J Anesth (2009) 23:51–56
DOI 10.1007/s00540-008-0688-1

Journal of
Anesthesia

Prediction of postoperative delirium after abdominal surgery in the elderly

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Abstract
Purpose. Indications for the surgical treatment of elderly patients have been increasing. Postoperative central nervous system dysfunction, including delirium, is one of the most common complications in elderly surgical patients. The relationship between patient factors, including cerebral oxygen saturation, and the incidence of postoperative delirium was evaluated.
Methods. Twenty American Society of Anesthesiologists (ASA) physical status I-II patients, older than 65 years, scheduled for elective abdominal surgery were enrolled in the study. The patients' cognitive function was assessed, using the Hasegawa dementia score (HDS) and kana-hiroi test, on the day before surgery and then again 1 week after the surgery. Regional cerebral oxygen saturation (rS_{O_2}) was continuously monitored during the surgery, using near-infrared spectroscopy (INVOS 3100). General anesthesia was induced with 3 $mg \cdot kg^{-1}$ thiopental and 5% sevoflurane. After tracheal intubation, the sevoflurane concentration was adjusted to maintain the bispectral index (BIS) value between 45 and 60. Postoperative delirium was diagnosed if DSM IV criteria were present and the patient scored 12 or more points on the Delirium Rating Scale.
Results. After surgery, 5 (25%) patients developed delirium. The age in the delirium (+) group (76 ± 4 years) was significantly higher than that in delirium (–) group (68 ± 3 years). Preoperative and postoperative HDS did not differ between the groups. The score on the preoperative kana-hiroi-test in the delirium (+) group (16 ± 5) was significantly lower than that in the delirium (–) group (32 ± 10). There were no significant differences between preoperative and postoperative kana-hiroi test scores in either group. Baseline rS_{O_2} in the delirium (+) group (60 ± 5%) was significantly lower than that in the delirium (–) group (66 ± 7%). However, there were no significant differences between the groups in the rS_{O_2} after the start of surgery.
Conclusion. Patients' age, low preoperative kana-hiroi test score, and low preoperative rS_{O_2} were important risk factors for postoperative delirium.

Key words Delirium · Kana-hiroi test · Cerebral oximetry · The elderly

Introduction

Indications for the surgical treatment for elderly patients have been increasing. Postoperative central nervous system (CNS) dysfunction is one of the most common complications in elderly surgical patients [1]. There are two main forms of postoperative CNS dysfunction: delirium and postoperative cognitive dysfunction. Postoperative delirium (POD) usually occurs 24–72 h after surgery and resolves within hours to days [1]. In contrast, postoperative cognitive dysfunction is noticed weeks to months after surgery. The causes of these CNS dysfunctions are not fully understood.

POD is an acute disorder of attention and cognition. POD is often associated with prolonged hospital stay and even increased mortality [2]. Therefore, the prevention, early diagnosis, and treatment of POD have been great challenges for the anesthesiologist. If patients who are predisposed to POD can be identified, interventions to prevent the disorder could be possible [3].

Various risk factors for POD have been reported, including aging and poor preoperative cognitive status [1,4]. A recent report suggests that impaired cerebral oxygenation, as evaluated by near-infrared spectroscopy (continuous monitoring of regional cerebral oxygen saturation [rS_{O_2}] during surgery is a predictor of postoperative cognitive dysfunction [5]. Because cognitive dysfunction is one of the characteristic symptoms of POD, strict monitoring of cerebral oxygenation during surgery under general anesthesia could predict POD.

In this study, we sought to evaluate the relationship between preoperative factors (including cognitive function), intraoperative factors (including cerebral oxygen

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Received: March 12, 2008 / Accepted: August 14, 2008

saturation during surgery), and the incidence of POD in elderly patients undergoing major abdominal surgery.

Patients and methods

The study protocol was approved by the Institutional Review Board of our hospital and written informed consent was obtained from each patient. Twenty-three patients (American Society of Anesthesiologists [ASA] physical status I-II) older than 65 years, scheduled for elective abdominal surgery were enrolled in the study. Surgical procedures included laparotomy and laparoscopic surgery. Patients with pre-existing cerebral pathology or a baseline Hasegwa dementia score (HDS) of less than 22 were excluded.

Before induction of anesthesia, a Bis Sensor (Aspect Medical Systems, Natick, MA, USA) was applied to the right forehead region. The EEG was monitored continuously using an Aspect A-1050 monitor (Bis ver. 3.4; Aspect Medical Systems). The EEG signal from the raw EEG port of the A-1050 monitor was introduced into a personal computer with Microsoft Windows XP, and BSA software [6] was used to record the bispectral index (BIS) value from the preinduction period to the end of surgery every 1 min.

