

Preoperative Hypovitaminosis D Can Predict Development of Postoperative Cognitive Dysfunction



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Submission: March 19, 2019; Published: April 10, 2019

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Abstract

Objectives: Preoperative estimation of serum 25OH-vitamin D (25OHD) level in patients undergoing surgical procedures extending for >60min under sevoflurane anesthesia and correlate these levels with frequency of postoperative (PO) cognitive dysfunction (POCD).

Patients & Methods: 254 patients; 127 Kuwaiti (Group A) and 127 Egyptian patients (Group B) were evaluated clinically and gave blood samples for ELISA estimation of serum 25OHD. Vitamin D sufficiency status was defined as sufficient (≥ 75 nmol/L), insufficient (50-75nmol/L) and deficient (<50nmol/L) level. Cognitive function was assessed preoperatively, 48-hr, 1-wk and 2-wk PO using the Digit span (DS) test. Anesthetic was induced using propofol, fentanyl and rocuronium, and was maintained with sevoflurane, fentanyl and rocuronium with continuous non-invasive hemodynamic monitoring. Study outcome included the frequency and severity of hypovitaminosis D (HVD) and POCD in studied patients.

Results: Only 31 patients (12.2%) had sufficient VD level with significant difference in favor of Group B. All surgeries were conducted uneventfully within mean operative time of 154.4 ± 37 min and mean blood loss of 415 ± 158 ml. Median preoperative DS score was 6, at 48-hr, 1-wk and 2-wk PO, 153, 124 and 95 patients, respectively had score of <6. Preoperative serum 25OHD level showed negative significant correlation with age and BMI, and positive significant correlation with male gender and duration of education. Median PO score on DS testing showed positive significant correlation with serum 25OHD, especially in Kuwaiti patients. Statistical analyses defined preoperative low serum 25OHD as significant specific predictor for POCD.

Conclusion: POCD is a common incident event among patients underwent major surgeries consuming long operative time under sevoflurane anesthesia. Old age, high BMI, duration and severity of surgery are co-factors for POCD. Preoperative HVD has a pronounced effect and correlated with these precipitating factors and could be used as independent significant predictor for POCD.

Keywords: Postoperative cognitive dysfunction; Hypovitaminosis D; Sevoflurane; Major surgery; Digit span test

Introduction

Postoperative cognitive dysfunction (POCD) is a neurologic dysfunction characterized by impairment of memory function and intellectual ability [1]. POCD is also associated with greatly reduced speech processing after surgery [2] as well as increased use of healthcare resources [1]. POCD may persist for a period ranging from weeks to months and affects patient's quality of life [3].

Increasing evidence links POCD to surgery and anesthesia and is recognized as an important neuropsychological adverse outcome in surgical patients [4]. Diagnosis of POCD requires complicated neuropsychological testing and is often delayed, so possible predictor for early detection or prediction of POCD is

essential for its prevention and treatment [5]. Also, increasing evidence defined age as a major risk factor for POCD [2].

Multiple studies tried to evaluate biomarkers for screening patients for an increased risk of POCD; preoperative neuron-specific enolase levels are more suitable for assessment of incidence of POCD [6]. The ratio of β -amyloid and Tau proteins, biomarkers of Alzheimer's disease, can be used in forecasting the occurrence of POCD, especially in elderly patients [7]. Preoperative salivary cortisol AM/PM ratio was significantly associated with the presence of early POCD [5].

Cognitive dysfunction, especially in geriatrics, was found to be associated with or predisposed to by multiple nutritional

deficiencies [8] with special regard to deficiency of folic acid [9], vitamin B6 [10], vitamin D [11] and vitamin B12 [12].

Vitamin D (VD) is an important secosteroid hormone in skeletal and non-skeletal systems [13]. After absorption, VD is bound to a binding protein to carry it in blood stream to liver to be hydroxylated into 25OHD [14], which in the kidneys it is hydroxylated to 1,25-dihydroxy VD; which is the biologically active form of VD [15]. Vitamin D can produce a number of biological effects in many non-skeletal tissues through binding to its receptors present in these tissues [16].

