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EDITORIAL

Preoperative management and postoperative delirium

The possibility of neuroprehabilitation using virtual reality

Kazuyoshi Hirota[1]

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Introduction

PubMed search shows that more than 140 articles on postoperative delirium (POD) have been published (28 articles in anesthesia journals) between January 1 and April 30, 2019. Two such articles regarding POD were published in the February issue of this journal [1, 2]. These articles raised two perioperative risk factors for POD, handover of anesthesia care [1] and postoperative hypotonic fluid administration [2]. As handover of anesthesia care for long-duration surgery is inevitable, this facet of POD may be difficult to reduce. However, careful intraoperative handover between anesthesiologists might prevent POD although there are no studies to address this. Regarding hypotonic fluid administration, although the National Institute for Health and Care Excellence (NICE) guideline has recommended administration of hypotonic fluid (sodium; 35 mmol/L) for postoperative maintenance, hypotonic fluid administration was associated with a higher risk of postoperative delirium with hyponatremia [2]. Serum sodium level should be monitored during hypotonic fluid administration.

Life expectancy is continuously increasing; this is estimated to be over 100 years for those born in 2007 in most developed countries and 107 years in Japan [3]. In Japan the aged population (> 65 years) was 27.7% in 2017 and this is predicted to rise to 38.4% in 2065 [4]. As POD is often observed in elderly patients, this has clinical and economic importance. Moreover, POD has been reported to be strongly associated with postoperative mortality and morbidity [5–8]. In this editorial, I discuss the cause and prevention of POD.

✉ Kazuyoshi Hirota
hirotak@hirosaki-u.ac.jp

1 Department of Anesthesiology, Hirosaki University Graduate School of Medicine, Hirosaki 036-8562, Japan

POD and mortality and morbidity

In a retrospective study Maniar and colleagues [5] determined whether the POD could predict mortality and morbidity. They found that POD was associated with longer intensive care unit (ICU) stay (70 vs. 27 h), ICU readmission and increases in mortality at 30 days and 1 year compared to patients without POD. POD did not affect 1-year mortality between aortic valve replacement approaches, surgical aortic valve replacement (SAVR) patients presented with POD more often than transcatheter aortic valve implantation (TAVI) patients. A prospective study also showed that POD predicts first-time readmissions and 180 days-mortality in octogenarian patients having undergone SAVR or TAVI therapy [7]. Systematic review and meta-analysis of 11 studies by Scholz et al. [6] also concluded that POD significantly increased the duration of hospital stay and there was a higher mortality rate. Another recent prospective study [8] found that POD is independently associated with a sevenfold increase in 5-year mortality and longer ICU stay in patients more than 50 years old undergoing elective surgeries.

Mechanism of POD

Neuroinflammation

Recent animal studies [9, 10] strongly suggest that POD may be caused by neuroinflammation in the central nervous system, caused by surgery-induced systematic inflammation. Vacas and colleagues [9] found that high-mobility group box 1 protein (HMGB1) caused memory decline and neutralizing anti-HMGB1 antibody could reduce postoperative memory decline in adult mice. Kawano et al. [10] showed that surgery-induced acute neuroinflammation caused trace and context memory dysfunction in the early postoperative period in aged rats. Kawano's group [11] also found that postoperative pain enhanced neuroinflammation and POD-like cognitive dysfunction in aged rats.

Intraoperative hemodynamics

Several clinical studies showed that intraoperative hypotension may be related to POD in spinal surgery [12] and severely burned patients undergoing early escharotomy [13] while several studies failed to show a relationship between intraoperative hypotension and POD [14, 15]. In elderly patients undergoing elective surgery, Yang and colleagues [14] found (using multivariate regression analysis) a significant association between POD and the incidence of intraoperative hypertension and tachycardia but not with hypotension and bradycardia. Hirsch and colleagues [15] reported that intraoperative blood pressure fluctuation but not absolute or relative hypotension was significantly associated with POD. These findings may indicate that adverse changes in cerebral perfusion or oxygen supply may lead to POD.

