

## CME

# Postoperative Delirium: Acute Change with Long-Term Implications

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Delirium is an acute change in cognition and attention, which may include alterations in consciousness and disorganized thinking. Although delirium may affect any age group, it is most common in older patients, especially those with preexisting cognitive impairment. Patients with delirium after surgery recover more slowly than those without delirium and, as a result, have increased length of stay and hospital costs. The measured incidence of postoperative delirium varies with the type of surgery, the urgency of surgery, and the type and sensitivity of the delirium assessment. Although generally considered a short-term condition, delirium can persist for months and is associated with poor cognitive and functional outcomes beyond the immediate postoperative period. In this article, we provide a guide to assess delirium risk preoperatively and to prevent, diagnose, and treat this common and morbid condition. Care improvements such as identifying delirium risk preoperatively; training surgeons, anesthesiologists, and nurses to screen for delirium; implementing delirium prevention programs; and developing standardized delirium treatment protocols may reduce the risk of delirium and its associated morbidity. (*Anesth Analg* 2011;112:1202–11)

Delirium is an acute change in cognition characterized by inattention, fluctuating levels of consciousness, and/or disorganized thinking. Postoperative delirium is common, with significant associated morbidity and cost. Patients with delirium after surgery have high in-hospital mortality (4%–17%),<sup>1–3</sup> and 1-month,<sup>4</sup> 6-month,<sup>5</sup> 12-month,<sup>6</sup> and long-term mortality remains elevated.<sup>7,8</sup> Additionally, delirium is associated with increased postoperative complications,<sup>9</sup> longer length of stay,<sup>1</sup> longer intensive care unit stay (ICU),<sup>3</sup> and much higher rates of discharge to a nursing home.<sup>4,10</sup> As a result, delirium adds significant cost to hospitalization and subsequent medical care.<sup>11</sup>

The incidence of postoperative delirium depends on the type of surgery. Table 1 highlights the incidence of delirium by surgical type. Hip fracture has the highest incidence of delirium, which is probably attributable to the urgent nature of the surgery and high comorbidity among these patients. Delirium is also common in patients after surgery for atherosclerosis pathology (cardiac, peripheral vascular, aneurysm repair). Elective and outpatient surgery have a lower, but still significant, incidence of delirium. A major factor in the variation of the reported incidence of delirium

is the method for delirium assessment. For example, in the cardiac surgery literature the methods used for delirium greatly influence the reported incidence of delirium: chart review only (3%),<sup>12</sup> delirium noted during routine clinical care (8%),<sup>13</sup> interviews with nurses (9%),<sup>7</sup> and daily mental status testing and application of a validated diagnostic algorithm (53%).<sup>14</sup>

## DEFINING AND DIAGNOSING DELIRIUM

Because of the morbidity associated with delirium, all patients, especially older patients, should be screened for delirium at least daily and more frequently if they are high risk. An algorithm for the diagnosis of delirium, the Confusion Assessment Method (CAM), which is based on *Diagnostic and Statistical Manual of Mental Disorders–III-R* criteria,<sup>15</sup> has been demonstrated to be reliable, sensitive, and specific for diagnosis of delirium compared with expert clinician examination.<sup>16,17</sup> The algorithm for the CAM is displayed in Figure 1. Briefly, the criteria are a combination of Feature 1 (acute onset and fluctuating course), Feature 2 (inattention), and either Feature 3 (disorganized thinking) or Feature 4 (abnormal level of consciousness).

There are important elements of the CAM that need to be clarified. First, attention is best assessed when formal testing (digit span, months of the year backward, serial 7s, etc.) is combined with interviewer observations.<sup>18</sup> Importantly, orientation items have low sensitivity for inattention, and delirium should not be considered the standard assessment for attention.<sup>19</sup> Additionally, there are 2 variants of delirium, which are characterized as the hyperactive (agitated) variant and the hypoactive (quiet) variant of delirium. The hyperactive variant, which accounts for only approximately 25% of cases, is rarely missed because the patient disrupts the flow of care.<sup>20</sup> The more common hypoactive variant is often missed because the patient is neither disruptive nor threatening.<sup>21</sup> For example, a patient with hypoactive delirium would briefly

