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Prospective observational study of the non-invasive assessment of immediate postoperative pain using the analgesia/nociception index (ANI)

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Editor's key points

- Objective measures of pain and analgesic efficacy are important in acute pain management.
- The analgesia/nociception index (ANI) is derived from heart rate variability (HRV).
- This study assessed whether the ANI was a useful surrogate postoperative pain measure.
- Changes in the ANI were related to changes in pain intensity.
- The ANI may have clinical utility in objectively assessing postoperative analgesia.

Background. The analgesia/nociception index (ANI), a 0–100 non-invasive index calculated from heart rate variability, reflects the analgesia/nociception balance during general anaesthesia. The aim of this study was to evaluate the ANI in the assessment of immediate postoperative pain in adult patients undergoing general anaesthesia.

Methods. Two-hundred patients undergoing scheduled surgery or endoscopy with general anaesthesia were included in this prospective observational study. Pain intensity was assessed using a 0–10 numerical rating scale (NRS) after arousal from general anaesthesia. Receiver-operating characteristic (ROC) curves were built to assess the performance of ANI to detect patients with NRS>3 and NRS≥7 on arrival in the postoperative care unit.

Results. A negative linear relationship was observed between ANI and NRS (ANI=−5.2×NRS+77.9, r^2=0.41, P<0.05). At the threshold of 57, the sensitivity and specificity of ANI to detect patients with NRS>3 were 78 and 80%, respectively, with a negative predictive value of 88%, corresponding to an area under the ROC curve (AUC) of 0.86. At the threshold of 48, the sensitivity and specificity of ANI to detect NRS≥7 were 92 and 82%, respectively, with a negative predictive value of 99%, corresponding to a ROC curve AUC of 0.91.

Conclusions. A measurement of ANI during the immediate postoperative period is significantly correlated with pain intensity. The measurement of ANI appears to be a simple and non-invasive method to assess immediate postoperative analgesia.

Keywords: analgesia/nociception index; assessment; pain; postoperative

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In a patient who is awake in the post-anaesthesia care unit (PACU), the presence of pain can be assessed using a 0–100 visual analogue scale (VAS), a 1–5 verbal rating scale (VRS), or a 0–10 numerical rating scale (NRS), although the standard method is still a topic of debate.[1–3] Analgesia or tolerable pain is usually defined as a VAS score of ≤30 mm or an NRS score of ≤3 and a VAS score of ≥70 mm or a NRS score of ≥7 should be considered indicative of severe pain.[1 4] However, some patient groups are at special risk for inadequate pain control and require additional analgesic considerations, including paediatric and geriatric patients, critically ill or cognitively impaired patients, or other patients who may have difficulty communicating.[5] Therefore, the objective assessment of postoperative analgesia would be valuable in the PACU setting to help optimize acute pain management.

It has been recently shown that pupillometer was an objective method to assess postoperative analgesia, with pupillary dilation reflex significantly correlated with VRS in PACU, helping titrating morphine in the immediate postoperative period.[6] The ANI, a 0–100 non-invasive index calculated from HRV, has also been recently proposed to reflect the analgesia/nociception balance during general anaesthesia.[7–10] However, to our knowledge, ANI has never been investigated for the evaluation of immediate postoperative pain. The aim of this study was to evaluate the clinical performance on ANI in the assessment of immediate postoperative analgesia in PACU in adult patients undergoing general anaesthesia.

Methods

Study design

This prospective observational study was approved by the Institutional Review Board (Comité de Protection des Personnes

Sud-Est III, study identifier CPP 2012–021 B, ClinicalTrials.gov identifier NCT01633320) and performed between June and July 2012 at Édouard Herriot Hospital, HCL, Lyon, France. The methodology followed the international guidelines for observational studies.[11]

After written informed consent was obtained, 200 ASA physical status I–II patients undergoing general anaesthesia were included. The procedures performed were ear, nose, and throat surgery or endoscopy and plastic surgery.

Exclusion criteria were age <18 yr or >75 yr old, arrhythmia, preoperative use of β-blockers, administration of anticholinergic drugs or neuromuscular block reversal in the 20 previous minutes, preoperative pain treated with opioids, psychiatric diseases, autonomic nervous system disorders, epilepsy, and inability to understand the verbal rating pain scale.

