Adverse Outcomes of Geriatric Patients Undergoing Abdominal Surgery Who Are at High Risk for Delirium

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Hypothesis: Among geriatric patients undergoing abdominal surgery who are at high risk for in-hospital delirium, clinical factors associated with delirium correlate with adverse outcomes.

Design: Retrospective case series study.

Setting: University-affiliated referral hospital.

Patients: Among 228 consecutive patients 70 years or older who underwent major abdominal surgery from September 1, 2002, through December 31, 2003, 89 patients with risk factors for delirium were included in the study.

Main Outcome Measures: Preoperative, intraoperative, and postoperative clinical factors known to affect the incidence of in-hospital delirium were tested for correlation with adverse outcomes. Incidence of delirium, mortality, and prolonged length of stay (LOS) of 14 days or longer were evaluated as adverse outcomes.

Results: Postoperative delirium occurred in 60%, death in 20%, and prolonged LOS in 32% of patients.

Conclusions: In a subset of geriatric patients undergoing abdominal surgery who are at high risk for in-hospital delirium, adverse outcomes correlate only with key clinical variables, such as hyperglycemia and poor nutritional and functional states. A high incidence of suboptimal care was observed in several clinical areas, suggesting opportunities for intervention.

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Delirium is present in 22% to 31% of hospitalized elderly patients and in 37% of postoperative geriatric patients, in some cases as many as 74%. Among patients undergoing cardiac, general, orthopedic, and vascular procedures, postoperative delirium has been found to correlate with a variety of preoperative, intraoperative, and postoperative clinical variables. The patients in these studies were not stratified according to their risks for delirium, and the findings apply to patient populations at low risk and high risk for delirium. Evidence has suggested that strategies for reducing postoperative delirium may be different for patients at various risk levels.

To our knowledge, no studies have evaluated geriatric patients undergoing major abdominal surgery who are identified at admission as high risk for postoperative delirium. With 60% of all general surgical procedures being performed on patients older than 65 years, prevention and treatment of delirium among patients who are at high risk of delirium are critical to affect both cost and outcome.

Inouye et al have created a validated prediction model for delirium in hospitalized, elderly patients based on 4 risk factors at admission: (1) severe illness, (2) visual impairment, (3) cognitive impairment, and (4) serum urea nitrogen to creatinine (SUN:Cr) ratio of 18 or higher. The model revealed an 83% incidence of delirium among patients with 3 or 4 risk factors compared with 9% among patients with no risk factors. A significant difference was demonstrated in mortality and nursing home placement outcomes based on risk factors at admission.

Using the model of Inouye and colleagues, we identified a group of geriatric patients undergoing abdominal surgery who were determined at admission to be at high risk for postoperative delirium. We reviewed their clinical characteristics and outcomes to study the hypothesis that ad-
verse outcomes would be frequent among these high-risk cohorts and would correlate with key clinical factors previously known to be associated with the development of delirium.

METHODS

STUDY INCLUSION CRITERIA

The study population consisted of patients who were admitted to a 650-bed teaching hospital from September 1, 2002, through December 31, 2003. A retrospective review of hospital medical records was conducted for all patients 70 years or older who underwent abdominal surgery. Inclusion criteria were applied, identifying patients with 3 or 4 of the following risk factors at admission for in-hospital delirium previously validated by Inouye et al: (1) severe illness, (2) visual impairment, (3) cognitive impairment, and (4) dehydration as determined by a SUN:Cr ratio of 18 or higher. In our study, we modified the original validation model by requiring severe illness as an inclusion criterion, defined as having diseases that needed major abdominal surgical procedures such as open abdominal explorations for bowel perforation, obstruction, bleeding, ischemia, infection, and cancer. We excluded less serious diseases that required procedures such as uncomplicated hernia repair or cholecystectomy. Visual impairment was identified in the medical records by a nurse’s documentation of the patient’s use of corrective lenses, presence of cataracts, diabetic retinopathy, or macular degeneration. Cognitive impairment was assessed by documentation of a prior history of dementia, Alzheimer disease, or significant recent memory loss.

