PACU setting after reaching an Aldrete score ≥9. The prevalence of

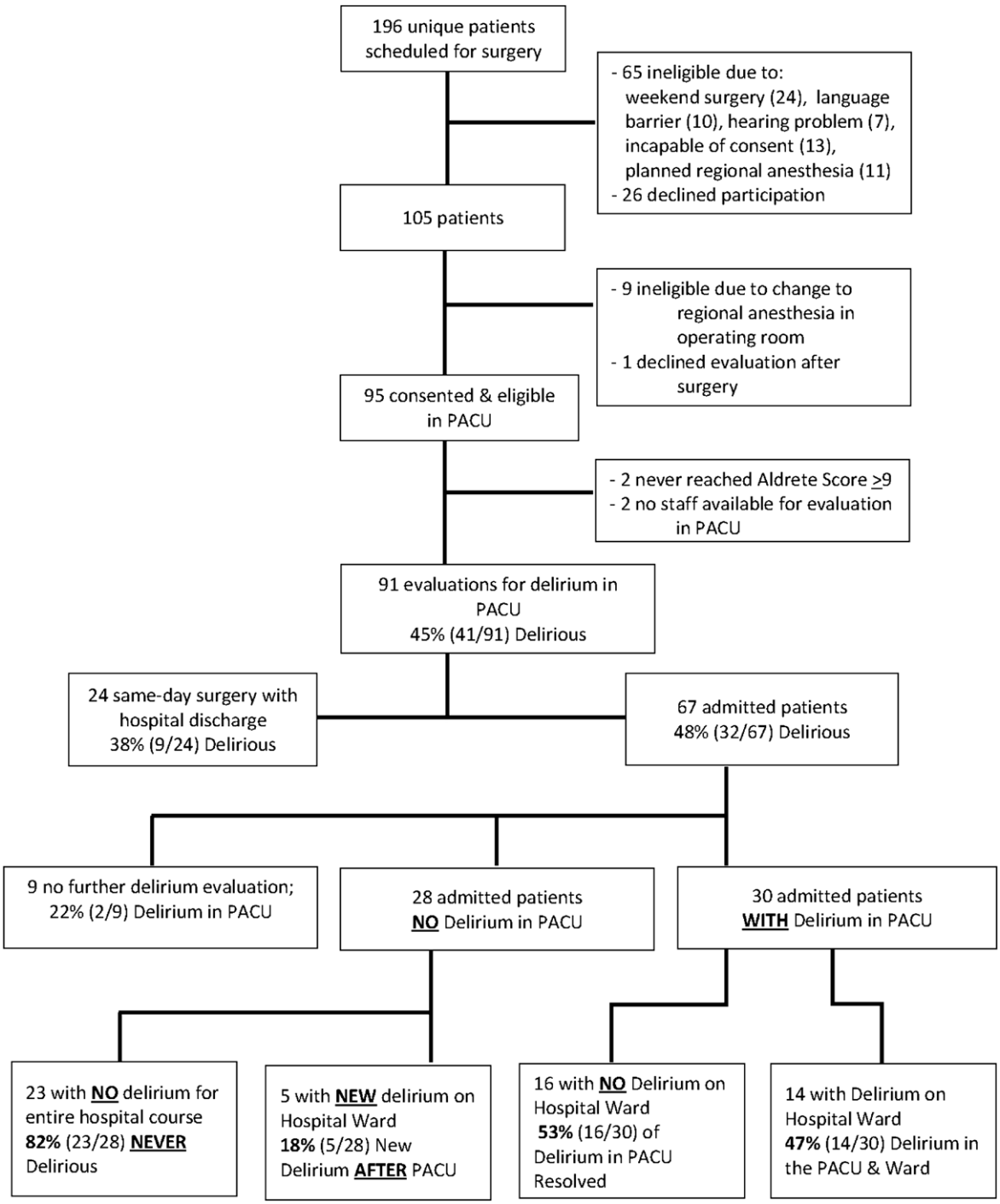


**Figure 1.** Consort flow diagram. PACU = postanesthesia care unit.

delirium in this sample was 45%. This phenomenon was not universal: more than half of elderly patients were not delirious despite general anesthesia, and 82% of these patients remained delirium free throughout their hospitalization. Delirium in the PACU was independently associated with decreased cognitive performance, from preoperative baseline, in verbal category fluency (a measure of working memory and frontal lobe and executive function), and possibly with institutionalization at hospital discharge. Half of patients (53%) with PACU delirium experienced resolution within 1 day of inpatient follow-up after surgery, while the remainder continued to have delirium during subsequent assessments with a median duration of 3 days. Delirium occurring only in the PACU (and not on the hospital ward) appeared to have negative consequences, demonstrating a potential dose–response relationship between delirium duration in the postoperative setting and negative outcomes.

Early diagnosis of delirium in the PACU is associated with delirium on hospital units. Of 19 episodes of delirium identified during the subsequent hospitalization, 74% were preceded by delirium in the PACU. In contrast to prior research,[11] our findings suggest that the majority of

**Table 1. Patient Characteristics**

| | All patients ($n$ = 91) | Delirium in recovery room ($n$ = 41) | No delirium in recovery room ($n$ = 50) |
|---|---|---|---|
| Sociodemographics | | | |
| Age, mean (SD), y | 79 (6) | 79 (6) | 77 (5) |
| Female | 53 (58%) | 26 (63%) | 27 (54%) |
| Caucasian | 81 (89%) | 35 (85%) | 46 (92%) |
| Education level | | | |