Anaesthetic technique

Premedication with oral alprazolam 0.1 mg kg^{-1} and hydroxyzine 1 mg kg^{-1} was administered 1 h before induction of anaesthesia. After arrival in the operating room, patients were monitored with a three-lead electrocardiogram (ECG), non-invasive arterial pressure measurement and pulse oxymetry. In order to provide excellent intubation conditions, the anaesthetic induction was performed using i.v. ketamine 0.1–0.5 mg kg^{-1}, i.v. propofol 2.5 mg kg^{-1}, and remifentanil 3–4 μg kg^{-1} as a 1 min bolus followed by a continuous infusion of 0.05–0.25 μg kg^{-1} min^{-1}.[12] After tracheal intubation, mechanical ventilation was initiated with a mixture of 60–70% O_2 and 30–40% air and adjusted to keep end-tidal CO_2 pressure between 30 and 35 mm Hg. Anaesthesia was maintained at the discretion of the anaesthesiologist with sevoflurane or desflurane adjusted to keep the minimal alveolar concentration between 0.8 and 1.2 or with propofol 6–10 mg kg^{-1} h^{-1} in continuous infusion. In case of endoscopic procedures without intubation, the anaesthetic induction was performed using i.v. propofol 1–2 mg kg^{-1} followed by a continuous infusion of 6–10 mg kg^{-1} h^{-1} and remifentanil 1 μg kg^{-1} as a 1 min bolus followed by a continuous infusion of 0.05–0.15 μg kg^{-1} min^{-1}.

The postoperative analgesia strategy was left to the discretion of the anaesthesiologist. Multimodal analgesia was provided using a combination of acetaminophen, ketoprofen, nefopam, tramadol, and morphine 0.1–0.2 mg kg^{-1} according to respective contraindications.[5] In some cases, regional analgesia techniques (peripheral nerve blocks or wound infiltration) were used. At the end of the procedure, remifentanil, propofol, and volatile agents were discontinued, and 100% O_2 was given with 10 litre min^{-1} fresh gas flow. Tracheal extubation was performed if necessary when the patient was alert, with a respiratory rate between 12 and 30 cycles min^{-1}, and a central core temperature >36°C, then the patient was sent to PACU.

Study protocol and ANI measurement

In the first 10 min after arrival in PACU, pain intensity was assessed by using a 0–10 NRS, with 0=no pain and 10=worst pain imaginable. All patients were educated about NRS before surgery. Patients experiencing NRS>3 received i.v. boluses of morphine 1–3 mg as titration at the discretion of the anaesthesiologist, with 5 min intervals between two injections, until pain returned to NRS of ≤3, which is the standard protocol in our unit.[13] Patients experiencing an initial NRS≤3 did not receive morphine titration. The use of non-opioid agents for multimodal postoperative analgesia during PACU stay was left to the discretion of the anaesthesiologist.

During NRS assessment, on arrival in PACU and at the end of PACU stay, ANI was recorded using the PhysioDoloris® monitor (MetroDoloris, Loos, France).[14] It is a non-invasive device that takes an ECG analogue output from the patient monitor and displays an average measurement of ANI made over the previous 120 s. The ANI computation is based on the integrative influence of the respiratory cycle on the RR interval derived from ECG. It allows a qualitative and quantitative measurement of HRV, primarily mediated by parasympathetic and sympathetic outflow from the central nervous system to the sinoatrial node.[14]

High-frequency (HF) fluctuations in HRV (0.15–0.5 Hz) are mediated predominantly by changes in parasympathetic outflow, while low-frequency (LF) changes are mediated by both parasympathetic and sympathetic activities. In case of prominent parasympathetic tone, each inspiration causes a brief increase in heart rate (HR) and decrease in the RRHF period (corresponding to the respiratory sinus arrhythmia), with the filtered RR analysis giving large variability.[9 10] On the contrary, if parasympathetic tone decreases, HR increases and the effect of respiration on the RR period interval can be used to assess sympathetic tone, and thus the analgesia-nociception balance.[9 10]

The ANI monitor uses mathematical analysis which permits differentiation of sympathetic and parasympathetic effects.[15] Local minima and maxima in the normalized RRHF series are automatically detected and the areas A1, A2, A3, and A4 are measured as the areas between the lower and upper envelopes in each 16 s subwindow (Fig. 1).[7 14] The AUC_{min} is defined as the sum of the minimum four sub-areas: AUC_{min}=min (A1, A2, A3, and A4). The ANI is then computed in order to express a fraction of the total window surface, leading to a measure between 0 and 100: $ANI=100\times(\alpha\times AUC_{min}+\beta)/12.8$, where $\alpha=5.1$ and $\beta=1.2$ have been determined in order to keep the coherence between the visual effect of respiratory influence on RR series and the quantitative measurement of ANI.[7 14] Continuous measurement of ANI can be performed by moving the 64 s window after each calculation.[7 14] In practice, a 4 s moving period gives an acceptable trend curve of the parameters values.[14]

