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Clinical research progress on the index of consciousness 2 in pain management

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Abstract: Effective perioperative pain management is essential for accelerating patient recovery and minimizing adverse events, in which sensitive and reliable pain monitoring plays an indispensable role. The index of consciousness (IOC) derived from electroencephalogram signal is an emerging index for monitoring the depth of anesthesia, and has been progressively applied during general anesthesia. The IOC2 is used for the monitoring of the degree of analgesia, and can be used as a pain management monitoring index in a variety of surgical types to evaluate the analgesic effect, guide the rational use of analgesic drugs, and reduce perioperative-related adverse events, and it has good advantages and application prospects in the clinic. The purpose of this paper is to summarize the basic principle, current status of clinical research, advantages and disadvantages of IOC2, and to make a simple comparison with other analgesic monitoring, so as to provide a reliable basis for the clinical application of IOC2.

Keywords: Index of consciousness 2; Anesthesia; Analgesic monitoring; Pain management

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Pain is defined as "a localized or generalized unpleasant bodily sensation or complex of sensations that causes mild to severe physical discomfort and emotional distress and typically results from bodily disorder (such as injury or disease)", including the patient's subjective perception of pain while conscious and objective responses to noxious stimuli during unconsciousness [1]. Currently, general anesthesia monitors anesthesia depth using indicators such as the bispectral index (BIS), entropy, Narcotrend index, etc., but these technologies primarily monitor changes in sedation depth and are not sensitive to the degree of analgesia [2-3]. Inadequate analgesia during general anesthesia can lead to strong autonomic responses in patients, even resulting in cardiovascular accidents; excessive analgesia can cause delayed recovery, respiratory depression, and potential harm to the immune system [4]. Historically, anesthesiologists have relied on empirical assessment of analgesic efficacy based on vital signs such as heart rate and blood pressure, but due to individual differences in pain sensitivity, this approach lacks precision. Therefore, effective and precise monitoring of analgesia during surgery is currently a critical issue in clinical anesthesia practice. In recent years, a new pain assessment index—Index of Consciousness 2 (IOC2)—has gained attention. IOC2 digitizes the analgesic effect for objective evaluation of pain in patients under general anesthesia, optimizing analgesic drug dosages to improve patient outcomes, demonstrating significant effectiveness in pain management. This review aims to summarize recent advances in clinical applications and research related to IOC2, comparing it with other techniques for monitoring analgesia in clinical practice.

1 Concept and Calculation Principles of IOC2

IOC2 is an index evaluating nociceptive/antinociceptive stimuli, derived from electroencephalogram (EEG) signals. IOC2 uses adaptive neuro-fuzzy inference systems and nonlinear analysis to process EEG signals in the frequency range of 0.5-42 Hz, separating linear and nonlinear components to reduce electromyographic interference. Symbolic dynamics are employed to convert the EEG time series into symbolic sequences, and burst suppression ratio parameters are used in fuzzy inference to compute the consciousness index (IOC1). Previous research indicated nociceptive stimuli could induce θ wave activity [5], and studies in mice showed aging increases θ waves as the dominant EEG waveform, with increased θ wave amplitudes correlating positively with pain intensity [6-7]. Additionally, insufficient opioid drugs can induce δ wave arousal, with δ band power increase (0.5-4 Hz) also related to nociceptive stimuli [8]. IOC2 measures θ and δ wave amplitudes, incorporating first-order differentials, wave morphology, and harmonics, combining results from IOC1 for final numerical assessment.

Common monitoring devices include the Wellanest Angel-6000D multi-parameter monitor and Quantium Medical qCON2000 monitor. IOC2 scores range from 0 to 99, with scores between 30 and 50 indicating appropriate general anesthesia depth; scores from 50 to 99 suggest inadequate intraoperative analgesia, while scores from 0 to 30 indicate excessive analgesia.

2 Clinical Applications of IOC2

2.1 Application in Total Intravenous Anesthesia (TIVA)

2.1.1 Guiding Endotracheal Intubation

There are individual differences in the onset and peak effects of analgesic drugs, and performing endotracheal intubation before adequate analgesic effect is achieved can lead to strong stress responses. Birendra [9] studied using IOC2 values to guide endotracheal intubation, finding that administering 0.6~0.7 μg/kg sufentanil compared to 0.5 μg/kg effectively controlled intubation stress for double-lumen endotracheal intubation. Sheng *et al.* [10] found that administering 0.4 μg/kg sufentanil maintained IOC2 values at 42±8, effectively suppressing intubation responses. These trials suggest different doses of opioid drugs may affect nociceptive responses to endotracheal intubation differently, possibly due to the greater irritability of double-lumen endotracheal tubes compared to single-lumen tubes, necessitating more balanced analgesic medication to balance nociceptive-antinociceptive responses. In addition to endotracheal tubes, Melia *et al.* [11] suggested IOC2 has predictive value for supraglottic airway devices as well.

2.1.2 Movement prevention during surgery

Painful stimuli during surgery can cause patient movement, which not only affects the surgeon's operation but also triggers adverse events. Jensen *et al.* [12] pointed out that under the same depth of anesthesia, IOC2 could predict whether patients will exhibit movements in response to noxious stimuli. Li *et al.* [13] suggested that when noxious stimuli occur, IOC2 could predict movement with a receiver operating characteristic (ROC) curve area under the curve (AUC) value of 0.827, effectively evaluating analgesic levels.

2.1.3 Guiding intraoperative analgesic medication

Multiple studies have found that compared to empirical use of remifentanil, maintaining IOC2 between 30-50 by adjusting the target concentration of remifentanil significantly reduces its dosage ($P<0.01$), while ensuring more stable patient vital signs [14-16]. Wu *et al.* [17] found that IOC2 monitoring increased the frequency and average dose of intraoperative remifentanil adjustments (P=0.003), but significantly reduced the incidence of intraoperative adverse events, consistent with the findings of Wei *et al.* [18] in their study on laparoscopic ovarian cystectomy. Currently, there is no definitive conclusion on whether IOC2 can reduce the perioperative dosage of medication A, requiring further research with expanded sample sizes.

2.1.4 Mitigating significant intraoperative stress hormone and blood glucose fluctuations

Surgery and anesthesia activate the patient's stress response system, leading to fluctuations in hormones (cortisol, prolactin, etc.) and interleukins (IL), causing metabolic disorders, increased postoperative infection rates, and even cardiovascular and cerebrovascular damage. Zhao *et al.* [19] found that maintaining IOC2 at 35-45 was optimal for analgesic depth during laparoscopic colorectal surgery, and controlling IOC2 at higher levels within the range of 30-50 could alleviate anesthesia-induced endocrine suppression (P=0.009), promoting anesthesia recovery. Besides, IOC2-guided perioperative medication significantly reduced blood glucose fluctuations (P=0.001) [17]. IOC2 monitoring technology effectively alleviates target organ damage caused by insulin resistance or hyperinsulinemia, demonstrating its clinical utility.