| Less than high school | 25 (28%) | 14 (34%) | 11 (22%)* |
| High school | 25 (28%) | 15 (37%) | 10 (20%) |
| Some college or college graduate | 30 (33%) | 10 (24%) | 20 (40%) |
| Post-graduate training | 11 (12%) | 2 (5%) | 9 (18%) |
| Employment status, retired | 75 (82%) | 36 (88%) | 39 (78%)* |
| Residence, living in own home | 71 (78%) | 28 (68%) | 43 (86%)* |
| Living arrangement, before surgery | | | |
| Alone | 21 (23%) | 11 (27%) | 10 (20%) |
| Spouse | 36 (40%) | 16 (39%) | 20 (40%) |
| Other | 34 (37%) | 14 (34%) | 20 (40%) |
| Status before surgery | | | |
| Charlson comorbidity index, mean(SD) | 2.2 (2.2) | 2.6 (2.6) | 1.9 (1.8) |
| ASA physical status classification score, >3 | 58 (64%) | 31 (76%) | 27 (54%)† |
| Activities of daily living, mean (SD)[a] | 5.5 (1.0) | 5.3 (1.3) | 5.6 (0.6) |
| Instrumental activities of daily living, mean(SD)[b] | 7.2 (1.4) | 6.9 (1.8) | 7.5 (1.0) |
| Self-reported memory problems | 37 (41%) | 21 (51%) | 16 (32%)† |
| Presurgery cognitive testing | | | |
| Verbal fluency (standardized T-score)[c,d] | | | |
| S word list, mean (SD) | 44 (11) | 44 (10) | 45 (12) |
| P word list, mean (SD) | 44 (12) | 44 (12) | 45 (12) |
| Animal word list category, mean (SD) | 47 (11) | 47 (11) | 46 (11) |
| Digit span (standardized T-score)[c] | | | |
| Forward, mean (SD)[d] | 48 (10) | 47 (9) | 49 (11) |
| Backward, mean (SD)[e] | 49 (12) | 47 (11) | 50 (12) |
| Mini-mental state exam score[e] mean (SD) | 25 (3) | 24 (4) | 26 (2)‡ |
| Surgery characteristics | | | |
| Type of surgery | | | |
| Orthopedics | 31 (34%) | 15 (37%) | 16 (32%) |
| Urinary and gynecologic | 25 (28%) | 8 (20%) | 17 (34%) |
| Gastrointestinal | 10 (11%) | 6 (15%) | 4 (8%) |
| Other | 25 (28%) | 12 (29%) | 13 (26%) |
| Surgery duration, mean (SD), h | 3.1 (1.7) | 3.7 (1.8) | 2.6 (1.5)‡ |