PATIENT CHARACTERISTICS

Clinical data were abstracted from hospital medical records of patients who met the inclusion criteria. Baseline patient characteristics were recorded, including age, sex, language, presence of advance directive, and family participation in care. Admission source and elective or emergency nature of surgery were noted. For each patient, the medical record was reviewed by at least 2 separate investigators (S.G., K.F.L., and A.M.) for concurrence to minimize investigator bias.

CLINICAL FACTORS ASSOCIATED WITH IN-HOSPITAL DELIRIUM

On the basis of previous reports, the following preoperative, intraoperative, and postoperative clinical variables were considered as factors associated with in-hospital delirium. They were tested for possible correlation with adverse outcomes.

Preoperative factors included poor nutritional status, poor functional status, and a history of diabetes mellitus. Poor nutritional status was defined as a serum albumin level less than 3.0 mg/dL (≤1.6 g/dL), poor glycemic control (serum glucose level >150 mg/dL; to convert to millimoles per liter, multiply by 0.0555), hypoxia (arterial oxygen saturation <95%), anemia (hematocrit <30%), uncontrolled pain, metabolic derangement, and hypoalbuminemia (albumin level <3.0 mg/dL). Potentially precipitative medications included meperidine, hydroxyzine, benzodiazepines, diphenhydramine, tricyclic antidepressants, muscle relaxants, and barbiturates.11,12 METABOLIC DERANGEMENT was defined as having one of the following serum abnormalities: pH less than 7.34 or greater than 7.55, serum sodium level greater than 150 or less than 130 mEq/L (to convert to millimoles per liter, multiply by 1.0), serum potassium level greater than 5.0 or less than 3.0 mEq/L (to convert to millimoles per liter, multiply by 1.0). Uncontrolled pain was defined as a pain score greater than 5 of 10 as documented by nursing staff along with assessment of vital signs.

In-hospital morbidity was assessed by reviewing complications that occurred throughout the hospital course. Complications were categorized by the associated organ system as follows: neurologic (stroke or seizures), cardiac (myocardial infarction, acute heart failure, or arrhythmias), respiratory (acute respiratory distress syndrome, pneumonia, or pleural effusion), gastrointestinal or hepatobiliary (hepatic insufficiency, jaundice, or prolonged ileus), renal (acute renal failure or electrolyte disturbances), infectious (bacterial sepsis, fungemia, or urinary tract infection), vascular (arterial or venous embolism), and wound (abdominal wall dehiscence or wound infection). The total number of organ system complications and morbidity rates were tabulated per patient.

SUBOPTIMAL CARE IN CLINICAL AREAS ASSOCIATED WITH DELIRIUM

Suboptimal care was defined as unexplained failure to recognize and/or treat a clinical situation. Continued use of physical restraint was considered suboptimal care if there was no clinical need for restraint for the protection of catheters, tubes (eg, endotracheal), or monitoring devices. Prolonged use of a bladder catheter was considered suboptimal care if a catheter was present despite adequate urine output, discontinuation of use of epidural anesthesia, or full ambulatory status. Prolonged bed rest was considered inappropriate in extubated patients if unexplained by a physician or a physical therapist.

If more than 4 new medications were administered, reasons for their use were evaluated. Appropriate uses for prophylactic antibiotics, diuretics, analgesics, or sedatives were excluded. Suboptimal care was noted when the medication list was not adjusted as clinical needs dissipated. When precipitative medications were given for analgesia or sedation, suboptimal care was noted if use of the drug could have been avoided by an alternate medication not associated with delirium. Pain was considered suboptimally managed if a pain score of greater than 5 was recorded during 8 hours without adequate analgesia to decrease the pain score below 5 of 10. Suboptimal care was also considered to be present if the pain score was not recorded at all by the physicians or nurses.

Malnutrition was considered suboptimally managed if documentation of nutritional status was absent, institution of nutri-
The symptoms included new onset of patient disorientation, diminished attention to external stimuli, disordered communication, confusion, agitation, or other indications of severe fluctuations in mental status. Mortality was defined as death before discharge from the hospital. Prolonged LOS was defined as 14 or more days of hospitalization.