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**Table 1. Incidence of Postoperative Delirium**

Surgery	Incidence of delirium (%)	References
Abdominal aortic aneurysm (infra-renal)	33–54	92–95
Abdominal	5–51	67, 92, 96, 97
Cataract	4	98
Coronary artery bypass graft surgery	37–52	14, 99
Elective orthopedic	9–15	92, 100
Head and neck (major)	17	101
Hip fracture	35–65	102
Peripheral vascular	30–48	93, 94
Urologic	4–7	99

wake when addressed and may comply with some requests, but then quickly falls back to sleep. Several studies have found that the hypoactive variant is detected less frequently and carries a higher mortality, presumably from the delay in diagnosis.<sup>21–23</sup> Thus, the CAM is a useful algorithm for diagnosis of delirium, but requires additional assessment of attention and observation.

The CAM-ICU operationalizes the CAM by adding objective assessments for attention, consciousness, and thought.<sup>24</sup> The CAM-ICU has been validated in nonverbal ICU patients.<sup>24</sup> The advantages of the CAM-ICU are that it can be performed by trained nurses or physicians; can be repeated over time to detect fluctuation and changes; and has been associated with ICU outcomes including mortality,<sup>25</sup> length of stay,<sup>26</sup> and cost.<sup>27</sup> The key elements of the CAM-ICU are the Richmond Agitation and Sedation Scale, a validated measure of consciousness,<sup>28</sup> the Attention Screening Examination,<sup>29</sup> and 5 thought questions. This information is used to complete the CAM algorithm for delirium.

### PREOPERATIVE ASSESSMENT FOR DELIRIUM RISK

Many preoperative risk factors for delirium have been described in the literature, and there are validated prediction rules for noncardiac and cardiac surgery to help identify those patients most at risk for postoperative delirium. The noncardiac surgery prediction rule identified 7 factors: age, impaired cognitive function, impaired physical

function, abnormal laboratory values, alcohol abuse, thoracic surgery, and open-aortic surgery.<sup>2</sup> The validated prediction rule for delirium after cardiac surgery identified 4 major risk factors: impaired cognitive function, low albumin, preoperative depressive symptoms, and prior stroke or transient ischemic attack.<sup>14</sup> Table 2 describes the point scoring system for the prediction rules. In both rules, the incidence of delirium increases with increasing points so that the highest risk group is more likely to develop delirium than the lowest risk group (25× in the noncardiac surgery rule and 4× in the cardiac surgery rule). To complete the prediction rules, a thorough history and physical examination with screening for cognition, mood, and physical function are required. The paragraphs below describe risk factors for delirium in more detail.

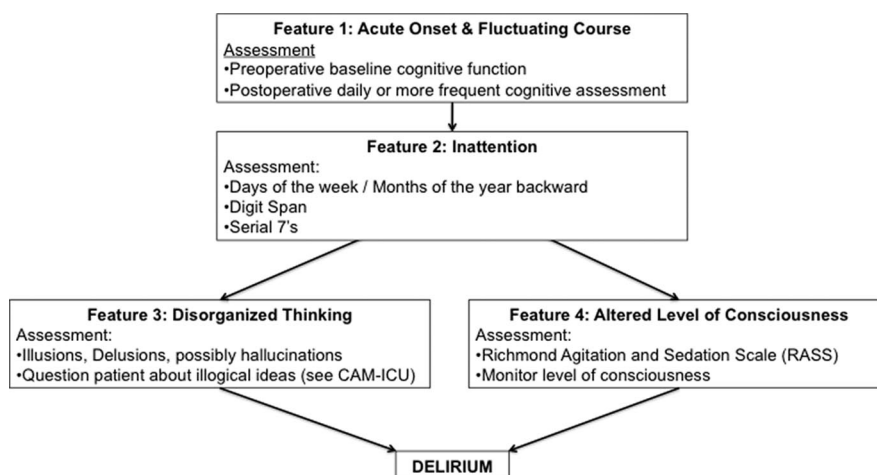
### Preexisting Cognitive Impairment

The most common independent risk factor for delirium across studies is preexisting cognitive impairment. Preoperative cognitive screening is beneficial for assessing delirium risk, as well as documenting baseline performance to detect delirium postoperatively. Cognitive screening should be performed with a standardized screening test. Many brief cognitive tests are available that require <10 minutes to complete.<sup>30,31</sup> Importantly, orientation items and observation of standard conversation are not sufficient to assess for preoperative cognitive deficits.