Hypothesis

The current study supposed that preoperative hypovitaminosis D (HVD) may induce or aggravate POCD.

Design

Prospective multi-center observational study

Setting

Anesthesia and Clinical Pathology Departments in Tanta University Hospital, Egypt and Sabah Al Ahmed Hospital, Kuwait

Objectives

Preoperative estimation of serum 25OH-vitamin D (25OHD) level in patients assigned for surgical procedures extending for >60min under sevoflurane anesthesia and correlate these levels with the frequency of development of POCD.

Patients & Methods

The current study intended to include >250 patients assigned for surgical procedures extending for >60 min under sevoflurane anesthesia. Exclusion criteria included duration of surgery for <60 min, age <18 years, endocrinopathy inducing HVD, orthopedic diseases or surgery, maintenance on VD supplemental therapy, pregnancy and/or lactation, chronic kidney diseases. The study protocol was approved by the Local Ethical Committee and all enrolled patients signed written fully informed consents. Group A included native Kuwaiti and Group B included native Egyptian patients and immigrants were excluded from either group. Preoperative preparation included general examination to determine demographic data, baseline clinical and hemodynamic data and to take blood samples for baseline investigations and ELISA estimation of serum 25OHD by a clinical chemist who is blinded about the hypothesis of the study or its outcome.

Sampling & investigations

Venous blood samples (5ml) were collected from the antecubital vein under complete aseptic conditions at booking time. The obtained sample was kept in a plane container and allowed to clot then serum was separated by centrifugation at 3000 rpm for 10 min. Serum was removed and placed in pyrogen-free Eppendorf tubes and stored at -70°C until ELISA assayed by Spectrophotometer for estimation of 25OHD using the Calbiotech Vitamin D Kit (Calbiotech, A Life Science Co, USA; Catalog No.

VD220B) which is a solid phase enzyme-linked immunoassay (ELISA) based on the principal of competitive binding [17].

Clinical evaluation

- Vitamin D sufficiency status was defined according to 25-OHD concentration as follows: ≥ 75 nmol/L sufficient level, 50-75nmol/L insufficient level and <50nmol/L deficient level. Vitamin D deficiency was categorized as mild, moderate and severe if 25-OHD concentration was 25-50nmol/L, 12.5-25nmol/L and <12.5nmol/L, respectively [18].
- Cognitive function was assessed preoperatively, 48-hr, 1-wk and 2-wk postoperatively (PO) using the Digit span (DS) test: Forward DS tests are used to measure short-term memory and general attention. Backward DS tests are used to measure verbal working memory [19-21].

Preoperative preparation

Patients were preoperatively evaluated for ASA grade and presence of associated co-morbidities. Patients with co-morbidities were adjusted and were maintained on their preoperative therapies till day of surgery and postoperatively to maintain the control state. Patients were premedicated by midazolam 0.02mg/kg.

Anesthetic procedure

Anesthesia was induced, in studied groups, using propofol 2mg/kg, fentanyl 1-2ug/kg, and rocuronium 0.6mg/kg, and was maintained with sevoflurane, fentanyl and rocuronium. After tracheal intubation, the lungs were ventilated with 100% O₂ in air using a semi-closed circle system for a tidal volume of 6-8ml/kg, and end-tidal carbon dioxide (paCO₂) of 32-35mmHg. Patients were continuously non-invasively monitored for Mean Arterial Pressure (MAP) and Heart Rate (HR).

Clinical Evaluation

- Primary outcome: The frequency and severity of preoperative HVD in patients of both communities
- Secondary outcome
- The frequency and severity of POCD in patients of both groups.
- The relationship between POCD and demographic data, preoperative 25-OHD levels, duration of anesthesia, and the need for ICU admission
- Intraoperative and PO hemodynamic changes
- operative and PO complications
- Frequency of ICU admission and duration of ICU stay

Sample size calculation

Review of literature showed that the overall incidence of HVD in Middle East ranged from 37.5% [22] to 26% [23], to get study

power of 80% with α value of 0.05 and β value of 0.2, sample size per group was calculated to be 120 patients.