**STATISTICAL ANALYSIS AND STUDY DESIGN**

The study methods received institutional review board approval. Statistical analysis was conducted with the Epi Info 3.2.2 software package (Centers for Disease Control and Prevention, Atlanta, Georgia). Statistical significance was determined with an α of .05 using 2-tailed P values. Differences in proportions were evaluated with the Mantel-Haenszel χ² test. The Mann-Whitney rank sum test was used to study differences in means. Means and relative risks (RRs) are indicated with 95% confidence intervals (CIs) in parentheses.

After performance of univariate analysis, clinical factors that achieved statistical significance were considered for inclusion in a stepwise unconditional multiple logistic regression analysis model. The Newton-Rhapson method was used to determine maximum likelihood estimates of the regression coefficient (β), the standard error of coefficient (SE), and the significance level (P) for each factor. The normal statistic (z) for each factor is the ratio between the regression coefficient and the SE and indicates the relative importance of that factor in determining outcome. The adjusted odds ratio for the variable represents the outcome for the patients with the factor present compared with the factor absent after adjusting for other factors. Clinical factors were entered into logistic regression models, with variables with a minimum normal statistic removed sequentially until statistically significant independent variables of association remained.

A total of 228 patients 70 years or older who underwent major abdominal surgery during the study period were evaluated for inclusion in the study. Of the 228 patients, 89 (39%) had 3 or more risk factors to meet the admission inclusion criteria for being at high risk for in-hospital delirium (mean age, 79 years; 95% CI, 77-80 years). Table 1 lists the clinical profiles of the patients. The Figure displays patients' admission sources and discharge destinations. Patients who developed postoperative delirium were less likely to be discharged to home than those who did not (31% vs 72%; P <.001). The indications for major abdominal surgical procedures are listed in Table 2. The mean hospital LOS was 12 days (95% CI, 10-13 days). Thirty-six of 89 patients (40%) were admitted to the intensive care unit (ICU) postoperatively, with a mean ICU stay of 6 days (95% CI, 4-8 days). No elective cases were associated with an ICU admission.

The overall incidence of delirium, mortality, and prolonged LOS was 60%, 20%, and 32%, respectively. Patients who required ICU admission had 50% mortality, of which all cases were associated with emergency operations. Table 3 indicates postoperative morbidity, involving a mean of 1.6 (95% CI, 1.2-1.9) organ systems per patient overall. Patients with delirium had mean of 1.9 organ systems with morbidity (95% CI, 1.5-2.4) compared with 1.0 (95% CI, 0.7-1.4) for those without delirium (P = .01).

### Table 1. Baseline Characteristics of 89 Patients at High Risk for Delirium

<table>
<thead>
<tr>
<th>Clinical Profile</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>42 (47)</td>
</tr>
<tr>
<td>English speaking</td>
<td>87 (98)</td>
</tr>
<tr>
<td>White race</td>
<td>81 (91)</td>
</tr>
<tr>
<td>Emergency admission</td>
<td>72 (81)</td>
</tr>
<tr>
<td>Family participation in care</td>
<td>79 (89)</td>
</tr>
<tr>
<td>Advance directive use</td>
<td>44 (49)</td>
</tr>
<tr>
<td>Presence of risk factors for in-hospital delirium</td>
<td>89 (100)</td>
</tr>
<tr>
<td>Severe illness</td>
<td>89 (100)</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>88 (98)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>31 (35)</td>
</tr>
<tr>
<td>SUN:Cr ratio ≥18</td>
<td>86 (96)</td>
</tr>
</tbody>
</table>

Abbreviations: Cr, creatinine; SUN, blood urea nitrogen.