### Function

Preoperative functional status is an independent risk factor for delirium after noncardiac surgery.<sup>2</sup> The activities of daily living and the instrumental activities of daily living provide an understanding of preoperative function. The activities of daily living measures the ability to perform 7 basic care skills (feeding, bathing, grooming, using the toilet, transferring, and walking).<sup>32</sup> The instrumental activities of daily living assesses the ability to perform 7 complex activities (using the telephone, grocery shopping, using transportation, cooking, house-keeping, taking medications, and handling finances).<sup>33</sup> In addition to providing risk stratification for delirium, assessing this information preoperatively can inform the

**Figure 1.** The algorithm of the Confusion Assessment Method (CAM). The diagnosis of delirium is made with the presence of Feature 1 and Feature 2 and either Feature 3 or Feature 4. Examples of assessments applicable in the postoperative period are included below the features. (Adapted from Inouye et al.<sup>16</sup> and Ely et al.<sup>106</sup>)



**Table 2. Preoperative Prediction Rules for Delirium After Noncardiac and Cardiac Surgery**

Risk factor	Criteria	Factor points	Total rule points <sup>a</sup>	Incidence of delirium (%)
<b>Noncardiac surgery</b>				
Cognitive impairment	TICS score <30	1	0	1–2
Age	≥70 y	1	1–2	8–19
Physical function	SAS class IV	1	≥3	45–55
Alcohol abuse		1		
Abnormal sodium (Na), potassium (K), or glucose	Na <130 or >150 mmol/L; K <3.0 or >6.0 mmol/L; glucose <60 or >300 mg/dL	1		
Aortic aneurysm surgery	Yes/no	2		
Noncardiac thoracic surgery	Yes/no	1		
<b>Cardiac surgery</b>				
Cognitive impairment	MMSE score <24	2	0	18–19
	MMSE score 24–27	1	1	43–47
Hypoalbuminemia	<3.5 g/dL	1	2	60–63
Depression	GDS score >6	1	≥3	86–87
Prior stroke or TIA	Yes/no	1		

TICS = Telephone Interview of Cognitive State<sup>103</sup>; MMSE = Mini-Mental State Examination<sup>104</sup>; SAS = Specific Activity Scale<sup>105</sup>; GDS = Geriatric Depression Scale<sup>43</sup>; TIA = transient ischemic attack.

<sup>a</sup> Total rule points are the sum of factor points for each patient.

patient, the family, and the surgical team about the expected course of recovery postoperatively.

### Abnormal Laboratory Values

Abnormal preoperative laboratory values including glucose, sodium, potassium, and albumin are risk factors for delirium (Table 2).<sup>2,14</sup> These abnormal laboratory values may represent underlying severe disease or organ system dysfunction, which is a predisposing risk factor for delirium. Hypoalbuminemia may be particularly important because of its association with malnutrition, drug binding, fluid management,<sup>34</sup> and perioperative mortality.<sup>35</sup> In the delirium prediction rule for medical patients, blood urea nitrogen to creatinine ratio ≥18, a marker of dehydration, was associated with incident delirium.<sup>36</sup> Consistent with current practice, preoperative assessment of laboratory values can provide information about patients at high risk for delirium.

### Depression

Many studies have identified depression as a risk factor for delirium after surgery.<sup>37–40</sup> Although the pathophysiology of this relationship remains to be determined, it is known that preoperative depression is associated with postoperative depression and incomplete recovery to independent functioning after surgery.<sup>41,42</sup> The assessment of depression in older patients can be easily performed with the 15-question Geriatric Depression Scale, which assesses depressive symptoms using 15 yes/no questions.<sup>43</sup> The advantage of the Geriatric Depression Scale is that it can be self-completed by the older patient and scored by the clinician in a short time frame (3 minutes).<sup>44</sup> In addition to delirium risk, assessment of depressive symptoms may provide insight into a patient's motivation for recovery.

