Postoperative delirium in elderly citizens and current practice

Siddareddygari Velayudha Reddy, Jawaharlal Narayanas Irkal, Ananthapuram Srinivasasumurthy
Department of Anaesthesiology and Critical Care, Navodaya Medical College and Research Center, Raichur, Karnataka, India

Abstract

Postoperative delirium (POD) represents an acute brain dysfunction in the postsurgical period. Perioperative physicians caring for the older adults are familiar with the care of dysfunction of organs such as lungs, heart, liver, or kidney in the perioperative setting, but they are less familiar with management of brain dysfunction. As early detection and prompt treatment of inciting factors are utmost important to prevent or minimize the deleterious outcomes of delirium. The purpose of this review is to prepare perioperative physicians with a set of current clinical practice recommendations to provide optimal perioperative care of older adults, with a special focus on specific perioperative interventions that have been shown to prevent POD. On literature search in EMBASE, CINAHL, and PUBMED between January 2000 and September 2015 using search words delirium, POD, acute postoperative confusion, and brain dysfunction resulted in 9710 articles. Among them, 73 articles were chosen for review, in addition, National Institute for Health and Clinical Excellence guidelines, American Geriatric Society guidelines, hospital elderly life program-confusion assessment method training manual, New York geriatric nursing protocols, World Health Organization’s International Classification of Diseases, 10th Revision classification of mental disorders, Food and Drug Administration requests boxed warnings on older class of antipsychotic drugs 2008 and delirium in Miller’s text book of anesthesia were reviewed and relevant information presented in this article.

Keywords: Current practice, elderly citizens, postoperative delirium, prevention

Introduction

Postoperative delirium (POD) is an acute disorder of cognition and attention, exhibits fluctuating symptoms of inattention, cognitive dysfunction, associated with disorganized thinking, and altered level of consciousness.[1] Other features of this syndrome include disorientation, impaired memory, perceptual instability, altered psychomotor activity, and altered sleep-wake cycles.[2] POD is one of the most unexpected and perplexing complications encountered following surgery. POD is associated with longer duration of hospital stays, more frequent discharge to long-term care amenities leading to greater cost with additional complications of poor recovery and increased mortality.[3] Even though POD is reversible in character, because of its long lasting sequelae in the form of cognitive deficits remaining for up to months, it can become chronic particularly in the elderly citizens following surgery.[4] In older patients, delirium can be a key factor in initiating a cascade of events that may lead to a, loss of independence, decline of executive function, institutionalization, and ultimately, death.[5]

The capability to predict patients at high risk for POD has enabled the physicians to do proactive interventions to prevent or to reduce the rate and severity of POD. Thus, a cornerstone in the management of POD is the detection and treatment of any underlying inciting factor. Therefore to familiarize the clinician in the management of POD a targeted literature search was performed, in EMBASE, CINAHL, and PUBMED between January 2000 and September 2015 using the keywords “delirium,” “postoperative delirium” “acute postoperative confusion” and “brain dysfunction”
resulted in 9710 articles, among them 73 articles were chosen for review. In addition National Institute for Health and Clinical Excellence guidelines, American Geriatric Society Guidelines, Hospital elderly life program-confusion assessment method (CAM) training manual, New York geriatric nursing protocols, World Health Organization’s International Classification of Diseases, 10th Revision (WHO ICD-10) classification of mental disorders, Food and Drug Administration requests boxed warnings on older class of antipsychotic drugs 2008 and delirium in Miller’s text book of anesthesia were reviewed.

Articles published in English language, describing precipitating, predisposing factors, pathophysiology, clinical features, diagnosis, preventive strategies, treatment regimens and outcomes of POD particularly in elderly, were analyzed and relevant information presented in this article. Excluded topics were delirium biomarkers, predictive models, prognostic methods, tools of assessment, alcohol or substance abuse, withdrawal, nonelderly populations (e.g., pediatric), dementia (e.g., Alzheimer disease), psychosis (e.g., schizophrenia), terminal illness (e.g., acute stroke), brain surgery, and traumatic brain injury.

The Epidemiology

The overall incidence of delirium is just 1%–2%, in the society, but in the hospital setting after admission this increases to 14%–24%. The rate of delirium occurring during a hospital stay increase from 6% to 56%, and this number is still higher in those admitted in the Postanesthesia Care Unit, Intensive Care Unit (ICU) and palliative-care settings. POD complicates in 15%–53% of surgical patients aged above 65 years, and among these patients admitted to ICU the occurrence of POD can reach as high as 70%–87%.