### Table 2. Admission and Discharge Venues for Patients

<table>
<thead>
<tr>
<th>Admission Source</th>
<th>Discharge Venue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>Home</td>
</tr>
<tr>
<td>Assisted Living</td>
<td>Home</td>
</tr>
<tr>
<td>Nursing Home</td>
<td>Rehabilitation</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>Hospital Transfer</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Patients, %</th>
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<tr>
<td>Home</td>
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<tr>
<td>Hospital Transfer</td>
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</tbody>
</table>

### Figure

Admission source of all 89 geriatric patients undergoing abdominal surgery and discharge destination of the 71 survivors.
No statistically significant difference was seen in age among patients who survived vs died ($P = .12$). A small but statistically significant difference in age was seen between the group that developed delirium (81 years; 95% CI, 79–82 years) vs those who did not (77 years; 95% CI, 75–79 years; $P = .005$). A LOS of 14 days or longer was seen in 28 patients (32%), of whom 11 (38%) had a delay in discharge after full restoration of oral dietary intake and bowel function. Primary reasons for discharge delay included management of complications in 9 (80%) and anticipation of institutional placement in 2 (20%). Patients with delirium were more likely to have an LOS of 14 days or longer than those without delirium (RR, 2.1; 95% CI, 1.02–4.5; $P = .03$). The presence of delirium correlated with increased risk of death (RR, 1.5; 95% CI, 1.3–1.8; $P < .001$). In addition, among patients who survived their hospitalization, patients who developed postoperative delirium were less likely to be discharged to home (RR, 0.4; 95% CI, 0.3–0.7; $P < .001$).

Table 4 summarizes various clinical factors previously described in the literature to be associated with delirium. Suboptimal care was noted in most patients affected by precipitative medications, prolonged bed rest, poor glycemic control, and hypoxia. Uncontrolled pain and anemia were also inadequately addressed in nearly half of the patients affected. Of the 89 patients studied, only 40 (45%) had albumin levels recorded within the first 3 postoperative days, with a mean albumin level of 2.5 mg/dL (95% CI, 2.3–2.7 mg/dL) (.0025 g/dL [95% CI, .0025–.0027 g/dL]). In contrast, suboptimal care was relatively infrequent in the areas of postoperative fluid status and metabolic derangements.

Table 5 gives the results of univariate analysis of clinical factors presumably associated with adverse outcomes. Table 6 gives the results of multiple logistic regression for variables associated with adverse outcomes. Preoperative nutritional and functional status were independent predictors of delirium. No intraoperative or postoperative clinical factors were associated with delirium after multivariate analysis. Poor glycemic control, preoperative nutritional status, and preoperative functional status were independent predictors of death. Hypoalbuminemia (albumin level <3.0 mg/dL [<.003 g/dL]) and morbidity (>2 organ systems involved) were independent predictors of prolonged LOS (>14 days).

**Comment**

In 1341 patients undergoing elective noncardiac procedures, Marcantiano et al reported that low-risk patients had a less than 1% incidence of postoperative delirium, whereas high-risk patients had an incidence of 45%. On the basis of a prediction model, postoperative delirium was predicted in high-risk patients with an accuracy of 70%.7 In addition to polypharmacy and dose-dependent correlation with age, various perioperative factors have been implicated in the development of delirium, including ineffective pain control and sleep cycle disturbances.10,19
The logical conclusion of these findings is that postoperative delirium depends on several preoperative, intraoperative, and postoperative clinical factors, with the potential for reduction in incidence by optimizing care by focusing on the subgroup of high-risk patients. Because postoperative delirium is believed to be linked to adverse outcomes, optimal management of the associated clinical factors may lead to improved clinical outcomes, such as mortality and LOS.

The present study was conducted as a retrospective exploration to test this rationale, specifically for geriatric patients undergoing abdominal surgery who are identifiable at admission as being at high risk for postoperative delirium. To our knowledge, this particular patient subset has not been previously studied in the literature. Certainly, it would have been ideal to conduct a prospective randomized trial to obtain a higher level of evidence. However, because of resource constraints, a carefully designed retrospective analysis was performed as a pilot exploration to answer, with some caution, the foregoing question.

Our patient population yielded a 60% incidence of postoperative delirium, which is higher than the 45% predicted by the study by Inouye et al.10 On a sample of nonsurgical patients. Their criterion, severe illness, was construed as equivalent to and therefore replaceable in our study by the stress of major abdominal surgery. Our definition of high risk was borrowed from the study by Inouye et al10 on a sample of nonsurgical patients. Their criterion, severe illness, was construed as equivalent to and therefore replaceable in our study by the stress of major abdominal surgery. Our 60% delirium rate was between the 43% reported by Marcantonio et al.11 We present this pilot study to test this rationale, specifically for geriatric patients undergoing abdominal surgery who are identifiable at admission as high risk for postoperative delirium. To our knowledge, this particular patient subset has not been previously studied in the literature. Certainly, it would have been ideal to conduct a prospective randomized trial to obtain a higher level of evidence. However, because of resource constraints, a carefully designed retrospective analysis was performed as a pilot exploration to answer, with some caution, the foregoing question.