Statistical analysis

Obtained data were presented as mean \pm SD, numbers and percentages. Results were analyzed using paired t-test, One-way ANOVA Test and Chi square test. Statistical analysis was conducted using the IBM SPSS (Version 23, 2015) for Windows statistical package. P value <0.05 was considered statistically significant.

Results

The study included 284 patients eligible for evaluation, 30 patients were excluded for not fulfilling the inclusion criteria and 254 patients were enrolled; 127 Kuwaiti (Group A) and 127 Egyptian patients (Group B) (Figure 1). Interestingly, mean educational duration was significantly longer and the frequency of employed patients was significantly higher among Egyptian than Kuwaiti patients. Patients collected from both communities showed non-significant ($p>0.05$) difference as regards preoperative data (Table 1).

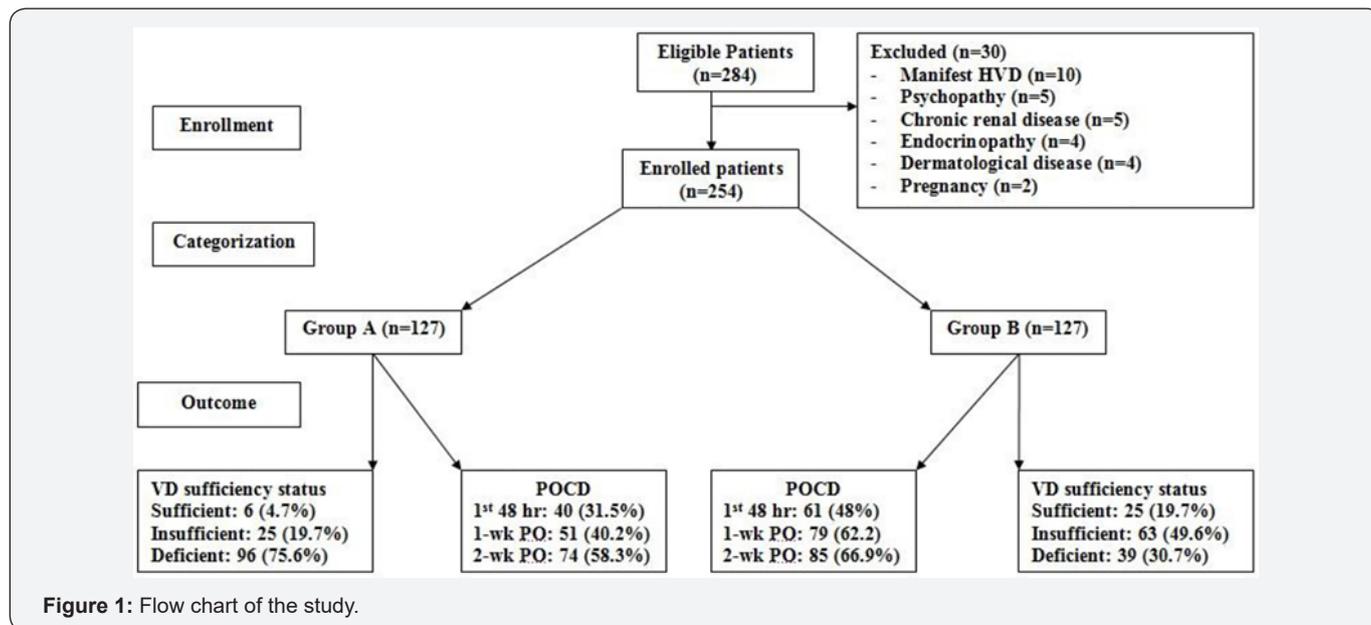


Figure 1: Flow chart of the study.

Table 1: Demographic and preoperative data of studied patients categorized according to patients' community.