2.1.5 Reducing postoperative complications and accelerate patient recovery

Opioids, as the core of perioperative analgesics, are the cornerstone of stress response inhibition and effective postoperative analgesia, but their various adverse reactions should not be underestimated. How to prevent or alleviate adverse reactions caused by opioid drugs is a hot topic of concern for clinical doctors and also one of the concepts of enhanced recovery after surgery (ERAS). Multiple studies have reported that IOC2 guided perioperative analgesic medication could accelerate postoperative gastrointestinal function recovery, reduce the incidence of intestinal dysfunction, significantly reduce postoperative nausea and vomiting (PONV), effectively alleviate postoperative organ pain, and improve patient comfort [18-20]. Feng *et al.* [21] optimized pain management based on IOC2 in anterior cervical decompression and fusion surgery, shortening the time for the patient's first anal exhaust and first meal after surgery, and also verifying the effectiveness of IOC2 in perioperative stress management. Huang *et al.* [22] used the QoR-15 scale in cerebral microvascular decompression surgery to evaluate patients' physiological comfort, emotional state, psychological support, pain perception, and physiological independence. They found that the IOC2 group had a higher total QoR-15 score on postoperative day 3, indicating that IOC2 could alleviate patients' psychological stress and improve the quality of early recovery.

2.2 Application of Compound Anesthesia

Liu *et al.* [23] found in their study on adult combined anesthesia that, the IOC2 value significantly decreased after 5 minutes of sevoflurane inhalation, and there was a highly positive correlation between sevoflurane inhalation and IOC2 (P<0.01). Related studies have also confirmed the reliability of IOC2 in pediatric sevoflurane anesthesia [24], suggesting that the combination of sevoflurane and propofol could inhibit nociceptive stimuli better and effectively reduce intraoperative stress reactions. Pan *et al.* [25] applied IOC2 in partial hepatectomy and pointed out that general anesthesia combined with epidural block has better analgesic effect, further confirming the clinical advantages of multimodal analgesia; Wang *et al.* [26] used IOC2 continuous monitoring and digital recording of peripheral nerve block patients' analgesic levels during knee fracture surgery. By comparing the ratio of dexmedetomidine and midazolam reaching the IOC2 target threshold (IOC2<90) and evaluating their analgesic effects in real-time based on IOC2, new ideas were provided for the use of dexmedetomidine as an adjuvant analgesic during the perioperative period. In addition, IOC2 plays an important role in evaluating the analgesic effect of classical and modified ultrasound-guided thoracolumbar fascial plane (TLIP) block in posterior lumbar decompression and stabilization surgery [27]. IOC2 is applied to evaluate the analgesic effect in compound anesthesia, optimize multi-mode analgesic schemes, better meet the needs of surgical anesthesia, and increase the safety and controllability of anesthesia.

2.3 Application of Anesthesia in Special Surgery

Under low temperature conditions, due to the slow physiological metabolism of patients and the delayed action time of opioid drugs, it is more likely to lead to various adverse reactions. Liu *et al.* [28] reported in their research on coronary artery bypass grafting that due to the increased analgesic effect of low temperature, IOC2 was positively correlated with body temperature, effectively reflecting the intensity of analgesia and providing real-time guidance for the rational use of analgesic drugs. This has opened up a new perspective for monitoring analgesia in such special surgical anesthesia and brought important breakthroughs in pain management in high-risk hypothermia surgeries.

2.4 Application of Anesthesia in Outpatient and Daytime Surgery

Liu et al. [29] found in a painless gastroscopy study that the IOC2 value was negatively correlated with the dose of remifentanil, with a correlation coefficient of -0.297. By adjusting the drug dosage and controlling IOC2 within the range of 30-50, the patient's recovery time can be shortened and postoperative pain can be reduced. In studies involving multiple types of gynecological short surgeries (painless abortion, staged curettage, conization, etc.), Duan *et al.* [30] found that remifentanil at a dose of 0.4 μ g/kg and sufentanil at a dose of 0.12 μ g/kg could achieve sufficient analgesic effects in short surgeries, that is, both can maintain IOC2 values at 30-50 during surgery. But it is generally believed that the analgesic efficacy ratio of remifentanil and sufentanil is 1:10, which means that the equivalent dose of remifentanil is calculated to be 1.2 μg/kg, but the actual dose used is 0.4 ug/kg, which can achieve sufficient analgesic effect. IOC2 compares the analgesic efficacy of different analgesics, selects the more suitable analgesic, regulates the dosage of opioid drugs reasonably, reduces postoperative dizziness and PONV incidence, and benefits patients.

3 IOC2 and Other Pain Monitoring Technologies

Various pain monitoring methods have to some extent reflected the degree of nociception. However, due to their relatively late development and limited clinical application, there is currently a lack of corresponding "gold standard". Nevertheless, precise pain monitoring remains a pressing issue in clinical anesthesia. Here introduces some commonly used pain monitoring techniques in clinical anesthesia for reference in the application of clinical analgesia technology.

3.1 IOC2 and Analgesia Nociception Index (ANI)

Unlike IOC2 based on EEG signals, ANI evaluates sympathetic nervous system tension by analyzing real-time changes in heart rate variability (HRV) affecting respiratory sinus arrhythmia, to assess the level of nociceptive stimuli and analgesia during general anesthesia [31]. Studies by Sabourdin *et al.* [32] indicated that ANI wad more sensitive in reflecting pain stimuli compared to hemodynamic parameters. Additionally, ANI can predict postoperative pain levels [33]. However, ANI has limitations: its parameters only reflect lung expansion recorded by pulmonary stretch receptors [34]. When patients are intubated and in a state of apnea, there is no stimulation of pulmonary stretch receptors, rendering ANI values typically uninformative. Compared to IOC2, ANI is susceptible to various autonomic nervous tension and heart rate changes, such as arrhythmias or the use of vasoactive drugs affecting sympathetic nerves, which may affect the accuracy of pain assessment.

3.2 IOC2 and Skin Conductance (SC)

SC reflects the degree of perioperative nociceptive stimuli and analgesia levels by evaluating the activation of peripheral sympathetic nerves. SC measurement is straightforward and effectively reflects the extent of nociceptive stimuli during general anesthesia [1]. Moreover, multiple studies indicated that SC could serve as a sensitive pain monitoring tool in critically ill infants, children, and adults [35]. However, SC measurements exhibit high individual variability, requiring researchers to observe continuous changes in SC values within the same patient, rather than relying on a single value to assess pain levels. Additionally, as an index of sympathetic nervous tension, SC is more susceptible to environmental factors such as ambient temperature and skin humidity compared to IOC2.

3.3 IOC2 and Pupil Distance (PD)

PD is the result of the coordination between the sympathetic and parasympathetic nervous systems and can be used as a pain assessment indicator. There are research reports that PD can effectively evaluate the degree of postoperative pain in patients and reduce the incidence of chronic pain [36]. However, Ledowski *et al.* [37] found no correlation between IOC2 and postoperative acute pain. In addition, Guglielminotti *et al.* [38] found that changes in PD also could be used to evaluate the level of uterine contractions and pain relief in obstetric patients. But PD monitoring also has shortcomings. For example, unlike IOC2 which can continuously and dynamically monitor, PD is not easy to track changes in pain; Environmental lighting, eye diseases, and drugs that affect the autonomic nervous system can also interfere with PD, affecting the accuracy of assessment.