The rS_{O_2} was continuously monitored, by near-infrared spectroscopy (WIRS, using the INVOS 3100; Somanetics, Troy, MI, USA). Sensors for cerebral oxymetry were applied over the left supraorbital region before the induction of anesthesia. Baseline rS_{O_2} was measured as the average saturation over a 1-min period before the induction of anesthesia, beginning approximately 3 min after the sensor was applied. The rS_{O_2} data were continuously recorded at 1-min intervals until the end of surgery. Cerebral desaturation was defined as a reduction of rS_{O_2} to less than 75% of the baseline value for more than 30 s.

After the insertion of an epidural catheter, general anesthesia was induced with 3 $mg \cdot kg^{-1}$ of thiopental and 5% sevoflurane. After tracheal intubation, the sevoflurane concentration was adjusted to maintain the BIS value between 45 and 60. Vecuronium and fentanyl were given as required. Mechanical ventilation was adjusted to maintain a Pa_{CO_2} of 35–40 mmHg. Bladder temperature was monitored and was maintained at 36.0°C–37.0°C, using a forced-air warming system (Warm touch; Mallinckrodt Medical, St. Luis, MO, USA). Noninvasive mean arterial blood pressure (MAP), heart rate (HR), and pulse oximetry (Sp_{O_2}) were monitored continuously and maintained within normal ranges (MAP, >60 mmHg; HR, 50–100 bpm; Sp_{O_2}, >96%). To maintain MAP greater than 60 mmHg, an 8-mg bolus of ephedrine was administered, and repeated as needed. After discontinuation of the sevoflurane at the end of surgery, the time required to recover responsiveness (recovery time) to name or light touch, answering to: "Do you know your name and age?" were recorded. Epidural infusion of 0.1% ropivacaine (4 $ml \cdot h^{-1}$) and morphine (2 $mg \cdot day^{-1}$) was started about 1 h before the end of surgery and continued for the first 48 h after surgery.

The cognitive function of the patients was assessed using the HDS and kana-hiroi test on the day before surgery and then again 1 week after the surgery. The HDS is a modification of the Mini-Mental State Examination, with a score range of 0 to 30, with higher scores representing a better cognitive state [7]. In the kana-hiroi test, the patient should correctly pick out and circle the following five Japanese "kana" letters "A, I, U, E, and O" (Japanese vowels) while reading an old story written in kana. The total number of kana letters is 406, 61 of which are one of these five vowels. The number of letters correctly recognized in 2 mins is scored. A decrease in the HDS or kana-hiroi test score of more than 2 SD from baseline was considered as an index of decline in cognitive function. For the postoperative surgical follow up, patients were observed daily from 1 to 7 postoperative days. The defining criteria of postoperative delirium are described in the DSM IV. Delirium was diagnosed if DSM IV criteria were present and the patient scored 12 or more points on the Delirium Rating Scale (DRS) [8].

The two-sample *t*-test and χ^2 test were used to test the association of the presence of delirium and predictor variables. Two-way repeated analysis of variance and Scheffe's multiple comparison test were used to evaluate the changes in rS_{O_2}, sevoflurane concentrations, and BIS values during the surgery. $P < 0.05$ was considered significant. Data values are expressed as means ± SD.

Results

Before surgery, three patients had an HDS lower than 22. These patients were older than 80 years. Thus, 20 patients proceeded to the study. Surgery was performed uneventfully and no severe intraoperative complication occurred in any patients. After surgery, 5 (25%) patients developed delirium, from 1 day after the surgery to 4 days after the surgery (Table 1). Demographic and intraoperative factors were compared between the patients with delirium (delirium (+) group; $n = 5$) and those with no delirium (delirium (−) group, $n = 15$) (Table 2). There were no significant differences in hemoglobin, serum electrolytes, blood glucose level, temperature, dose of fentanyl, dose of vecuronium, and dose of ephedrine during surgery between the two groups. The age was significantly higher and the recovery time after anesthesia was significantly longer in the delirium (+) group than in the delirium (–) group.

Preoperative and postoperative HDS did not differ between the groups (Table 3). Baseline HDS in all patients was 28 ± 2. A decrease in HDS by 4 points or more 1 week after surgery as compared to the baseline value was observed in 2 (40%) patients in the delirium (+) group and 3 (20%) patients in delirium (–) group. There were no significant differences in the incidence of decline in cognitive function between the groups. The preoperative kana-hiroi-test score in delirium (+) group (16 ± 5) was significantly lower than that in the delirium (–) group (32 ± 10). There were no significant differences between preoperative and postoperative kana-hiroi-test scores in either group.