Risk Factors for Development of Postoperative Delirium

Development of POD depends on a compound interaction of multiple risk factors. A few of these risk factors are modifiable and are possible targets for delirium prevention. Health-care workers caring for elderly surgical patients should conduct a preoperative assessment for delirium risk factors, including age older than 65 years, dementia or chronic cognitive decline, poor vision, impaired hearing, severe illness, existence of infection, and any other risk factor as shown Table 1. Patients with two or more risk factors should have greater risk for POD than patients with no or single risk factor. The risk for POD, in general, is greater in the emergency situation in comparison with the elective setting.

Pathophysiology

Many possible pathophysiologic mechanisms were postulated for the development of delirium. The widely

| Table 1: Risk factors for development of postoperative delirium |
|---------------------------------------------------------------|
| **Modifiable risk factors**                                   | **Nonmodifiable risk factors** |
| Preoperative predisposing factors                             | Age > 65 years                 |
| Immobilization or limited mobility                           | Male gender                    |
| Hearing or vision impairment                                 | ASA physical status ≥III       |
| Presence of infection or shock                               | History of delirium, stroke, neurological disease, falls, or gait disorder |
| Inadequately controlled pain, use of opioid analgesic commonly mepridine | Current hip fracture            |
| Depression                                                   | Dementia or cognitive impairment |
| Alcohol abuse or smoking                                     | Functional impairment           |
| Anemia and hypoalbuminemia                                   | Renal or hepatic insufficiency  |
| Decreased oral intake and malnutrition                       |                                |
| Intra-operative precipitating factors                        |                                |
| Hypoxia or hypercarbia                                       |                                |
| Dehydration-oliguria                                         |                                |
| Use of psychotrophic medications (antipsychotics, benzodiazepines, anticholinergics, antihistamines, meperidine) |                                |
| Electrolyte abnormalities (hyper- or hypo-natremia)          |                                |
| Poly-pharmacy: More than 5 drugs at a time                   |                                |
| Postoperative precipitating factors                          |                                |
| Risk of urinary retention or constipation                     |                                |
| Presence of urinary catheter                                 |                                |
| Pain, emotional distress                                     |                                |
| Sustained sleep deprivation                                  |                                |

ASA = American Society of Anesthesiologists, ICU = Intensive Care Unit
suggested mechanisms include alterations in one of several neurotransmitter systems, inflammatory mediators, physiological stress, metabolic disorders, and electrolyte disturbances. An extensive evidence supports an imbalance between dopaminergic and cholinergic neurotransmitters as a key factor in the genesis of delirium. In fact, drugs with anticholinergic properties can incite delirium and therapy with cholinesterase inhibitors such as physostigmine can effectively reverse delirium in some occasions. The antipsychotics, which block dopamine receptors are successful in the treatment of delirium. Thus, a reduced cholinergic reserve and relative excess of dopaminergic transmission in certain regions of the brain were related to the development of delirium. Pro-inflammatory mediators, such as interferon α or β, interleukin (IL)-1β, IL-6, IL-8, IL-10 and tumor necrosis factor-alpha, may contribute to the genesis of delirium by increasing the blood brain barrier permeability, thereby altering neurotransmission. In addition, biological stressor response from anesthesia and surgery is known to incite sympathetic over activity to liberate glucocorticoids which may play a key role in the genesis of delirium.

Although the basic pathophysiologic mechanisms of delirium are not yet completely understand, in the geriatrics prototype, delirium characterizes an atypical presentation of disease, in which acute disease is manifested through weakest link of the most susceptible organ system, in this case, it is brain, results in delirium. This hypothesis explains that the normal course of aging can be characterized as homeostenosis, the progressive shrinkage and constriction of homeostatic reserve in every organ system’s ability to respond to stress. In addition, the aging brain is more prone to be affected by drugs and that cloud the sensorium of brain. The sum of all these effects leads some older adults to be teetering on the edge of neurodysfunction. If these elderly people are subjected to the stressor, is now beyond the reserve limits as a result of homeostenosis of aging. In this case, it is brain centered, decompensation occurs, because compensatory mechanisms are over whelmed, results in delirium.