Statistical analysis

The statistical analysis was performed using Medcalc® version 12.1.4.0 (MedCalc Software, Mariakerke, Belgium). For the comparison between patients with NRS≤3 and NRS>3, Student *t*, Mann-Whitney *U* and χ^2 tests were

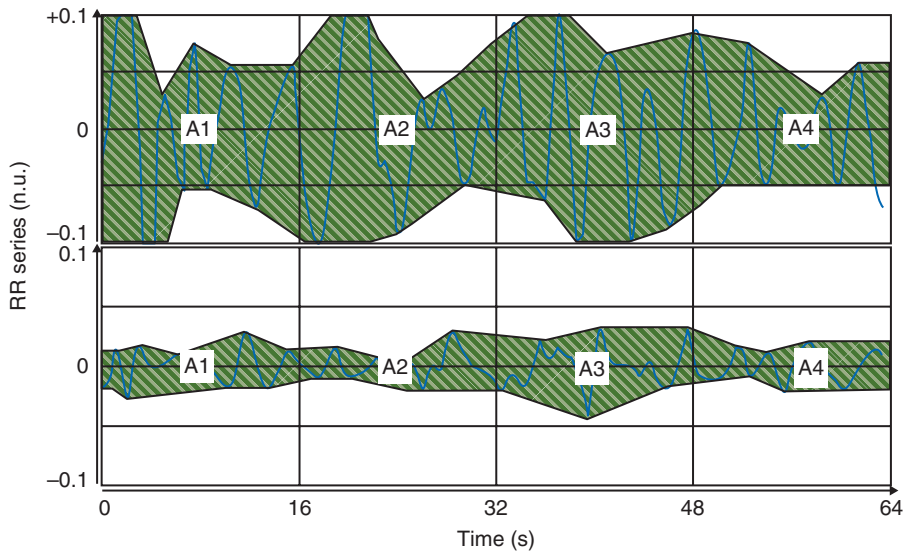

Fig 1 Normalized and filtered RR series (plain line) in two different states of antinociception/nociception balance during general anaesthesia. The grey surfaces A1, A2, A3, and A4 measure the respiratory influence in the RR series and are proportional to the relative parasympathetic tone. Upper panel shows high relative parasympathetic tone in case of adequate analgesia; lower panel shows low relative parasympathetic tone in case of nociception leading to an increase of HR and arterial pressure (reprinted with permission from Jeanne *et al.* [8]).

Table 1 Characteristics of study subjects. BMI, body mass index; ENT, ear, nose and throat; NRS, 0–10 numerical rating scale

	NRS≤3 (*n*=132)	NRS>3 (*n*=68)	*P*-value
Age (yr), mean (SD)	41 (18)	44 (15)	0.30
Gender, *n* (%)			0.15
Male	70 (53)	42 (62)	
Female	62 (47)	26 (38)	
BMI (kg m^{-2}), mean (SD)	25 (5)	25 (6)	0.42
ASA class, *n* (%)			
I	82 (62)	34 (50)	
II	50 (38)	34 (50)	0.07
Type of procedure, *n* (%)			
ENT surgery	91 (69)	47 (69)	
ENT endoscopy	26 (20)	3 (4)	
Plastic surgery	15 (11)	28 (27)	<0.01
Maintenance of anesthesia, *n* (%)			
Propofol	69 (52)	18 (28)	
Halogenated anesthetic	63 (48)	49 (72)	<0.01
Morphine consumption in PACU (mg), median [IQR]	0	4 [2–6]	<0.01

performed where appropriate. We hypothesized that ANI on arrival in PACU would have a linear relationship with initial NRS. The linear relationship and the coefficient of determination (r^2) were determined with linear regression. The ANI and NRS at arrival in PACU and at the end of PACU stay were compared with analysis of variance (ANOVA) for repeated measures. The results were expressed as mean (SD), median [IQR] or *n* (%). The threshold for statistical significance was set at $P<0.05$.

