Published in final edited form as:

J Perianesth Nurs. 2011 August ; 26(4): 231–241. doi:10.1016/j.jopan.2011.03.001.

Factors Associated with Recovery from Early Postoperative Delirium

Susan K. DeCrane, PhD, RN[Assistant Professor],

Purdue University School of Nursing, 502 North University Street, West Lafayette, Indiana 47907-2069

Laura Sands, PhD,

Purdue University School of Nursing

Meghan Ashland, MS, RN, ANP-BC,

Purdue University School of Nursing

Eunjung Lim, MS,

Purdue University Department of Statistics

Tiffany L. Tsai, BA,

University of California, San Francisco, Department of Anesthesia and Perioperative Care

Sudeshna Paul, PhD, and

Harvard Medical School, Department of HealthCare Policy

Jacqueline M. Leung, MD, MPH

University of California, San Francisco, Department of Anesthesia and Perioperative Care

Abstract

Background—Delirium has been shown to occur in 14-56% of postoperative, hospitalized elderly persons, making it one of the most common postoperative complications for the older patient.

Objective—The aim of this study was to determine factors associated with recovery of delirium from postoperative day one (POD 1) to postoperative day two (POD 2). The hypothesis was that those with less pain are more likely to recover from delirium by POD 2.

Methods—Patients aged 65 or older who were scheduled for noncardiac surgery, spoke English, and who developed delirium on POD 1 as detected by the Confusion Assessment Method (CAM) were included. Total sample size was 176 patients. Postoperative delirium on day two was also measured with the CAM. Postoperative pain was assessed on POD 1 and 2 using the Numeric Rating Scale (NRS). Postoperative pain medications were abstracted from patient medical records.

Results—One hundred seventy six patients developed delirium on POD 1 with 66 (38%) recovering from delirium by POD 2. The mean age of those patients who recovered from delirium was 72.5 ± 5.7 (N=66) while the mean age of those patients who did not recover from delirium was 75.9 ± 6.5 (N=110). Multivariate logistic regression revealed that patients less than age 75

© 2011 The American Society of PeriAnesthesia Nurses. Published by Elsevier Inc. All rights reserved.

Corresponding Author: Susan K. DeCrane, PhD, RN, Assistant Professor, Purdue University School of Nursing, 502 North University Street, West Lafayette, Indiana 47907-2069, Phone: 765-494-4028, Fax: 765-494-6339, sdecrane@purdue.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

were more likely to recover from delirium (OR=2.31; 95% CI=1.18-4.53; p=0.015) as were patients who had pain scores of less than 5 on day two (OR=2.59; 95% CI=1.26-5.35; p=0.0098).

Conclusion—Patients with lower pain levels (NRS 4 or less) were more likely to recover from delirium on POD 2. The type of postoperative pain therapy (the use or non-use of patient controlled analgesia) was not related to the recovery of delirium. The results suggest that aggressive pain management in the first 48 hours postoperatively may be important in promoting recovery from postoperative delirium.

Keywords

Postoperative delirium; pain management; geriatrics; research

Delirium is defined as an acute disturbance of consciousness characterized by a fluctuating change of cognitive capacity. It has been shown to occur in 14-56% of postoperative hospitalized elderly patients and is one of the most frequent postoperative complications of older surgical patients.^[1,2] Clinical features of delirium include inattention, disorganized thinking, altered level of consciousness, cognitive deficits, perceptual disturbances, psychomotor disturbances, altered sleep-wake cycle, and emotional disturbances.^[2]

Delirium can increase risk for poor outcomes.^[3, 4] Mortality rates among hospitalized patients with delirium range from 22-76%, with the one year mortality rate being 35-40%.^[2] In a recent study, patients with persistent delirium were 2.9 times more likely to die after 1 year compared to those whose delirium had resolved.^[5] Delirium is costly with nearly half of delirious patients' length of stay attributable to delirium.^[2] Those with delirium have average costs per day that are 2.5 times more costly than those patients without delirium.^[2] Total hospital cost attributed to delirium ranges from \$16,303 to \$64,421 per patient.^[2] The national burden of delirium on the entire healthcare system ranges from \$38 billion to \$152 billion each year.^[6]

Patients that do not resolve delirium by discharge have higher rates of nursing home placement, rehospitalization, and death.^[7-9] In order to improve outcomes, there is a need to determine characteristics associated with recovery from early postoperative delirium in hospitalized elderly patients. Prior studies have identified non-modifiable (e.g. age)^[2, 4, 10-13] and modifiable risks (e.g. dehydration)^[2,14] and precipitating factors (e.g. surgery or medications)^[2, 15-20] associated with development of delirium; however, little is known about factors associated with early recovery of delirium.