3.4 IOC2 and surgical plethysmography index (SPI)

SPI is a multivariate index obtained by collecting the amplitude and frequency of photoplethysmography pulses using a blood oxygen saturation probe, and combining the two to calculate them [39]. Struys *et al.* [40] reported a significant correlation between SPI values and remifentanil effect concentrations. One major advantage of SPI as an analgesic monitoring tool is that it is not affected by the concentration of propofol, which is different from the IOC2 calculated based on monitoring sedation IOC1. However, changes in patient position, volume, and the use of vasoactive drugs can affect the reliability of SPI monitoring [41], which still requires careful evaluation in clinical practice.

4 Limitations of IOC2

(1) When placing the electrode patch of IOC2, facial areas need to be cleaned of grease to enhance skin conductivity. This poses difficulties for patients with facial injuries or those undergoing head and facial surgeries. Additionally, electrical signals from devices like electrosurgical units during surgery may interfere with IOC2 signal acquisition [42], affecting the precision of pain assessment.

(2) The premise of IOC2 monitoring requires adequate sedation, and its values are derived based on IOC1. Therefore, IOC2 values are significantly influenced by IOC1, and both must be monitored concurrently. In the induction phase of anesthesia, as the dose of anesthetic increases, IOC1 decreases faster than IOC2, indicating a potential time delay in IOC2 reflecting changes in analgesic state [11].

(3) IOC2 is a pain monitoring index based on EEG signals. Factors such as muscle relaxants, vasoactive drugs affecting central excitation, age, and body temperature can influence EEG activity [43]. Additionally, diseases causing abnormal EEG activity such as epilepsy may also affect the accuracy of IOC2 values.

5 Summary and Outlook

IOC2 monitoring reflects the sensitivity of unconscious patients to nociceptive stimuli. It offers advantages such as non-invasiveness, real-time continuous monitoring, and quantification. It has significant application value in guiding endotracheal intubation, predicting hemodynamic changes, adjusting opioid doses rationally, optimizing multimodal analgesia regimens, reducing postoperative complications, and monitoring the effectiveness of perioperative analgesia in hypothermic surgery. It is particularly valuable for patients requiring individualized adjustment of anesthetic drug doses, such as infants, elderly, and critically ill patients. With the development of the concept of "precision anesthesia" and further clinical research, specific quantification monitoring indicators for analgesic levels have extremely important implications for personalized precision medicine. IOC2 holds great potential in perioperative pain management. Large sample sizes, diverse surgical types, various patient populations, and deeper mechanistic research are necessary in future clinical work and scientific experiments to further confirm the reliability and sensitivity of IOC2 and explore broader clinical applications.

Conflict of Interest None

References

[1] Xie YL, Chen SH, Yang JJ, et al. Progress in analgesia monitoring during general anesthesia[J]. Chin J Anesthesiol, 2022, 42(5): 629-636. **[In Chinese]**

[2] Kang JM, Fang CL, Li YJ, et al. Effects of qCON and qNOX-guided general anaesthesia management on patient opioid use and prognosis: a study protocol[J]. BMJ Open, 2023, 13(5): e069134.

[3] Yang YC, Shuai SC, Han J, et al. Sedative effect of low-dose remidazolam combined with propofol in elderly patients received gastrointestinal endoscopy[J]. Chin J Clin Res, 2023, 36(8): 1205-1209. **[In Chinese]**