Clinical Features

All health-care workers need familiarity with the symptoms and signs of delirium. POD can develop from the 1st to 3rd postoperative day. The clinical manifestations of delirium vary and can often be vague. On the basis of psychomotor behavior Robinson et al. using validated instruments measured and broadly classified delirium into three subtypes.

• The hypoactive type, in which patients are withdrawn and quiet, unaware, with prominent lethargy or apathy, decreased alertness, staring, psychomotor slowing, slowed movements, sparse, or slow speech

• The hyperactive type, featuring prominent agitation, hyperarousal, hypervigilance, irritability, restlessness, combativeness, fast or loud speech, singing, swearing, laughing, fast motor responses, hallucinations, impatience, anger, uncooperative, wandering, easy startling tangentiality, distractibility, nightmares, or persistent thoughts, often associated with life-endangering autonomic instability

• The last mixed type in which patients frequently fall somewhere along a spectrum between the hyperactive and hypoactive extremes, sometimes swinging from one to the other type within minutes.

In most cases, the clinical features of delirium have a tendency to fluctuate both in severity and type, with a lucid interval in between. It has been implicated that each subtype of delirium can result from a different pathological mechanism, and that each one might carry a varied prognosis.

Delirium Screening Tools

A range of bedside screening devices are available to help the clinician in the recognition of delirium. Many screening instruments have been narrated in the published articles, among them 11 tools were identified for the evaluation of delirium. The CAM was reported as the best validated and most accurate of the tools reviewed. The CAM operates on the Diagnostic and Statistical Manual, 4th edition (DSM-IV) criteria, increased reliability is demonstrated when health-care professionals trained in the use of a screening tool evaluated the patients for delirium. CAM is used by many as a screening instrument (short form) and diagnostic tool (long form with algorithm). The CAM is a bedside rating scale developed to assist clinicians not trained in psychiatry for rapid and accurate diagnosis of delirium in clinical settings, can be administered by any health-care worker and may also be administered by trained lay interviewers. The sensitivity of the CAM is 94%–100%, with specificity 90%–95% against the gold standard of psychiatric diagnosis. Other validated instruments commonly used for screening delirium are delirium symptom interview and nursing delirium screening scale. The CAM-ICU and Intensive Care Delirium Screening Check List has been adapted for measuring delirium of ventilated patients in the ICU. For elective surgery, patients should have their preanesthetic cognitive testing to record their baseline level.

Diagnosis of Delirium

Early diagnosis and treatment of POD are crucial components for precise surgical care of older adults. The most important step
to establish the diagnosis of delirium is obtaining history from
an observer (e.g., caregiver or family member), doing a brief
cognitive assessment (e.g., level of arousal for verbal stimulus,
low arousal states of acute onset, disorientation to time place
and changes in language indicate cognitive deficit. Attention
can easily be assessed by simple bedside tests such as digit
span or telling the months of the year backwards) and review of
medical records. For laboratory investigations, targeted testing
is the best strategy. Table 2\[^{11,35}\] summarizes the recommended
work-up and diagnostic assessments (e.g., laboratory testing
or neuroimaging) on the basis of the patient’s history and
physical examination.\[^{35}\]

A high degree of clinical suspicion is the mainstay to discern
delirium in older patients after surgery.\[^{36}\] ”The hallmark
of delirium is acute fluctuating cognition from baseline,
inattention is the cardinal feature of delirium, associated with
either disorganized thinking or an altered level of consciousness
are diagnostic of delirium. Use of a cognitive test is required
for accurate diagnosis, a formal delirium diagnostic tool such as
the DSM-V,\[^{37,38}\] the WHO ICD-10,\[^{39}\] or CAM diagnostic
algorithm”\[^{29}\] used by a competent health care professionals will
make the diagnosis of delirium more accurately.