A receiver-operating characteristic (ROC) curve was built by plotting the sensitivity, or true positive rate, as a function of the false positive rate (100-specificity) at different ANI points. The software generated the ANI value with the highest sensitivity and specificity to conclude that a patient had moderate to severe pain (NRS>3) requiring morphine titration. A subgroup analysis was performed to compare ROC curve AUCs according to the anaesthetic agent used (halogenated or propofol). Another ROC curve was built to determine the performance of ANI for the detection of severe pain (NRS≥7). The performance of a diagnostic test with a ROC curve AUC of 0.8 can be classified as good.[16]

Results

Two hundred patients were included in the study (Table 1). Pain assessment was performed within 10 min after arrival in PACU in all cases. Measurements of ANI and NRS were easily performed in all cases with no missing data. During this first pain evaluation, 132 patients (66%) had no or mild pain (NRS≤3), all of them having received effective i.v. or regional analgesia during surgery, and 68 patients (34%) had moderate to severe pain (NRS>3), including 12 (6%) patients with severe pain (NRS≥7). Age, gender, body mass index (BMI), and ASA class were similar between patients with NRS≤3 and NRS>3 (Table 1). More patients with NRS>3 underwent plastic surgery and received halogenated-based anaesthesia and less patients with NRS>3 underwent

endoscopic procedures and received propofol-based anaesthesia ($P<0.05$).

A statistically significant negative linear relationship was observed between ANI and NRS (ANI$=-5.2\times$NRS$+77.9$, $r^2=0.41$, $P<0.05$) at arrival in PACU, with 41% variations of ANI explained by NRS (Fig. 2). The ROC curve determining the performance of ANI for predicting NRS>3 is shown in Figure 3A [AUC=0.86, 95% confidence interval (CI) 0.8–0.91]. At the threshold of 57, the sensitivity and specificity (95% CI) of ANI to discriminate between patients with NRS≤3 and NRS>3 were 78% (66–87) and 80% (73–87), respectively (Table 2). In a subgroup analysis considering the hypnotic agent used during anaesthesia, there was a significant difference ($P=0.03$) between ROC curves AUCs when propofol (Fig. 3B) or halogenated anaesthetics (Fig. 3C) were used: 0.93 (95% CI 0.85–0.97) *vs* 0.82 (95% CI 0.73–0.88), respectively (Table 2). The ROC curve determining the performance of ANI for predicting severe pain (NRS≥7) is shown in Figure 3D (AUC=0.91, 95% CI 0.86–0.95). At the threshold of 48, the sensitivity and specificity of ANI to discriminate patients with NRS≥7 were 92% (62–100) and 82% (76–88), respectively.

There was a statistically significant difference ($P<0.01$) between mean (SD) ANI and NRS values on arrival in PACU [49(14) and 5(1), respectively] and at the end of PACU stay [71(17) and 2(1), respectively] in the 68 patients with initial NRS >3 (Fig. 4). Mean (SD) ANI values were statistically different between patients with initial NRS≤3 and NRS>3 [73(17) *vs* 49(14), respectively, $P<0.01$] but in the end of PACU stay, after morphine titration and i.v. analgesia, no statistically significant difference was observed (Fig. 4). The median [IQR] morphine consumption during PACU stay was statistically higher ($P<0.05$) in patients with initial NRS>3 in comparison with patients with NRS≤3, respectively 4 mg [2–6] *vs* 0 mg [0–0].

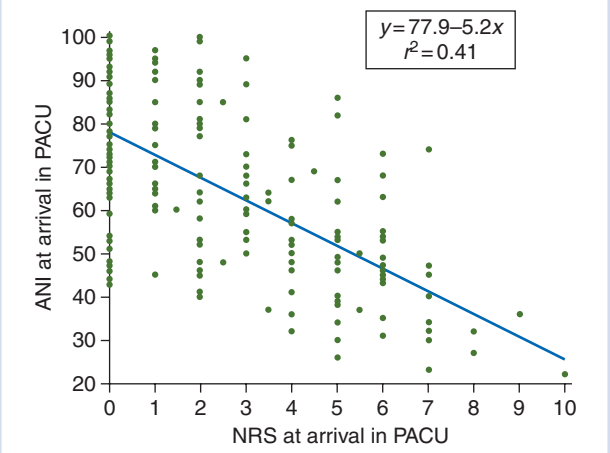

Fig 2 Negative linear relationship between ANI and NRS (linear regression).