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et al and the predicted incidence of 83% for the high-risk nonsurgical patients reported by Inouye et al.10

The postoperative mortality rates in our study were consistent with the findings of Hamel et al20 from the Veterans Administration National Surgical Quality Improvement Project (VA-NSQIP). In the VA-NSQIP database of elderly patients, patients with more than 48 hours of ventilatory assistance, acute renal failure, and systemic sepsis had mortality rates of 38.5%, 52.1%, and 45.2%, respectively, which is similar to the 50% mortality rate among our patients who required postoperative ICU care. Our mortality rates were also consistent with a recent review21 of the literature on the outcomes of critically ill, geriatric postoperative patients.

In univariate analysis, our patients undergoing abdominal surgery who were at high risk for in-hospital delirium showed clinical correlates of postoperative delirium similar to those of the patients undergoing mixed surgical and vascular procedures.4 However, in multivariate analysis using stepwise logistic regression, only the preoperative clinical factors (poor functional and nutritional status) remained as independent clinical correlates. In analysis of mortality, postoperative clinical variables such as inadequate fluid hydration and hypoalbuminemia—both significant in univariate analysis—dropped out after logistic regression. Once again, preoperative functional and nutritional status remained as independent clinical correlates of mortality, along with a sole postoperative clinical variable, namely, inadequate glycemic control. These findings conflict with some of the previous reports on postoperative delirium.4,7,11,12,18,22 in which additional intraoperative and postoperative clinical factors were reported to significantly influence the occurrence of postoperative delirium.

One explanation may be the difference in the stratification of risks for postoperative delirium. In previous reports9,11,14 based on unstratified subsets of patients with a wide range of risks for postoperative delirium, intraoperative and postoperative clinical factors may exhibit heterogeneity with differences that affected the clinical outcome. In our study, all or nearly all of the patients in our subset had severe illness that required major abdominal surgery (100%), emergency surgery (81%), and acute dehydration leading to azotemia (96%). Delirium notwithstanding, these clinical characteristics describe a narrowly defined, acutely ill patient population, portending a generally adverse postoperative course in which many clinical factors may not have made any difference in the outcome.

The only independent correlates of adverse outcomes during intraoperative and postoperative periods were inadequate glycemic control for mortality and postoperative hypoalbuminemia and morbidity (involving >2 organ systems) for prolonged LOS. These clinical factors have been described in the literature more in association with critical care and surgical outcomes than in relation to postoperative delirium. Van den Berghe et al21 have reported level I evidence that intensive insulin therapy for hyperglycemia in critically ill patients reduces mortality and morbidity. Khuri et al22 have also reported level I evidence from the VA-NSQIP database that hypoalbuminemia is first among clinical variables that correlate with adverse postsurgical outcomes.

The findings in the present study cast doubt on the role of conventional interventions (eg, multicomponent management of putative risk factors23,26) designed to prevent postoperative delirium, particularly among patients undergoing abdominal surgery who are at high risk for in-hospital delirium. This suggestion is also consistent with the data reported in the literature. A systematic review20 of 8 studies that involved patients undergoing surgery concluded that interventions to prevent delirium were only modestly effective. Among patients with chronic cognitive impairment, a recent review26 in the Cochrane database determined that evidence was inadequate to warrant a clinical guideline for a multidisciplinary team intervention. Even the clinical investigators who have pioneered the multicomponent intervention to reduce in-hospital delirium pointed out that it was not found to be cost-effective in patients at high risk for delirium.8 The intervention was found to be cost-effective only in patients with an intermediate risk for delirium.