### Prevention

Prevention is the most effective strategy to minimize the
detrimental outcomes of delirium, and an estimated 30%–40%
of cases of POD can be preventable by early treatment of
predisposing factors.\[^{5}\] Although the evidence is weaker
for prevention of delirium, several moderate to high quality
studies demonstrated benefit from non-pharmacologic
measures [Box 1].\[^{9,40-44}\] Implementing and monitoring these
interventions by an interdisciplinary team, may successfully

---

**Table 2: Approach to a patient for evaluation of delirium**

| Approach |
|-------------------------|
| An organic cause should be ruled out first by detailed history, physical examination, laboratory investigations, or other diagnostic tests |
| Any risk-associated medications, doses may be minimized or stopped temporarily |

| History |
|-------------------------|
| Baseline cognitive function, attention and acute changes in mental status (history from staff or surrogates) can be assessed while taking history from the patient |
| Recent changes in condition, new diagnoses |
| Review all current drugs (including herbal preparations and over-the-counter purchases); pay special attention to new drugs and drug interactions |
| Review sleep disturbances, sedative and alcohol use |
| Assess discomfort and pain (e.g., thirst, urinary retention and constipation) |

| Physical examination |
|-----------------------|
| Vital signs, record postural vital signs as required |
| Measure core body temperature, oxygen saturation |
| Thorough physical examination and review of all systems |
| The neurologic examination requires a careful assessment of mental status |
| Search for signs of systemic infection, dehydration, deep vein thrombosis, acute abdominal pain and other acute illness |
| Look for sensory impairments e.g., visual and hearing |
| Investigate for meningitis signs and focal neurological changes |
| Explore for evidence for nonconvulsive status epilepticus |

| Laboratory investigations (selected tests based on history and physical)* |
|--------------------------|
| Consider complete hemogram; urinalysis; measurement of concentrations of serum glucose, electrolytes and calcium |
| Tests for renal, liver, pulmonary, and thyroid function |
| Send urine, blood and sputum for cultures |
| Measure serum concentrations of drugs, cortisol, ammonia, and vitamin B12 |
| Arterial blood gas analysis |
| Do ECG |
| Lumbar puncture should be reserved for evaluation of fever with headache and meningitis signs or suspicion of encephalitis |

| Targeted imaging (in selected patients) |
|-----------------|
| X-ray, chest and abdomen |
| Electroencephalography (in selected patients of suspected encephalitis and head trauma) |
| Computed tomography brain (stroke can present as delirium) |

| Review all medical records including nursing notes |
|-----------------|
| Differentiate other psychiatric disorder from delirium |

*Conducting all these tests in all patients is not necessary; rather, specific tests should be performed guided by history, physical examination, and previous results. ECG = Electrocardiography
reduce the rate of POD about 30%–40% in the postsurgical period.\[42,44\]

**Perioperative Preventive Measures**

Although several intra-operative issues were studied for their effect on POD, however there is inadequate information on the topics studied earlier, which including regional anesthesia versus general anesthesia (GA), specific anesthesia agents, intra-operative blood transfusion, systemic arterial pressure monitoring and use of medications such as statins or dexamethasone. Previous studies have found deep sedation was associated with increased rates of POD and lighter planes of anesthesia will reduce POD in comparison with deeper sedation.\[45\] A Randomized use of Bispectral Index by anesthesia providers to guide anesthesia depth during GA have reduced the incidence of POD in older patients when compared with those who received regular care. Monitoring anesthetic depth during intravenous sedation or GA for older patients using processed electroencephalographic (EEG) monitors may reduce POD. The idea is that by EEG monitoring and providing a lighter depth of anesthesia by administering lower doses or fewer anesthetic agents will reduce POD in comparison with deeper sedation.\[46,47\]

Inadequate postoperative analgesia contributes to development of POD. Postoperative pain control is paramount to curtail the frequency of delirium.\[48,49\] A magnitude of evidence suggests that nonopioid analgesics diminish POD in comparison with opioid-only analgesic regimes.\[50,51\] The use of regional anesthesia has been found to reduce POD in two studies.\[52,53\] Current practice guidelines to improve the safety of medication use in older adults advocated avoidance of drugs prone to enhance the severity or risk of delirium [Table 3].\[54,55\]

Prescribing antipsychotic medications to prevent POD has limited, conflicting, and contradictory support in the literature. Several studies found decreased incidence of delirium with prophylactic antipsychotics,\[57-59\] and a few did not.\[60-62\] Potential tribulations of this class of medication are considerable; therefore, antipsychotics are not recommended to thwart delirium.\[63-66\] Prophylactic administration of newly approved cholinesterase inhibitors are not effective in reducing POD,\[67,69\] and may cause increased harm including mortality,\[70\] hence, no prophylaxis is currently recommended with these agents in the current practice guidelines.