		Total	Group A (Kuwaiti)	Group B (Egyptians)	P value
Age (years)		55.9 \pm 16.3	56.3 \pm 16.1	55.5 \pm 16.6	0.587
Gender; M: F	Males	113 (44.5%)	58 (46.7%)	55 (43.3%)	0.705
	Females	141 (55.5%)	69 (54.3%)	72 (56.7%)	
BMI data	Weight (kg)	84.7 \pm 11.6	83.7 \pm 10.9	85.7 \pm 12.2	0.184
	Height (cm)	169.4 \pm 3.6	169.7 \pm 3.8	169.6 \pm 3.7	0.481
	BMI (kg/m ²)	29.4 \pm 4.1	29.2 \pm 4	29.5 \pm 4.2	0.501
Educational years	5-10	91 (35.8%)	62 (48.8%)	29 (22.8%)	0.0001
	>10-15	106 (41.7%)	43 (33.9%)	63 (49.6%)	
	>15	57 (22.5%)	22 (17.3%)	35 (27.6%)	
	Total	11.7 \pm 3.5	10.8 \pm 3.6	12.6 \pm 3.2	0.089
Employment	Yes	153 (60.2%)	69 (54.3%)	85 (66.9%)	0.039
	No	101 (39.8%)	58 (46.7%)	42 (33.1%)	
ASA grade	I	50 (19.7%)	24 (18.9%)	26 (20.5%)	0.825
	II	143 (56.3%)	70 (55.1%)	73 (57.5%)	
	III	61 (24%)	33 (26%)	28 (22%)	
Ass. Medical co-morbidities	No	69 (27.2%)	33 (26%)	36 (28.3%)	0.782
	Yes	185 (72.8%)	94 (74%)	91 (71.7%)	

Data are presented as numbers and mean \pm SD; percentages are in parenthesis; VD: Vitamin D; P value indicates the significance of difference between both groups.

At time of enrolment; 31 patients (12.2%) had sufficient and 88 patients (34.6%) had insufficient, while 135 patients (53.2%) had deficient VD level with significant ($p=0.00001$) in favor of Group B. Among patients had deficient VD level, 48 patients (35.6%) had mild, 55 patients (40.7%) had moderate and 32 patients (23.7%) had severe HVD with significant ($p=0.0001$) difference in favor of

Group B. Mean serum VD levels were non-significantly ($p=0.262$) higher in patients of group B than those of group A. Despite of the significantly higher level of VD in patients of group B who had insufficient and deficient VD than corresponding patients of group A, patients of group B having sufficient VD had non-significantly ($p=0.515$) higher serum VD levels than those of group A (Table 2).

Table 2: At enrolment serum VD status of studied patients categorized according to patient's community.

Parameters	Group VD status	Total	Group A (Kuwaiti)	Group B (Egyptians)	P value	
Patients' distribution	Sufficient	31 (12.2%)	6 (4.7%)	25 (19.7%)	0.00001	
	Insufficient	88 (34.6%)	25 (19.7%)	63 (49.6%)		
	Deficient	135 (53.2%)	96 (75.6%)	39 (30.7%)		
Level (nmol/L)	Sufficient	77.7±2.9	77±1.5	77.9±3.2	0.515	
	Insufficient	66±6.4	61.5±5.6	67.8±5.9	0.00002	
	Deficient	Mild	31.8±3.8	31.9±3.9	31.8±1	0.943
		Moderate	18.7±4.1	19.3±4.1	17.4±3.9	0.111
		Severe	10.9±0.9	10.7±1.1	10.9±0.7	0.545
		Total	21.8±8.9	24.3±8.6	16.1±6.8	0.00001
Total		44.1±24.9	34.4±19.2	53.9±26.2	0.00001	

Data are presented as numbers, percentages and mean ± SD; VD: Vitamin D; P value indicates the significance of difference between both groups

All surgeries were conducted uneventfully within a mean operative time of 154.4 ± 37 ; range 70-215 minutes. Mean intraoperative blood loss was 415 ± 158 ml, but no patient required blood transfusion. HR and MAP measures recorded at end of surgery were significantly lower in patients of group A compared to that recorded at time of induction of anesthesia. In group B, at end of surgery, MAP measures were significantly lower, while HR measures were non-significantly lower than them at-induction measures. MAP measures at end of surgery were non-significantly higher, while HR measures were significantly ($p=0.036$) higher in patients of group B compared to patients of group A (Figure 1).

