Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/ggxx1a43

SURGICAL PLETH INDEX AS A RELIABLE INDICATOR OF NOCICEPTION AND STRESS HORMONE RESPONSE DURING GENERAL ANESTHESIA

Dr. Seelam Bhagyavi*

*Assistant Professor, Department of Anaesthesia, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Osudu, Puducherry – 605502

***Corresponding Author:** Dr. Seelam Bhagyavi
*Assistant Professor, Department of Anaesthesia, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Osudu, Agaram Village, Koodapakkam Post, Puducherry - 605502

Abstract

Background: Surgical nociceptive stimulation can increase the risk of infection, prolong hospitalization, and raise healthcare costs. Managing surgical stress during general anesthesia is crucial to maintain hemodynamic stability. The Surgical Pleth Index (SPI), derived from normalized heart rate and pulse wave amplitude, has emerged as a potential tool to monitor nociception more accurately than traditional measures such as blood pressure and heart rate. This study evaluated the relationship between SPI and stress hormones during elective ENT surgery under general anesthesia.

Methods: Eighty ASA I-II patients undergoing elective ENT procedures were randomized into two groups: SPI-guided remifentanil titration (SPI group) and traditional remifentanil dosing (control group). SPI, BIS, arterial blood pressure, heart rate, and stress hormones (ACTH, cortisol, epinephrine, norepinephrine) were monitored at baseline, intubation, maximal surgical stimulus, and post-maximal stimulus. Hormone assays were performed using reversed-phase high-performance liquid chromatography. Statistical analyses included t-tests, chi-square, Spearman's correlation, and ROC curve analysis.

Results: Baseline demographics were comparable between groups. The SPI group demonstrated significantly lower ACTH and cortisol levels during intubation, maximal stimulation, and after maximal stimulus compared to controls. Hemodynamic parameters, including heart rate and mean arterial pressure, were more stable in the SPI group. Moderate to strong correlations were observed between SPI and stress hormone concentrations, especially ACTH. SPI showed better predictive capability for stress hormone levels than heart rate, blood pressure, or BIS.

Conclusion: SPI monitoring during general anesthesia provides a reliable, real-time measure of nociception and surgical stress, outperforming traditional indicators. SPI-guided analgesic administration results in improved hormonal stress response suppression and better cardiovascular stability. Incorporating SPI into anesthetic practice may enhance patient care by optimizing analgesia and reducing physiological stress during surgery.

Keywords: Surgical Pleth Index, nociception, stress hormones, general anesthesia, analgesia monitoring.

INTRODUCTION

Infection, the duration of hospitalization and health costs may all worsen from surgical nociceptive stimulation [1]. Since stress during surgery is mostly related to decreases in blood flow, general anesthesia helps assess the proper balance of pain and its control which blunts the haemodynamic changes that stress invokes. Getting such a perfect variable to direct how analgesics are delivered to manage stress responses is still challenging [2]. Until now, monitoring movement and autonomic responses has been the standard method to test analgesia effectiveness. Even so, these symptoms are not very specific. A proposal for the surgical pleth index is based on measuring normalized heart rate and pulse wave amplitude to measure nociception following general anesthesia. SPI was more accurate than blood pressure and heart rate in monitoring patients during general anaesthesia, reports [3]. In addition, there was a negative relationship between SPI and remifentanil concentration at the anesthetic site in patients receiving total intravenous anesthesia with propofol and remifentanil. By using SPI, propofol-remfenanil anesthesia used less remifentanil and preserved more stable hemopatic conditions. This research shows that using the SPI may measure the level of stress or nociception caused during an operation. Many studies confirm that epinephrine, cortisol and ACTH are true stress hormones. This method requires obtaining blood and analyzing it in the laboratory for intraoperative stress observation [5]. In order to evaluate the performance of the SPI, we relied on stress hormones in people's blood because there is no established standard. During the use of propofol and remifentanil, researchers looked at the RLS, BIS, arterial blood pressure, heart rate and stress hormones as the event unfolded. Linked according to time points. SPI improves when there is a loss of consciousness, but measures poorly during waking conditions and is a better marker for stress hormones compared to ABP, HR or the BIS.