### Comorbidities

Patients with multiple comorbidities are at increased risk of delirium. Alcohol abuse and prior stroke or transient ischemic attack deserve particular mention. Withdrawal from alcohol use has long been understood to precipitate delirium tremens, a variant of delirium.<sup>45</sup> However, most

postoperative delirium is not delirium tremens. Screening for alcohol use preoperatively can allow prevention of alcohol withdrawal with standardized protocols. Additionally, preexisting cerebral damage from prior strokes and transient ischemic attacks,<sup>14</sup> or a long history of alcohol abuse even in the absence of active drinking, has been independently associated with postoperative delirium.<sup>2</sup> Collection of this historical information from the patient or proxy before surgery is sufficient, and routine cerebral imaging is *not* required for assessment of delirium risk.

### Practical Preoperative Screening Considerations

In many older patients, the 5 senses decline with age. The combination of decreased sensory input (e.g., no glasses or hearing aids), cognitive impairment, and the perioperative environment may lead to misinterpretation of communication (i.e., talking back to television conversation), alarms (i.e., telephone ringing), and elements of the environment (i.e., window is a picture frame). Additionally, there is evidence in patients that increasing cognitive stimulation through improved sensory input may prevent delirium.<sup>46,47</sup> As a result, preoperative assessment should include vision and hearing assessments and patients should be encouraged to bring their glasses and hearing amplifiers for use in the postoperative period to improve sensory input.

### PREVENTION OF DELIRIUM

#### Nonpharmacological

Delirium can be prevented in operative and medical patients<sup>46,47</sup> by targeting moderate- and high-risk patients with clinical modules to improve baseline vulnerabilities and avoid iatrogenic complications. A summary of modules for prevention of postoperative delirium based on successful prevention models is presented in Table 3. For example, the nonpharmacological sleep protocols involve environmental changes conducive to sleep (i.e., lights off, creating a relaxing environment, minimizing nighttime interruptions, dedicated time for sleep), which are successful in reducing psychoactive medication use and,

**Table 3. Prevention of Delirium After Surgery**

Module	Postoperative interventions
Cognitive stimulation	<ul style="list-style-type: none"> <li>● Orientation (clock, calendar, orientation board)</li> <li>● Avoid cognitively active medications</li> </ul>
Improve sensory input	<ul style="list-style-type: none"> <li>● Glasses</li> <li>● Hearing aids/amplifiers</li> </ul>
Mobilization	<ul style="list-style-type: none"> <li>● Early mobilization and rehabilitation</li> </ul>
Avoidance of psychoactive medication	<ul style="list-style-type: none"> <li>● Elimination of unnecessary medications</li> <li>● Pain management protocol</li> </ul>
Fluid and nutrition	<ul style="list-style-type: none"> <li>● Fluid management</li> <li>● Electrolyte monitoring and repletion</li> <li>● Adequate nutrition protocol</li> </ul>
Avoidance of hospital complications	<ul style="list-style-type: none"> <li>● Bowel protocol</li> <li>● Early removal of urinary catheters</li> <li>● Adequate central nervous system O<sub>2</sub> delivery, including supplemental oxygen and transfusion for very low hematocrit</li> <li>● Postoperative complication monitoring protocol</li> </ul>

ultimately, delirium.<sup>47</sup> Other key modules include improving sensory input, nutrition, ambulation, and preventing complications.

### Pharmacological

Haloperidol is a high-potency dopamine antagonist (antipsychotic) medication. In a single-site study, prophylactic administration of haloperidol did not reduce the incidence of delirium after hip fracture, but did reduce the severity and duration of delirium.<sup>48</sup> However, severity scales tend to overweight hyperactive symptoms of delirium, so a possible explanation of these findings is the conversion of hyperactive delirium to hypoactive.<sup>49</sup> As noted above, such a conversion may be a convenience for the care team, but actually worsens the prognosis of the patient. A follow-up study comparing high-potency antipsychotic, atypical antipsychotic, and placebo in ICU patients found no difference in the days alive without delirium.<sup>50</sup> As a result, the practice of prophylaxis with antipsychotics should be avoided at present because of increased risk of death, delirium, and complications in older patients attributed to this class of drugs.<sup>51</sup>