**Treatment of Delirium**

Even though, the quality of evidence is low for recognizing and treating the underlying inciting factors of a patient’s delirium, health-care professionals are strongly recommended to carry out a medical evaluation, make environmental and medication adjustments, and perform appropriate investigations to identify and treat underlying contributors for development of POD. Neuroimaging is generally limited to patients with recent head trauma or falls, focal neurologic signs, use of anticoagulation and fever of unknown explanation [Table 2].\[11,35\] Thus, the treatment of POD consists of treating the underlying cause, correcting fluid, electrolyte imbalance, hypoxia, and removing catheters if present. The next step consists of initiating the nonpharmacological measures, which are similar to preventive measures [Box 1] \[9,40-44\] but also include regimens for de-escalation of agitation, education of nurses, physicians, and proactive geriatric consultation, the last step is treating the patients who are restless, aggressive, agitating and harm to self or others with antipsychotics [Table 4].\[39,55,71,72\]

Current practice guidelines recommended lowest effective dose and shortest duration of antipsychotics to treat patients who are severely violent or aggressive, and are threatening sizeable harm to others or self. In all patients, management with antipsychotics should be started only if behavioral procedures have failed or are not possible, and continuing use should be assessed daily with physical examination of patients. Antipsychotic or benzodiazepines [Table 4]\[39,55,71,72\] are not prescribed for treatment of POD in older adults who are not agitated or distressed.\[23\] No current evidence supports the routine use of benzodiazepines in the delirium treatment. There
Reddy, et al.: Postoperative delirium in elderly

is a significant evidence that benzodiazepines promote delirium.\textsuperscript{[23]} Conversely, benzodiazepines remains the suggested therapy for treatment of alcohol and drug withdrawal induced delirium.\textsuperscript{[24]}

**Outcome**

POD, which results from dissimilar multiple etiologies, can contribute to poor patient outcome, irrespective of the
underlying cause. It has been reported that POD is associated with poor outcomes even after controlling basic patient personality and etiological factors,[73] and the more severe the occurrence of POD, the poorer will be the outcome.[76] Some patients (33%) never get back to their baseline state of cognitive function following an attack of delirium and show persistent functional and cognitive deficits. Patients with dementia who subsequently develop delirium, besides demonstrating worst outcomes, have higher rates (33%) of institutionalization, hospitalization and death than those who do not suffer from this condition.[77-80]

