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Long-Term Cognitive Decline in the Elderly is not Attributable to Surgery/Anesthesia

Research Article

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Abstract

Postoperative cognitive dysfunction (POCD) is a topic of special importance for elderly patients. Based upon the results of a combination of retrospective human studies, experiments in animals, and a number of prospective human studies, the anesthesia research community has advanced the notion that surgery/anesthesia might precipitate permanent incident dementia. A careful analysis of the data, however, reveals numerous methodological problems with the clinical trials that have examined long-term POCD, including the vague definition of POCD, poorly matched controls (or lack of controls in some investigations), arbitrary diagnostic criteria, etc. More recent evidence suggests that the vast majority of patients without pre-existing disease recover cognition in the long term. In fact, there are studies that suggest that in some cases surgery improves cognitive functioning (e.g. carotid endarterectomy, weight reduction surgery, etc.). This report critically analyzes the methodological concerns of the older studies and presents current evidence rejecting the long-term POCD hypothesis. In addition, it reviews the pre-existing conditions that may result in long term POCD.

Introduction

Cognitive function is an important outcome measure of surgical intervention that affects patient well-being and function. It is expected that surgery would improve quality of life. However, a preponderance of literature during the last two decades questions this precept and suggest that "surgery may heal the body but harm the brain" especially among the elderly patients [1]. As the number of publications on a subject of postoperative cognitive dysfunction (POCD) has dramatically increased, the concept become a "hot topic" among the anesthesiologists. It appears, however, that this postoperative complication (either perceived or real) is not an issue widely recognized by surgeons or other specialists. Surgical volume continues to grow, particularly in the elderly. It increased from 226 million operations in 2004 to 313 million operation in 2012 [2]. Clearly, concerns regarding POCD played minimal if any role in patients/surgeons decision to proceed with the surgery. Moreover, recent more carefully conducted research indicates that surgery may actually improve cognition in the majority of patients [3, 4]. The objection of this narrative is to critically evaluate the POCD literature and assess clinical implications of the phenomena if it indeed exists.

Drawbacks of POCD Research

POCD is defined as a decline in cognitive performance arising after surgical procedure. Its diagnosis requires both preoperative psychometric testing (baseline) and an arbitrary definition of how much of a decline is called cognitive dysfunction. The testing, however, rarely performed outside of research setting. Neither ICD10 nor DSM V recognized POCD as a clinical state. Currently there is no nomenclature or diagnostic criteria for this condition.

Criteria for POCD typically rests on a battery of neurobehavioral assessments that measure various cognitive domains. Tests vary from complex combinations of neuropsychological measures (e.g. Hopkins Verbal Learning Tests, Visuospatial Learning Test, various subtests from Wechsler Adult Intelligence Scale, etc.) to simple Mini Mental Exam (MMSE).

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Reported incidence of POCD varies from 0 to 70% after cardiac and from 0 to 50% after non-cardiac operations [5, 6]. The significant variability of the data is related to the rather arbitrary diagnostic criteria of the condition that have been used by the various research groups. The other limitations of the POCD research include:

a. Uncertainty about the time course of the disease; the researchers assess cognitive decline anywhere from 1 week to 7 years after surgery
b. Difficulties in accounting for the learning effect of repeat cognitive testing
c. Lack of a properly matched control group
d. Inability to account for the underlying comorbidities
e. A single point assessments of cognitive capacity of a subject; it is plausible that a patient is cognitively declining irrespective of a surgery
f. Emotional state may contribute to decline in cognitive performance

It is impossible to compare the results of various studies (or even the existence of the condition) until there is an unambiguous definition of this disorder.

Critical Analysis of the Studies that show POCD after Cardiac Surgery

The perception that a cognitive decline is a common complication after cardiac surgery has existed since the introduction of open heart procedures. The reported incidence of POCD varies from 10% to 70% and is highly dependent on the number of cognitive tests used, time of assessment and statistical analysis used to define a significant change. There are literally 100s reports propagating this perception. In this presentation we will review methodology of the most impactful publications disseminating this notion.

Newman et al. have published first and one of the most influential publication in 2001 that addressed the issue of long-term cognitive deterioration after open heart surgery [7]. The authors reported that incidence of POCD was 53% at discharge, 36% at 6 weeks, 24%, at 6 months and 42% five years after surgery. They also show that 47% and 64% of patients had no change on discharge and 6 weeks respectively, 76% of patients improved at 6 month and 58% had no change five years after surgery. The study had no control group so it is impossible to compare this date with the expected age-related decline in cognition. A number of earlier articles showed similar rates of POCD, but all of them suffered from the similar methodological flaws [8].

A number of other prominent groups reported cognitive decline in patients undergoing open heart surgery [9-11]. Most of them, however, are cohort studies and, as such, are lacking a non-surgical control group. Other common limitations include a rather arbitrary, inconsistent, and liberal definition of the POCD, suboptimal statistical approach and a failure to account for underlying co-morbidities (i.e. vascular disease which are associated with cognitive decline).

Review of the Studies that do not Demonstrate POCD after Cardiac Surgery

Despite the common believe that POCD after cardiac surgery is major problem, most of the recent well conducted studies addressing this issue do not show a cognitive decline in this patient population [3, 12]. There was a common believe based on uncontrolled cohort studies (see above) that cognitive decline is related to a brain injury caused by cardiopulmonary bypass (commonly referred to as "pump head"). Several investigations compared cognitive changes in patients who had surgery with versus without extracorporeal circulation ("off-pump") and found no difference in outcomes [13, 14]. Similarly, there is no difference in cognitive outcome in patients treated with angioplasty versus off-pump coronary bypass surgery [15]. A number of publications by Selnes et al. have convincingly demonstrated that although subjective memory complaints are more frequent in the early postoperative period, there is no measurable long-term cognitive changes [16]. A recent publication by Bruce et al., confirmed these results [17]. These authors compared cognitive changes in the on-pump surgical patients, thoracic surgical patients, and nonsurgical control group. They concluded that approximately one-third of surgical patients had impaired cognition 1 week after surgery (i.e. no effect of cardiopulmonary bypass), most recover to baseline or better 8 weeks after operation. Notably, all of these studies have included an appropriately matched controlled group.