Acetylcholinesterase inhibitors are medications used to stabilize cognitive function in patients with Alzheimer disease. A randomized controlled trial of rivastigmine for delirium prevention in cardiac surgery found no effect of treatment on delirium incidence or cognitive performance.<sup>52</sup> In elective orthopedic surgery, the results have been mixed, with one trial showing no effect<sup>53</sup> and another suggesting benefit.<sup>54</sup> A randomized controlled trial of rivastigmine for delirium treatment was stopped early because of increased mortality in the treatment arm and no effect on delirium.<sup>55</sup> Thus, at this time, prevention or treatment of delirium with acetylcholinesterase inhibitors should be avoided.<sup>56</sup>

Dexmedetomidine is an  $\alpha$ -2 adrenergic receptor agonist that is used for sedation. Two recent studies have found

that the use of dexmedetomidine for sedation in the ICU setting reduces the rate of delirium compared with midazolam and lorazepam.<sup>57,58</sup> Additionally, a randomized trial of intraoperative sedation with dexmedetomidine, propofol, or midazolam found that dexmedetomidine was associated with a lower incidence of postoperative delirium.<sup>59</sup> Thus, the use of dexmedetomidine in patients at intermediate risk and high risk for delirium may have benefits that outweigh the potential adverse events.

### PRECIPITATING FACTORS FOR DELIRIUM

The delirium risk factors described above are classified as predisposing factors, that is, factors that can be assessed before surgery and increase the patient's risk. Precipitating factors, a distinct class of risk factors, occur intraoperatively and postoperatively and are thought to acutely precipitate the delirium episode. Precipitating factors for delirium have been more difficult to identify than predisposing factors. A primary challenge has been heterogeneity, attributed to patient factors (age, education, comorbidity), surgery factors (type of surgery, techniques used, hypothermia, bleeding), physiologic factors (inflammation, microembolization, blood-brain barrier function), intraoperative factors (anesthesia, cerebral oxygenation, hypotension), perioperative factors (medication, sleep, complications), and postoperative factors (rehabilitation, depression, social supports). Thus, not all of the precipitating factors for postoperative delirium have been fully elucidated. Table 4 summarizes predisposing (preoperative) and known precipitating (intraoperative and postoperative) factors that may be associated with delirium.

### Intraoperative Medications

During surgery, numerous medications with properties that affect cognition are given to patients. Inhaled anesthetics alter electrical activity in the brain<sup>60</sup> and have been associated with amyloid deposition and apoptosis.<sup>61</sup> Induction drugs and benzodiazepines have significant properties that affect cognition that may precipitate delirium.<sup>62</sup> Although regional anesthesia has the potential to reduce this exposure, studies of general versus regional anesthesia have not demonstrated a reduction in delirium.<sup>63</sup> One reason for this may be the concomitant administration of sedatives in addition to the regional anesthetic. In a recent randomized study, lighter depth of sedation, measured with the bispectral index, resulted in 50% less postoperative delirium than deep sedation.<sup>64</sup>

Pain medications may precipitate delirium, particularly meperidine, which increases the odds of delirium over other opioids.<sup>62</sup> Many of these medications are necessary for the operation; however, the clinically important point is to recognize the risk for delirium associated with medications with properties that affect cognition and minimize the exposure to these medications, especially in older patients with cognitive impairment.

### Postoperative Medications: Sedation and Analgesia

After surgery, many patients are given medications that can impair cognitive function. For example, in the postoperative tracheally intubated patient, sedatives such as benzodiazepines or propofol are given. In these patients, dexmedetomidine used for sedation may reduce the risk of