[a]Activities of daily living based is scored from a minimum of 0 to a maximum of 6 which indicates full independence.
[b]Instrumental activities of daily living is scored from 0 to 8 with 8 indicating full independence.
[c]Raw test scores for verbal fluency and digit span were transformed to T-scores based on population norms standardized for age, sex, education, and race with mean = 50 and SD = 10.
[d]$n$ = 74 with 41 without delirium and 33 with delirium: 17 patients did not complete verbal fluency tasks and digit span forwards preoperatively due to a lack of time before surgery or patient declining.
[e]$n$ = 73 with 41 without delirium and 32 with delirium: 18 patients did not complete digit span backwards preoperatively due to a lack of time before surgery or patient declining.
[e]Mini-mental state examination (MMSE) scores range from 0 to 30 with 30 indicating good cognitive function; MMSE was missing in 3 patients, all found to be delirious in the postanesthesia care unit.
$P$ values are calculated from Fisher exact test or a Wilcoxon rank-sum test: *$P$ < 0.05; †$P$ = 0.05; ‡$P$ < 0.01.

**Table 2. Cognitive and Health Care Resource Utilization Outcomes for Inpatients**

| | All patients | Delirium in recovery room | No delirium in recovery room |
|---|---|---|---|
| Cognitive testing at discharge | | | |
| Verbal fluency (standardized T-score)[a,b] | | | |
| S word list, mean (SD) | 42 (12) | 41 (12) | 44 (11) |
| P word list, mean (SD) | 43 (11) | 40 (10)* | 46 (10)* |
| Animal word list, mean (SD) | 46 (10) | 42 (10)† | 49 (8)† |
| Digit Span (standardized T-score)[a,c] | | | |
| Forward, mean (SD) | 46 (12) | 45 (12) | 47 (13) |
| Backward, mean (SD) | 44 (9) | 40 (9)† | 47 (9)† |
| Health care resource utilization | | | |
| Discharge to institution versus home | 18 (20%) | 15 (37%)‡ | 3 (6%)‡ |

[a]Raw test scores for verbal fluency and digit span were transformed to T-scores based on population norms standardized for age, sex, education, and race with mean = 50 and SD = 10.
[b]$n$ = 55 with 28 no delirium and 27 with delirium: 12 patients did not complete verbal fluency tasks postoperatively before discharge.
[c]$n$ = 54 with 28 no delirium and 26 with delirium: 13 patients did not complete digit span tasks postoperatively before discharge.
$P$ values are calculated from Fisher exact test or a Wilcoxon rank-sum test: *$P$ < 0.01;†$P$ < 0.05; ‡$P$ < 0.001.

**Table 3. Association of Recovery Room Delirium with Change in Cognitive and Health Care Resource Utilization Outcomes**

| | Unadjusted | | | Adjusted[c] | | |
|---|---|---|---|---|---|---|
| **Change (SE) in cognitive T-scores (hospital discharge minus presurgery baseline)[a,b]** | | | | | | |
| | Recovery room delirium (*n* = 22) | No recovery room delirium (*n* = 28) | *P* | Recovery room delirium (*n* = 22) | No recovery room delirium (*n* = 28) | *P* |
| Verbal fluency (letters "s" and "p") | −1.55 (1.47) | −0.02 (1.31) | 0.44 | −1.55 (1.47) | −0.02 (1.31) | 0.44 |
| Verbal fluency (animal category) | −4.91 (1.74) | 1.11 (1.54) | 0.01 | −4.91 (1.74) | 1.11 (1.54) | 0.01 |
| Digit span forward | −2.33 (2.09) | −0.50 (1.81) | 0.51 | −2.33 (2.09) | −0.50 (1.81) | 0.51 |
| Digit span backward | −5.25 (2.04) | −2.07 (1.72) | 0.23 | −5.25 (2.04) | −2.07 (1.72) | 0.23 |
| **Difference in health care resource utilization with and without recovery room delirium, *n* = 67** | | | | | | |
| | Unadjusted | | *P* | Adjusted[d] | | *P* |
| Discharge to institution, odds ratio (95% confidence interval) | 9.0 (2.4–34.1) | | 0.001 | 4.2 (0.9–19.7) | | 0.07 |

PACU = postanesthesia care unit.