The conceptual framework for this study builds upon a biological model of known risk factors for delirium among postoperative older adults as a specific risk group of hospitalized older adults. Current evidence supports concepts of pre-existing patient factors, intraoperative factors, and postoperative factors in this model, specifically finding increased occurrence of delirium with use of meperidine,^[18-19] abnormal blood pressure^[19] higher pain scores at rest,^[15] and moderate or severe pain levels and increase in pain from baseline to post-operative day (POD) 1.^[17] The current evidence further demonstrates that undertreatment of pain can raise the risk of multiple complications, including delirium, in the postoperative period.^[21] Knowledge of the unique context of factors in surgical patients has been directed at prevention of delirium in the postoperative period. More knowledge is needed regarding specific early post-operative period (48 hours) interventions that may lead to recovery from delirium once it occurs, and whether early recovery from delirium can attenuate negative outcomes associated with postoperative delirium as well as decrease hospital length-of-stay (LOS).

The purpose of this study was to determine factors associated with recovery from early postoperative delirium. Early postoperative delirium may have different etiologies than delirium that develops later in the recovery period, and may require different types of intervention. [22] Identifying factors that are associated with early postoperative delirium could assist in the development of hospital-based interventions that could possibly reduce the duration of delirium before patient discharge. Our hypothesis was that those with lower Numeric Rating Scale (NRS) pain levels are more likely to recover from delirium by postoperative day 2 (POD 2) as compared to those with higher NRS scores.

Methods

Sample

The study was conducted at the University of California, San Francisco Medical Center from 2001 to 2007. After approval by the Institutional Review Board for human research, informed consent was obtained preoperatively from those patients meeting the inclusion criteria. Patients were selected from an ongoing larger study investigating the pathophysiology of postoperative delirium in older surgical patients. The sample was comprised of English speaking patients 65 years of age or older who were scheduled to undergo major elective non-cardiac surgery requiring anesthesia and who were expected to have a length-of-stay (LOS) of greater than 48 hours postoperatively. Common surgical procedures included knee arthroplasty, hip arthroplasty, prostatectomy, laminectomy/diskectomy, foraminotomy/spinal fusion, femoral artery bypass graft, hepatectomy, nephrectomy, glossectomy, cystectomy, and ureterostomy. Patients who did not or could not provide informed consent were excluded from the sample. A subset of this sample (109 from a larger sample of 333) was included in a previous manuscript evaluating the predictors of postoperative delirium that included the measurements of pain, postoperative medications, and other co-variables. [17]

Timing of Assessments

Patients were personally interviewed three times (preoperatively, 24 hours postoperatively, and 48 hours postoperatively) by the same trained research assistant. Preoperative interviews occurred less than 48 hours prior to surgery and were conducted in the preoperative clinic. These interviews consisted of a medical history focusing on neurological status, assessment of cognitive status, pain, functional status, and assessment of depressive symptoms. The first postoperative assessment occurred 24 hours after surgery and focused on the patient's cognitive status and pain. The second postoperative assessment also focused on the patient's cognitive status and pain and occurred 48 hours after the surgery. Both postoperative assessments were done in the patients' hospital rooms between the hours of 9AM and noon.

Dependent Variable

The dependent variable was postoperative delirium occurring within 24 hours of surgery that resolved by 48 hours postoperatively. This variable represents whether or not the patient recovered from delirium on POD 2. Delirium was measured by trained interviewers using the Confusion Assessment Method (CAM). To ensure consistency in the evaluation, each patient was evaluated by the same research assistant for all three interviews. The research assistant was trained in the use of the CAM based on a detailed manual developed by Inouye *et al.* for administration of the CAM. [23] Postoperative delirium assessments were validated by a second investigator with advanced training in psychology. The CAM consists of nine operationalized criteria taken from the Diagnostic and Statistical Manual of Mental Disorders and can be completed in five minutes. The CAM is scored positive for delirium based upon the findings of acute onset and fluctuating course and inattention, along with either disorganized thinking or altered level of consciousness. Sensitivity has been shown to

range from 94% to 100% and specificity has been shown to range from 90% to 95%. The inter-rater reliability of the CAM is high with a kappa= 0.81-1.0. [23]

Independent Variables

Domains of variables known to be associated with postoperative delirium including demographic and patient factors, functional status, cognitive status, surgical and anesthetic factors, pain level, and the type of pain management were examined.

Demographics

Both gender and age were included in the analysis. Age was used as a continuous variable for descriptive statistics, but dichotomized into less than or equal to 75 years of age and greater than 75 years of age for multivariate analyses.

