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Editorial

Time is Brain: A Preoperative Neurological Evaluation Before Surgery?

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The preoperative evaluation of the function of vital organs including heart, lungs, liver and kidney is established practice across all surgical specialities. Effective perioperative evaluation and optimization has been shown to reduce postoperative medical complications, but nowadays there is a gap in the perioperative evaluation of neurological status [1]. Brain health is largerly overlooked by current modalities of perioperative assessment. On the other hand, existing protocols and guidelines focusing on modifiable risk factors for cardiac, pulmonary, renal, and metabolic-related complications have clearly demonstrated that prehabilitation strategies can decrease not only complication rates, but also 30-day mortality and length of hospital stay [2]. Frailty in the elderly population is strongly associated with the risk of postoperative complications, delirium, institutionalization, and mortality. Delirium remains the most common postoperative adverse event, with a pooled risk ratio of 2.13 (95% CI 1.23-3.67), but it can also be a marker of preclinical dementia and may contribute to delayed neurocognitive recovery [3]. It is indeed time to appreciate that surgical stress and systemic inflammation may lead to neuroinflammation, worsen preoperative neurologic status, and increase neurological complication rates in vulnerable individuals who lack physiological reserve and present with multisystemic functional deterioration. Use of Electroencephalography (EEG) monitoring as a guide to anesthetic titration to reduce the rate of perioperative cognitive disorders may prove a useful adjunct in this category of patients, but it is currently under investigation [4]. EEG is essential for differentiating delirium (a state of usually reversible global brain disfunction) and seizure disorders (a condition of spontaneous, recurrent paroxysmal electrical dysfunction), enabling the distinctly different treatment: Antiepileptic Drugs (AEDs) are a class of medications that have indeed received considerable attention as possible treatments for agitation and aggression, despite a lack of high-quality data and despite neurologist and psychiatrist often disagree on terminology.

We believe that preoperative assessment of elderly and frail patients is often neglected in everyday practice but remains the foundation for a safe surgical practice. In United Kingdom, the proactive care of older patients undergoing surgery (POPS) model has integrated the Comprehensive Geriatric Assessment (CGA) in the elective and emergency surgical setting, and has provided a robust evidence based methodology to identify the elderly population at risk and to optimize the surgical pathway and the follow-up after hospital discharge [5]. A randomized clinical trial showed that preoperative CGA and optimization according to the POPS model result in fewer non-surgical complications and reduce the length of hospital stay by 40% compared to standard care [6].

Normal Pressure Hydrocephalus (NPH), a condition most commonly seen in older adults is often misdiagnosed (less than 20% of patients in a Neurological unit receive an appropriate diagnosis) but has emerged as a “treatable movement disorder”, and represents a cause of delirium or cognitive decline in elderly adults who undergo cardiac surgery [7].