Discussion

The results of this study demonstrate that there is a negative relationship between ANI derived from HRV and pain evaluation for patients in the immediate postoperative period. The ANI values decrease when pain intensity increases with an ANI ≤57 corresponding to the subjective threshold of moderate pain. With a ROC curve AUC of 0.86 at the threshold of 57, the performance of ANI for the detection of moderate to severe pain (NRS>3) at arrival in PACU may be classified as good[16] and is improved with propofol-based in comparison with halogenated-based anaesthesia. Moreover, with a ROC curve AUC of 0.91, the performance of ANI at the threshold of 48 is highly discriminant between no severe pain (NRS<7) and severe pain (NRS≥7) whatever hypnotic agent used. Besides, with respective negative predictive values of 88 and 99% in our study, an ANI value of >57 may predict that 88% of patients have adequate analgesia (NRS≤3), therefore not requiring morphine titration, and an ANI value of >48 may predict that 99% of patients have no severe pain, which might be of importance in the treatment of postoperative pain in poorly communicative patients. The positive predictive value appears to be somewhat low (67%) at an ANI threshold of 57 to detect NRS>3, and even lower (25%) at the threshold of 48 to detect NRS≥7. So, an alternative interpretation would be that ANI may be a useful screening tool for adequate analgesia and particularly for the absence of severe pain.

Current ASA guidelines recommend that anaesthesiologists and other healthcare providers should use standardized,

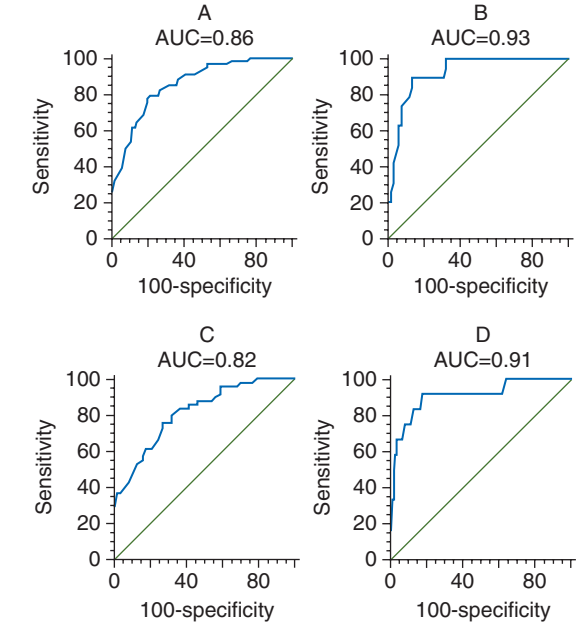

Fig 3 ROC curves. (A) All patients with NRS>3. (B) Propofol-anaesthetized patients with NRS>3. (C) Halogenated-anaesthetized patients with NRS>3. (D) All patients with NRS≥7.

Table 2 Performance of ANI in the detection of immediate postoperative pain. AUC, area under the curve; NLR, negative likelihood ratio; NPV, negative predictive value; NRS, 0–10 numerical rating scale; PLR, positive likelihood ratio; PPV, positive predictive value. Values in parentheses are 95% CI. *$P<0.05$ *vs* propofol

	Moderate to severe pain (NRS>3)			Severe pain (NRS≥7)
	All patients	Propofol	Halogenated	All patients
ANI threshold	≤57	≤57	≤57	≤48
ROC curve AUC	0.86 (0.80–0.91)	0.93 (0.85–0.97)	0.82 (0.73–0.88)*	0.91 (0.86–0.95)
Sensitivity (%)	78 (66–87)	89 (67–98)	76 (61–87)	92 (62–100)
Specificity (%)	80 (73–97)	87 (77–94)	73 (60–83)	82 (76–88)
PPV	67 (56–77)	65 (44–83)	69 (54–81)	25 (13–41)
NPV	88 (80–93)	97 (99–100)	79 (67–89)	99 (97–100)
PLR	4.0 (3.4–4.6)	6.9 (5.7–8.2)	2.8 (2.2–3.5)	5.2 (4.3–6.3)
NLR	0.3 (0.2–0.5)	0.1 (0.0–0.5)	0.3 (0.2–0.6)	0.1 (0.0–0.7)