Functional Status

Independence in five Activities of Daily Living (ADLs) was measured using Katz Index of Independence of Daily Living, which evaluates an individual's ability to perform activities of daily living independently. The activities assessed include: toileting, eating, bathing, dressing, and transferring. Independence was defined the ability of the patient to perform each of the activities without assistance. [24, 25]

Independence in seven Instrumental Activities of Daily Living (IADLs) was also used to determine functional status. This measured use of the telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, and ability to handle finances. [26]

Cognitive Status

Cognitive status was measured with the Telephone Interview for Cognitive Status (TICS), chosen because it can be administered reliably either face-to-face or by telephone. The TICS was adapted from and compared to the Mini Mental State Examination, having a sensitivity of 1.00 and specificity of 0.83.[27]

The TICS was administered face-to-face at three time points: before surgery during the preoperative workup, and at 24 and 48 hours after surgery. The TICS score obtained prior to surgery was used in the analysis as a baseline of cognitive function. A cutoff score of less than 25 was indicative of dementia. The Geriatric Depression Scale (GDS), a 15-item questionnaire, was used preoperatively to detect depression in the participating patients. The GDS has a test-retest reliability correlation of 0.85. [28] Sensitivity and specificity are 84% and 95% respectively when using a cut off score of 11, and 80% and 100% when using a cut off score of 14. [29]

Assessment also included history of central nervous system (CNS) disorders such as cerebrovascular accidents, dementia, delirium, seizure disorder, or Parkinson's disease. Other co-variates such as alcohol use and the highest level of education obtained were abstracted from patient medical records.

Surgical Factors

The Charlson Comorbidity Index is a chart-review based comorbidity instrument used to measure the number and severity of preoperative coexistent conditions in order to predict mortality. [30] The American Society of Anesthesiologists' (ASA) classification incorporates the severity and number of comorbid conditions the patient has prior to surgery and was obtained from the medical chart review, as was the type of surgery. The type of surgery was

classified into categories as follows: orthopedic/neurological, general/ENT/thoracic/plastic, and urological/gynecological/vascular. Surgical risk was estimated using the American College of Cardiology and the American Heart Association guidelines for perioperative cardiovascular evaluation for those patients undergoing non-cardiac surgery. [31] This variable takes into consideration the type and duration of surgery along with the intra-operative blood loss and is divided into three categories: low risk, intermediate risk, and high risk. Clinical covariates such as type of anesthesia, postoperative hemoglobin value, and postoperative systolic blood pressure were abstracted from patient medical records.

Pain

Pain was measured by trained research assistants using an 11-point Numerical Rating Scale (NRS) [32-35] in which a rating of 0 indicated 'no pain' and a rating of 10 indicated the 'worst possible pain.' The NRS was stratified per institutional practice, with patients having a NRS score of 4 or less considered to have 'pain under control' which met the criterion for discharge from the PACU after surgery. [21] Patients were asked preoperatively, on POD 1, and POD 2 to rate 'pain at rest' using this scale. This variable was coded as a number from 0-10 according to patient self-report of pain using the NRS. Use of patient-controlled analgesia (PCA) as the method of postoperative pain management was recorded from the medical record as was the use of pre- and postoperative benzodiazepines.

Statistical Methods

Bivariate associations were determined using t-tests for continuous variables and chi-square tests or Fisher exact tests for categorical variables. A multiple logistic regression was conducted to determine variables that were associated with recovery from delirium by POD 2. Variables having a *P* value of 0.20 or less with recovery from delirium in the bivariate analyses were included in the multiple logistic regression analyses. The Wald stepwise method was used in the logistic regression analysis so that the variable explaining the most variation in the dependent variable was added first. The variable explaining the most variation in the dependent variable of those variables remaining is added next and the statistics are recalculated. The addition of the variables stops once the addition of another variable doesn't significantly improve the prediction of the dependent variable.

All statistical analyses were performed with SAS, version 9.2. [36] In all tests, *P* values less than 0.05 (two-tailed) were considered statistically significant. All data were presented as means with standard deviation unless stated otherwise.

Results

One hundred and seventy-six (176) patients developed delirium on postoperative day one (POD 1). Three patients did not have delirium data on postoperative day two because of early discharge (*n*=1), sedation (*n*=1), and refusal to be interviewed (*n*=1), and were not included in the subsequent analysis. Table 1 provides a summary of bivariate analyses for the demographic and patient factors.

Sixty-six of 173 (38%) did not recover from their delirium by postoperative day two (POD 2). Younger patients were more likely to recover from delirium by day two; the average age of those who recovered was 72.5 versus 75.9 for those who did not recover (*P*=0.0005). The mean TICS score differed significantly between the two groups. The mean score for the patients whose delirium did not resolve was significantly lower than the mean score in those whose delirium resolved (30.2 ± 5.2 vs. 32.0 ± 3.4 , *P*=0.01). Other factors that were not related to the recovery of delirium include functional status, independence in Instrumental

Activities of Daily Living, alcohol use, preoperative Geriatric Depression Scale scores, history of CNS disorders, and highest level of education.

Bivariate analyses of surgical and anesthetic factors are shown in Table 2. Patients with intra-operative blood loss of less than 1000 ml were more likely to recover by POD 2 ($P=0.02$). No other surgical or anesthetic factors examined reached statistical significance including Charlson Comorbidity Index, type of anesthesia, ASA classification, surgical risk, surgery type, postoperative hemoglobin, and minimum postoperative systolic blood pressure on either POD 1 or POD 2.