The most effective way to influence adverse outcomes may be to focus, if possible in elective cases, on preoperative optimization of nutritional status and physical activity to enhance protein metabolism and prevent deconditioning and sarcopenia. In emergency preoperative settings, risk stratification of functional and nutritional status will be important to identify patients with prohibitive risks who may require modification of the type of surgery offered. Intensive perioperative recognition and treatment of hyperglycemia and aggressive perioperative nutritional support may also favorably affect the adverse outcomes.

These inferences must be considered in light of several limitations of the present study, which is based on a cohort of only 89 patients. Clearly, a major weakness of our study is the lack of a control group, which enables direct comparison of the study group in terms of RRs and odds ratios. With use of a control group, this study may have yielded different results. Furthermore, performance of a retrospective review is limited by reliance on the accuracy of documentation by caregivers. Investigator bias looms large in any retrospective study design in which medical records are examined long after hospital discharge. However, consistency of these findings with those in the literature suggests that these confounders exerted minimal influence on the results.

Another limitation was that the determination of poor preoperative functional status and nutritional status was not rigorous. We did not use any standard assessment tools because paucity and inconsistency of the nurse and physician notes made it difficult to use a standard checklist of clinical variables. Instead, we looked for keywords in the medical records that suggested clear evidence of functional and nutritional deficits. It is possible that we may have underestimated the true incidence of preoperative functional deficits and malnutrition.

Retrospective analysis has been shown to underestimate the incidence of true delirium, with physicians and nurses missing or neglecting to document 29% of cases of postoperative delirium when medical records were compared against prospective clinical interviews.24 This finding suggests that the incidence of delirium in this study might have been a conservative estimate.

The accuracy of our definition for delirium may also have been inadequate and may represent more of an as-
sessment of the presence of altered mental status rather than the strict DSM-IV-TR criteria. However, a prospective study has demonstrated that geriatric patients with a partial diagnosis of delirium closely resemble those with delirium defined according to the DSM-III, with consistent outcomes of a low rate of resolution after discharge and a prolonged hospital stay.

Some may question the choice of the high-risk inclusion criteria based on the prediction model developed by Inouye and colleagues on a cohort of medical rather than surgical patients. We chose this model because of its simplicity and high predictability of delirium among its high-risk subset. The high incidence (60%) of delirium among our high-risk patients fell within the range of other prediction models derived from patients undergoing surgery. This finding suggested that the choice of inclusion criteria did not significantly affect the study results.

Other issues are open for debate but are likely inconsequential to the study conclusion. These issues include whether or not the SUN:Cr ratio of 18 or higher truly reflected dehydration and hypovolemia. Inadequate glycemic control was defined as a serum glucose level of more than 110 mg/dL in the study by van den Berghe et al., but we chose a higher level of 150 mg/dL in the present study. Furthermore, not only is hypoalbuminemia a marker of long-term nutritional status but it also fluctuates during acute illness and physiologic stress; it may not be interpreted simply as an indicator for nutritional state. Also open to criticism may be the criteria used to define suboptimal care. Failure to document either recognition or treatment of various clinical problems (eg, urine output or pain score) has not proved to be associated with adverse outcomes, and designation of suboptimal care may not have been fair. However, the data summarized in Table 4 may be construed as descriptive, and as such, the findings remain striking and noteworthy.

Despite the importance of perioperative nutrition such as enteral feeding, delay or neglect of nutritional support was seen in nearly a third of the patients with poor nutritional status. Inadequate glycemic control was unrecognized or undertreated in 56% of patients with glucose levels greater than 150 mg/dL, despite the knowledge of level I evidence of its correlation with high morbidity and mortality. Inadequate postoperative fluid hydration was suboptimally managed in only 22% of the affected patients. One may postulate that the surgical team in a university-affiliated teaching hospital is more educated, and therefore more aggressive, in the treatment of postoperative hypovolemia than hyperglycemia or nutritional deficit. Clearly, opportunities exist for continuing education, improvement of care, and reduction of adverse outcomes when caring for high-risk geriatric patients undergoing major abdominal surgery.

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Author Contributions: Drs Ganai and Lee had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Ganai, K. F. Lee, Merrill, Bellantonio, Brennan, and Lindauer. Acquisi-


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