**Table 4. Predisposing and Precipitating Factors for Delirium After Surgery**

Predisposing factors, preoperative	Precipitating factors	
	Intraoperative	Postoperative
Demographics	Type of operation	Early complications of operation
Increasing age	Hip fracture	Low hematocrit
Male gender	Cardiac surgery	Cardiogenic shock
Comorbidities	Vascular surgery	Hypoxemia
Impaired cognition	Complexity of operation	Prolonged intubation
Dementia	Operation time	Sedation management
Mild cognitive impairment	Shock/hypotension	Pain
Preoperative memory complaint	Arrhythmia	Later complications of operation
Atherosclerosis	Decreased cardiac output	Low albumin
Intracranial stenosis	Emergency surgery	Abnormal electrolytes
Carotid stenosis	Operative factors	Iatrogenic complications
Peripheral vascular disease	Intraoperative temperature	Pain
Prior stroke/transient ischemic attack	Benzodiazepine administration	Infection
Diabetes	Propofol administration	Liver failure
Hypertension	Blood transfusion	Renal failure
Atrial fibrillation	Anesthesia factors	Sleep-wake disturbance
Low albumin	Type of anesthesia	Alcohol withdrawal
Electrolyte abnormalities	Duration of anesthesia	
Psychiatric disease	Cognitively active medications	
Anxiety		
Depression		
Benzodiazepine use		
Function		
Impaired functional status		
Sensory impairment		
Lifestyle factors		
Alcohol use		
Sleep deprivation		
Smoking		

delirium.<sup>59</sup> Out of the ICU setting, benzodiazepine and sedative use may be minimized by improving sleep hygiene using nonpharmacological measures such as decreasing environmental noise, creating a relaxing environment, and preserving the circadian rhythm.<sup>47</sup>

Although opioids may precipitate delirium, uncontrolled pain may also precipitate delirium.<sup>62</sup> When opioid pain medication is needed after surgery, standardized age-adjusted protocols should be used to treat pain and taper opioid doses. Strong consideration should be given to standing pain medication, especially acetaminophen, which has been shown to reduce total opioid needs and improve patient reports of pain in a postoperative randomized controlled trial.<sup>65</sup> The advantage of acetaminophen is its limited cognitive properties, compared with opioids. Even in patients who require opioids, administration on a schedule has been shown to reduce total dose needs relative to as-needed dosing.<sup>66</sup> Patient-controlled analgesia improves pain control; however, caution should be used in older patients with cognitive impairments and those who have developed delirium.<sup>67</sup> In summary, postoperative sedative use should be minimized, and postoperative analgesia should be administered using rational, carefully designed protocols designed to minimize systemic exposure to opioids with psychoactive properties.

### Postoperative Environment

After cardiac surgery, patients are transferred to the ICU environment, which is busy, noisy, and light-filled, where

patients are approached, assessed, and stimulated constantly. Recent work in the ICU setting found that the environment may contribute to delirium through sleep deprivation and overstimulation.<sup>68</sup> Although this environment may be required in the immediate postoperative period, early transfer of medically stable patients to less-intense wards should be considered. Additionally, consideration should be given to balancing the patient's monitoring needs with the sleep requirements of the patient (i.e., Does the patient need a standing order for vital signs at midnight and 4 AM?). Even the non-ICU environment can be disorienting: preservation of the sleep-wake cycle (minimized nighttime interruptions, adequate lighting, sleep hygiene), provision of orienting supplies (clock, calendar, orientation board), and cognitively stimulating activities (glasses, hearing amplifiers, puzzles) may minimize precipitation of delirium.<sup>46,47</sup>

### Iatrogenic Events

Complications of hospitalization and surgery can precipitate delirium. For example, a leading identifiable cause of delirium in older inpatients is urinary tract infection associated with catheter use.<sup>69</sup> Preventable medical processes such as deep venous thrombosis, pressure ulcer, deconditioning, malnutrition, and dehydration should be assessed using a standardized team-based approach.<sup>46</sup> Additionally, reduced mobility through formal restraints or informal tethers (i.e., IV lines, oxygen tubing, urinary catheters, etc.) can contribute to delirium, loss of function, falls, and increased rehabilitation placement.<sup>70</sup> The routine use of

care systems to prevent postoperative complications may also prevent delirium.

## EVALUATION AND TREATMENT OF DELIRIUM

### Identify and Treat the Etiology

The primary treatment of delirium is to identify and treat its underlying causes. Thus, it is recommended that the clinician begin with a broad differential diagnosis and systematically eliminate potential causes. It should be noted that delirium is associated with significant morbidity and mortality, and thus, all patients with delirium should be assessed promptly with an interim history, thorough physical examination with a focus on the neurological examination, and targeted laboratory testing based on the history and examination. Most patients with delirium require at least basic laboratory testing including a complete blood count, basic metabolic panel including renal function, and urinalysis. It is also important to carefully review the patient's medications, particularly the nursing administration record where it is clear exactly what medications the patient received and when. It is also important to note that the causes of delirium are often multifactorial, and therefore the search for additional causes and contributors to delirium should not be terminated when a single cause has been identified.