Thirty-eight (15%) patients required transfer to ICU for hemodynamic and respiratory stabilization; 25 patients of group A and 13 patients of group B with significantly ($p=0.035$) higher frequency among patients of group A. Mean ICU stay duration was 31.7 ± 17.8 ; range: 12-72hr with non-significant ($p=0.302$) difference between both groups. The remaining patients were transferred to post-anesthetic care unit (PACU) and shifted to surgical ward after a mean duration of 87 ± 45.8 ; range: 30-240min, with non-significant ($p=0.363$) difference between patients of both groups (Table 3).

Table 3: IO and immediate PO data of studied patients categorized according to patient's community.

Group Parameter	Total	Group A (Kuwaiti)	Group B (Egyptians)	P value	
Operative time (min)	154.4±37	150±38.8	158.8±34.6	0.698	
Intraoperative blood loss (ml)	415.7±158.2	421.5±162.2	409.8±154.6	0.762	
Hemodynamic changes	HR (beats/min)	Pre	77.1±7.9	76.7±8.9	0.331
		PO	75.3±6.7	74.1±6.2*	0.036
	MAP (mmHg)	Pre	87.3±5	86.8±5.5	0.634
		PO	83.3±10.2	82±10.7*	0.102
Immediate PO care at	ICU	38 (15%)	25 (19.7%)	13 (10.2%)	0.035
	PACU	216 (85%)	102 (80.3%)	114 (89.8%)	
Duration till shift to ward	ICU stay (hrs)	31.7±17.8	33.8±19.4	27.5±14	0.302
	PACU stay (min)	87±45.8	90±45.9	84.2±46.3	0.363

Data are presented as numbers, percentages and mean ± SD; IO: Intraoperative; HR: Heart rate; MAP: Mean arterial pressure; PO: Postoperative; ICU: Intensive care unit; PACU: Postanesthetic care unit; P value indicates the significance of difference between both groups; *: indicates significant difference between pre- and PO measures; $p < 0.05$ indicates significant difference.

Preoperative median DS score for studied patients was 6; considering this figure as cutoff point; on forward testing, 153 patients (60.2%) had score of < 6 at 48-hr, 124 patients (48.8%)

at 1-wk and 95 patients (37.4%) at 2-wk PO and on backward 127 patients (50%) had score of < 6 at 48-hr, 106 patients (41.7%) at 1-wk and 86 patients (33.9%) at 2-wk PO. The frequency of

patients had DS score <6 on forward testing was significantly higher in patients of group A than in group B. However, on backward testing the difference was non-significantly higher between both groups, but in favor of group B (Table 4).

Table 4: PO scores on DS testing of studied patients categorized according to patient's community.

Test	Parameter	Time	Total	Group A (Kuwaiti)	Group B (Egyptians)	P value
DS Forward testing	Frequency of DS score ≥6	48-hr PO	101(39.8%)	40 (31.5%)	61 (48%)	0.007
		1-wk PO	130(51.2%)	51 (40.2%)	79 (62.2%)	0.0004
		2-wk	159(62.6%)	74 (58.3%)	85 (66.9%)	0.154
	Score	Preoperative	6.9±0.8	6.9±0.9	6.8±0.6	0.218
		48-hr PO	5.5±1.1**	5.3±1**	5.7±1.2**	0.002
		1-wk PO	5.9±1.4**	5.5±1.4**	6.2±1.3*	0.00012
		2-wk	6.3±1.3*	6.2±1.3	6.4±1.3	0.191
DS Backward testing	Frequency of DS score ≥6	48-hr PO	127 (50%)	63 (49.6%)	64 (50.4%)	0.902
		1-wk PO	148(58.3%)	69 (54.3%)	79 (62.2%)	0.203
		2-wk	168(66.1%)	83 (65.4%)	85 (66.9%)	0.467
	Score	Preoperative	7±1.4**	7±1	7.1±0.7	0.456
		48-hr PO	5.8±1.1**	5.7±1.1**	5.8±1.1**	0.442
		1-wk PO	6.2±1.4*	5.9±1.3**	6.5±1.5*	0.002
		2-wk	6.4±1.5	6.2±1.5*	6.5±1.4	0.083