Depth of anesthesia

A previous report [16] suggested that bispectral index (BIS)-guided anesthesia reduced the incidence of POD as extremely low BIS value may precipitate POD. Depth of anesthesia monitoring may decrease anesthetic exposure and produce a faster neurological recovery and consequently reduce POD. Indeed, a recent systematic review concluded that depth of anesthesia monitoring-guided anesthesia significantly reduced the risk of POD and long-term cognitive dysfunction [17]. However, most recent randomized clinical trials (RCTs) clearly question the efficacy of depth of anesthesia monitoring for POD [18]. These RCTs showed that depth of anesthesia monitoring-guided anesthesia did not decrease the incidence of POD in elderly patients undergoing major surgery. Further RCTs are required to clarify the efficacy of depth of anesthesia monitoring in POD.

Preoperative risk factors for POD and prehabilitation

Significant risk factors for POD have been identified: advanced age, vascular diseases, diabetes, anemia, psychoneurologic diseases, chronic pain and alcohol excess, preexisting cognitive impairment, severe illness [American Society of Anesthesiologists (ASA) physical status ≥ III] [6, 19, 20]. Elderly patients often show frailty which is strongly associated with POD after both non-cardiac and cardiac surgery [21–23]. Prehabilitation program including exercise, nutritional support, psychological support and behavioral modification has been suggested to decrease the incidence of POD by improving patients' baseline health [24]. Thus, prehabilitation programs are strongly recommended in these populations to prevent POD [25]. Indeed, several clinical trials are currently running to investigate the preventive effects of multimodal prehabilitation programs on physical functions and postoperative complications including POD [26, 27]. However, elderly patients are often not able to perform physical exercise, which is the most important component of prehabilitation programs. This inability is due to neurological diseases including stroke, Parkinson's disease and cognitive dysfunction, impaired cardiac and/or pulmonary function, lumbago, coxalgia, and gonalgia. Recent articles [28–30] show the efficacy of rehabilitation using virtual reality (VR). Kober et al. [28] set up a VR route-finding training program for neurologic patients with severe impairments in spatial orientation performance. The patients learned and recalled different routes for navigation in a VR city over 5 training sessions. Prasertsakul et al. [29] designed a VR balance training system for sedentary adults having a falling risk. The users can interact with the object in the VR training system consisting of 3 game modes, such as matching color, bakery and memo number. In addition, the users have to stand and require rapid movement of the dominant arm to control the virtual hand inside the VR environment for completion of the games. Cho and colleagues [30] established a VR-immersive training program with head-mount display for acute stroke patients which consists of two performances: fishing and picture matching. Fishing has 3 levels such as easy, normal, and hard depending on the accuracy of hand and finger movements. In the picture-matching program, the patient flips cards and finds a match. Indeed, these programs could improve cognitive and physical function. Thus, VR training programs may also be useful for prehabilitation in patients with limitations of exercise tolerance.

Application of VR to prehabilitation for prevention of POD

VR has emerged as a promising tool in many domains of therapy and rehabilitation. This technique has also been introduced as a physical, cognitive, and psychological interventional tool for neurorehabilitation in patients with neurological diseases [31]. Several recent systematic reviews and meta-analysis covering the efficacy of neurorehabilitation suggest that VR interventions may improve motor function, psychological and cognitive function in those patients [31–33]. VR may also be applicable to prehabilitation for the prevention of POD in patients who cannot perform standard prehabilitation programs.

Conclusion

POD has recently been recognized to increase postoperative morbidity and mortality. Prehabilitation is important in the prevention of POD. However, elderly patients are often frail with several pre-existing comorbidities and have difficulty participating in 'standard' prehabilitation programs, VR-prehabilitation may be a promising tool for the prevention of POD. Clinical trials are essential to test this with VR-neuroprehabilitation for the prevention of POD in the elderly patients offering an attractive prospect for these vulnerable patients.

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