Of the pain management factors, 42% of those whose delirium did not resolve had a POD 2 pain NRS score of 5 or higher as compared to 24% of those whose delirium resolved ($P=0.02$). Pain management factors that were not significantly related to recovery of delirium included POD 1 pain NRS score, preoperative oral narcotic use, type of postoperative pain regimen, and use of benzodiazepines on POD 1. Bivariate analyses of pain management factors are provided in Table 3.

Variables that had a P -value of less than 0.2 from each of the domains (demographic/patient factors, surgical/anesthetic factors, and pain management factors) were entered into a stepwise logistic regression, which revealed two variables that were significant in predicting whether a patient's delirium would be resolved by the second postoperative day (Table 4). Patients younger than 75 years of age ($OR=2.42$; 95% $CI=1.16-5.07$) and patients who had resting NRS pain scores of less than 5 on POD 2 ($OR=2.59$; 95% $CI=1.15-5.83$) were statistically more likely to have a resolution of delirium by the second postoperative day (POD 2).

Lastly, information regarding length-of-stay (LOS) and 30 day outcome measures is displayed in Table 5. The mean duration of hospital stay was measured for patients with POD 2 delirium resolution and those without (still having delirium on POD 2). Those patients who recovered from delirium by POD 2 had a mean duration of stay of 6.43 days while those who did not recover had a mean duration of stay of 8.82 days ($P = 0.02$). Further examination of recovery and outcome variables show greater 30-day ADL dependency ($P=0.05$) and 30-day IADL dependency ($P=0.10$) among patients who did not recover from delirium by POD 2. While 49.15% of patients who recovered from delirium by POD 2 were discharged home versus 37.11% for those who did not recover, this difference was not significant ($P=0.14$).

Discussion

Many studies have determined risks for developing delirium, and risks for prolonged delirium that lasts until discharge or longer. [2,7,10,13,17,19,37] To our knowledge, this is the first study that has considered factors associated with surgical patients' recovery from delirium early in the postoperative period. Prior studies have mainly focused on interventions that were specifically designed to identify 'at-risk' patients, with the intent of preventing delirium development from occurring. This study is the first to examine specific factors in the early postoperative window. Further research is needed to determine whether components of interventions directed towards preventing delirium may be effective in treating delirium early in its course.

Of the two variables that were found to be significant in recovery from early delirium (age and pain), only pain is modifiable. Improvement in pain management in the early postoperative period is an important factor,^[18, 38] however, it often involves complex assessment, pain management, and recovery needs of older adult patients with multiple comorbidities. Interestingly, lower POD 2 pain scores were more likely to lead to delirium

recovery than were lower POD 1 pain scores. Improved patient guidelines or algorithms for the early postoperative period could assist clinicians with complex clinical decision-making, as well as identify areas in need of improvement or target areas for specific evidence-based pain management protocols. One particular model could include the development of a pain practice index tool to determine potential practice gaps in pain guidelines that can be modified to intervention-level practice changes and resulting outcome measures.^[39] Potential outcomes of improved postoperative pain management may be reduced number of days of delirium and shorter length-of-stay.

A recently published meta-analysis concludes that delirium is independently associated with poor outcomes including mortality.^[40] Our study shows that surgical patients who experienced early recovery from delirium have better outcomes (shorter hospital stays and lower dependence on ADL's at 30 days) compared to patients who did not recover from delirium. Pain management in postoperative older patients is known to have significant effects on length-of-stay,^[38] reduction in delirium development,^[15, 19] and resolution of postoperative cognitive decline.^[41] Given the high cost of longer hospital stays, discharge disposition to long-term care, and other negative sequelae associated with delirium, the use of evidenced-based pain management guidelines, as well as careful scrutiny of how those guidelines are best implemented in the early perioperative period, is essential.

Pain management is not commonly incorporated into delirium prevention protocols; however, one intervention designed to prevent delirium included a protocol for the treatment of severe pain.^[42] The patient was to receive around-the-clock acetaminophen (1 gram four times daily). For early-stage break-through pain, low dose subcutaneous morphine was given with specific instructions to avoid meperidine. For late-stage break-through pain, oral oxycodone was used as needed. Because this was one module of ten that was addressed in the geriatrics consultation, it is not known how much this pain protocol reduced the incidence of delirium; however, the entire intervention reduced the incidence of delirium by 18%.^[42] The development of pain management protocols aimed at improving recovery from delirium should consider that the use of patient controlled analgesia puts patients at a greater risk for developing delirium and postoperative cognitive dysfunction than narcotics taken orally.^[17, 18, 41] The protocol in the Marcantonio et al study did not involve pain medication delivery by patient controlled analgesia.^[42] Additional evidence is needed to determine which post-operative pain management methods are most effective at simultaneously reducing pain and days of postoperative delirium.