Table 4 shows intraoperative anesthetic conditions. Intraoperative sevoflurane concentrations and BIS values did not differ between the delirium (–) group and the delirium (+) group. The percentage of time at which BIS values were lower than 45 or higher than 60 were 38 ± 30 (%) in the delirium (–) group and 27 ± 22 (%) in the delirium (+) group. There were no differences between the groups.

Figure 1 shows the changes in rS_{O_2} during the surgery. Baseline rS_{O_2} in the delirium (+) group was significantly

Table 1. Development and time course of postoperative delirium

Patients	Age (years)/Sex	Postoperative days 1	2	3	4	5
1	75, Male		○	○		
2	72, Male	○	○	○	○	
3	83, Male	○	○			
4	73, Male		○			
5	75, Male	○	○			

○, Diagnosed with delirium

Table 2. Demographic and intraoperative data

	Delirium (–)	Delirium (+)
Age (years)	68 ± 3	76 ± 4*
Weight (kg)	58 ± 12	59 ± 10
Height (cm)	159 ± 10	166 ± 6
Sex (male/female)	10/5	4/1
Duration of surgery (min)	337 ± 109	249 ± 53
Laparoscopic surgery	7 (47%)	1 (20%)
Blood loss (g)	516 ± 620	386 ± 152
Hb ($g \cdot dl^{-1}$)	10.8 ± 1.9	10.7 ± 2.1
Na ($mmol \cdot l^{-1}$)	139 ± 4	140 ± 2
Blood glucose ($mg \cdot dl^{-1}$)	133 ± 25	119 ± 28
Recovery time (min)	19 ± 6	26 ± 8*
Dose of fentanyl (μg)	486 ± 123	480 ± 259
Dose of vecuronium (mg)	20 ± 8	17 ± 2
Dose of ephedrine (mg)	15 ± 5	19 ± 8

* $P < 0.05$ versus delirium (–)
Values are means ± SD

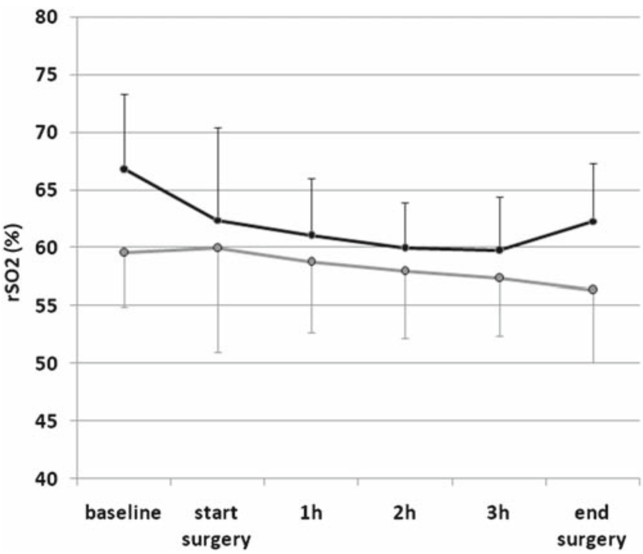

Fig. 1. Changes in regional cerebral oxygen saturation (rS_{O_2}) during the surgery. *Black dots*, Delirium (–); *gray dots*, delirium (+). $P < 0.05$ versus delirium (–). Values are means ± SD

Table 3. Results of cognitive function tests

	Pre-surgery	Post-surgery
HDS (delirium (–))	28 ± 2	26 ± 1
HDS (delirium (+))	28 ± 1	26 ± 4
Kana-hiroi test (delirium (–))	32 ± 10	35 ± 11
Kana-hiroi test (delirium (+))	16 ± 5*	22 ± 7*

* $P < 0.05$ versus delirium (–)
Values are means ± SD
HDS, Hasegawa dementia scale

Table 4. Intraoperative anesthetic conditions

	Start of surgery	1 h	2 h	3 h	End of surgery
Sevoflurane concentration (%)					
Delirium (–)	1.3 ± 0.3	1.3 ± 0.2	1.3 ± 0.2	1.3 ± 0.2	1.2 ± 0.1
Delirium (+)	1.5 ± 0.5	1.5 ± 0.4	1.5 ± 0.6	1.5 ± 0.6	1.4 ± 0.3
BIS					
Delirium (–)	48 ± 6	47 ± 6	47 ± 5	48 ± 5	51 ± 7
Delirium (+)	50 ± 5	46 ± 4	46 ± 2	50 ± 4	49 ± 2