METHODOLOGY

Altogether, 80 patients identified as I-II ASA status were studied, each aged between 18 and 70 years, scheduled for elective ENT procedures. This analysis did not include participants who had conditions related to the nervous system, were on psychoactive drugs, had problems with alcohol or drugs or significant illnesses in the heart, kidney, liver or metabolism. Patients were allocated to one of two groups: SPI in the first group, where remifentanil was titrated using the SPI values during anesthesia maintenance and Control, where remifentanil dosing relied on the traditional approach. The report has been published previously. The night prior to surgery, all groups were given 20-30 mg dipotassium clorazepate, then 3.75-7.5 mg midazolam. Forearm vein catheters were put in and the patient's blood pressure, ECG and oxygen saturation were monitored without penetration.

Both sets of participants were under observation by SPI and BIS. The foremost and manufacturer-recommended BIS positions were used and impedance was monitored below 7.5kΩ for optimum contact. An index finger sensor was used to track pulse oximetry during the treatment. SPIs were taken every 10 seconds. SPI, BIS, SpO2 and ECG were continuously monitored during anaesthesia. We used target-controlled infusion pumps to give propofol and remifentanil before tracheal intubation. We followed Schnider et al. for propofol and Minto et al. for remifentanil. A concentration of 35 mmHg for end-tidal carbon dioxide was established following intubation. The BIS level was kept between 40 and 60 using Ceprop every four minutes; Ceremi was not adjusted until surgery started.

Ceprop was titrated by 0.5 mL/1 every 4 minutes for every patient, group assignment aside. Traditional indications of insufficient anesthesia led to a Ceremi adjustment in the Control group. When the patient displayed signs in Table 1 [6-8], anaesthesia was viewed as being inadequate and Ceremi was increased by steps to the ceiling concentration. Urapidil 10 mg was given intravenously as required. They ramped up the speed of the intravenous infusion, gradually lowered the amount of Ceremi and gave Akrinor 0.5 ml. We gave the patient 0.5 mg of atropine for slow heart rate. Concentrations of remifentanil in the blood stayed between 20 to 50 stepwise. The method for treating a failed anesthesia included: urapidil 10 mg i.v.; akrinor 0.5 mL i.v.; atropine 0.5 mg i.v.; and atropine atropine. Eligible participants were given rescue medication when somatic arousal was normal within approved limits. Those whose BIS was greater than 60 and smaller than 65 could decrease their PECprop fifteen minutes prior to being wheeled into the OR, as their PECremi did not need to be

changed. In each patient, piritramide was used as an analgesic after surgery. At the same time as remifentanil, our team stopped propofol when the surgical suture was done.
Stress hormone assay and blood sampling are used in this study. At each event, each group took blood from the participants at four specific points in time. Keep the samples refrigerated as soon as you get them, spin them down within 15 minutes and keep the temperature at 25°C. Employing reversed phase high-performance liquid chromatography. A standard ACTH level falls between 7.2 and 63.6 pg/mL, 6.2 and 19 g/dL, with epinephrine between 84 pg/mL and 420 pg/mL.

STATISTICS

In various situations, results are given as mean and standard deviation or median and the range of values. The statistical analysis in this paper was done using Prism from GraphPad. Numerical data was analyzed with student t-tests, data variance was investigated using one-way student t-tests or SNK tests and nominal data was explored with chi-square tests. For finding and studying relationships between variables, Spearman's rank correlation was implemented and F-tests for testing regression slopes. The goal was to figure out if SPI could reliably predict stress hormone blood concentration and that is why ROCs were used. Furthermore, ROC analysis was used to show the right thresholds for SPI. We considered a P value of 0.05 to show statistical significance.