Implications for Practice, Research, and Education

Previous literature has described the importance of reducing environmental contributors to delirium. This includes orienting the patient through clear and concise communication by family and nursing staff, and the use of clear signs (e.g. clock, calendar, or chart with the day's schedule).^[43] Patients who have resolved delirium stated that interventions such as these gave a heightened sense of control during delirium. Future interventions that include components to optimize early post-operative pain, including non-pharmacologic approaches, may increase patients' sense of control in the postoperative setting. A recent study demonstrated that pain management can be achieved even among persons with delirium.^[44] Finally, more intensive surveillance of patients during and after delirium would provide evidence whether interventions to reduce the length of early post-operative delirium reduces other downstream negative sequelae in these patients such as higher mortality and longer hospital stays that have been demonstrated in the literature.^[8-9,12]

Limitations

This study focused on measuring the prevalence of delirium in the early postoperative period because nearly one in three patients in this non-cardiac surgical cohort were discharged two days after surgery. As a result, we may have missed the occurrence of delirium in the late postoperative period for those patients with longer length-of-stay. The fluctuating nature of delirium could also have resulted in missed cases of delirium on or after POD 3; consequently, we were not able to describe factors associated with delirium recovery of those that developed delirium later in their hospital stay. It is possible that patients who develop delirium early in the postoperative period have different etiologies or conditions which could then be addressed with specific interventions.

Another limitation of this study was that timing of POD 2 pain medications was not known; therefore, we do not know whether they were given before or after the delirium and pain ratings assessments. Because of this, we did not include the pain medications given on POD 2 in our analysis. Our research assistants completed both the delirium measurement and NRS scores together (not blinded), making some chance of bias a possibility. We do not believe this occurred, as the NRS was a 'self-report,' however, not having these assessments done independently should be considered a limitation. We do not have evidence about the validity of NRS pain scores in delirious patients, although our prior work suggests that pain reports in patients with and without delirium have similar reliability.^[44] Finally, we did not have 30-day follow-up data on all patients from the original data collection, so there is a possibility that missing data could influence the 30-day outcome analyses. Although completed data on all subjects would have created a larger sample size, it is possible that trends in the missing data could differ from the increased dependency that we found in the completed subjects.

Conclusions

Older age and NRS pain score of 5 or higher are associated with lack of recovery from delirium on POD 2. The finding of higher NRS pain scores in patients not recovering from delirium provides evidence of the need for systematic pain assessments as well as clinical guidelines for managing pain in complex patient recovery situations. Such pain management strategies could reduce continuation of delirium early in the post-operative period. Our findings suggest that other outcomes such as length-of-stay and discharge disposition might also be reduced as a result of earlier recovery of delirium in the first 48 hours postoperatively.

Acknowledgments

Funding: National Institutes of Health 1R01AG031795-02

We gratefully acknowledge the Perioperative Medicine Research Group at the University of California, San Francisco, for their support and assistance with this study.

References

1. Gillick M, Serrell N, Gillick L. Adverse consequences of hospitalization in the elderly. *Social Science Medicine*. 1982; 16:1033–1038. [PubMed: 6955965]
2. Inouye SK. Delirium in older persons. *The New England Journal of Medicine*. 2006; 354(11):1157–1165. [PubMed: 16540616]
3. Lowery D, Wesnes K, Ballard C. Subtle attentional deficits in the absence of dementia are associated with an increased risk of post-operative delirium. *Dementia and Geriatric Cognitive Disorders*. 2007; 23(6):390–394. [PubMed: 17396030]