Values are means ± SD

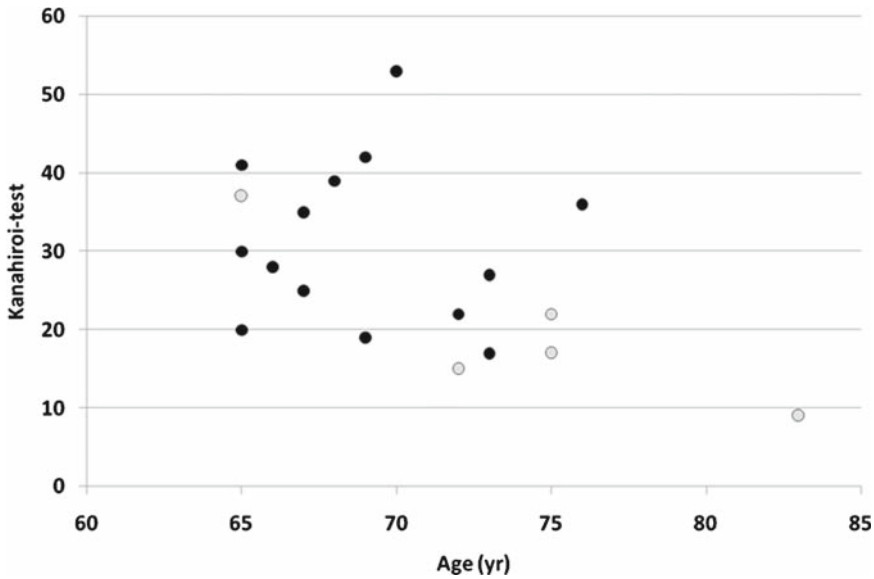

Fig. 2. The relationship between age and preoperative kana-hiroi test scores. The kana-hiroi test scores were linearly correlated with age (kana-hiroi test = 108 − 1.14 × age; $r = 0.49$; $P < 0.05$). *Black dots* show the patients without postoperative delirium. *Gray dots* show the patients with postoperative delirium

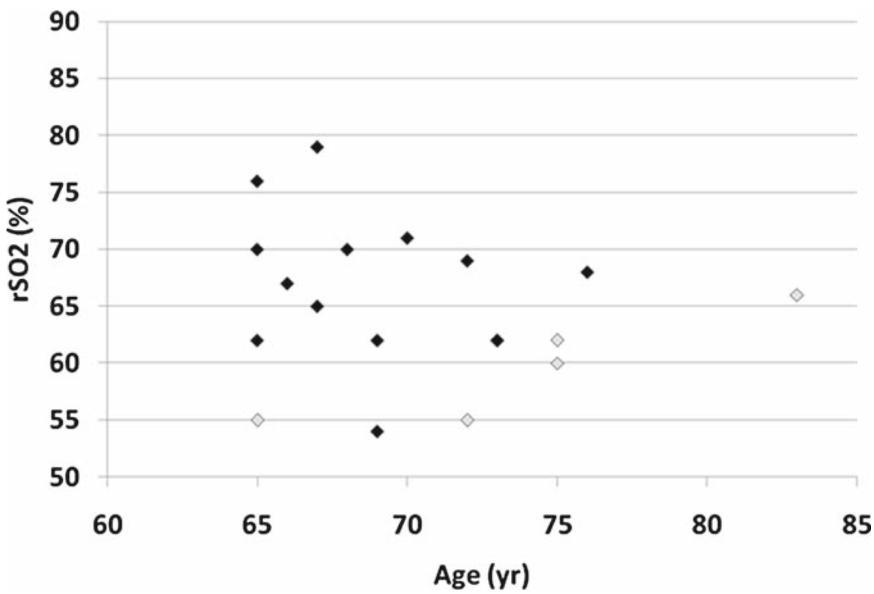

Fig. 3. The relationship between age and baseline rS_{O_2}. There was no correlation between these factors ($P = 0.48$). *Black dots* show the patients without postoperative delirium. *Gray dots* show the patients with postoperative delirium

lower than that in the delirium (−) group. However, there were no significant differences between the groups in the rS_{O_2} after the start of surgery. The numbers of patients with cerebral desaturation, defined as a reduction of rS_{O_2} values below 75% of baseline were 0 in the delirium (+) group and 3 (20%) in the delirium (−) group. There were no significant differences in the incidence of cerebral desaturation between the groups.

Figure 2 shows the relationship between age and preoperative kana-hiroi test scores. The kana-hiroi test scores were linearly correlated with age (kana-hiroi test = 108 − 1.14 × age; $r = 0.49$; $P < 0.05$).