RESULTS

Inadequate anesthesia was determined when the patient's anesthetic depth was not sufficient and they responded displeasingly or through purposeful actions or apparent signs such as coughing or grimacing. Hypertension was diagnosed when mean arterial pressure was higher than 120% of the baseline or lower than 100 mmHg and hypotension occurred when mean arterial pressure was less than 80% of baseline or less than 60 mmHg. A heart rate of more than 90 beats per minute was tachycardia and a rate below 80% of your normal rate or below 45 beats per minute was bradycardia (Table 1).
The study samples had equal demographics. The overallmean age for both groups was very similar, with the SPI group at 49 years (±18) and the control group at 48 years (±18). The height and weight of both groups did not differ significantly, with averages of 175 cm (plus or minus 19) and 173 cm (plus or minus 95) for height and 80 kg (plus or minus 14) and 77 kg (plus or minus 19) for weight. No significant difference was found in gender, physical condition or the time between surgery and intubation among groups, showing the study population was well balanced (see Table 2).
Initial levels of ACTH and cortisol were somewhat higher in the SPI group (25 ± 16 pg/mL and 16 ± 7 pg/mL) than in the control group (21 ± 15 pg/mL and 15 ± 8 pg/mL). Before exposure, epinephrine and norepinephrine levels were lower in the SPI group (40 ± 20 pg/mL and 190 ± 117 pg/mL) than in controls (36 ± 20 pg/mL and 256 ± 175 pg/mL). No significant differences in mean arterial pressure or heart rate were found between groups at the start. ACTH and cortisol levels were significantly lower in the SPI group than at baseline (17 ± 9 pg/mL for ACTH and 13 ± 6 pg/mL for cortisol), but remained relatively high in the control group. In addition, norepinephrine and epinephrine both decreased in both groups and the SPI group had a slightly lower mean arterial pressure and heart rate, reflecting a more controlled hemodynamic state compared to the other group (Table 3).
For both groups, ACTH and cortisol levels decreased even farther when the maximal stimulation was applied, but the SPI group maintained levels still lower than the controls (12 ± 7 pg/mL, 10 ± 6 pg/mL compared to 14 ± 67 pg/mL and 10 ± 5 pg/mL). Both groups had lower mean arterial pressure and heart rate, yet the SPI group had notably less. Besides, their SPI and BIS indices indicated reduced autonomic activity and greater anesthesia. After the maximum stimulation session, both groups returned to nearly normal hormone and hemodynamic levels, but the SPI group sustained a reduced response to stress through continually lower ACTH, cortisol and catecholamine levels and a decreased heart rate and mean arterial pressure.
In general, the results found that the group using the SPI protocol had more control over their stress hormones and stronger heart stability than those not using the protocol. It means that watching the

SPI might help manage the depth of anesthesia, decreasing the effects of surgery on a patient's body, without putting the patient at risk.

Table 1: Inadequate anesthesia and hypotension or bradycardia criteria

Condition	Definition
Inadequate Anesthesia	Insufficient depth of anesthesia causing patient discomfort or physiological response
Hypertension	Mean arterial pressure exceeding 120% of baseline or >100 mmHg
Tachycardia	Heart rate exceeding 90 beats per minute
Somatic Arousal	Physical signs such as coughing, jaw movement, or facial grimacing indicating light anesthesia
Somatic Response	Purposeful body movements indicating inadequate anesthesia depth
Hypotension	Mean arterial pressure less than 80% of baseline or <60 mmHg
Bradycardia	Heart rate less than 80% of baseline or below 45 beats per minute

Table 2: Demographic data

Parameter	SPI (n = 80)	Control (n = 80)	P values
Age (years)	49 ± 18	48 ± 18	0.839
Height (cm)	175 ± 19	173 ± 95	0.657
Weight (Kg)	80 ± 14	77 ± 19	0.438
Gender-M/F (n)	29/255	45/41	0.254
ASA I/II (n)	39/47	41/45	1.000
Duration of	155 ± 69	176 ± 86	0.076
Duration of surgery	112 ± 63	135 ± 83	0.108
Intubation to surgery	26 ± 10	27 ± 12	0.534

Table 3: Bp, heart rate, SPI, and BIS values at different times related to events.

Time Point	Group	ACTH (pg/mL)	Cortisol (pg/mL)	Epinephrine (pg/mL)	Norepinephrine (pg/mL)	Mean (mmHg)	HR (beat/min)	SPI	BIS
Base SSI	SSI	25 ± 16	16 ± 7	40 ± 20	190 ± 117	96 ± 16	73 ± 15	55 ± 13	94 ± 17
Base Control	Control	21 ± 15	15 ± 8	36 ± 20	256 ± 175	101 ± 16	72 ± 14	55 ± 13	99 ± 4
Intu SSI	SSI	17 ± 9**	13 ± 6**	30 ± 21	132 ± 72**	96 ± 22	74 ± 14	53 ± 15	39 ± 12**
Intu Control	Control	18 ± 11	13 ± 6*	28 ± 11	135 ± 75**	95 ± 18	77 ± 17	77 ± 17	379 ± 15**
Maxi SSI	SSI	12 ± 7**#	10 ± 6**##	36 ± 9	86 ± 53**##	76 ± 12**##	61 ± 12**##	45 ± 14**##	41 ± 13**