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An important aspect of perioperative care is that several drugs may have a significant impact on neurological perioperative outcomes, especially in elderly patients in whom polypharmacy is common practice. Multiple prescriptions and non-prescription medications have the potential for drug-to-drug interaction and perioperative adverse events. Although electronic health records have the potential to detect errors and interactions, having the patient bringing in all medications they use at home is a critical step at the time of office visit to prevent adverse outcomes due to drug abuse, withdrawal or interactions. Many group of drugs can cause delirium and this includes many prescriptions over the counter, complementary ("natural") and alternative products (some examples of herbal products that have cholinergic effects are henbane, jimson weed and mandrake and some teas). The mechanism of drug induced delirium are not well defined, but evidence support a major role for cholinergic failure. Anticholinergic intoxication causes a classical delirium syndrome that may be reversible with cholinesterase inhibitors; drugs which can cause a muscarinic blockade can leads to delirium and drugs such as digoxine, lithium and histamine (H2) antagonists shoes measurable cholinergic receptor binding. The most common drugs associated with delirium are sedative hypnotics (benzodiazepines), analgesic, and medications with an anticholinergic effect. Serotoninergic drugs may also indirectly contribute to delirium by causing serotonin syndrome (in particular paroxetine due to greatest affinity for muscarinic receptors), and neuroleptic malignant syndrome [8]. This reciprocal relationship between cholinergic and dopaminergic brain effects indicate a role for dopaminergic excess in delirium and explain why dopaminergic medications such as levodopa or dopamine agonist can contribute to delirium in a dose related manner. Dopamine dysregulation syndrome and punding are encountered with levodopa therapy particularly if delivered in an intermittent fashion, with slow-release formulations and it it's crush a slow release formulation in a nasogastric tube, as levodopa competes with amino acids for uptake in proximal small intestine. Even gastric emptying can result in erratic absorption and bioavailability. For these necessary medications, a dosage reduction or adjusting the dosage schedule may be helpful; for example, if antiparkinsonism medications are suspected of causing confusion, anticholinergic medications should be the first to be discontinued, followed by selegiline, dopamine agonist and finally and most important, by tapering levodopa, as many patients can develop an acute "akinetic attack" with hyperpyrexia and diaphoresis resembling the clinical picture of neuroleptic malignant syndrome that it may follow an abrupt change in dopaminergic medication [9-13]. Also, use of herb medications should be carefully reviewed. Patients should be counselled and monitored regarding pharmacological therapy in preparation for the surgical procedure. Deprescribing may be necessary, and alternative routes for neurotropic drug administration should be considered in the immediate postoperative period, especially after foregut procedures that may transiently impair the ability to swallow or bowel absorption.

Concurrent medical problems may also contribute to "drug induced delirium", for example in heart failure, hepatic insufficiency and renal failure; antibiotics mainly cephalosporins and macrolids may induced delirium; the mechanism behind this phenomenon is still not fully understood but has been hypothesized that may lower the seizure threshold by binding competitively to the GABA-A receptor inducing a Non-Convulsive Status Epilepticus (NCSE) manifested by an altered mental state. Frailty, rather than chronological age, is increasingly recognized as a predictor of adverse postoperative events. Interestingly, a large cohort study conducted across 9 noncardiac specialties showed that there was a greater than 10% 180-day mortality for frail patients following even low-stress procedures in low-intensity specialties [6]. This confirms that triage and optimization of preoperative assessment should be mandatory for all surgical specialties regardless of the planned procedure. Furthermore, it is time to expand the concept of pre-habilitation to include optimization of neurological functional status among the therapeutic targets. It is possible that screening for depression, anxiety, movement disorders and stroke, and a period of structured cognitive exercise along with pharmacological modulation, if necessary, can help to identify reversible deficits and strengthen the capacity of the patient to withstand surgical stress. In stroke and many neurological disorders there is impaired integrity of blood-brain barrier function, which allows more of a potentially toxic drug to reach the brain and reduced integrity of blood-brain barrier function is strongly associated with susceptibility to delirium. A comprehensive evaluation of the neurological status in elderly patients who are surgical candidates and the adoption of a collaborative neuro-geriatric perioperative care pathway could fill an existing gap, and successful treatment of delirium

depend on identifying the reversible contributing factors, as drugs are the most common reversible cause of delirium. Some recent studies suggest that dexmedetomidine , a sympatholytic drug that acts as agonist to alpha-2-receptor, use for sedation in mechanically ventilated adults may reduce time to extubation in neurological disorders, may be associated with less delirium and appears to be associated with less neurocognitive dysfunction compared to other sedatives, but these findings were inconclusive because of publication bias, heterogeneity and limited sample size. These factors can improve current modalities of anesthesiological and surgical risk stratification, and reduce the risk of postoperative cognitive disorders and functional decline [11]. Finally, discharged patients form intensive care to general ward have a better neurological outcome and less subclinical delirium using the "ABCDE bundle" (Awakening and breathing coordination, delirium monitoring and exercise/early mobility"): we should investigate better if ward-transfers, arriving in the Emergency Department (ED) at nighttime, time spent in ED and visits from other specialists at nighttime could be possibly associated with development of "incident delirium" and delirium motor subtypes; the transfer of patients from the Intensive Care Unit (ICU) to a general ward can present several challenges, ensuring optimal care and reducing delirium; let us change our attitude as neurologists and clinicians, "from bed to wheelchair" [12].

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