Figure 3 shows the relationship between age and baseline rS_{O_2}. There was no correlation between these factors ($P = 0.48$).

Discussion

In reports in the literature, POD occurs in 10%–60% of patients, and the rate of occurrence is most frequent in the elderly [4,9]. The occurrence of POD appears to be associated with the type of surgery, preoperative cognitive dysfunction, electrolyte abnormalities, and alcohol abuse [1,9–11]. In the present study, it was found that patient age, low preoperative kana-hiroi test score, low preoperative rS_{O_2}, and delayed recovery from anesthesia were the important risk factors for POD.

We sought to evaluate the relation between the decrease in cerebral blood flow (assessed indirectly by NIRS) and POD. However, cerebral desaturation during the surgery was not a predictor for POD despite the lower baseline rS_{O_2} values observed in the patients who exhibited delirium. Preoperative factors, including age and low kana-hiroi test scores, were more relevant for POD than intraoperative factors. The intraoperative anesthetic conditions, including sevoflurane concentration and BIS value, had no relation with POD.

Our results that the mean age in the delirium (+) group was higher than that in the delirium (–) group are in accordance with those in previous reports. In contrast, regarding the preoperative cognitive status assessed by the HDS, no apparent relation was observed in the present study. Our result is different from that reported by Kaneko et al. [12], who demonstrated that patients having preoperative cognitive impairment exhibited POD. However, they determined that an HDS of less than 20 represented preoperative cognitive impairment. In our present study, we excluded the patients in whom preoperative HDS was less than 22 because we believe that these patients should be classified in a different group.

Recent studies have highlighted subtle preoperative cognitive deficits as a hallmark of delirium. Lowery et al. [13] reported that subtle attentional deficits in the absence of dementia were associated with an increased risk of POD. The battery of tests performed in their study were "simple reaction time", "digit vigilance", and "choice reaction time". Similar to the results observed in the study by Lowery et al. [13], low scores on the preoperative kana-hiroi test were associated with the development of POD in our study. Especially, those patients whose preoperative kana-hiroi test score was less than 20 belong to a high-risk group for POD.

The kana-hiroi test is considered to be the most suitable for the screening of frontal lobe function and to have excellent sensitivity for the discrimination of predementia [14]. Therefore, the kana-hiroi test is generally affected by age [15], as was shown in our study. Fukunaga et al. [15] evaluated the relationship between changes in kana-hiroi test scores and cerebral blood flow study, assessed by single photon emission computed tomography (SPECT) in patients with nonruptured cerebral aneurysms before and after surgery. They found a close relation between low kana-hiroi test scores and low cerebral blood flow and they suggested that the kana-hiroi test was a good indicator of cerebral blood flow. The low rS_{O_2} at baseline and delayed recovery from anesthesia on the delirium (+) group in our study also suggest this hypothesis.

The application of NIRS to allow continuous noninvasive monitoring of rS_{O_2} through the scalp and skull provides information on the balance between brain oxygen supply and demand [16]. Low rS_{O_2} values at baseline indicate low brain oxygen supply unless metabolic demand is high. Therefore, it is possible that preoperative cerebral blood flow may have been low in the patients who exhibited delirium in our study.

We hypothesized that intraoperative cerebral desaturation may be responsible for the occurrence of POD. Cerebral desaturation may impair central nervous system function and may be involved in the etiology of postoperative cognitive dysfunction. Casati et al. [5] reported that, in their cohort of elderly patients, brain desaturation (rS_{O_2} decrease <75% of baseline) occurred in 40% of the patients, and the occurrence of cerebral desaturation was associated with a high incidence of postoperative cognitive dysfunction. Cerebral hypoxia is also associated with disturbances in the neurotransmitter system and POD. However, we found no positive relation between this intraoperative factor of cerebral desaturation and POD. One difference was that the incidence of cerebral desaturation in our study was lower (15% of the patients) than that in the study of Casati et al. [5] (40%). In this present study, we monitored rS_{O_2} only during the surgery but not postoperatively, and therefore the occurrence of a postoperative decrease in rS_{O_2} might have been overlooked.

A recent study has shown a relationship between delirium and reduced regional cerebral blood flow in the frontal, temporal, and occipital cortex [17]; accordingly, further studies are warranted to evaluate the relationship between cerebral desaturation and POD.

In summary, we found that patient age, low preoperative kana-hiroi test score, low preoperative rS_{O_2}, and delayed recovery from anesthesia were the important risk factors for POD.

Assessment of preoperative cognitive function with the kana-hiroi test could make a useful contribution to the diagnosis of POD. We note the limitation of our study because of its small sample size. In future, larger-scale studies will be needed to confirm the results of this study.

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