**Conclusion**

POD is a serious cause and complication of hospitalized elderly patients. Irrespective of the specific etiology, POD has the potential to distinctly affect the overall outcome and prognosis of severely ill patients, as well as significantly increasing health-care costs. Nonpharmacologic prevention strategies have shown to be effective at diminishing the incidence of delirium; as pharmacological prevention strategies have no trial-based support. Assessing and recognizing delirium risk preoperatively, implementing delirium prevention strategies, and applying standardized treatment protocols when it occurs are essential components of optimal perioperative care for elderly citizens.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Dasgupta M, Dumbrell AC. Preoperative risk assessment for delirium after noncardiac surgery: A systematic review. J Am Geriatr Soc 2006;54:1578-89.
2. Kalisvaart KJ, Vreeswijk R, de Jonghe JF, van der Ploeg T, van Gool WA, Eikelenboom P. Risk factors and prediction of postoperative delirium in elderly hip-surgery patients: Implementation and validation of a medical risk factor model. J Am Geriatr Soc 2006;54:817-22.
3. Yildizeli B, Ozuyurtkan MO, Batirel HF, Kuscuk K, Bekiroglu N, Yüksel M. Factors associated with postoperative delirium after thoracic surgery. Ann Thorac Surg 2005;79:1004-9.
4. Cavaliere F, D’Ambrosio F, Volpe C, Masieri S. Postoperative delirium. Curr Drug Targets 2005;6:807-14.
5. Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: Diagnosis, prevention and treatment. Nat Rev Neurol 2009;5:210-20.
6. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: A systematic literature review. Age Ageing 2006;35:350-64.
7. Girard TD, Ely EW. Delirium in the critically ill patient. Handb Clin Neurol 2006;90:39-56.
8. Bruce AJ, Ritchie CW, Blizzard L, Lai R, Raven P. The incidence of delirium associated with orthopedic surgery: A meta-analytic review. Int Psychogeriatr 2007;19:197-214.
9. Inouye SK. Delirium in older persons. N Engl J Med 2006;354:1157-65.
10. Pisani MA, McNicol L, Inouye SK. Cognitive impairment in the Intensive Care Unit. Clin Chest Med 2003;24:727-57.
11. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet 2014;383:911-22.
12. National Institute for Health and Clinical Excellence. Delirium: Diagnosis, Prevention, and Management; July, 2010. Available from: http://www.nice.org.uk/cg103. [Last accessed on 2015 Sep 19].
13. Chaput AJ, Bryson GL. Postoperative delirium: Risk factors and management: Continuing professional development. Can J Anaesth 2012;59:304-20.
14. Simone MJ, Tan ZS. The role of inflammation in the pathogenesis of delirium and dementia in older adults: A review. CNS Neurosci Ther 2011;17:506-13.
15. Trezpac T. Is there a final common neural pathway in delirium? Focus on acetylcholine and dopamine. Semin Clin Neuropsychiatry 2000;5:132-48.
16. Campbell N, Boustani M, Limbili T, Ott C, Fox C, Maidment I, et al. The cognitive impact of anticholinergics: A clinical review. Clin Interv Aging 2009;4:225-33.
17. Deiner S, Silverstein JH. Postoperative delirium and cognitive dysfunction. Br J Anaesth 2009;103 Suppl 1:i41-46.
18. Sieber F, Pauldine R. Geriatric anesthesia. In: Miller RD, editor. Miller’s Anesthesia. 8th ed. Vol 2. Philadelphia: Elsevier Churchill Livingstone; 2015. p. 2412-4.
19. Marcoantoni E. Ask the expert question and answer how can a urinary tract infection precipitate delirium in an older patient? Ann Longterm Care 2002;10:56-60.
20. Clinical Practice Guideline for Postoperative Delirium in Older Adults. The American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. Available from: http://www.geriatricscareonline.org/toc/postoperative_delirium/CL018. [Last accessed on 2015 Oct 05].
21. Robinson TN, Raeburn CD, Tran ZV, Brenner LA, Moss M. Motor subtypes of postoperative delirium in older adults. Arch Surg 2011;146:295-300.
22. Peterson JF, Pun BT, Dittus RS, Thomason JW, Jackson JC, Shintani AK, et al. Delirium and its motoric subtypes: A study of 614 critically ill patients. J Am Geriatr Soc 2006;54:479-84.
23. McCusker J, Cole M, Abramowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. Arch Intern Med 2002;162:457-63.
24. Meagher DJ, Leonard M, Donnelly S, Conroy M, Adams D, Trezpac T. A longitudinal study of motor subtypes in delirium: Relationship with other phenomenology, etiology, medication exposure and prognosis. J Psychosom Res 2011;71:395-403.
25. Adams D, Sharma N, Whelan PJ, Macdonald AJ. Delirium scales: A review of current evidence. Aging Ment Health 2010;14:543-55.
26. Wong CL, Holroyd-Leduc J, Simel DL, Straus SE. Does this patient have delirium? value of bedside instruments. JAMA 2010;304:779-86.
27. Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The confusion assessment method: A systematic review of current usage. J Am Geriatr Soc 2008;56:823-30.
28. Confusion Assessment Method (CAM) Training Manual. Available from: http://www.hospitalelderlifeprogram.org/
delirium-instruments/confusion-assessment-method-long-cam/ confusion-assessment-method-long-cam-manual/. [Last accessed on 2015 Oct 19].

30. Gaudreau JD, Gagnon P, Harel F, Tremblay A, Roy MA. Fast, systematic, and continuous delirium assessment in hospitalized patients: The nursing delirium screening scale. J Pain Symptom Manage 2005;29:368-75.

31. Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L, et al. Delirium in mechanically ventilated patients: Validity and reliability of the confusion assessment method for the Intensive Care Unit (CAM-ICU). JAMA 2001;286:2703-10.

32. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive care delirium screening checklist: Evaluation of a new screening tool. Intensive Care Med 2001;27:859-64.

33. Chow WB, Rosenthal RA, Merkow RP, Ko CY, Esnaola NF; American College of Surgeons National Surgical Quality Improvement Program; American Geriatrics Society. Optimal preoperative assessment of the geriatric surgical patient: A best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society; J Am Coll Surg 2012;215:453-66.

34. Milisen K, Braes T, Foreman MD. Assessing cognitive function. In: Boltz M, Capezuti E, Fulmer T, Anne ZD, O'Meara A, editors. Evidence-Based Geriatric Nursing Protocols for Best Practice. 4th ed. New York: Springer Publishing Company; 2012. p. 122-34.