POCD after Non-Cardiac Surgery

It is expected that acute pain, inflammation, anxiety associated with surgery and drugs that are used to treat pain may affect cognition in the immediate postoperative period. The POCD is diagnosed by assessing subject's performance on the battery of neuropsychological tests administered immediately before and after surgery. As the time course of this "disease" is unknown, the assessments are performed at the arbitrary time points. This transient decline can last for several weeks [18]. Although some uncontrolled cohort studies have claimed a whopping 46% incidence of POCD at 1 year after surgery [19], the most prominent trials report that approximately 10% of patients show cognitive decline at three months after surgery when compared with their preoperative mental state [20, 21]. Notably, the difference in cognitive performance between post-surgical and age/disease matched controls patients disappears at 1-2 years follow up [22].

Most of the methodologically well conducted recent studies do not show the association between surgery/anesthesia and cognitive decline when measure beyond first 3 months. Avidan et al. analyzed a cognitive decline in patients tested annually at the Washington University Alzheimer's Disease Research Center. They compared patients who had noncardiac surgery, illness, or neither and found no difference in cognitive decline attributable to surgery [23]. Dokkedal et al., studied a relationship between surgery and long-term POCD in 8500 twins and found no clinically relevant association [4]. A meta-analysis of 17 studies that assessed POCD in patients undergoing hip/knee arthroplasty concluded that there is no decline in cognitive performance at 3 to 6 months [24].

Postoperative Cognitive Improvement

The purpose of performing surgery is to prolong survival, reduce morbidity, and/or improve a quality of live. Although cognitive function can be negatively affected immediately after surgery, it is expected that it should return to a level consistent with patient's cognitive trajectory within a short (currently undefined) period of time. Numerous clinical studies, meta-analysis and systematic reviews have formally assessed post-surgical outcomes and confirmed this assertion.

POCI as a Likely Effect of the Surgery

It is expected that cognition will actually improve if a purpose of the surgery is to reestablish cerebral blood flow, restore metabolic milieu, or remove a brain lesion associated with cognitive impairment. Recent studies demonstrated that approximately 10% of patients undergoing CEA show postoperative improvement in cognitive function, particularly in patients with a preoperative low perfusion in the cerebral cortex ipsilateral to the side of surgery [25, 26]. Similarly, a number of studies show improvement in cognitive function after bariatric surgery. Cognitive benefits, particularly in memory and executive function, are maintained up to 3 years postoperatively [27, 28]. Although the majority of patients with meningioma have mild to moderate cognitive deficits preoperatively, resection of the brain lesion significantly improved functioning in the following cognitive domains: memory, attention, cognitive flexibility, processing flexibility and executive functioning [29].

There was (is) a widespread believe that POCD is associated to the use of cardiopulmonary bypass. A number of high-profile studies have credibly demonstrated that neither on-pump nor off-pump are associated with a higher risk of cognitive decline when compared to medical or non-surgical treatments [30]. In fact, Sauer et al., recently reported a trend towards lower cognitive performance in the Percutaneous Coronary Intervention group when compared to CABG [15]. Bruce et al., confirmed these results [17]. These investigators found that patients in the CABG group scored higher than non-surgical controls 8 weeks after the operation. A meta-analysis of cognitive outcomes following CABG also reported a significant improvement across all 4 measures of cognitive performance analyzed by the authors [31].

A number of recent studies also demonstrated cognitive improvement in patients after Total Joint Arthroplasty. Ancelin et al., studied cognitive changes in patients over the age of 65 after orthopedic surgery [32]. These authors found that although patients performance decline in Geometric form association test (visuospatial ability), it improved significantly in object naming, immediate verbal recall, narrative recall and delayed verbal recall. Meta-analysis of 17 studies that assessed cognitive changes in patients after total joint arthroplasty indicated no evidence of decline in any neurocognitive domains and notable improvements in immediate verbal recall, delayed visual recall and speed of processing [24].

POCD in the Vulnerable Population

Although there is a little evidence that POCD is a major problem in general surgical population, a number of investigators attempted to identify subgroups of patients who are predisposed to develop a long-term cognitive decline. Individuals with mild cognitive impairment (intermediate state between normal aging and dementia) are at risk to progress to dementia. It is reasonable to hypothesize that surgery may accelerate progression to dementia in patients at high risk for this complication. Bekker et al., have reported that surgery negatively impacted attention concentration in patients with MCI but not in normal individuals [33]. Kline et al., examined the data from Alzheimer Disease Neuroimaging Initiative (ADNI) and reach similar conclusion: only patients with MCI experienced POCD at approximately 6 months after operation; cognitive performance of elderly patients without preoperative compromise improved after surgery [34].

Conclusion

Despite a widespread perception that surgery and/or anesthesia may lead to long term cognitive decline in elderly patients, a careful analysis of the available literature questions this sentiment. In fact, a growing body of clinical research suggests that cognitive performance of the majority of patients improves after surgery. There are vulnerable subgroups of the elderly patients whose cognitive performance maybe negatively affected by the surgery.

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