4. McCusker J, Cole M, Dendukuri N, et al. The course of delirium in older medical inpatients: A prospective study. *Journal of General Internal Medicine*. 2003; 18(4):696–704. [PubMed: 12950477]
5. Kiely DK, Marcantonio ER, Inouye SK, et al. Persistent delirium predicts greater mortality. *Journal of the American Geriatric Society*. 2009; 57(1):55–61.
6. Leslie DL, Marcantonio ER, Zhang Y, et al. One year health care costs associated with delirium in the elderly population. *Archives of Internal Medicine*. 2008; 168(1):27–32. [PubMed: 18195192]
7. Inouye SK, Zhang Y, Jones RN, et al. Risk factors for delirium at hospital discharge: development and validation of a predictive model. *Archives of Internal Medicine*. 2007; 167:1406–1413. [PubMed: 17620535]
8. Kakuma R, Galbaud du Fort G, Arsenault L, et al. Delirium in older emergency department patients discharged home: Effect on survival. *Journal of the American Geriatric Society*. 2003; 51:443–450.
9. McAvay GJ, Van Ness PH, Bogardus ST, et al. Older adults discharged from the hospital with delirium: 1-year outcomes. *Journal of the American Geriatric Society*. 2006; 54(8):1245–1250.
10. Inouye SK, Viscoli CM, Horwitz RI, et al. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. *Annals of Internal Medicine*. 1993; 119(6):474–481. [PubMed: 8357112]
11. Murray AM, Levkoff SE, Wetle T, et al. Acute delirium and functional decline in the hospitalized elderly patient. *Journal of Gerontology*. 1993; 48(5):M181–M186. [PubMed: 8366260]
12. O'Keefe ST, Lavan JN. The prognostic significance of delirium in older hospital patients. *Journal of the American Geriatric Society*. 1997; 45(2):174–178.
13. Leung JM, Sands LP, Mullen EA, et al. Are preoperative depressive symptoms associated with postoperative delirium in geriatric surgical patients? *Journal of Gerontology*. 2005; 60A(12):1563–1568.
14. Radtke FM, Franck M, MacGuill M. Duration of fluid fasting and choice of analgesic are modifiable factors for early postoperative delirium. *European Journal of Anaesthesiology*. 2010; 27(5):411–416. [PubMed: 19887950]
15. Lynch E, Lazor MA, Gellis JE, et al. The impact of postoperative pain on the development of postoperative delirium. *Anesthesia and Analgesia*. 1998; 86(4):781–785. [PubMed: 9539601]
16. Sharma PT, Sieber FE, Zakriya KJ, et al. Recovery room delirium predicts postoperative delirium after hip fracture repair. *International Journal of Anesthesia Research Society*. 2005; 101(4):1215–1220.
17. Vaurio LE, Sands LP, Wang Y, et al. Postoperative delirium: The importance of pain and pain management. *Anesthesia and Analgesia*. 2006; 102:1267–1273. [PubMed: 16551935]
18. Fong HK, Sands LP, Leung JM. The role of postoperative analgesia in delirium and cognitive decline in elderly patients: A systematic review. *Anesthesia and Analgesia*. 2006; 102:1255–1266. [PubMed: 16551934]
19. Morrison SR, Magaziner J, Gilbert M, et al. Relationship between pain and opioid analgesics on the development of delirium following hip fracture. *Journal of Gerontology*. 2003; 58A:1, 76–81.
20. Han L, McCusker J, Cole M, et al. Use of medications with anticholinergic effect predicts clinical severity of delirium symptoms in older medical inpatients. *Archives of Internal Medicine*. 2001; 161(8):1099–1105. [PubMed: 11322844]
21. American Society of Anesthesiologists. Practice guidelines for acute pain management in the perioperative setting. *Anesthesiology*. 2004; 100(6):1573–1581. [PubMed: 15166580]
22. Kiely DK, Jones RN, Bergmann MA, et al. Association between delirium resolution and functional recovery among newly admitted postacute facility patients. *Journal of Gerontology*. 2006; 61A(2):204–208.
23. Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: The confusion assessment method. *Annals of Internal Medicine*. 1990; 113:941–948. [PubMed: 2240918]
24. Katz S, Ford AB, Moskowitz RW, et al. Studies of the illness in the aged: the index of ADL: a standardized measure of biological and psychosocial function. *Journal of the American Medical Association*. 1963; 185(12):914–919. [PubMed: 14044222]
25. Katz S, Downs TD, Cash HR, et al. Progress in the development of the ADL index. *The Gerontologist*. 1970; 10(1 Part 1):20–30. [PubMed: 5420677]

