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Review article

Prevention of post-operative delirium in older patients with cancer undergoing surgery

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ABSTRACT

Prevention has been shown to be the most effective strategy for minimizing the occurrence of delirium as well as delirium-associated complications.[5] Therefore prevention of delirium in older adults undergoing surgery is a top research priority given the extent of the problem in this patient population. In this review, we will describe the POD syndrome, previously identified risk factors that predict POD in surgical cancer patients, long-term outcomes of POD and both non-pharmacologic and pharmacologic therapies aimed at preventing POD.

Contents

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1. Introduction

Post-operative delirium (POD) occurs in as much as 50% of all surgical patients with cancer, with older patients being particularly at risk.[1–3] Population aging is a real concern for the surgical oncologists[4] who are treating patients who would not have been considered for surgery in the past. There is a strong association between increasing age, a cancer diagnosis, and the need for surgical intervention. Therefore the identification of pre-surgical risk factors and those patients at higher risk of POD is especially important.

2. Post-operative Delirium Defined

With the introduction of the Diagnostic and Statistical Manual of Mental Disorders—5th Edition (DSM-5), delirium is included in the broader category of Neurocognitive Disorders, which includes syndromes in which acquired cognitive dysfunction is the principal symptom. DSM-5 criteria for delirium consist of a fluctuating disturbance in attention and awareness that represents a decline from baseline status, accompanied by cognitive dysfunction (in orientation, memory, language function, etc.), and may have multiple possible causes (i.e. intoxication, withdrawal, surgical intervention, infection). Delirium is additionally sub-typed as either: *hyperactive*, characterized by increased psychomotor activity, agitation, and mood lability; *hypoactive*, characterized by reduced psychomotor activity and lethargy; or *mixed*, characterized by fluctuating psychomotor activity between hyper- and hypoactive states or, more rarely, normal psychomotor activity with disordered attention and awareness. POD is distinguished from the syndrome of emergence delirium,[6] which is characterized by behavioral disorganization and disorientation in the immediate period following emergence and recovery from anesthetic exposure and more common in pediatric surgical patients. While emergence delirium may in some cases precede POD, the latter generally refers to cases in which symptoms emerge within the first three days of the post-operative course.

While most of the work on POD has focused on general and cardiac surgical cohorts, POD in patients undergoing surgery for resection of primary cancers has received less attention. Despite this, the nature of cancer diagnosis and treatment prior to surgery may confer an even greater risk for POD following surgery, and this area continues to be understudied. Indeed, POD occurs in as much as 50% of all surgical patients with cancer, with older patients being particularly at risk.[1,3,7,8] Radiation therapies that may precede surgery, presence of induction (or neo-adjuvant) chemotherapy treatment, suboptimal nutrition and hydration, pain medications, stress of diagnosis and treatment, primary central nervous system (CNS) cancer pathology, inflammatory dysregulation, pharmacologic interactions, and the possibility for multiple surgical interventions in the presence of recurrence all may lead to higher rates of POD in a cancer cohort.

3. Post-operative Delirium Outcomes

A growing body of research strongly suggests that post-operative delirium is associated with an increased risk of long-term decreased functional independence, cognitive decline, dementia risk, and shortened survival time.[9,10] Evidence for cognitive decline following resolved delirium appears early in the course of recovery (3–6 months) as indicated by decreased Mini-Mental State Exam (MMSE) scores[11] and decreased performance on neuropsychological measures compared to unaffected individuals.[12] Most significantly, evidence of chronic long term decline is demonstrated at two to five year follow-up; following a delirium episode, affected individuals exhibit decreased MMSE performance,[13,14] a higher incidence of diagnosed mild cognitive impairment and dementia[15–18] and increased mortality.[19–21] In addition to increased burdens and risks to the affected patient, POD is associated with increased caretaker burden, increased health care costs largely due to lengthened hospital stays, additional staff required for the patient's care, and extensive medical and supervision needs following discharge to home or institutional care.[22–24]

4. Risk Factors

Several risk factors that may predispose surgical patients to POD have been identified in both general and cardiac surgical groups, and, most recently, in patients undergoing surgical resection for primary cancers (Table 1).[25,26] For cardiac surgical patients, preoperative comorbidities including cardiovascular disease, intraoperative procedures that influence blood pressure and perfusion, as well as potential for CNS emboli, suggest specific risk factors and interventions that may not be representative of patients undergoing surgical intervention for primary cancers. In non-cardiac surgical patients (emergent and elective orthopedic, thoracic, and peripheral vascular procedures), which may be more representative of risk factors for POD in surgical cancer patients, several factors have been identified with some regularity.[26] The general concept of "frailty"[27] in patients has been used to aggregate a collection of specific factors that are associated with treatment outcomes in general, and following surgical

Table 1 – Risk factors for delirium.

Major risk factors[41,42]
Cognitive impairment
Severity of illness
Visual impairment
Dehydration
Minor risk factors[41,42]
Polypharmacy
Catheterization
Use of restrains
Malnutrition
Any iatrogenic event
Other risk factors for POD
Older age[26,29,30]
Increased number of comorbidities[25,26]
Increased functional dependency[25,30]
History of falls in the last 6 months[25]
Pre and post surgical pain[31]
Increased white matter pathology[33]