



## Decrease in spectral entropy by low tidal volume ventilation-associated severe hypercapnia -a case report-

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Severe hypercapnia can be predicted by a decrease in cerebral electrical activity. The authors describe a sudden decrease in spectral entropy due to severe hypercapnia-induced respiratory acidosis in a patient with chronic pulmonary obstructive disease during lung resection. After two and a half hours of low tidal volume ventilation in the lateral position, the state entropy suddenly dropped from 45 to 7, without any changes in the effect-site concentration of propofol, end-tidal carbon dioxide (CO<sub>2</sub>) tension, oxygen saturation, or arterial pressure. However, arterial blood gas analysis showed severe respiratory acidosis (pH 7.01, PaCO<sub>2</sub> 115 mmHg and PaO<sub>2</sub> 246 mmHg with FIO<sub>2</sub> of 0.5). Immediate hyperventilation improved the state entropy and acid-base balance. Electroencephalography-based spectral entropy can detect severe hypercapnia in chronic pulmonary obstructive disease patients with a large arterial to end-tidal CO<sub>2</sub> difference due to prolonged hypoventilation during thoracic surgery.

**Key Words:** Electroencephalography, Entropy, Hypercapnia, Hypoventilation.

End-tidal carbon dioxide pressure (PetCO<sub>2</sub>) is a well-known surrogate marker of ventilation adequacy during general anesthesia under mechanical ventilation. However, significant ventilation-perfusion mismatch during a thoracic procedure in the lateral position results in a large PetCO<sub>2</sub> to PaCO<sub>2</sub> discrepancy and makes PetCO<sub>2</sub> unreliable for the estimation of PaCO<sub>2</sub> to determine ventilation adequacy [1,2].

Electroencephalography (EEG)-based cerebral monitors, such as spectral entropy or bispectral index (BIS), are widely

used to titrate anesthetic-induced cerebral depression in clinical practice as they provide measures of cortical electrical activity. BIS can detect systemic hypoperfusion-induced depression in the central nervous system [3]. In contrast to BIS, which combines the spectrogram, bispectrum, and a time domain assessment of EEG burst suppression into a single index, spectral entropy produces two different indices by quantifying the irregularity, complexity, and unpredictability of processed EEG signals (state entropy, SE) and frontal electromyography (EMG) signals (response entropy, RE). Although acute ventilatory failure due to CO<sub>2</sub> insufflation and subcutaneous emphysema can lead to a sudden decrease in the BIS and increase in PetCO<sub>2</sub> in anesthetized patients [4], the effects of progressive hypercapnia due to prolonged hypoventilation on spectral entropy and PetCO<sub>2</sub> have not been determined.

We report a sudden and marked drop in spectral entropy without a PetCO<sub>2</sub> change, associated with severe hypercapnia due to prolonged low tidal volume ventilation in a patient with chronic obstructive pulmonary disease (COPD) undergoing lung resection.

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## Case Report

A 66-year-old, heavy smoker (male, 62 kg, 166 cm) with lung cancer was scheduled for elective left upper lobectomy. He was medicated for chronic bronchitis and emphysema with obstructive pulmonary dysfunction (EFV<sub>1</sub>/FVC 55%) preoperatively. Upon arrival in the operating room, standard anesthesia monitoring and spectral entropy were established. Anesthesia was induced and maintained with intravenous propofol and remifentanyl anesthesia. After administering rocuronium 0.75 mg/kg, an Arndt endobronchial blocker was introduced through a single-lumen endotracheal tube to provide one-lung ventilation (OLV) and properly placed in the left bronchus via flexible fiberoptic bronchoscopy. However, the hypoxemia persisted with OLV despite correct endobronchial blocker positioning and ventilator adjustments, and thus, surgery proceeded under two-lung ventilation at a tidal volume (TV) of 4–5 ml/kg and a respiratory rate (RR) of 15 breaths/min to maintain PetCO<sub>2</sub> at 45–50 mmHg (PaCO<sub>2</sub> was 50–55 mmHg). The SE was maintained between 40 and 50 under target controlled propofol infusion during surgical procedure.