26. Lawton MP, Brody EM. Assessment of older people: Self-maintaining and instrumental activities of daily living. *The Gerontologist*. 1969; 9(3 Part 1):179–186. [PubMed: 5349366]
27. Desmond DW, Tatemichi TK, Hanzawa L. The telephone interview for cognitive status (TICS): Reliability and validity in a stroke sample. *International Journal of Geriatric Psychiatry*. 1994; 9(10):803–807.
28. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research*. 1983; 17(1):37–49. [PubMed: 7183759]
29. Brink TL, Yesavage JA, Lum O, et al. Screening tests for geriatric depression. *Clinical Gerontologist*. 1982; 1:37–44.
30. Charlson ME, Pompei P, Ales KL, et al. A new method for classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases*. 1987; 40(5):373–383. [PubMed: 3558716]
31. ACC/AHA guideline update for the perioperative cardiovascular evaluation for noncardiac surgery executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Anesthesia & Analgesia*. 2002; 94:1052–1064. [PubMed: 11973163]
32. Jensen MP, Turner JA, Romano JM, et al. Comparative reliability and validity of chronic pain intensity measures. *Pain*. 1999; 83:157–162. [PubMed: 10534586]
33. Lundeborg T, Lund I, Dahlin L, et al. Reliability and responsiveness of three different pain assessments. *Journal of Rehabilitation Medicine*. 2001; 33:279–283. [PubMed: 11766958]
34. Turk DC, Rudy TE, Sorkin BA. Neglected topics in chronic pain treatment outcome studies: Determination of success. *Pain*. 1993; 53:3–16. [PubMed: 8316386]
35. Farrar JT, Young JP Jr, LaMoreaux L, et al. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical rating scale. *Pain*. 2001; 94:149–158. [PubMed: 11690728]
36. SAS Institute. Help and documentation. 3rd. Cary, North Carolina: SAS Institute, Inc.; 2003.
37. Elie M, Cole MG, Primeau FT, et al. Delirium risk factors in elderly hospitalized patients. *Journal of General Internal Medicine*. 1998; 13(3):204–212. [PubMed: 9541379]
38. Kerr P, Shever L, Titler MG, et al. The unique contribution of the nursing intervention pain management on length of stay in older patients undergoing hip procedures. *Applied Nursing Research*. 2010; 23:36–44. [PubMed: 20122509]
39. Herr K, Titler M, Fine P, et al. Assessing and treating pain in hospices: Current state of evidence-based practice. *Journal of Pain and Symptom Management*. 2010; 39(5):803–819. [PubMed: 20471542]
40. Witlox J, Eurelings LS, deJongue JF, et al. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia. *Journal of the American Medical Association*. 2010; 304(4):443–451. [PubMed: 20664045]
41. Wang Y, Sands LP, Vaurio L, et al. The effects of postoperative pain and its management on postoperative cognitive dysfunction. *American Journal of Geriatric Psychiatry*. 2007; 15(1):50–59. [PubMed: 17194815]
42. Marcantonio ER, Flacker JM, Wright RJ, et al. Reducing delirium after hip fracture: A randomized trial. *Journal of the American Geriatric Society*. 2001; 49(5):516–522.
43. Meagher DJ. Delirium: Optimising management. *British Medical Journal*. 2001; 322:144–149. [PubMed: 11159573]
44. Leung JM, Sands LP, Paul S, et al. Does postoperative delirium limit the use of patient controlled analgesia in older surgical patients. *Anesthesiology*. 2009; 111(3):625–631. [PubMed: 19672166]

Table 1

Demographics/patient factors

Variable	Recovery from delirium on post-op day 2				P-value
	N ₁ *	No (N = 110)	N ₂ *	Yes (N = 66)	
Age	110	75.9 ± 6.5	66	72.5 ± 5.7	0.0005
Age (categorical variable)	110		66		0.0074
< 75		47 (42.73%)		42 (63.64%)	
≥ 75		63 (57.27%)		24 (36.36%)	
Gender	107		69		0.4992
Female		69 (62.73%)		38 (57.58%)	
Male		41 (37.27%)		28 (42.42%)	
Pre-op GDS scores	102	3.6 ± 3.2	59	3.2 ± 3.0	0.5327
Pre-op GDS scores	102		59		0.8291
0-5		81 (79.41%)		46 (77.97%)	
≥ 6		21 (20.59%)		13 (22.03%)	
Pre-op TICS scores	101	30.2 ± 5.2	57	32.0 ± 3.4	0.0235
Pre-op TICS scores	101		57		0.0944
<30		38 (37.62%)		14 (24.56%)	
≥30		63 (62.28%)		43 (75.44%)	
Functional Status	110		66		0.3901
1-3		46 (41.82%)		32 (48.48%)	
4-6		64 (58.18%)		34 (51.52%)	
Dependence of 5 ADLs	109		65		0.7263
No		83 (76.15%)		51 (78.46%)	
Yes		26 (23.85%)		14 (21.54%)	
Dependence of 7 IADLs	106		60		0.3373
No		52 (49.06%)		34 (56.67%)	
Yes		54 (50.94%)		26 (43.33%)	
Alcohol use	108		65		0.3180
≤ 2 drinks		101 (93.52%)		58 (89.23%)	
> 2 drinks		7 (6.48%)		7 (10.77%)	

Variable	Recovery from delirium on post-op day 2				P-value
	N ₁ *	No (N = 110)	N ₂ *	Yes (N = 66)	
History of CNS disorders	109		65		0.3466
No		44 (40.37%)		31 (47.69%)	
Yes		65 (59.63%)		34 (52.31%)	
Highest level of education	110		66		0.5987
High school graduate or lower		41 (37.27%)		22 (33.33%)	
Attended college or higher		69 (62.73%)		44 (66.67%)	

N₁ * = Actual number of non-missing observations from subjects with delirium on post-op day2.

N₂ * = Actual number of non-missing observations from subjects w/o delirium on post-op day2.