[a]Adjusted change in cognitive scores based on linear regression model with random intercept; the equation is $Y_{ij} = \beta_0 + \alpha_{0i} + \beta_1 \times \text{time} + \beta_2 \times \text{PACU}_{\text{delirium}} + \beta_3 \times \text{time} \times \text{PACU}_{\text{delirium}} + e_{ij}$, where $Y_{ij}$ represents the measurement for the ith patient at the jth timepoint.

[b]A total of 22 delirious patients had both preoperative and discharge testing with 10 patients missing 1 set of testing for verbal fluency; digit span forward included 21 delirious patients with 11 patients missing 1 set of testing and 20 delirious patients for digit span backward with 12 patients missing 1 set of testing; a total of 28 nondelirious patients had both preoperative and discharge testing with 7 patients missing 1 set of testing.

[c]Adjusted for baseline Mini-Mental State Exam (MMSE) and surgery duration with no changes demonstrated from the unadjusted results.

[d]Adjusted for baseline MMSE, residence before admission, and surgery duration.

episodes of postoperative delirium are temporally associated with recovery from anesthesia and begin in the PACU without a period of lucidity.

The 45% prevalence of PACU delirium in this study is the same as observed by Sharma et al.[12] who evaluated 50 elderly patients exclusively undergoing hip surgery. Our data demonstrate that delirium prevalence is high in elderly patients, even across a wide variety of major surgical procedures (mean surgery duration in our study was 3 hours) performed under general anesthesia.

Sharma et al.[12] also reported that 75% of patients with delirium in the PACU had delirium on subsequent inpatient days. In a study of 910 younger patients (mean age 50 years) recovering from general anesthesia after a wide variety of surgical procedures, Radtke et al.[30] documented a delirium prevalence of 11% in the PACU and noted that 84% of all delirium episodes measured on subsequent inpatient days were preceded by delirium in the PACU. The similarity between our findings and these 2 prior studies underscores the link between delirium in the PACU after general anesthesia and delirium during subsequent postoperative days on the ward.

The finding that patients with delirium in the PACU declined in cognitive performance on verbal category fluency between admission and hospital discharge, even after controlling for baseline MMSE and surgery duration, suggests that the impact of even brief episodes of delirium on cognition may be important; this has been demonstrated in studies that followed cognitive function of older patients after cardiac surgery.[10,31] Initiating monitoring for delirium on the first postoperative day, instead of in the PACU, in this sample would have missed 53% of the patients who experienced delirium, suggesting that beginning surveillance early after general anesthesia may be important.

The decline in cognitive performance on verbal category fluency testing, but not verbal letter fluency testing, is likely due to the more cognitively taxing nature of the category test.[32] Recent neuroimaging investigations suggest that category and letter fluency are dependent on partially distinct neural networks with category fluency involving temporal lobe activation and letter fluency involving frontal lobe activation.[33] Studies have shown that decreased verbal fluency in general, and category word fluency in particular, are associated with greater functional impairment among older adults.[34]

**Table 4. Change in Cognitive and Health Care Resource Utilization Outcomes by Delirium Subgroup**

| | Never delirious (*n* = 23) | Recovery room only delirium (*n* = 16) | Recovery room and hospital delirium (*n* = 14) | *P*-value for recovery room only versus never delirium | *P*-value for recovery room only versus recovery room and hospital delirium |
|---|---|---|---|---|---|
| Change (SE) in cognitive T-Scores (hospital discharge minus presurgery baseline)[a] | | | | | |
| Verbal fluency (letters "s" and "p") | 0.46 (1.34) | 1.79 (1.86) | −5.55 (2.03) | 0.56 | **0.008** |
| Verbal fluency (animal category) | 2.74 (1.55) | −2.00 (2.15) | −8.40 (2.36) | 0.07 | 0.05 |
| Digit span forward | −0.96 (1.98) | −0.73 (2.86) | −4.10 (3.00) | 0.95 | 0.42 |
| Digit span backward | −1.17 (1.84) | −2.60 (2.79) | −7.90 (2.79) | 0.67 | 0.18 |
| Difference in health care resource utilization[b] | | | | | |
| Discharge to institution as a probability (95% confidence interval) | 3% (0%–10%) | 26% (1%–51%) | 39% (0%–81%) | 0.05 | 0.48 |

PACU = postanesthesia care unit.