[4] Santa Cruz Mercado LA, Liu R, Bharadwaj KM, et al. Association of

intraoperative opioid administration with postoperative pain and opioid use[J]. JAMA Surg, 2023, 158(8): 854-864.
[5] Chang P, Fabrizi L, Olhede S, et al. The development of nociceptive network activity in the somatosensory cortex of freely moving rat pups[J]. Cereb Cortex, 2016, 26(12): 4513-4523.
[6] Koyama S, LeBlanc BW, Smith KA, et al. An electroencephalography bioassay for preclinical testing of analgesic efficacy[J]. Sci Rep, 2018, 8(1): 16402.
[7] LeBlanc BW, Bowary PM, Chao YC, et al. Electroencephalographic signatures of pain and analgesia in rats[J]. Pain, 2016, 157(10): 2330-2340.
[8] García PS, Kreuzer M, Hight D, et al. Effects of noxious stimulation on the electroencephalogram during general anaesthesia: a narrative review and approach to analgesic titration[J]. Br J Anaesth, 2021, 126(2): 445-457.
[9] Birendra SB. The effect of sufentanil on the index of analgesic status (IoC2) change and hemodynamic responses after double-lumen endobronchial intubation[D]. Chongqing: Chongqing Medical University, 2017.
[10] Sheng K, Zhang Y, Hu XW, et al. The changes of IoC2 value during tracheal intubation induced with various dose of sufentanil[J]. Guangdong Med J, 2018, 39(16): 2519-2522. **[In Chinese]**
[11] Melia U, Gabarron E, Agustí M, et al. Comparison of the qCON and qNOX indices for the assessment of unconsciousness level and noxious stimulation response during surgery[J]. J Clin Monit Comput, 2017, 31(6): 1273-1281.
[12] Jensen EW, Valencia JF, López A, et al. Monitoring hypnotic effect and nociception with two EEG-derived indices, qCON and qNOX, during general anaesthesia[J]. Acta Anaesthesiol Scand, 2014, 58(8): 933-941.
[13] Li Z, Cao YT, Wang S, et al. Evaluation of index of consciousness on anesthesia depth in patients underwent laparoscopy in the Department of Gynecology[J]. J China Jpn Friendsh Hosp, 2022, 36(6): 323-326, 339. **[In Chinese]**
[14] Yuan BH, Liu XN. Application of the consciousness index (IoC1) combined with injury sensitive index (IoC2) in cesarean section under general anesthesia[J]. Basic Clin Med, 2021, 41(9): 1329-1332. **[In Chinese]**
[15] Wang N, Zhang ZN, Li X, et al. Application of closed-loop target controlled infusion (TCI)of propofol combined with pain and nociception index-guided remifentanil TCI in gynecological laparoscopic surgery[J]. J Shanxi Med Univ, 2016, 47(6): 574-577. **[In Chinese]**
[16] Ma YH, Du SH, Wu J, et al. Application of index of consciousness in elderly patients undergoing video-assisted thoracoscopic lobectomy[J]. J Clin Anesthesiol, 2023, 39(7): 683-687. **[In Chinese]**
[17] Wu GS, Zhang L, Wang XX, et al. Effects of indexes of consciousness (IoC1 and IoC2) monitoring on remifentanil dosage in modified radical mastectomy: a randomized trial[J]. Trials, 2016, 17: 167.
[18] Wei JJ, Xiao W, Kan MH, et al. The effect of intraoperative analgesia monitored by index of consciousness 2 on laparoscopic ovarian cyst exfoliation[J]. Int J Anesthesiol Resusc, 2022, 43(9): 933-939. **[In Chinese]**
[19] Zhao J, Kang ZM, Xie WQ, et al. Effects of depth of anesthesia monitored by IoC on patients undergoing laparoscopic radical resection of colorectal cancer[J]. Mol Ther Methods Clin Dev, 2020, 18: 304-311.
[20] Wang YL. Effect of opioid-free anesthesia on intestinal function in patients undergoing laparoscopic cholecystectomy[D].Chengde: Chengde Medical College, 2021. **[In Chinese]**
[21] Feng S, Yang SY, Wang TL, et al. Effects of index of consciousness 1 and index of consciousness 2 monitoring on postoperative recovery of gastrointestinal function in patients undergoing anterior cervical decompression and fusion[J]. Beijing Med J, 2022, 44(2): 132-135. **[In Chinese]**
[22] Huang M, Li J, Yang CW. Effect of index of consciousness monitoring on early recovery quality in patients after cerebral microvascular decompression[J]. J Clin Anesthesiol, 2020, 36(6): 555-558. **[In Chinese]**
[23] Liu HX, Song ZW, Ma T, et al. The effect of sevoflurane on non-invasive nociceptive index qNOX and sedation index qCON during lobectomy[J]. Beijing Med J, 2019, 41(8): 660-663. **[In Chinese]**
[24] Li Q. The Clinical Research of Index of Consciousness to Monitor the Depth of Anesthesia[D]. Jinan: Shandong University, 2014. **[In Chinese]**
[25] Pan Y, Liao QW, Ge SJ. Clinical value of qCON and qNOX monitoring for anesthesia in partial hepatectomy[J]. Chin J Clin Med, 2019, 26(3): 494-498.
[26] Wang XH, Zhang SY, Wang CX, et al. Real-time evaluation of the independent analgesic efficacy of dexmedetomidine[J]. BMC Anesthesiol, 2023, 23(1): 68.
[27] Tantri AR, Sukmono RB, Lumban Tobing SDA, et al. Comparing the effect of classical and modified thoracolumbar interfascial plane block on postoperative pain and IL-6 level in posterior lumbar decompression and stabilization surgery[J]. Anesth Pain Med, 2022, 12(2): e122174.
[28] Liu B, Nie CR, Tian ZL, et al. Clinical evaluation of IOC2 analgesia monitoring under hypothermic cardiopulmonary bypass during coronary artery bypass grafting[J]. Beijing Med J, 2018, 40(6): 517-519. **[In Chinese]**
[29] Liu MQ, Wu HY, Yang DL, et al. Effects of small-dose remifentanil combined with index of consciousness monitoring on gastroscopic polypectomy: a prospective, randomized, single-blinded trial[J]. Trials, 2018, 19(1): 392.
[30] Duan Y, Zhang H, Gao CR, et al. Comparison of propofol combined with remifentanil or sufentanil in gynecological short surgery under the guidance of index of consciousness[J]. J Clin Anesthesiol, 2019, 35(12): 1189-1192. **[In Chinese]**
[31] Kim MK, Choi GJ, Oh KS, et al. Pain assessment using the analgesia nociception index (ANI) in patients undergoing general anesthesia: a systematic review and meta-analysis[J]. J Pers Med, 2023, 13(10): 1461.
[32] Sabourdin N, Constant I. Monitoring of analgesia level during general anesthesia in children[J]. Curr Opin Anaesthesiol, 2022, 35(3): 367-373.
[33] Boselli E, Bouvet L, Bégou G, et al. Prediction of immediate postoperative pain using the analgesia/nociception index: a prospective observational study[J]. Br J Anaesth, 2014, 112(4): 715-721.
[34] Jeanne M, Logier R, De Jonckheere J, et al. Heart rate variability during total intravenous anesthesia: effects of nociception and analgesia[J]. Auton Neurosci, 2009, 147(1/2): 91-96.
[35] Hu JL, Harrold J, Squires JE, et al. The validity of skin conductance for assessing acute pain in mechanically ventilated infants: a cross-sectional observational study[J]. Eur J Pain, 2021, 25(9): 1994-2006.
[36] Sabourdin N, Barrois J, Louvet N, et al. Pupillometry-guided intraoperative remifentanil administration versus standard practice influences opioid use: a randomized study[J]. Anesthesiology, 2017, 127(2): 284-292.
[37] Ledowski T, Schmitz-Rode I. Predicting acute postoperative pain by the Qnox score at the end of surgery: a prospective observational study[J]. Br J Anaesth, 2020, 124(2): 222-226.
[38] Guglielminotti J, Mentré F, Gaillard J, et al. Assessment of pain during labor with pupillometry: a prospective observational study[J]. Anesth Analg, 2013, 116(5): 1057-1062.
[39] Huang M, Li J. Advances in the clinical application of surgical pleth index in general anesthesia[J]. Int J Anesthesiol Resusc, 2021, 42(5): 501-504. **[In Chinese]**
[40] Struys MMRF, Vanpeteghem C, Huiku M, et al. Changes in a surgical stress index in response to standardized pain stimuli during propofol-remifentanil infusion[J]. Br J Anaesth, 2007, 99(3): 359-367.
[41] Kim JH, Jwa EK, Choung Y, et al. Comparison of pupillometry with surgical pleth index monitoring on perioperative opioid consumption and nociception during propofol-remifentanil anesthesia: a prospective randomized controlled trial[J]. Anesth Analg, 2020, 131(5): 1589-1598.
[42] Fan SW, Luo YJ, Xue S, et al. Clinical research progress on anesthesia depth monitoring based on index of consciousness[J]. Int J Anesthesiol Resusc, 2021, 42(11): 1208-1212. **[In Chinese]**
[43] Lichtenfeld F, Kratzer S, Hinzmann D, et al. The influence of electromyographic on electroencephalogram-based monitoring: putting the forearm on the forehead[J]. Anesth Analg, 2024, 138(6): 1285-1294.

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· 研究进展 ·

伤害敏感指数在疼痛管理中的研究进展

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摘要： 有效的围手术期疼痛管理对于加速患者康复和减少不良事件的发生至关重要，而敏感且可靠的疼痛监测在其中起到了不可或缺的作用。基于脑电图信号衍生的意识指数(index of consciousness，IoC)是一种新兴的麻醉深度监测指标，已经逐步应用于全身麻醉过程中。伤害敏感指数(IoC2)用于镇痛程度的监测，也可作为多种手术类型中的疼痛管理的监测指标评价镇痛效果，指导合理使用镇痛药物，减少围术期相关不良事件，在临床上具有良好的优势及应用前景。本文旨在综述 IoC2 的基本原理、临床研究现状以及优劣势等方面，并与其他镇痛监测作比较，为 IoC2 的临床应用提供可靠的依据。

关键词： 伤害敏感指数；麻醉；镇痛监测；疼痛管理

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Research progress on the index of consciousness 2 in pain management

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Keywords: Index of consciousness2; Anesthesia; Analgesic monitoring; Pain management