35. Gofton TE. Delirium: A review. Can J Neurol Sci 2011;38:673-80.

36. Hall RJ, Meagher DJ, MacLullich AM. Delirium detection and monitoring outside the ICU. Best Pract Res Clin Anaesthesiol 2012;26:367-83.

37. Kalish VB, Gillham JE, Unwin BK. Delirium in older persons: Evaluation and management. Am Fam Physician 2014;90:150-8.

38. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013. p. 596-602.

39. WHO. The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research. Geneva: World Health Organization; 1993. Available from: http://www.who.int/classifications/icd/en/GRNBOOK.pdf. [Last accessed on 2016 Mar 10].

40. Björkelund KB, Hommel A, Thorngren KG, Gustafson L, Larsson S, Lundberg D. Reducing delirium in elderly patients with hip fracture: A multi-factorial intervention study. Acta Anaesthesiol Scand 2010;54:678-88.

41. Inouye SK, Bagardus ST Jr., Baker DJ, Leo-Summers L, Cooney LM Jr. The Hospital Elder Life Program: A model of care to prevent cognitive and functional decline in older hospitalized patients. Hospital Elder Life Program. J Am Geriatr Soc 2000;48:1697-706.

42. Milisen K, Foreman MD, Abraham IL, De Geest S, Godderis J, Vandermeulen E, et al. A nurse-led interdisciplinairy intervention program for delirium in elderly hip-fracture patients. J Am Geriatr Soc 2001;49:523-32.

43. Zaubler TS, Murphy K, Rizzuto L, Santos R, Skotzko C, Giordano J. Quality improvement and cost savings with multi component delirium interventions: Replication of the Hospital Elder Life Program in a community hospital. Psychosomatics 2013;54:219-26.

44. Rubin FH, Neal K, Fenlon K, Hassan S, Inouye SK. Sustainability and scalability of the hospital elder life program at a community hospital. J Am Geriatr Soc 2011;59:359-65.

45. Sieber FE, Zakriya KJ, Gottschalk A, Blute MR, Lee HB, Rosenberg PB, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Mayo Clin Proc 2010;85:18-26.

46. Chan MT, Cheng BC, Lee TM, Gin T; CODA Trial Group. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol 2013;25:33-42.

47. Radtke FM, Franck M, Lendner J, Krüger S, Wernecke KD, Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. Br J Anaesth 2013;110 Suppl 1:i98-105.

48. Vauroio LE, Sands LP, Wang Y, Mullen EA, Leung JM. Postoperative delirium: The importance of pain and pain management. Anesth Analg 2006;102:1267-73.

49. Robinson S, Vollmer C. Undermedication for pain and precipitation of delirium. Medsurg Nurs 2010;19:79-83.

50. Leung JM, Sands LP, Rico M, Petersen KL, Rowbotham MC, Dahl JB, et al. Pilot clinical trial of gabapentin to decrease postoperative delirium in older patients. Neurology 2006;67:1251-3.

51. Krenk L, Rasmussen LS, Hansen TB, Bogs S, Soballe K, Kehlet H. Delirium after fast-track hip and knee arthroplasty. Br J Anaesth 2012;108:607-11.

52. Mouzopoulos G, Vasiiliadis G, Lasonianos N, Nikolaras G, Morakis E, Kaminaris M. Fasica iliaca block prophylaxis for hip fracture patients at risk for delirium: A randomized placebo-controlled study. J Orthop Traumatol 2009;10:127-33.

53. Kinjo S, Lim E, Sands LP, Bozic KJ, Leung JM. Does using a femoral nerve block for total knee replacement decrease postoperative delirium? BMC Anesthesiol 2012;12:4.

54. Fick DM, Semla TP. American Geriatrics Society Beers Criteria: New year, new criteria, new perspective. J Am Geriatr Soc 2012;60:614-5.

55. Short MR, Winstead PS. Delirium dilemma. Orthopedics 2007;30:273-6.

56. Allen SR, Frankel HL. Postoperative complications: Delirium. Surg Clin North Am 2012;92:409-31, x.

57. Larsen KA, Kelly SE, Stern TA, Bode RH Jr., Price LL, Hunter DJ, et al. Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: A randomized, controlled trial. Psychosomatics 2010;51:409-18.