[a]Adjusted change in cognitive scores based on linear regression model with random intercept and adjusted for baseline Mini-Mental State Exam (MMSE) and surgery duration; The model equation is $Y_{ij} = \beta_0 + \alpha_{0i} + \beta_1 \times \text{time} + \beta_2 \times \text{PACU}_{\text{delirium}} + \beta_3 \times \text{time} \times \text{PACU}_{\text{delirium}} + e_{ij}$, where $Y_{ij}$ represents the measurement for the ith patient at the jth timepoint.

[b]Adjusted for baseline MMSE, residence before admission, and surgery duration.

Our result is similar to a prior multicenter study that measured postoperative changes in cognitive function and demonstrated an association between delirium in the postoperative course and cognitive dysfunction 7 days later[35] and another recent study that documented cognitive decline after postoperative delirium up to 6 months later.[10] Other investigators studying the impact of delirium after cardiac surgery used cognitive testing similar to our study, including digit span (forward and backward) and verbal letter fluency and also found that category fluency was particularly affected.[36,37] They compared the unadjusted change in scores in delirious versus nondelirious patients, demonstrating a significant change in a composite digit span and a trend toward a difference in verbal letter fluency. An adjusted analysis was not provided to control for baseline factors, such as surgery duration and baseline MMSE, which were found to be important confounders in our current study.

An important strength of this current study is the use of expert reference raters who prospectively and rigorously assessed delirium according to DSM-IV criteria using a neuropsychiatric examination, concurrent with independent and blinded prospective screening evaluations of baseline and discharge cognitive function. To our knowledge, this is the first report using this kind of rigorous PACU examination in the delirium literature. Prior studies have used screening tools not yet validated in this patient population that were based on nursing observation or rating of the CAM algorithm in the PACU,[12,30] and not on direct and prospective neuropsychiatric examination of the patient in this setting.

The current study has limitations. First, our sample size reduces the power to detect clinically important differences in some of the outcomes including some of the cognitive measures. However, our sample size is comparable with several prior studies of postoperative delirium.[12,35–37] We caution readers to interpret the associations of PACU delirium and patient outcomes as hypothesis-generating for future studies. However, we have successfully demonstrated the feasibility of delirium evaluation once an Aldrete score of ≥9 is obtained after general anesthesia. Second, cognitive assessments were not always possible in a relatively small number of the pre- and postsurgery assessments. However, comprehensive efforts were made to minimize missed assessments, with our rates being similar to prior studies.[10,30,31,35] Ongoing delirium might account for poorer performance on cognitive testing at hospital discharge; however, our results persisted even after excluding those patients in a sensitivity analysis. Finally, our evaluation of only in-hospital outcome measures does not permit insights into any long-term associations of PACU delirium on cognition and subsequent health care utilization. Future studies should include prospective long-term follow-up of individuals with delirium found in the PACU setting as well as the hospital ward.

In conclusion, this prospective study of 91 elderly patients undergoing general anesthesia and surgery identified a 45% prevalence of delirium in the PACU. The majority of patients with postoperative delirium had delirium starting in the PACU. Hence, recognizing delirium in the PACU may be important for identifying patients at higher risk of in-hospital harms (e.g., falls), as well as cognitive impairment and institutionalization at hospital discharge. Early identification and intervention for delirium in the PACU setting requires evaluation of its potential to improve patient outcomes.