### Cerebral Imaging in the Evaluation of Delirium

Prior work has found that in the absence of focal neurological deficits, a head computed tomography has low diagnostic value in the assessment and treatment of the delirious patient.<sup>71</sup> Magnetic resonance imaging in the postoperative patient is difficult because of the acuity of illness, recently implanted hardware (e.g., staples, prostheses, grafts, and valves), and the time and cooperation required for scanning. In the patient with delirium, sedation, which can worsen or prolong the delirium, may be needed for imaging.<sup>72</sup> In the patient after cardiac surgery, there will likely be new foci on imaging related to microemboli during the operation.<sup>73</sup> Because the causal link between microemboli and delirium has not been established,<sup>74</sup> the clinical significance of such findings is unknown. Additionally, stroke thrombolysis is contraindicated in the postoperative surgery patient,<sup>75</sup> so the potential treatments for stroke are limited in this setting. The treatment of occlusive infarct in postoperative patients is identical to the treatment of cardiac disease (e.g., aspirin, statin, arterial blood pressure control, cardiac risk reduction, and rehabilitation). Therefore, cerebral imaging should be restricted to those with new focal neurological findings, or those at very high risk in whom no other cause of delirium can be identified.

### Management of Agitation Associated with Delirium

For patients who develop agitation, a thorough review of the medications and physical examination, including pain assessment, is required. First, the offending precipitant of the delirium (constipation, urinary retention, etc.) should be relieved. Nonpharmacological treatments should also be initiated, regardless if the cause is identified. For example, elimination of environmental noise, allowing the patient to

sleep at night, and reorientation efforts should be implemented. A model of care for the delirious patient found that environmental modifications and staff training could produce reductions in patient agitation and use of psychoactive medications, with similar length of stay.<sup>76</sup> Another useful resource is family members who can serve as a reorienting and reassuring stimulus. Because of the low risk of adverse events, nonpharmacological methods are recommended as a first step.

For patients in whom these nonpharmacological interventions are not sufficient, antipsychotics are considered the first line for the pharmacological management of agitation associated with delirium.<sup>51,77</sup> For most patients, haloperidol at a low initial dose of 0.5 to 1.0 mg is a reasonable choice. If there is no response within 1 hour, a repeat dose may be considered. If there is no effect after 2 to 3 mg of haloperidol, it is unlikely that the patient is going to respond. Higher doses administered IV are frequently used in ICU patients.<sup>50</sup> Antipsychotics administered in the acute setting have not demonstrated to increase mortality, but even intermediate-term (6–12 weeks) use of antipsychotics is considered to carry an increased mortality, especially in cognitively impaired patients.<sup>78,79</sup> Additionally, electrocardiograms should be performed at baseline and monitored in high-risk patients (i.e., older age, atherosclerosis pathology, major surgery) taking high-dose antipsychotics because of the risk of QTc prolongation.<sup>80</sup> Finally, early evidence suggests that acute administration of antipsychotics may be associated with oropharyngeal dysphagia, which may further delay recovery.<sup>81</sup> At this time, there is no evidence for an incremental benefit of atypical antipsychotics beyond that of haloperidol for the treatment of delirium.<sup>51</sup>

For patients with contraindications to antipsychotics such as Parkinson disease, Lewy Body dementia, prior seizures, and prior neuroleptic malignant syndrome, agitation may be better managed with benzodiazepines. In general, benzodiazepines disinhibit patients and patients should be monitored for a paradoxical reaction, whereby administration of the benzodiazepine results in agitation. Additionally, prior work has shown that benzodiazepines may actually prolong or worsen the course of delirium.<sup>72</sup> Finally, respiratory depression becomes a risk in older patients with respiratory comorbidities who have just undergone surgery. Thus, other than the specific case of alcohol or chronic sedative withdrawal, use of benzodiazepines should not be considered a first-line therapy and should be reserved for cases in which clinical circumstances limit use of antipsychotics.