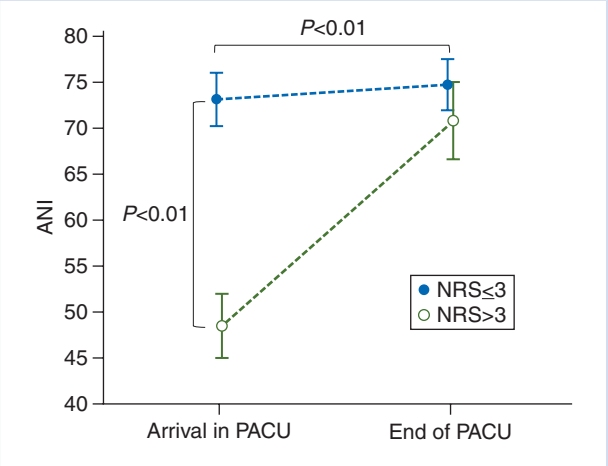

Fig 4 Mean ANI values at arrival in PACU and at the end of PACU in patients with NRS≤3 and NRS>3 (ANOVA for repeated measures). Filled circles represent patients with NRS≤3. Open circles represent patients with NRS>3. Error bars represent 95% CI for mean. The dotted lines represent the thresholds for moderate to severe pain (ANI≤57 and NRS>3).

validated instruments to facilitate the regular evaluation and documentation of pain intensity, the effects of pain therapy, and side-effects caused by the therapy.[5] There is also evidence that, although the reasons for lower perioperative analgesic doses in the elderly are unclear, undertreatment of pain in elderly persons is widespread.[5] Therefore, it is recommended that pain assessment and therapy should be integrated in the perioperative care of geriatric patients and that pain assessment tools should be adapted to patients' cognitive abilities. Opioid dose titration should be done to optimize pain treatment therapy while avoiding adverse effects such as somnolence in this vulnerable group, and extensive evaluation of analgesia should be conducted to overcome barriers that hinder communication regarding unrelieved pain.[5]

The objective assessment of the immediate postoperative analgesia using pupillary reflex measurement has been recently reported.[6] The measurement of ANI might offer theoretical advantages over pupillary reflex measurement as the method is totally non-invasive, with no need for noxious stimulation or patient mobilization and without any direct contact with patients' skin. Moreover, this equipment could offer a continuous evaluation of pain both during surgery and in the non-communicative immediate recovery phase. It is, therefore, important to determine the clinical performance of ANI in regard to pain assessment, giving an objective tool to measure analgesia where using pain scores might lead to more subjectivity.[17]

In a preliminary study performed in patients undergoing orthopaedic surgical procedures, ANI was measured after induction of general anaesthesia, during the surgical procedure then in PACU when VAS was >50 mm (defined as pain) and after suppression of pain by regional anaesthesia (VAS<10 mm).[14] In this study, ANI was significantly lower during surgical procedure than after induction of anaesthesia. In PACU, measurements made with VAS>50 mm were similar to those made during surgery, but ANI increased significantly when postoperative pain was alleviated by regional anaesthesia (VAS<10 mm). The authors concluded that ANI showed significant changes between painful periods (surgical incision and immediate postoperative period) and no pain periods (before surgical procedure and after regional analgesia).

More recently, it has been suggested that ANI may be a useful indicator of the antinociception/nociception balance during total i.v. anaesthesia in patients undergoing laparoscopic abdominal surgery.[8] Patients received cisatracurim and target-controlled infusions of propofol, adjusted to maintain the bispectral index in the range 40–60, and remifentanil, with target increase in case of 20% increase of baseline in HR, systolic arterial pressure (SAP). Anaesthesia induction decreased HR and SAP, while high median ANI values (88) were recorded, indicating parasympathetic predominance. After start of surgery, median ANI decreased to 60 and further to 50 after pneumoperitoneum inflation while there was no significant change in HR or SAP. When haemodynamic reactivity occurred, median ANI decreased

to 40 and returned to 90 after completion of surgery. The authors concluded that ANI monitoring seems more sensitive than HR and SAP to detect moderate nociceptive stimuli in propofol-anaesthetized patients, and that it may be helpful to optimize remifentanil administration.

A negative linear relationship between ANI and NRS has been observed during labour in 45 women before initiation of epidural analgesia.[18] In this study, pain scores were higher and ANI scores lower during uterine contractions ($P<0.001$). Uterine contractions significantly affected ANI with a mean (SD) decrease of 9.3(1.8) in comparison with contraction-free values. Using VAS>30 mm to define a painful sensation, the lower 95% confidence limit for ANI was 49. The authors concluded that ANI may provide a non-invasive continuous assessment of pain in parturients, although the influence of epidural anaesthesia on this index is still to be determined.