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疼痛被定义为一种“与实际或潜在的组织损伤相关的不愉快的情感体验”，包括患者在意识状态下对疼痛的主观感受及意识消失时对伤害性刺激的客观反应[1]。目前全身麻醉可通过脑电双频指数(bis pectral index，BIS)、脑电熵指数(entroy)、Narcortrend 指数等指标监测麻醉深度，但这些技术主要监测镇静深度变化，对镇痛程度的反映并不敏感[2-3]。全身麻醉期间镇痛不足可导致患者强烈的自主神经反应，甚至发生心脑血管意外；镇痛过度可导致苏醒延迟、呼吸抑制甚至损害免疫系统等严重后果[4]。长期以来麻醉医师主要依据心率、血压等生命体征变化经验性地评估镇痛效果，但由于个体之间存在疼痛敏感性差异，其精确性远远不够。因此，术中进行有效精确的镇痛监测是目前临床麻醉工作中亟待解决的问题。近年来，一项新的疼痛评估指标——伤害敏感指数(index of consciousness 2，IoC2)开始备受关注。IoC2 将镇痛效果以数字化的形式呈现，用于客观评价全身麻醉患者的疼痛情况，从而优化镇痛药物用量，改善患者预后，在疼痛管理中展现出显著的效果。本综述旨在总结近年来有关 IoC2 的临床应用研究进展，并比较了临床监测镇痛的其他技术，为临床实践提供参考。

1　IoC2 概念及计算原理

IoC2 是评价伤害性刺激/抗伤害性刺激的指标，由脑电图

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(electroencephalogram, EEG)信号衍生而来。IoC2 通过使用自适应神经模糊推理系统和非线性分析计算,采集脑电频率范围为 0.5~42 Hz 的 EEG 信号,将其线性成分和非线性成分分离,以减少肌电活动的干扰,再通过符号动力学法,将 EEG 信号分为若干分区,且每个分区用一个符号作为标记,将时间序列转化成符号序列,并结合爆发抑制比等参数识别差异功能后进行模糊推理,通过判别函数组合计算得出意识指数(index of consciousness 1, IoC1)。既往研究表示伤害性刺激可以引起 θ 波活动[5];且多项小鼠实验表明,随着小鼠年龄的增长,θ 波逐渐成为 EEG 中的主导波形,并且疼痛刺激诱发的 θ 波振幅增加,给予镇痛药物后,θ 波增强现象受抑制[6-7],提示 θ 波振幅与疼痛程度之间存在良好的正相关。此外,在阿片类药物不足的情况下,会导致 δ 波唤醒,即 δ 波段功率增加 0.5~4 Hz 也与伤害性刺激有关[8]。IoC2 通过监测 θ 和 δ 频段上的波幅,结合一阶分差、波的形态、谐波进行区分后结合 IoC1 的结果进行二次计算,得出最终数值。

目前常用的监测仪器有威浩康 Angel-6000D 脑电麻醉深度监护仪及 Quantium Medical qCON2000 监护仪。IoC2 测试范围为 0~99,在 30~50 范围内表示处于适合的全身麻醉状态,IoC2 数值在 50~99 时提示术中镇痛效果不佳,在 0~30 时则提示镇痛过度。

2　IoC2 的临床应用

2.1　全凭静脉麻醉中的应用

2.1.1　指导气管插管　镇痛药物起效和达到峰值的时间存在个体差异,镇痛药还没有充分起效时进行气管插管会出现强烈应激反应。Birendra[9]研究利用 IoC2 数值指导气管插管操作,发现相比于 0.5 μg/kg 舒芬太尼,给予 0.6~0.7 μg/kg 舒芬太尼时行双腔支气管插管更有效地控制插管所造成的应激。而盛奎等[10]结果提示,静注 0.4 μg/kg 舒芬太尼可以维持 IoC2 值在 42±8,有效抑制插管反应。这两项试验表明,不同剂量的阿片类药物应对插管引起的伤害性刺激可能存在一定差异。这种差异可能是因为双腔支气管导管较单腔气管导管插管对患者而言具有更大的刺激性,需要更多的镇痛药平衡伤害/抗伤害性刺激反应。除气管导管外,Melia 等[11]提出 IoC2 对于声门上气道装置也有较好的预测价值。

2.1.2　预防术中体动　手术中疼痛刺激会导致患者体动,不仅影响手术医生操作,还会诱发不良事件。Jensen 等[12]指出在麻醉深度相同的情况下,IoC2 能够预测患者是否会对伤害性刺激产生体动;李昭等[13]研究提示,当伤害性刺激发生时,IoC2 预测体动的受试者工作特征(receiver operating characteristic, ROC)曲线下面积(area under curve, AUC)为 0.827,,能较准确地评价镇痛水平。

2.1.3　指导术中镇痛用药　多项研究发现,相较于经验性应用瑞芬太尼,通过调节瑞芬太尼靶浓度维持 IoC2 在 30~50 之间,可显著减少瑞芬太尼用量($P<0.01$),同时患者生命体征更加平稳[14-16]。Wu 等[17]研究认为,IoC2 监测增加了术中瑞芬太尼调整次数和平均剂量($P=0.003$),但术中不良事件发生率明显降低,这与魏晶晶等[18]在腹腔镜下卵巢囊肿剥除术的研究中所得结果一致。目前关于 IoC2 是否能减少围术期阿片类药物使用剂量尚未得出明确的定论,需要扩大样本量继续研究。

2.1.4　缓解术中应激激素及血糖大幅波动　手术及麻醉会激活患者体内应激反应系统,并引起相关激素(皮质醇、催乳素等)和白细胞介素(IL)水平的波动,导致代谢紊乱,术后感染率增高,甚至心脑血管损伤等一系列并发症。Zhao 等[19]研究发现,IoC2 在 35~45 是最合适腹腔镜结直肠手术的镇痛深度。将 IoC2 控制 30~50 范围内的较高水平,可以减轻麻醉对于内分泌的抑制($P=0.009$),有利于麻醉恢复;此外,IoC2 监测指导围术期用药还可明显降低血糖波动($P=0.001$)[17]。IoC2 监测技术有效减轻胰岛素抵抗或高胰岛素血症造成的靶器官受损,体现其临床应用价值。

2.1.5　减少术后并发症,加速患者康复　阿片类药物作为围术期镇痛药物的核心,是抑制应激反应和有效术后镇痛的基石,但其带来的各种不良反应不容小觑。如何预防或减轻阿片类药物导致的不良反应是临床医生关注的热点,也是快速康复外科(ERAS)理念之一。多项研究报道称,IoC2 指导围术期镇痛用药,可加快术后胃肠功能恢复速度、降低肠功能障碍的发生率,还可明显减轻术后恶心呕吐(PONV),有效缓解术后脏器疼痛,提高患者舒适度[18-20]。冯帅等[21]在颈椎前路减压融合术中根据 IoC2 优化疼痛管理,缩短了患者术后首次肛门排气及首次进食时间,也验证了 IoC2 在围术期抗应激管理的有效性。黄媚等[22]在脑部微血管减压手术中使用 QoR-15 量表来评价患者生理舒适度、情感状态、心理支持、疼痛感觉以及生理独立性,发现 IoC2 组患者术后 3 d 的 QoR-15 总评分更高,即 IoC2 可缓解患者术后的心理应激,提高了早期恢复质量。