GDS=Geriatric Depression Scale

TICS=Telephone Interview for Cognitive Status

ADL=Activities of Daily Living

IADL=Instrumental Activities of Daily Living

CNS= Central Nervous System

Table 2

Surgical /anesthetic factors

Variable	N1*	Recovery from delirium on post-op day 2			P value
		No (N = 110)	N2*	Yes (N = 66)	
Charlson Comorbidity index	110	1.6 ± 1.9	66	1.4 ± 1.5	0.5976
Intra-operative blood loss	110		65		0.0129
<1000 ml		74 (67.27%)		54 (83.08%)	
≥1000 ml		36 (32.73%)		11 (16.92%)	
Type of anesthesia	110		66		0.9329
I (general)		76 (69.09%)		46 (69.70%)	
II (non-general *)		34 (30.91%)		20 (20.30%)	
ASA classification	110		66		0.3435
I-II		68 (61.82%)		36 (54.55%)	
III-IV		42 (38.18%)		30 (45.45%)	
Surgical risk	110		66		0.1066
I-II		78 (70.91%)		54 (81.82%)	
III		32 (29.09%)		12 (18.18%)	
Surgery Type	110		66		0.5716
Orthopedic/Neurological		75 (68.18%)		40 (60.61%)	
General/ENT/Thoracic/Plastic		16 (14.55%)		11 (16.67%)	
Urological/Gynecological/Vascular		19 (17.27%)		15 (22.73%)	
Postoperative hemoglobin	102	12.8 ± 1.6	60	12.8 ± 1.7	0.7315
Min systolic blood pressure on post-op day 1	102	107.8 ± 18.0	63	109.4 ± 22.2	0.6206
Min systolic blood pressure on post-op day 2	101	113.7 ± 18.7	62	117.2 ± 17.3	0.2364

N1* = Actual number of non-missing observations from subjects with delirium on post-op day2.

N2* = Actual number of non-missing observations from subjects w/o delirium on post-op day2.

* Non-general anesthesia was either regional anesthesia or intravenous sedation

ASA= American Society of Anesthesiologists

ENT=Ear/Nose/Throat

Table 3

Pain management factors

Variable	N ₁ *	Recovery from delirium on post-op day 2		P value
		No (N = 110)	Yes (N = 66)	
Post-op day 1 NRS pain score	102			0.1426
0-4		50 (49.02%)	40 (60.61%)	
≥5		52 (50.98%)	26 (39.39%)	
Post-op day 2 NRS pain score	95			0.0232
0-4		55 (57.89%)	49 (75.38%)	
≥5		40 (42.11%)	16 (24.62%)	
Preoperative oral narcotic use	110			0.0919
No		68 (61.82%)	49 (74.24%)	
Yes		42 (38.18%)	17 (25.76%)	
Type of post-op pain regimen	110			0.3350
PCA		87 (79.09%)	48 (72.73%)	
No PCA		23 (20.91%)	18 (27.27%)	
Use of benzodiazepines on post-op day 1	110			0.1118
No		73 (70.19%)	52 (81.25%)	
Yes		31 (29.81%)	12 (18.75%)	

N₁*= Actual number of non-missing observations from subjects with delirium on post-op day2.N₂*= Actual number of non-missing observations from subjects w/o delirium on post-op day2.

NRS=Numeric Rating Scale

PCA=Patient Controlled Analgesia

Table 4
Results from the final multivariate stepwise logistic model (c-statistic = 0.64 N=360)

Effect	Estimate	P value	Odds ratio	95% Wald CL
Age				
<75 vs. ≥75	0.84	0.015	2.31	1.18 4.53
Rest pain on POD 2				
<5 vs. ≥5	0.95	0.0098	2.59	1.26 5.35
POD=Postoperative Day				

Table 5
Bivariate association of delirium recovery and outcome variables

Variable	Recovery from delirium on post-op day 2				P value [†]
	N ₁ [*]	No (N = 110)	N ₂ [*]	Yes (N = 66)	
Length of hospital stay (in days)	108		64		0.02
2 – 4		24 (22.22%)		24 (37.50%)	
5 – 7		40 (37.04%)		23 (35.94%)	
8 – 71		44 (40.74%)		17 (26.56%)	
Discharge Disposition	97		59		0.14
Home only		36 (37.11%)		29 (49.15%)	
Other long-term care or rehabilitative facilities		61 (62.89%)		30 (50.85%)	
ADL dependency at 30 day follow-up	62		38		0.05
No		25 (40.32%)		23 (60.53%)	
Yes		37 (59.68%)		15 (39.47%)	
IADL dependency at follow-up	62		38		0.10
No		12 (19.35%)		13 (34.21%)	
Yes		50 (80.65%)		25 (65.79%)	

N₁^{*}= Actual number of non-missing observations from subjects with delirium on post-op day2.

N₂^{*}= Actual number of non-missing observations from subjects w/o delirium on post-op day2.

[†] P-values are obtained by Chi-square test (Mantel-Haenszel Chi-square is used for ordered variable) or by Fisher's exact test (if a cell has less than 5 incidences)

ADL=Activities of Daily Living

IADL=Instrumental Activities of Daily Living