The current study shows for the first time a negative linear relationship between ANI value and the level of pain reported by the patient on NRS during the immediate postoperative period. Moreover, the performance of ANI seems better in propofol-anaesthetized than in halogenated-anaesthetized patients. This might probably be explained by the differential effects of propofol and volatile anaesthetics on HRV. Indeed, it has been shown after induction of anaesthesia that propofol reduces cardiac parasympathetic tone depending on the depth of hypnosis whereas sevoflurane has little or no effect.[19] Different results were observed in patients undergoing dental implantation on conscious sedation with propofol.[20] In this study, propofol induced significant decreases in LF, HF, and LF/HF ratio with no change in HR, indicating predominance of parasympathetic activity during sedation, whereas in the recovery period, propofol induced significant increases in HF and decreases in LF and LF/HF, resulting in parasympathetic activation and sympathetic depression. It has also been shown that desflurane reduces the total autonomic neural system activity and alters the balance between sympathetic and parasympathetic activities during maintenance of anaesthesia.[21]

Comparisons of the current study performed in awake patients having the sympathetic component predominant during the conscious state to studies performed in anaesthetized patients are difficult. Regardless of the mechanism, which remains poorly understood, it may be concluded from our results that the measurement of ANI at arrival in PACU may be a reliable indication of postoperative pain, in particular after propofol-based anaesthesia.

Our study presents several limitations. First, the differences in ROC curve AUCs between anaesthetic agents must be interpreted with caution as more patients with NRS>3 received halogenated-based anaesthesia, which might be a source of potential bias.

However, ROC curves show the relationship between the sensitivity of a test and its specificity and are not affected by the prevalence of the disease.[22] Secondly, the selected population with respect to age, comorbidities (ASA I and II), and type of surgery included in the current study represents only a small proportion of patients seen in daily clinical practice, so that these results cannot be extrapolated to all patients requiring anaesthesia. Indeed, medications known to affect HRV such as β-blocking agents or antiepileptic drugs were avoided.[23 24] Moreover, HRV is influenced by multiple other factors including age, awareness, different effects of hypnotics and analgesics, changing autonomic or haemodynamic conditions or inspired oxygen fraction and the interaction between these variables is unclear.[9 23 25 26] Further studies are thus needed to evaluate the usefulness of ANI in various anaesthesia and surgery conditions, and in different patient groups including geriatric or paediatric patients and critically ill or cognitively impaired patients.

In conclusion, the assessment ANI during the immediate postoperative is significantly correlated with pain intensity. In our study population, an ANI value of ≤57 corresponded to the subjective threshold of moderate pain (NRS>3) with better performance in propofol-anaesthetized patients in comparison with halogenated-anaesthetized patients, and an ANI value of ≤48 corresponded to the subjective threshold of severe pain (NRS≥7), whatever hypnotic agent was used. Considering the high negative predictive values at these thresholds, the measurement of ANI appears to be a simple and non-invasive method to assess adequate analgesia and particularly the absence of immediate postoperative severe pain in PACU and therefore may help clinicians and other healthcare providers to improve pain management, especially in patients with communication impairments.

Declaration of interest

None declared.

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References

1 Aubrun F, Langeron O, Quesnel C, Coriat P, Riou B. Relationships between measurement of pain using visual analog score and morphine requirements during postoperative intravenous morphine titration. *Anesthesiology* 2003; **98**: 1415–21

2 DeLoach LJ, Higgins MS, Caplan AB, Stiff JL. The visual analog scale in the immediate postoperative period: intrasubject variability and correlation with a numeric scale. *Anesth Analg* 1998; **86**: 102–6

3 Hjermstad MJ, Fayers PM, Haugen DF, *et al.* Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage* 2011; **41**: 1073–93

4 Gerbershagen HJ, Rothaug J, Kalkman CJ, Meissner W. Determination of moderate-to-severe postoperative pain on the numeric rating scale: a cut-off point analysis applying four different methods. *Br J Anaesth* 2011; **107**: 619–26

5 American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology* 2012; **116**: 248–73

6 Aissou M, Snauwaert A, Dupuis C, Atchabahian A, Aubrun F, Beaussier M. Objective assessment of the immediate postoperative analgesia using pupillary reflex measurement: a prospective and observational study. *Anesthesiology* 2012; **116**: 1006–12