2.2　复合麻醉中的应用

刘海霞等[23]在成人静吸复合麻醉的研究中发现,七氟醚吸入 5 min 后 IoC2 数值显著降低,二者之间存在高度正相关性($P<0.01$);小儿七氟醚麻醉中也有相关研究证实 IoC2 的可靠性[24],这提示七氟醚联合异丙酚可以更好抑制伤害性刺激,有效减轻术中应激反应。潘艳等[25]在肝部分切除术中应用 IoC2,指出全麻复合硬膜外阻滞具有更佳的镇痛效果,进一步确证了多模式镇痛的临床优势;Wang 等[26]在膝关节骨折手术中采用 IoC2 连续监测并数字化记录外周神经阻滞患者镇痛水平,通过比较右美托咪定与咪达唑仑达到 IoC2 目标阈值(IoC2<90)的比率,并根据 IoC2 实时评价二者镇痛效果,为右美托咪定围术期辅助镇痛用药提供新思路。此外,IoC2 在后路腰椎减压稳定术中评估经典和改良的超声引导下胸腰筋膜平面阻滞(TLIP)的镇痛效果中也起到了重要作用[27]。IoC2 应用于复合麻醉中评价镇痛效果,优化多模式镇痛方案,更好地满足了手术麻醉需求,增加了麻醉的安全性及可控性。

2.3　特殊手术麻醉中的应用

低温情况下由于患者生理代谢减慢,阿片类药物作用时间延缓,更容易导致各种不良反应。刘贝等[28]在冠状动脉旁路移植术的研究中报道,由于低

温能够增加镇痛效果,IoC2 与体温成正相关,有效反映了镇痛强度,实时指导镇痛药物合理使用,为此类特殊手术麻醉的镇痛监测开创了全新的视角,也为高危低体温手术中疼痛管理带来重要的突破。

2.4　门诊及日间手术麻醉中的应用　Liu 等[29]在无痛胃肠镜研究中发现,IoC2 数值与瑞芬太尼剂量呈负相关,其相关系数为-0.297。通过调节药物剂量,控制 IoC2 在 30~50 范围内,可以缩短患者苏醒时间并减轻术后疼痛;在涉及多类妇科短小手术(无痛人流术、分段诊刮、锥切术等)的研究中,段怡等[30]发现剂量为 0.4 μg/kg 的瑞芬太尼与 0.12 μg/kg 的舒芬太尼在短小手术中均可以达到足够的镇痛效果,二者术中均能使 IoC2 值维持在 30~50。但通常认为,瑞芬太尼和舒芬太尼的镇痛效能比为 1 ∶ 10,即测算瑞芬太尼等效剂量为 1.2 μg/kg,但实际使用剂量为 0.4 μg/kg 即可达到足够镇痛效果。IoC2 通过比较不同镇痛药物的镇痛效能,选用更合适的镇痛药物,合理调控阿片类药物用量,减轻术后眩晕感及 PONV 发生率,使得患者受益。

3　IoC2 与其他镇痛监测技术

多种镇痛监测手段均在一定程度上反映伤害性感受的程度,但由于起步较晚且未在临床广泛应用,目前仍缺乏相应的“金标准”。然而,精准的镇痛监测是临床麻醉中亟待解决的问题,下面介绍一些临床麻醉中较为多见的镇痛监测,为临床镇痛技术的应用提供参考。

3.1　IoC2 与镇痛伤害感受指数(ANI)　与基于 EEG 信号的 IoC2 不同,ANI 通过实时分析心率变异性(heart rate variability, HRV)刺激对呼吸性窦性心律的影响,得出副交感神经张力的指标值,来评估全身麻醉期间伤害性刺激及镇痛水平[31]。Sabourdin 等[32]研究指出,在反映疼痛刺激方面,ANI 比血流动力学参数敏感度更高;除此之外,ANI 还可用于预测术后疼痛程度[33]。但 ANI 也存在一定局限性,其参数仅能反映肺部的牵张感受器记录到的肺膨胀情况[34]。当气管插管时患者处于无通气无呼吸状态,肺部牵张感受器刺激消失,此时 ANI 数值通常无参考价值。相比 IoC2,ANI 易受到各种自主神经张力及心率变化的影响,如心律失常、使用各种影响副交感神经的血管活性药物等情况下,ANI 评估镇痛效果的精确性还有待进一步考量。

3.2　IoC2 与皮肤电导(SC)　SC 是通过评价外周交感神经的激活程度来反映围术期伤害性刺激及镇痛水平的指标。SC 操作简单,可以有效反映患者全麻期间伤害性刺激的程度[1]。此外,多项研究表明,SC 在危重婴幼儿及成人中也可作为敏感的疼痛监测工具[35]。但 SC 测量值具有高度个体化差异,研究者需要观察同一患者的连续 SC 值变化,而不仅仅是凭借单一数值来评估患者疼痛程度。此外,由于 SC 是交感神经张力指标,较 IoC2 而言,更容易受到环境温度、皮肤湿度等影响。

3.3　IoC2 与瞳孔直径(pupil distance, PD)　PD 是交感神经和副交感神经相互协调的结果,可作为疼痛评估指标。有研究报道,PD 可有效评估患者术后疼痛程度并减少慢性疼痛发生率[36]。而 Ledowski 等[37]研究发现,IoC2 与术后急性疼痛无相关性。此外,Guglielminotti 等[38]研究指出,PD 变化还可用于评估产科患者宫缩痛水平以及镇痛情况。但 PD 监测也存在缺陷。比如,与 IoC2 可连续动态监测,PD 不易跟踪疼痛变化;环境光线、眼部疾病、影响自主神经的药物等也会对 PD 造成干扰,影响评估精确性。

3.4　IoC2 与手术体积描记指数(SPI)　SPI 是基于血氧饱和度探头采集光电容积脉搏波幅及脉冲频率,并将二者结合运算后得出的多元指数[39]。Struys 等[40]研究报道,SPI 值与瑞芬太尼效应浓度存在显著的相关性。SPI 作为镇痛监测的一大优势在于其不受丙泊酚效应浓度的影响,这与基于监测镇静的 IoC1 计算得出的 IoC2 不同。但患者体位改变、容量变化和血管活性药物的使用会影响 SPI 监测的可靠性[41],在临床工作中仍需谨慎评估。

4　IoC2 的局限性

(1)在贴置电极片时,需要将面部粘贴部位进行油脂清洗,以增加皮肤导电性能。对于面部外伤以及头面部手术患者而言,存在一定困难。此外,术中电刀等设备产生的电信号可能会干扰 IoC2 信号采集[42],影响疼痛评估的精确性。(2)IoC2监测的前提是充分镇静,其数值是在 IoC1 的基础上计算获得,因此 IoC2 数值受 IoC1 的影响较大,且两者必须同时监测,不能通过单一的 IoC2 来进行术中疼痛管理。在麻醉诱导过程中,随着麻醉药物剂量的增加,IoC1 值下降的速度比 IoC2 更快,即 IoC2 反映镇痛状态改变时可能会有一定的时间延迟[11]。(3)IoC2 是基于 EEG 信号的疼痛监测指标,而肌肉松弛剂、兴奋中枢的血管活性药物、年龄、体温等均是影响脑电活动的相关因素[43]。此外,癫痫等引发异常脑电活动的疾病也可能会在某种程度上影响 IoC2 数值的准确性。