Data are presented as numbers, percentages, mean±SD; DS: Digit Span test; P indicates significance of difference between groups A and B; *: indicates significant difference versus preoperative score; *: significance at <0.05 level; **: significance at <0.001 level.

Mean DS score at 48-hr and 1-wk PO was significantly lower on both forward and backward testing of all patients in comparison to preoperative scores with significantly lower score for patients of group A than group B at 48-hr and 1-wk PO for forward and at 1-wk PO on backward testing. At 2-wk PO, mean DS score was non-significantly lower in patients of group B on forward and backward testing on comparison to preoperative score, while in patients of group A, the difference in score on backward testing was still significantly lower than their preoperative score (Table 4).

Median value of the three PO scores of forward testing was significantly (Z=3.629, p=0.0003) higher in group B (6; IQR: 5-7) than in group A (5; IQR: 5-6) and for backward testing was significantly (Z=3.012, p=0.003) higher in group B (6; IQR: 5-7)

than in group A (6; IQR: 5-6). However, for total patients the median value of the three PO scores of forward testing (6; IQR: 5-6) was non-significantly (Z=1.679, p=0.092) higher than for backward testing (6; IQR: 5-7).

In total studied population, preoperative serum 25OHD level showed negative significant correlation with age and BMI, while showed positive significant correlation with male gender, duration of education. Moreover, median value of estimated PO score on DS testing showed positive significant correlation with preoperative serum 25OHD on both forward and backward DS test evaluation. These correlations with preoperative serum 25OHD levels were more pronounced in Kuwaiti patients than in Egyptian patients (Table 5).

Table 5: Pearson's correlation coefficient between patients' preoperative data and median value of DS test score, and preoperative serum VD levels.

Parameter Group	Group A (Kuwaiti)		Group B (Egyptians)		Total		
	r	p	r	p	r	p	
Age	-0.249	0.005	-0.138	0.120	-0.197	0.002	
Male gender	0.241	0.006	0.178	0.045	0.211	0.001	
BMI	-0.227	0.010	-0.234	0.008	-0.226	<0.001	
Duration of Education	0.360	<0.001	0.413	<0.001	0.388	<0.001	
Employment	0.315	<0.001	0.252	0.004	0.284	<0.001	
DS testing	Forward	0.272	0.002	0.321	<0.001	0.300	<0.001
	Backward	0.218	0.014	0.338	<0.001	0.285	<0.001

Regression analysis defined preoperative low serum 25OHD (β=0.379, p<0.001), short duration of education (β=0.203,

p=0.002), high BMI (β=0.173, p=0.006) and old age (β=0.171, p=0.007) as positive predictors for POCD. ROC curve analysis for

these predictors defined high BMI as a significant ($p=0.006$) sensitive predictor for POCD with AUC=0.371 (95% CI: 0.283-0.460),

while low serum 25OHD as significant ($p=0.006$) specific predictor with AUC=0.630 (95% CI: 0.543-0.717) for POCD (Figure 2).