Maxi Control	Control	14 ± 67**#	10 ± 5**##	38 ± 26#	85 ± 52**#	79 ± 18**##	61 ± 12**##	47 ± 16*#	40 ± 11**
After-Maxi SSI	SSI	11 ± 8**##	7 ± 5**##&	21 ± 20**#&&	38 ± 20**##&&	79 ± 15**##	61 ± 11**##	31 ± 13**##&&	46 ± 13**
After-Maxi Control	Control	11 ± 7**##	8 ± 6**##	21 ± 12**&&	38 ± 20**##&	84 ± 17**##	60 ± 12**##	33 ± 15**##&&	42 ± 9**

Figure 1: Demographic Data Comparison: SPI vs Control Groups

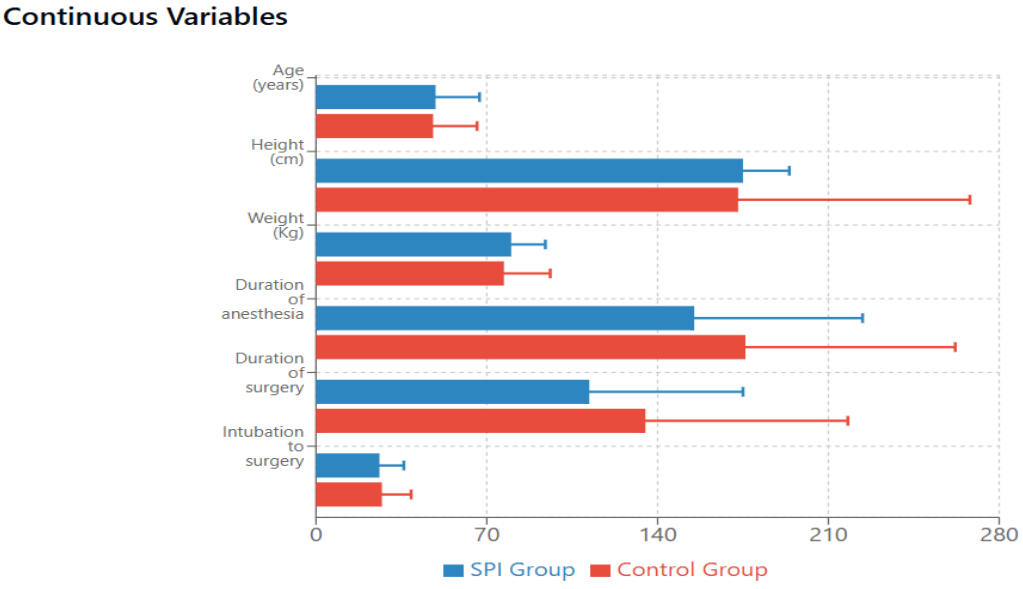


Figure 2: Gender Distribution

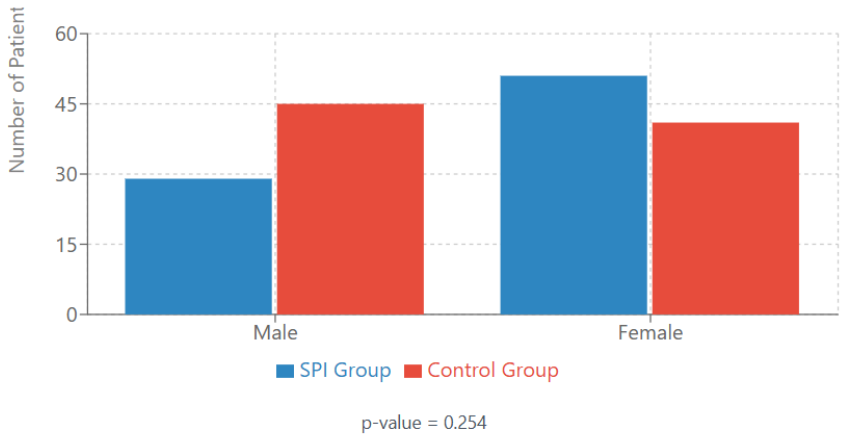
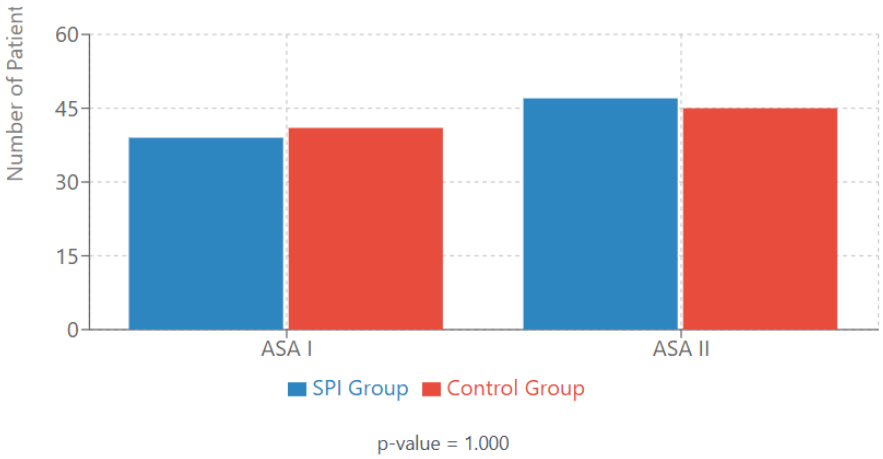


Figure 3: ASA Classification



DISCUSSION

We looked at how SPI changes in relation to levels of nociception during general anesthesia, using photoplethysmography. While no links with stress hormones were found at Base in our prospective, randomized, single-blinded study, a moderate-to-good relationship was visible with these hormones at the other measured times, especially ACTH, whose levels were strongly predictable from SPI. No direct tools exist for detecting stress or nociception during general anaesthesia. Usually, anesthesiologists watch a patient's blood pressure, heart rate, sweating and tearing for signs of stress, but these factors have been found to be poor markers. Analgesic endpoints such as how quickly a patient moves their limb when exposed to pain, are generally used to detect unsuccessful analgesia, but their reliability is poor and muscle relaxants can make the tests less reliable. In addition to state entropy (SE) and response entropy (RE), variables measured from EEGs are helpful signs of the pain-inhibiting effects of anaesthesia. Stress and nociception can both be spotted by looking at the varying amplitude of photoplethysmography. As a rule, these variables show weak performance. Four parameters of pulse wave velocity and normalized heart rate are recorded by SPI during general anesthesia to provide a measure of nociception or stress [12]. The effect-site concentrations of remifentanil at total i.v. anesthesia were shown to be negatively correlated with the SPI. FN demonstrated better results than SE, RE, heart rate and PPGA at recognizing nociceptive stimulation when patients received propofol anesthesia and Esmolol made no difference in its performance. Evaluating performance of new measurement tools, like SPI [13], is very important with general anaesthesia. Production of