Two and a half hours after commencing surgery, the SE and RE suddenly dropped from 45 to 7 and 43 to 16, respectively, without any change in the effect-site concentration of propofol (Table 1). Although the heart rate increased progressively from 73 to 110 beats/min, no changes in oxygen saturation (98–99%), PetCO<sub>2</sub> (48 mmHg), or invasive arterial pressure (125/65–110/60 mmHg) were observed. However, arterial blood gas analysis (ABGA) showed severe respiratory acidosis (pH 7.01, PaCO<sub>2</sub> 115 mmHg, and PaO<sub>2</sub> 246 mmHg with FIO<sub>2</sub> of 0.5).

On realizing inadvertent hypercapnia, we requested the surgeon stop the surgical procedure and immediately initiated

hyperventilation. The SE then progressively increased to 30 and then to 51 after 10 and 30 minutes of hyperventilation, respectively. Changes in PetCO<sub>2</sub> were observed after 15 minutes and reached 33 mmHg at 30 minutes (Table 1). At 30 minutes after hyperventilation, ABGA showed the following; pH 7.34, PaCO<sub>2</sub> 47 mmHg and PaO<sub>2</sub> 221 mmHg with FIO<sub>2</sub> of 0.5. Because resection of the left upper bronchus was almost complete, surgery uneventfully proceeded with a TV of 500 ml and RR of 12 breaths/min. After surgery, the patient was extubated because he was alert with an acceptable range of oxygenation and ventilation and a SE of 91. No neurological deficit was detected postoperatively.

## Discussion

In this case, low tidal volume ventilation-associated severe hypercapnia induced a marked reduction in state entropy without a concomitant increase in PetCO<sub>2</sub> during a thoracic surgical procedure. Generally, changes in entropy scores can reflect the effect of various contributors on cerebral function, including anesthetic concentration, cerebral blood flow, cerebral oxygen metabolism, and hypothermia, in patients with general anesthesia [5–7]. However, changes in the anesthesia depth, hypothermia, and cerebral hypoperfusion were unlikely to have reduced the SE because an effect-site propofol concentration of 3.0 µg/ml was maintained without temperature and hemodynamic changes during surgery. The reason for the sudden SE decrease from 45 to 7 in our patient may have been related to severe hypercapnia (peak PaCO<sub>2</sub> 115 mmHg).

It has been reported that changes in the arterial CO<sub>2</sub> tension can alter EEG patterns. Hypercapnia-induced respiratory acidosis can not only increase cerebral blood flow and intracranial

**Table 1.** Changes in Ventilation, Oxygenation, Circulation, and Spectral Entropy and Arterial Blood Gas Analysis

	After Induction of Anesthesia	During Surgery				End of surgery
		30 min	180 min	190 min	210 min	
Tidal volume (ml/kg)	8	4–5	4–5	8–9	8–9	8
Respiratory rate (bpm)	12	15	15	20	20	12
PIP (mmHg)	16	12	20	20	20	21
ABP (mmHg)	110/60	120/65	120/65	115/63	125/72	105/60
Heart rate (bpm)	65	72	110	100	91	72
SpO <sub>2</sub> (%)	99	100	98	99	99	98
ETCO <sub>2</sub> (mmHg)	35	45	48	48	33	34
State entropy	52	46	7	30	51	49
Response entropy	55	48	16	37	53	52
pH		7.31	7.01		7.34	7.35
PaCO <sub>2</sub> (mmHg)		58	115		47	47
PaO <sub>2</sub> (mmHg)		240	246		221	268
PaCO <sub>2</sub> -PetCO <sub>2</sub> (mmHg)		13	63		15	13

ABP: arterial blood pressure, PIP: peak inspiratory pressure.