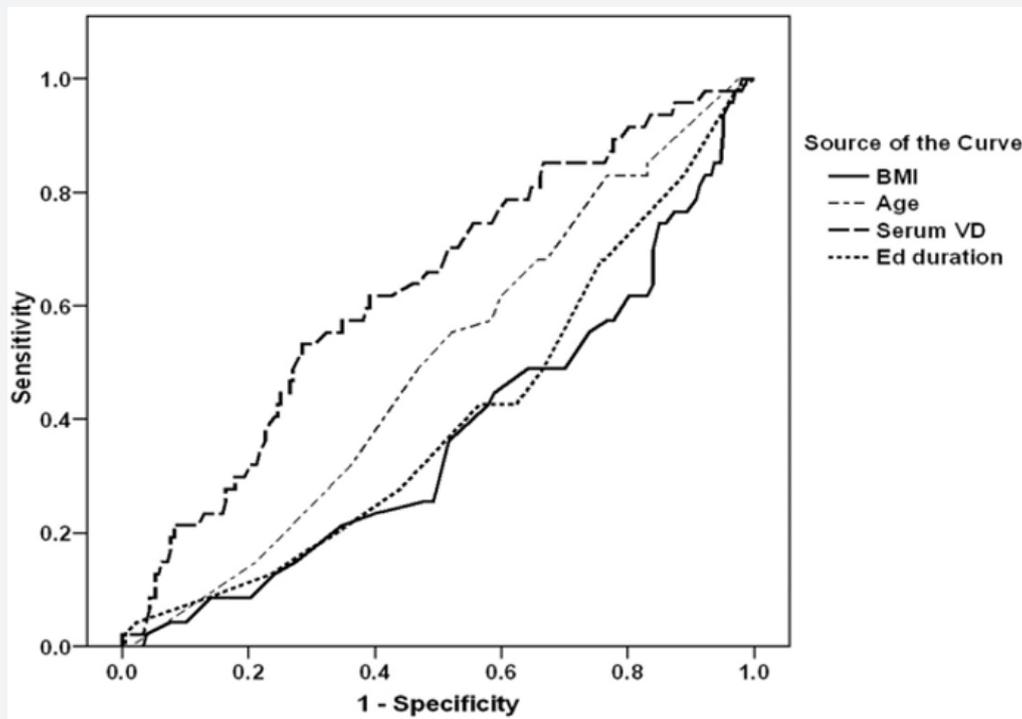


Figure 2: ROC curve analysis for preoperative parameters as predictor for POCD development.

Discussion

The current study included 254 patients underwent major surgical procedures under sevoflurane anesthesia within a mean operative time of 154.4 (± 37) min and 38 patients had admitted to ICU for a mean duration of 31.7 (± 17.8) hr. All patients showed significantly lower score on DS test in relation to their preoperative score and despite of the progressively regained Cognitive Function (CF), the 2-wk PO scores were still significantly lower than their preoperative scores.

These findings illustrate the deleterious effects of long-duration surgery and sevoflurane anesthesia, especially if surgery induced excessive blood loss on CF of patients. However, the underlying etiology and pathogenesis is still a matter of debate, where multiple studies attributed the development of POCD to sevoflurane anesthesia [24-27] secondary to sevoflurane-induced higher levels malondialdehyde [24], TNF- α and IL-6 [26,27] and caspase-3 [27] and/or reduced levels S100B protein [24,26,28]. Other studies reported non-significant difference between frequency and severity of POCD after either of sevoflurane or propofol anesthesia [29-31]. The situation was made worse by Guo et al. [32] who found sevoflurane could improve cerebral oxygenation even in patients with impaired cerebral oxygenation. Moreover, Shoair et al. [25] found using highly anticholinergic or sedative-hypnotic drugs prior to surgery are risk factors for POCD

and Sato et al. [33] suggested that the risk of early PO attention dysfunction may be magnified in patients experiencing other risk factors of POCD, as severity of surgery, occurrence of complications, and pre-existing cognitive impairments. Furthermore, Fan et al. [34] found the use of LMA reduced the prevalence of POCD during pediatric neurosurgery than with endotracheal intubation.

The reported continued CD for 2-wk after surgery could be explained depending on the experimental findings of Huang et al. [35] who detected neuro-inflammation, glia activation, aberrant tau phosphorylation and DNA damage in the hippocampus of aged rats underwent a midline laparotomy or exposed to sevoflurane anesthesia alone up to 14 days PO.