pituitary hormones is greater after surgery because of stress. Cortisol, epinephrine and norepinephrine can all change how we detect pain during surgery. Too many stress hormones are linked to poorer results in patients. When patients experienced mental stress despite premedication, all four stress hormones were highest among those studied [14, 15]. In addition, we found stress hormone levels at Max were much higher than 15 min After-Max which happened when the surgeon said stress was at its highest during surgery. By contrast, we observed that there were moderate to good relationships between stress hormones and SPI concentrations. To design the SPI, researchers studied anaesthetized patients to measure surgical stress during anesthesia. Since the patient is asleep under general anaesthesia, their mind does not influence them. There was likely some preoperative stress among the patients in the Base group while they were still awake. Therefore, many believe that surgical induced nociception greatly increases stress during general anesthesia. Stress hormone amounts and SPI levels may change as a person's state of consciousness changes. SPI could only be useful for practitioners of anaesthetics. Stress correlations are explained by these three hormone releases: (1) Stimulation during surgery causes the hypothalamus-pituitary-adrenal axis, releasing ACTH, to encourage cortisol production. Whenever stress occurs, the HPA axis starts producing the hormones epinephrine and norepinephrine. Over time, the amounts of these hormones produced may vary as set by the timing of stress in the group. Samples were taken from the blood

with 30-60 seconds of the incident and then tested for stress hormones. Stress hormone levels can be greater at their highest points than at their lowest. Having surgery bodily stimulates responses related to stress hormones. The choice of anaesthetics made very little difference to epinephrine and norepinephrine, but catecholamines changed with surgical stress at the same rate, unlike ACTH and cortisol which rose with the severity of the surgery. Over the course of the procedure, both epinephrine and norepinephrine remained stable, whereas ACTH and cortisol increased. The body's hormones varied in terms of when they peaked. There seems to be a difference in how the stress hormones are released depending on what type of stimulus is involved.