pressure but can also inhibit excitatory synaptic transmission in the forebrain cortex by elevating extracellular adenosine concentrations [8]. The suppression of synaptic potentials by hypercapnia can result in substantial EEG depression, i.e., a reduction in the amplitude of fast (alpha and beta) waves and a relative increase in the slow frequency delta wave in conscious and anesthetized individuals [9-11]. Therefore, we suppose that severe hypercapnia-related EEG changes caused a decrease in the EEG-derived state entropy in our patient. Because spectral entropy reveals separate courses for EEG-based SE and combined EEG and EMG-based RE simultaneously, more drastic changes in SE than RE in our patient suggests that severe hypercapnia-induced respiratory acidosis predominantly affects cerebral electrical activity (EEG) rather than muscular activity (EMG).

The effects of CO<sub>2</sub>-related changes on EEG-derived cerebral activities have been mentioned previously. During general anesthesia, the BIS was not influenced by moderate changes in PetCO<sub>2</sub> in the range of 22.5 to 90 mmHg [12]. However, severe respiratory acidosis (pH 6.94, PaCO<sub>2</sub> 137 mmHg) induced by acute ventilatory failure due to CO<sub>2</sub> insufflation and subcutaneous emphysema resulted in a marked reduction of the BIS to 4, PetCO<sub>2</sub> elevation (from 37 to 63 mmHg), hypertension, and tachycardia in a laparoscopic surgery patient [4]. Lee and Chang [13] reported that inadvertent muscular paralysis-associated CO<sub>2</sub> narcosis (pH 6.875, PaCO<sub>2</sub> 130 mmHg) resulted in loss of consciousness, with BIS values between 35 and 40 in a conscious patient. Considering the differences in BIS observed in anesthetized and conscious patients, it would appear that severe hypercapnia seems to have an anesthetic property equivalent to general anesthesia. In our patient, an abrupt decrease in SE occurred when PaCO<sub>2</sub> reached 115 mmHg despite the progressive development of hypercapnia due to prolonged hypoventilation during general anesthesia. Furthermore, when normocapnia was reestablished, SE dramatically increased to a value acceptable for general anesthesia. These findings also suggest that only severe hypercapnia can reduce cerebral electrical activity more

than general anesthesia, and the effect of moderate hypercapnia on EEG is possibly masked by general anesthesia or is above the cut-off level required to cause substantial synaptic transmission suppression.

In contrast to spectral entropy, continuous capnography did not provide useful information about the marked PaCO<sub>2</sub> changes observed. Prolonged low tidal volume ventilation may have exacerbated arterial to end-tidal CO<sub>2</sub> pressure discrepancy in our COPD patient undergoing a thoracic procedure in the lateral position. In cases with PaCO<sub>2</sub> in the range of 30–50 mmHg, transcutaneous CO<sub>2</sub> partial pressure monitoring more accurately predicts PaCO<sub>2</sub> than PetCO<sub>2</sub> monitoring during thoracic surgery [14,15]. However, its validity at higher PaCO<sub>2</sub> levels is yet to be proven. In addition, in our patient, severe hypercapnia was accompanied by only a gradual, modest increase in heart rate without hypertension or arrhythmia. Unlike the sudden onset of acute hypercapnia caused by acute ventilatory failure [4,13], low tidal volume ventilation-induced prolonged, accumulating arterial CO<sub>2</sub> tension seems to have blunted a prominent cardiovascular response in our patient. These observations caution that when a significant arterial to end-tidal CO<sub>2</sub> pressure gradient is suspected in a patient with ventilation-perfusion mismatch, timely and serial measurements of arterial CO<sub>2</sub>, rather than end-tidal CO<sub>2</sub> or hemodynamic parameters, are necessary to ensure ventilation adequacy.

In summary, we report a case of severe hypercapnia detected by a sudden decrease in EEG-derived spectral entropy without changes in PetCO<sub>2</sub> in a COPD patient ventilated with a low-tidal volume during thoracic surgery.

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