58. Wang W, Li HL, Wang DX, Zhu X, Li SL, Yao GQ, et al. Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: A randomized controlled trial. Crit Care Med 2012;40:731-9.

59. van den Boogaard M, Schoonhoven L, van Achterberg T, van der Hoeven JG, Pickkers P. Haloperidol prophylaxis in critically ill patients with a high risk for delirium. Crit Care 2013;17:89.

60. Page VJ, Ely EW, Gates S, Zhao XB, Abe T, Shintani A, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): A randomised, double-blind, placebo-controlled trial. Lancet Respir Med 2013;1:515-23.

61. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: A randomized placebo-controlled study. J Am Geriatr Soc 2005;53:1658-66.

62. Vochteloo AJ, Moerman S, van der Burg BL, de Boo M, de Vries MR, Niesten DD, et al. Delirium risk screening and haloperidol prophylaxis program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr 2011;11:39.

63. Trifirò G. Antipsychotic drug use and community-acquired pneumonia. Curr Infect Dis Rep 2011;13:262-8.

64. Masand PS. Side effects of antipsychotics in the elderly. J Clin Psychiatry 2000;61 Suppl 8:43-9.

65. Administration US FDA. FDA Requests Boxed Warnings on Older Class of Antipsychotic Drugs; 2008. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ ucm116912.htm. [Last accessed on 2015 Sep 24].

66. Crawford GB, Agar MM, Quinn SJ, Phillips J, Liseter C, Michael N, et al. Pharmacovigilance in hospice/palliative care: Net effect of haloperidol for delirium. J Palliat Med 2013;16:1335-41.

67. Sampson EL, Raven PR, Ndhlovu PN, Phillips J, Liseter C, Michael N,
et al. A randomized, double-blind, placebo-controlled trial of donepezil hydrochloride (Aricept) for reducing the incidence of postoperative delirium after elective total hip replacement. Int J Geriatr Psychiatry 2007;22:243-9.

68. Gambertini M, Bolliger D, Lurati Buse GA, Burkhart CS, Gropow M, Gagneux A, et al. Rivastigmine for the prevention of postoperative delirium in elderly patients undergoing elective cardiac surgery – A randomized controlled trial. Crit Care Med 2009;37:1762-8.

69. Marcantonio ER, Palinhich K, Appleton P, Davis RB. Pilot randomized trial of donepezil hydrochloride for delirium after hip fracture. J Am Geriatr Soc 2011;59 Suppl 2:S282-8.

70. van Eijk MM, Roes KC, Honing ML, Kuiper MA, Karakus A, van der Jagt M, et al. Effect of rivastigmine as an adjunct to usual care with haloperidol on duration of delirium and mortality in critically ill patients: A multicentre, double-blind, placebo-controlled randomised trial. Lancet 2010;376:1829-37.

71. Lacasse H, Perreault MM, Williamson DR. Systematic review of antipsychotics for the treatment of hospital-associated delirium in medically or surgically ill patients. Ann Pharmacother 2006;40:1966-73.

72. Briton ME. Drugs, delirium and older people. J Pharm Pract Res 2011;41:233-8.

73. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, et al. Lorazepam is an independent risk factor for transitioning to delirium in Intensive Care Unit patients. Anesthesiology 2006;104:21-6.

74. Amato L, Minozzi S, Vecchi S, Davoli M. Benzodiazepines for alcohol withdrawal. Cochrane Database Syst Rev 2010;(3):CD005063.

75. Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subacute delirium after on-pump cardiac surgery in the elderly: A randomized trial. Anesthesiology 2012;116:987-9.

76. Girard TD, Pandharipande PP, Carson SS, Schmidt GA, Wright PE, Canonico AE, et al. Feasibility, efficacy, and safety of antipsychotics for Intensive Care Unit delirium: The MIND randomized, placebo-controlled trial. Crit Care Med 2010;38:428-37.

77. Fick D, Foreman M. Consequences of not recognizing delirium superimposed on dementia in hospitalized elderly individuals. J Gerontol Nurs 2000;26:30-40.

78. Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia: A systematic review. J Am Geriatr Soc 2002;50:1723-32.

79. Steis MR, Fick DM. Delirium superimposed on dementia: Accuracy of nurse documentation. J Gerontol Nurs 2012;38:32-42.

80. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: A meta-analysis. JAMA 2010;304:443-51.