About 88% of studied patients had insufficient-deficient serum 25OHD levels, a prevalence which coincided with Chakhtoura et al. [36] who documented that the Middle East and North Africa region is of the lowest serum 25OHD concentrations, worldwide. However, HVD was more evident in Kuwaiti than Egyptian patients as manifested by significantly higher frequency of patients had HVD and significantly lower serum 25OHD among Kuwaiti patients. These findings spot light on the impact of cultural, environmental and educational factors on VD status. In support of this assumption, the reported significantly higher educational duration and frequency of employee among Egyptian patients and this most probably provided greater opportunity for

sunlight exposure with subsequent increased VD synthesis. In line with these data and explanation Al-Taiar et al. [37] reported that despite the abundant sunshine in Kuwait, prevalence of VD deficiency and severe deficiency was 81.21% and 39.48%, respectively and this reflects strong sun avoidance behavior, so adequate outdoor daytime activities should be encouraged.

Preoperative serum VD levels of studied patients showed negative significant correlation with age and BMI, while showed positive significant correlation with male gender, duration of education. Similarly, Golan-Cohen et al. [38] in multivariate analysis of results of cross-sectional study found older age, female gender, higher BMI, sunscreen use, and low sun exposure were associated with lower VD levels and Hashem et al. [39] found most Kuwaiti adolescents are physically inactive and attributed this to low/medium maternal educational levels.

Collectively, median value of PO score on DS test was positively correlated with preoperative serum VD. This finding supported previous reports concerning the association between HVD and poorer mental flexibility [40] or higher likelihood of functional deficits among patients with memory complaint [41], CD in specific domains in old adults [42], and increased problems of memorizing new information [43]. Moreover, these data are consistent with results of VD supplemental intake and slowing, prevention, or improvement of neurocognitive decline [44], decline in verbal fluency [45], or memory loss [46].

Moreover, statistical analyses defined preoperative HVD as positive specific predictor for the possibility for development of POCD. These findings point to a close relationship between VD and cognitive function (CF), so HVD could give an objective predictor for the possibility of development of POCD. Similarly, Sakuma et al. [47] found HVD was independently associated with a higher prevalence of CD and De Oliveira et al. [48] documented that the independent and inverse relation between low 25OHD levels and elevated depressive symptoms suggests that HVD may be a risk factor for late-life depression, particularly among women.

Few studies evaluated the relation between HVD and CF disturbances in middle aged populations; the current study included patients in age range of 28-79 years and all these patients showed POCD. Moreover, Similarly, Shu et al. [49] reported that the depth of anesthesia under combined intravenous-inhalational anesthesia yielded milder influence on POCF in young and middle-aged patients.

Unfortunately, previous studies dealt with the relation between HVD and POCD were deficient. However, the obtained results go in hand with Zhang et al. [50] who documented that after adjusting for confounding factors, preoperative VD deficiency was associated with an increased risk of POCD. In trial to explore the association between HVD and disturbed CF, Annweiler et al. [51] suggested an association between HVD and dysfunction of the frontal-subcortical neuronal circuits,

particularly the dorsolateral circuit in patients with disturbed CF and HVD. Thereafter, Annweiler [51] documented that VD is essential to neurotransmitters and neurotrophins regulation with anti-inflammatory and antioxidant neuroprotective action, so HVD may result in neurological dysfunction that may explain part of the cognitive disorders.

Conclusion

POCD is a common incident event among patients undergoing major surgical procedures consuming long operative time under sevoflurane anesthesia. Sevoflurane anesthesia could not be accused as the sole precipitating factor. Old age, high BMI, duration and severity of surgery and development of complications are co-factors for upcoming CD. Preoperative HVD has a pronounced effect and correlated with all of these precipitating factors and could be used as an independent significant predictor for POCD.

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DOI: [10.19080/JAICM.2019.08.555746](https://doi.org/10.19080/JAICM.2019.08.555746)

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