## IMPLICATIONS OF DELIRIUM BEYOND THE PERIOPERATIVE PERIOD

### Persistent Delirium

Although generally thought of as a short-term disorder, delirium can have lasting effects beyond the perioperative period. First, delirium itself can persist for months. In a study of patients with delirium upon admission to a rehabilitation facility after hospitalization, delirium persisted for 6 months in one-third of patients.<sup>82</sup> Persistent delirium increased the 1-year mortality and prevented functional recovery.<sup>82,83</sup> There is an increasing body of

evidence that persistent delirium can delay both cognitive and functional recovery.<sup>10</sup>

## Postdelirium Mental Health

Delirium may accelerate the cognitive decline in patients with Alzheimer disease.<sup>84</sup> Although delirium is thought to be distinct from postoperative cognitive dysfunction, the 2 syndromes may be highly correlated in the short term (1 week).<sup>85–87</sup> The impact of delirium on long-term postoperative cognitive dysfunction has been less consistent.<sup>85,86,88</sup> In addition to cognitive function, delirium has been associated with postoperative depression,<sup>37,38</sup> another factor that may impede recovery. Finally, newer evidence is emerging that (younger) patients with delirium may develop a posttraumatic stress disorder–like syndrome.<sup>89,90</sup> As a result, delirium may have long-term mental health complications that are not fully studied and may affect functional recovery.

## Functional Decline

Several studies have demonstrated that postoperative delirium is associated with functional decline and nursing home placement 1 to 3 months after surgery.<sup>4,91</sup> However, these same studies have not demonstrated a consistent association between delirium and functional decline  $\geq 6$  months after surgery. This difference may be related to reduced statistical power because of decreased functional decline rates in the long term and dropout of the patients with delirium.<sup>4,91</sup> Future work in larger epidemiological studies will help determine the relationship between the incidence of delirium and long-term functional change after surgery.

## CONCLUSION

Delirium is an acute change in cognitive function, specifically attention, with associated disorganization of thought and abnormal level of consciousness. Postoperative delirium is very common, especially in older surgical patients, and is associated with substantial morbidity, costs, and mortality. Preoperative delirium risk assessment is critical for identification of those patients who would most benefit from delirium prevention and surveillance protocols. Non-pharmacological delirium prevention strategies have proven effective at reducing delirium incidence, but pharmacological prevention strategies do not yet have trial-based support. The primary treatment of delirium is to identify and treat the underlying causes. Delirium has substantial long-term consequences, which are currently being better defined through large-scale epidemiological studies. Assessing preoperative delirium risk, using delirium prevention strategies, and implementing standardized treatment protocols are important components of optimal care for older patients undergoing surgery. ■

## DISCLOSURES

**Name:** James L. Rudolph, MD, SM.

**Contribution:** Study design, conduct of study, data collection, data analysis, and manuscript preparation.

**Name:** Edward R. Marcantonio, MD, SM.

**Contribution:** Study design, conduct of study, data collection, data analysis, and manuscript preparation.

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### **Dolasetron for Preventing Postanesthetic Shivering: Retraction**

The editor in chief of *Anesthesia & Analgesia* requests the retraction of the article “Dolasetron for preventing postanesthetic shivering” by Swen N. Piper, Kerstin D. Röhm, Wolfgang H. Maleck, Moritz T. Fent, Stefan W. Suttner, and Joachim Boldt (*Anesthesia & Analgesia*, January 2002, volume 94, pages 106–111). Please see Editor’s Note: Notices of Retraction on page 1246 in this issue.

#### **Reference:**

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### **Colloids Versus Crystalloids and Tissue Oxygen Tension in Patients Undergoing Major Abdominal Surgery: Retraction**

The editor in chief of *Anesthesia & Analgesia* requests the retraction of the article “Colloids versus crystalloids and tissue oxygen tension in patients undergoing major abdominal surgery” by Katrin Lang, Joachim Boldt, Stefan Suttner, and Günther Haisch (*Anesthesia & Analgesia*, August 2001, volume 93, pages 405–409). Please see Editor’s Note: Notices of Retraction on page 1246 in this issue.

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