## DISCLOSURES

**Name:** Karin J. Neufeld, MD, MPH.
**Contribution:** This author helped design the study, conduct the study, analyze the data, and write the manuscript.
**Attestation:** Karin J. Neufeld has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**Name:** Jeannie-Marie S. Leoutsakos, PhD, MHS.
**Contribution:** This author helped analyze the data and write the manuscript.
**Attestation:** Jeannie-Marie S. Leoutsakos has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**Name:** Frederick E. Sieber, MD.
**Contribution:** This author helped design the study, conduct the study, analyze the data, and write the manuscript.
**Attestation:** Frederick E. Sieber has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**Name:** Brett L. Wanamaker.
**Contribution:** This author helped design the study, conduct the study, and write the manuscript.
**Attestation:** Brett L. Wanamaker has seen the original study data and approved the final manuscript.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**Name:** Jennifer J. Gibson Chambers, MS.
**Contribution:** This author helped design the study, conduct the study, analyze the data, and write the manuscript.
**Attestation:** Jennifer J. Gibson Chambers has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**Name:** Veena Rao.
**Contribution:** This author helped design the study, conduct the study, and write the manuscript.
**Attestation:** Veena Rao has seen the original study data and approved the final manuscript.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**Name:** David J. Schretlen, PhD.
**Contribution:** This author helped design the study, analyze the data, and write the manuscript.
**Attestation:** David J. Schretlen has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
**Conflicts of Interest:** David J. Schretlen received royalties from Psychological Assessment Resources, Inc. Under an agreement with Psychological Assessment Resources, Inc., Dr. Schretlen receives royalties for sales of a test used in this study. The terms of this agreement are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.

**Name:** Dale M. Needham, MD, PhD.
**Contribution:** This author helped design the study, conduct the study, analyze the data, and write the manuscript.
**Attestation:** Dale M. Needham has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
**Conflicts of Interest:** The author has no conflicts of interest to declare.
**This manuscript was handled by:** Gregory J. Crosby, MD.

## ACKNOWLEDGMENTS

The authors would also like to acknowledge Drs. Jose Rios Robles and Dhruv Joshi who were instrumental in data collection for this study, and Ms. Caroline Lassen-Greene for assistance with scoring the cognitive tests.

## REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association, 1995:223
2. Pun BT, Ely EW. The importance of diagnosing and managing ICU delirium. Chest 2007;132:624–36
3. Inouye SK. Delirium in older persons. N Engl J Med 2006;354:1157–65
4. Siddiqi N, House A. Delirium: an update on diagnosis, treatment and prevention. Clin Med 2006;6:540–3
5. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr, Inouye SK, Bernard GR, Dittus RS. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA 2004;291:1753–62
6. Young J, Inouye SK. Delirium in older people. BMJ 2007;334:842–6
7. Marcantonio E, Ta T, Duthie E, Resnick NM. Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. J Am Geriatr Soc 2002;50:850–7
8. Sanders RD, Pandharipande PP, Davidson AJ, Ma D, Maze M. Anticipating and managing postoperative delirium and cognitive decline in adults. BMJ 2011;343:d4331
9. Rudolph JL, Jones RN, Rasmussen LS, Silverstein JH, Inouye SK, Marcantonio ER. Independent vascular and cognitive risk factors for postoperative delirium. Am J Med 2007;120:807–13
10. Saczynski JS, Marcantonio ER, Quach L, Fong TG, Gross A, Inouye SK, Jones RN. Cognitive trajectories after postoperative delirium. N Engl J Med 2012;367:30–9
11. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth 2009;103 Suppl 1:i41–46
12. Sharma PT, Sieber FE, Zakriya KJ, Pauldine RW, Gerold KB, Hang J, Smith TH. Recovery room delirium predicts postoperative delirium after hip-fracture repair. Anesth Analg 2005;101:1215–20
13. Appelbaum PS. Assessment of patient's competence to consent to treatment. N Engl J Med 2007;357:1834–40
14. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. Gerontologist 1970;10:20–30
15. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179–86
16. Baddeley AD. Working Memory. Oxford, UK: Oxford University Press, 1986
17. Hester RL, Kinsella GJ, Ong B. Effect of age on forward and backward span tasks. J Int Neuropsychol Soc 2004;10:475–81
18. Schretlen DJ, Vannorsdall TD. Calibrated Ideational Fluency Assessment (CIFA) Professional Manual. Lutz, FL: Psychological Assessment Resources Inc., 2010
19. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98
20. Newkirk LA, Kim JM, Thompson JM, Tinklenberg JR, Yesavage JA, Taylor JL. Validation of a 26-point telephone version of the Mini-Mental State Examination. J Geriatr Psychiatry Neurol 2004;17:81–7
21. Schretlen DJ, Testa SM, Pearlson GD. Calibrated Neuropsychological Normative System Professional Manual. Lutz, FL: Psychological Assessment Resources, Inc., 2010
22. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83
23. Aldrete JA. Modifications to the postanesthesia score for use in ambulatory surgery. J Perianesth Nurs 1998;13:148–55
24. Lipowski ZJ. Delirium: Acute Confusional States. New York, NY: Oxford University Press, 1990
25. Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. Ann Intern Med 1993;118:201–10
26. Harrell RE, Lee KL, Matchar DB, Reichert TA. Regression models for prognostic prediction: advantages, problems, and suggested solutions. Cancer Treat Rep 1985;69:1071–77
27. StataCorp. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP, 2009
28. Fitzmaurice GM, Laird NM, Ware JH. Applied Longitudinal Analysis. Hoboken, NJ: Wiley-Interscience, 2004:506. Available at: http://www.loc.gov/catdir/toc/wiley041/2004040891.html. Accessed May 14, 2013
29. Girard TD, Jackson JC, Pandharipande PP, Pun BT, Thompson JL, Shintani AK, Gordon SM, Canonico AE, Dittus RS, Bernard GR, Ely EW. Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. Crit Care Med 2010;38:1513–20
30. Radtke FM, Franck M, MacGuill M, Seeling M, Lütz A, Westhoff S, Neumann U, Wernecke KD, Spies CD. Duration of fluid fasting and choice of analgesic are modifiable factors for early postoperative delirium. Eur J Anaesthesiol 2010;27:411–6
31. Monsch AU, Bondi MW, Butters N, Salmon DP, Katzman R, Thal LJ. Comparisons of fluency tasks in detection of dementia of the Alzheimer's type. Arch Neurol 1992;49;1253–8
32. Birn RM, Kenworthy L, Case L, Caravella R, Jones TB, Bandettini PA, Martin A. Neural systems supporting lexical search guided by letter and semantic category cues: a self-paced overt response fMRI study of verbal fluency. Neuroimage 2010;49:1099–107
33. Koehler M, Kliegel M, Wiese B, Bickel H, Kaduszkiewicz H, van den Bussche H, Eifflaender-Gorfer S, Eisele M, Fuchs A, Koenig HH, Leicht H, Luck T, Maier W, Moesch E, Riedel-Heller S, Tebarth F, Wagner M, Weyerer S, Zimmermann T, Pentzek M; AgeCoDe study group. Malperformance in verbal fluency and delayed recall as cognitive risk factors for impairment in instrumental activities of daily living. Dement Geriatr Cogn Disord 2011;31:81–8
34. Rudolph JL, Jones RN, Grande LJ, Milberg WP, King EG, Lipsitz LA, Levkoff SE, Marcantonio ER. Impaired executive function is associated with delirium after coronary artery bypass graft surgery. J Am Geriatr Soc 2006;54:937–41
35. Rudolph JL, Marcantonio ER, Culley DJ, Silverstein JH, Rasmussen LS, Crosby GJ, Inouye SK. Delirium is associated with early postoperative cognitive dysfunction. Anaesthesia 2008;63:941–7
36. Brown LJ, Ferner HS, Robertson J, Mills NL, Pessotto R, Deary IJ, MacLullich AM. Differential effects of delirium on fluid and crystallized cognitive abilities. Arch Gerontol Geriatr 2011;52:153–8
37. Robinson TN, Raeburn CD, Tran ZV, Angles EM, Brenner LA, Moss M. Postoperative delirium in the elderly: risk factors and outcomes. Ann Surg 2009;249:173–8