5　总结和展望

IoC2 监测可反映患者无意识生理状态下的伤害刺激敏感程度,具有无创、实时、连续、量化等优势,在指导气管插管、预测血流动力学变化、合理调整阿片类药物用量、优化多模式镇痛方案、减少术后不良事件、监测低温手术镇痛效果等方面都有很好的应用价值。尤其是对于幼儿、老年人、危重症等特别需要个体化调整麻醉药物剂量的患者,其价值更为重要。随着“精准麻醉”观念的发展和临床研究的深入,特异性镇痛程度量化监测指标对个体化精准医疗有极其重要的意义,IoC2 在围术期疼痛管理方面具有很大的应用潜力。在日后的临床工作与科学试验中,需要大样本量、多类型手术、多种类患者以及更深层次的研究(包括机制等方面)来继续证实 IoC2 的可靠及敏感性,并开辟更广阔的临床应用前景。

利益冲突　无

参考文献

[1]　谢艳乐,陈书涵,杨建军,等.全身麻醉期间镇痛监测的研究进展

[J].中华麻醉学杂志,2022,42(5):629-636.
Xie YL, Chen SH, Yang JJ, et al. Progress in analgesia monitoring during general anesthesia[J]. Chin J Anesthesiol, 2022, 42(5): 629-636.
[2] Kang JM, Fang CL, Li YJ, et al. Effects of qCON and qNOX-guided general anaesthesia management on patient opioid use and prognosis: a study protocol [J]. BMJ Open, 2023, 13 (5): e069134.
[3] 杨亚崇,帅世超,韩静,等.小剂量瑞马唑仑复合丙泊酚在老年患者胃肠镜诊疗中的镇静效果[J].中国临床研究,2023,36(8): 1205-1209.
Yang YC, Shuai SC, Han J, et al. Sedative effect of low-dose remidazolam combined with propofol in elderly patients received gastrointestinal endoscopy[J]. Chin J Clin Res, 2023, 36(8): 1205-1209.
[4] Santa Cruz Mercado LA, Liu R, Bharadwaj KM, et al. Association of intraoperative opioid administration with postoperative pain and opioid use[J]. JAMA Surg, 2023, 158(8): 854-864.
[5] Chang P, Fabrizi L, Olhede S, et al. The development of nociceptive network activity in the somatosensory cortex of freely moving rat pups[J]. Cereb Cortex, 2016, 26(12): 4513-4523.
[6] Koyama S, LeBlanc BW, Smith KA, et al. An electroencephalography bioassay for preclinical testing of analgesic efficacy[J]. Sci Rep, 2018, 8(1): 16402.
[7] LeBlanc BW, Bowary PM, Chao YC, et al. Electroencephalographic signatures of pain and analgesia in rats[J]. Pain, 2016, 157(10): 2330-2340.
[8] García PS, Kreuzer M, Hight D, et al. Effects of noxious stimulation on the electroencephalogram during general anaesthesia: a narrative review and approach to analgesic titration[J]. Br J Anaesth, 2021, 126(2): 445-457.
[9] Birendra SB. The effect of sufentanil on the index of analgesic status (IoC2) change and hemodynamic responses after double-lumen endobronchial intubation[D]. 重庆:重庆医科大学, 2017.
[10] 盛奎,张野,胡宪文,等.意识指数 2 在不同剂量舒芬太尼气管插管时的数值变化[J].广东医学,2018,39(16):2519-2522.
Sheng K, Zhang Y, Hu XW, et al. The changes of IoC2 value during tracheal intubation induced with various dose of sufentanil[J]. Guangdong Med J, 2018, 39(16): 2519-2522.
[11] Melia U, Gabarron E, Agustí M, et al. Comparison of the qCON and qNOX indices for the assessment of unconsciousness level and noxious stimulation response during surgery[J]. J Clin Monit Comput, 2017, 31(6): 1273-1281.
[12] Jensen EW, Valencia JF, López A, et al. Monitoring hypnotic effect and nociception with two EEG-derived indices, qCON and qNOX, during general anaesthesia[J]. Acta Anaesthesiol Scand, 2014, 58 (8): 933-941.
[13] 李昭,曹妍婷,王思,等.意识指数对妇科腹腔镜患者麻醉深度监测效果的评价[J].中日友好医院学报,2022,36(6):323-326,339.
Li Z, Cao YT, Wang S, et al. Evaluation of index of consciousness on anesthesia depth in patients underwent laparoscopy in the Department of Gynecology[J]. J China Jpn Friendsh Hosp, 2022, 36(6): 323-326, 339.
[14] 袁保红,刘小男.意识指数(IoC1)联合伤害敏感指数(IoC2)监测在全麻剖宫产中的应用效果[J].基础医学与临床,2021,41 (9):1329-1332.
Yuan BH, Liu XN. Application of the consciousness index (IoC1) combined with injury sensitive index (IoC2) in cesarean section under general anesthesia [J]. Basic Clin Med, 2021, 41 (9): 1329-1332.
[15] 王宁,张珍妮,李雪,等.丙泊酚闭环靶控输注联合伤害敏感指数指导下的瑞芬太尼靶控输注在妇科腹腔镜手术中的应用[J].山西医科大学学报,2016,47(6):574-577.
Wang N, Zhang ZN, Li X, et al. Application of closed-loop target controlled infusion(TCI) of propofol combined with pain and nociception index-guided remifentanil TCI in gynecological laparoscopic surgery[J]. J Shanxi Med Univ, 2016, 47(6): 574-577.
[16] 马艳辉,杜淑卉,吴洁,等.意识指数在老年患者胸腔镜肺叶切除术中的应用[J].临床麻醉学杂志,2023,39(7):683-687.
Ma YH, Du SH, Wu J, et al. Application of index of consciousness in elderly patients undergoing video-assisted thoracoscopic lobectomy [J]. J Clin Anesthesiol, 2023, 39(7): 683-687.
[17] Wu GS, Zhang L, Wang XX, et al. Effects of indexes of consciousness (IoC1 and IoC2) monitoring on remifentanil dosage in modified radical mastectomy: a randomized trial[J]. Trials, 2016, 17: 167.
[18] 魏晶晶,肖玮,阚敏慧,等.意识指数 2 指导下术中镇痛对腹腔镜卵巢囊肿剥除术的影响[J].国际麻醉学与复苏杂志,2022,43 (9):933-939.
Wei JJ, Xiao W, Kan MH, et al. The effect of intraoperative analgesia monitored by index of consciousness 2 on laparoscopic ovarian cyst exfoliation [J]. Int J Anesthesiol Resusc, 2022, 43 (9): 933-939.
[19] Zhao J, Kang ZM, Xie WQ, et al. Effects of depth of anesthesia monitored by IoC on patients undergoing laparoscopic radical resection of colorectal cancer [J]. Mol Ther Methods Clin Dev, 2020, 18: 304-311.
[20] 王亚丽.无阿片药物麻醉对腹腔镜胆囊切除术患者肠功能的影响[D].承德:承德医学院,2021.
Wang YL. Effect of opioid-free anesthesia on intestinal function in patients undergoing laparoscopic cholecystectomy [D]. Chengde: Chengde Medical College, 2021.
[21] 冯帅,杨舒怡,王天龙,等.意识指数与伤害敏感指数监测对颈椎前路减压融合术患者术后胃肠道功能的影响[J].北京医学,2022,44(2):132-135.
Feng S, Yang SY, Wang TL, et al. Effects of index of consciousness 1 and index of consciousness 2 monitoring on postoperative recovery of gastrointestinal function in patients undergoing anterior cervical decompression and fusion [J]. Beijing Med J, 2022, 44 (2): 132-135.
[22] 黄媚,李娟,杨成伟.意识指数监测对脑微血管减压术患者术后早期恢复质量的影响[J].临床麻醉学杂志,2020,36(6): 555-558.
Huang M, Li J, Yang CW. Effect of index of consciousness monito-