7 Logier R, Jeanne M, Tavernier B, De Jonckheere J. Pain/analgesia evaluation using heart rate variability analysis. *Conf Proc IEEE Eng Med Biol Soc* 2006; **1**: 4303–6

8 Jeanne M, Clément C, De Jonckheere J, Logier R, Tavernier B. Variations of the analgesia nociception index during general anaesthesia for laparoscopic abdominal surgery. *J Clin Monit Comput* 2012; **26**: 289–94

9 Jeanne M, Logier R, De Jonckheere J, Tavernier B. Heart rate variability during total intravenous anesthesia: effects of nociception and analgesia. *Autonomic Neurosci* 2009; **147**: 91–6

10 Jeanne M, Logier R, De Jonckheere J, Tavernier B. Validation of a graphic measurement of heart rate variability to assess analgesia/nociception balance during general anesthesia. *Conf Proc IEEE Eng Med Biol Soc* 2009; **2009**: 1840–3

11 von Elm E, Altman DG, Egger M, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; **147**: 573–7

12 Bouvet L, Stoian A, Rimmelé T, Allaouchiche B, Chassard D, Boselli E. Optimal remifentanil dosage for providing excellent intubating conditions when co-administered with a single standard dose of propofol. *Anaesthesia* 2009; **64**: 719–26

13 Aubrun F, Mazoit JX, Riou B. Postoperative intravenous morphine titration. *Br J Anaesth* 2012; **108**: 193–201

14 Logier R, Jeanne M, De Jonckheere J, Dassonneville A, Delecroix M, Tavernier B. PhysioDoloris: a monitoring device for analgesia/nociception balance evaluation using heart rate variability analysis. *Conf Proc IEEE Eng Med Biol Soc* 2010; **2010**: 1194–7

15 Pichot V, Gaspoz JM, Molliex S, *et al.* Wavelet transform to quantify heart rate variability and to assess its instantaneous changes. *J Appl Physiol* 1999; **86**: 1081–91

16 Galley HF. Editorial II: Solid as a ROC. *Br J Anaesth* 2004; **93**: 623–6

17 van Dijk JF, van Wijck AJ, Kappen TH, Peelen LM, Kalkman CJ, Schuurmans MJ. Postoperative pain assessment based on numeric ratings is not the same for patients and professionals: a cross-sectional study. *Int J Nurs Stud* 2012; **49**: 65–71

18 Le Guen M, Jeanne M, Sievert K, *et al.* The Analgesia Nociception Index: a pilot study to evaluation of a new pain parameter during labor. *Int J Obst Anesth* 2012; **21**: 146–51

19 Kanaya N, Hirata N, Kurosawa S, Nakayama M, Namiki A. Differential effects of propofol and sevoflurane on heart rate variability. *Anesthesiology* 2003; **98**: 34–40

20 Win NN, Fukayama H, Kohase H, Umino M. The different effects of intravenous propofol and midazolam sedation on hemodynamic and heart rate variability. *Anesth Analg* 2005; **101**: 97–102

21 Widmark C, Olaison J, Reftel B, Jonsson LE, Lindecrantz K. Spectral analysis of heart rate variability during desflurane and isoflurane anaesthesia in patients undergoing arthroscopy. *Acta Anaesthesiol Scand* 1998; **42**: 204–10

22 Obuchowski NA. Receiver operating characteristic curves and their use in radiology. *Radiology* 2003; **229**: 3–8

23 Lotufo PA, Valiengo L, Bensenor IM, Brunoni AR. A systematic review and meta-analysis of heart rate variability in epilepsy and antiepileptic drugs. *Epilepsia* 2012; **53**: 272–82

24 Silke B, Guy S, Riddell JG. Effects of beta-adrenoceptor agonists and antagonists on heart-rate variability in normal subjects assessed using summary statistics and nonlinear procedures. *J Cardiovasc Pharmacol* 1997; **30**: 817–23

25 Lauscher P, Kertscho H, Enselmann P, Lauscher S, Habler O, Meier J. Effects of alterations of inspiratory oxygen fractions on heart rate variability. *Br J Anaesth* 2012; **108**: 402–8

26 Boettger MK, Schulz S, Berger S, *et al.* Influence of age on linear and nonlinear measures of autonomic cardiovascular modulation. *Ann Noninvasive Electrocardiol* 2010; **15**: 165–74

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