ring on early recovery quality in patients after cerebral microvascular decompression[J]. J Clin Anesthesiol, 2020, 36(6): 555-558.

[23] 刘海霞,宋志伟,马挺,等.肺叶切除术中七氟醚对非侵入性伤害感受指数 qNOX 与镇静指数 qCON 的影响[J].北京医学,2019,41(8):660-663.
Liu HX, Song ZW, Ma T, et al. The effect of sevoflurane on non-invasive nociceptive index qNOX and sedation index qCON during lobectomy[J]. Beijing Med J, 2019, 41(8): 660-663.

[24] 李茜.意识指数用于麻醉深度监测的临床研究[D].济南:山东大学,2014.
Li. The Clinical research of index of consciousness to monitor the depth of anesthesia[D]. Jinan: Shandong University, 2014.

[25] 潘艳,廖庆武,葛圣金.qCON、qNOX 监测用于肝部分切除术麻醉管理的临床价值[J].中国临床医学,2019,26(3):494-498.
Pan Y, Liao QW, Ge SJ. Clinical value of qCON and qNOX monitoring for anesthesia in partial hepatectomy[J]. Chin J Clin Med, 2019, 26(3): 494-498.

[26] Wang XH, Zhang SY, Wang CX, et al. Real-time evaluation of the independent analgesic efficacy of dexmedetomidine[J]. BMC Anesthesiol, 2023, 23(1): 68.

[27] Tantri AR, Sukmono RB, Lumban Tobing SDA, et al. Comparing the effect of classical and modified thoracolumbar interfascial plane block on postoperative pain and IL-6 level in posterior lumbar decompression and stabilization surgery[J]. Anesth Pain Med, 2022, 12(2): e122174.

[28] 刘贝,聂超然,田肇隆,等.体外循环低温条件下冠状动脉旁路移植术中 IoC2 镇痛监测的临床应用评价[J].北京医学,2018,40(6):517-519.
Liu B, Nie CR, Tian ZL, et al. Clinical evaluation of IoC2 analgesia monitoring under hypothermic cardiopulmonary bypass during coronary artery bypass grafting[J]. Beijing Med J, 2018, 40(6): 517-519.

[29] Liu MQ, Wu HY, Yang DL, et al. Effects of small-dose remifentanil combined with index of consciousness monitoring on gastroscopic polypectomy: a prospective, randomized, single-blinded trial[J]. Trials, 2018, 19(1): 392.

[30] 段怡,张欢,高翠荣,等.意识指数监测下瑞芬太尼或舒芬太尼复合丙泊酚在妇科短小手术中的比较[J].临床麻醉学杂志,2019,35(12):1189-1192.
Duan Y, Zhang H, Gao CR, et al. Comparison of propofol combined with remifentanil or sufentanil in gynecological short surgery under the guidance of index of consciousness[J]. J Clin Anesthesiol, 2019, 35(12): 1189-1192.

[31] Kim MK, Choi GJ, Oh KS, et al. Pain assessment using the analgesia nociception index (ANI) in patients undergoing general anesthesia: a systematic review and meta-analysis[J]. J Pers Med, 2023, 13(10): 1461.

[32] Sabourdin N, Constant I. Monitoring of analgesia level during general anesthesia in children[J]. Curr Opin Anaesthesiol, 2022, 35(3): 367-373.

[33] Boselli E, Bouvet L, Bégou G, et al. Prediction of immediate postoperative pain using the analgesia/nociception index: a prospective observational study[J]. Br J Anaesth, 2014, 112(4): 715-721.

[34] Jeanne M, Logier R, De Jonckheere J, et al. Heart rate variability during total intravenous anesthesia: effects of nociception and analgesia[J]. Auton Neurosci, 2009, 147(1/2): 91-96.

[35] Hu JL, Harrold J, Squires JE, et al. The validity of skin conductance for assessing acute pain in mechanically ventilated infants: a cross-sectional observational study[J]. Eur J Pain, 2021, 25(9): 1994-2006.

[36] Sabourdin N, Barrois J, Louvet N, et al. Pupillometry-guided intraoperative remifentanil administration versus standard practice influences opioid use: a randomized study[J]. Anesthesiology, 2017, 127(2): 284-292.

[37] Ledowski T, Schmitz-Rode I. Predicting acute postoperative pain by the Qnox score at the end of surgery: a prospective observational study[J]. Br J Anaesth, 2020, 124(2): 222-226.

[38] Guglielminotti J, Mentré F, Gaillard J, et al. Assessment of pain during labor with pupillometry: a prospective observational study[J]. Anesth Analg, 2013, 116(5): 1057-1062.

[39] 黄媚,李娟.手术体积描记指数在全身麻醉手术中的临床应用研究进展[J].国际麻醉学与复苏杂志,2021,42(5):501-504.
Huang M, Li J. Advances in the clinical application of surgical pleth index in general anesthesia[J]. Int J Anesthesiol Resusc, 2021, 42(5): 501-504.

[40] Struys MMRF, Vanpeteghem C, Huiku M, et al. Changes in a surgical stress index in response to standardized pain stimuli during propofol-remifentanil infusion[J]. Br J Anaesth, 2007, 99(3): 359-367.

[41] Kim JH, Jwa EK, Choung Y, et al. Comparison of pupillometry with surgical pleth index monitoring on perioperative opioid consumption and nociception during propofol-remifentanil anesthesia: a prospective randomized controlled trial[J]. Anesth Analg, 2020, 131(5): 1589-1598.

[42] 范帅伟,罗玉军,薛杉,等.基于意识指数的麻醉深度监测临床研究进展[J].国际麻醉学与复苏杂志,2021,42(11):1208-1212.
Fan SW, Luo YJ, Xue S, et al. Clinical research progress on anesthesia depth monitoring based on index of consciousness[J]. Int J Anesthesiol Resusc, 2021, 42(11): 1208-1212.

[43] Lichtenfeld F, Kratzer S, Hinzmann D, et al. The influence of electromyographic on electroencephalogram-based monitoring: putting the forearm on the forehead[J]. Anesth Analg, 2024, 138(6): 1285-1294.

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