Certain constraints are present in the design of this study. People have diverging opinions about when to draw blood during an MRI scan. Event-related time points involve the levels of nociceptive stimulation during anesthesia. It is hard to find out how close to the access point the cancer is. Blood samples were taken within a minute after stress began and the SPI figures were noted 15 seconds after the stress ended. ENT surgery is much less involved surgically than large surgeries which could be the cause for a lower stress hormone level. Future investigations should look at more different surgical procedures.

CONCLUSION

The findings indicate that SPI can reliably measure nociception and stress reactions during a general anesthesia operation. The relationship between SPI and stress hormone levels, especially ACTH, was stronger across many perioperative events when compared to heart rate, blood pressure and BIS.

Patients treated using the SPI-guided remifentanil titration had much lower ACTH and cortisol levels during intubation, the highest level of surgery and after. Hemodynamic stability improved in the SPI group, as manifestaed by lower and more even heart rate and mean arterial pressure than in the controls. As a result, monitoring SPI may allow safer and more effective delivery of analgesics, with little or no strain on the heart or respiratory systems.

SPI did not vary consistently with baseline hormone measures, likely because patients were aware and anxious ahead of surgery; even so, SPI seemed to track the changing levels of stress hormones during anesthesia, supporting its use as a quick indicator of nerve activity during sleep. The amount and timing of hormone release are evidence of the complex nature of surgical stress, because catecholamines do not change much, whereas ACTH and cortisol react more directly to what the surgery involves.

The fact that most of the participants had simple ENT procedures may explain why stress hormone levels were lower than those seen in other types of surgery. Blood sampling may vary throughout the course of surgery and could hence change the accuracy of hormone measurements. Work should be done to apply these results to different surgical cases and understand the effects of SPI-based analgesia on recovery, success of treatment and how well patients are satisfied.

In short, SPI works without surgery and seems promising since it gives a more reliable and sensitive signal of pain inside the body than current monitoring does. Applying SPI in an operating room may improve stress management during anesthesia, avoid inadequate analgesia and benefit patients throughout their care.

REFERENCE

1. S. D. Parker, M. J. Breslow, S. M. Frank *et al.,* "Catecholamine and cortisol responses to lower extremity revascularization: correlation with outcome variables," *Critical Care Medicine*, 23(12), 1995, 1954–1961,
2. P. S. Myles, J. O. Hunt, H. Fletcher *et al.,* "Remifentanil, fentanyl, and cardiac surgery: a double-blinded, randomized, controlled trial of costs and outcomes," *Anesthesia and Analge- sia*, 95(4), 2002, 805–812,
3. M. M. R. F. Struys, C. Vanpeteghem, M. Huiku, K. Uutela,N. B. K. Blyaert, and E. P. Mortier, *et al*., "Changes in a surgical stress index in response to standardized pain stimuli during propofol-remifentanil infusion," *British Journal of Anaesthesia*, 99(3), 2007, 359–367,

4. W. Buhre and R. Rossaint*, et al*., "Perioperative management and monitoring in anaesthesia," *Lancet*, 362(9398), 2003, 1839–1846,.
5. J. Bruhn, P. S. Myles, R. Sneyd, and M. M. R. F. Struys, *et al*., "Depth of anaesthesia monitoring: what's available, what's validated and what's next?" *British Journal of Anaesthesia*, 97(1), 2006, 85–94,
6. T. Heier and P. A. Steen, *et al.,* "Assessment of anaesthesia depth," *Acta Anaesthesiologica Scandinavica*, 40(9),1996, 1087– 1100,
7. M. Rantanen, A. Yli-Hankala, M. van Gils *et al.,* "Novel multiparameter approach for measurement of nociception at skin incision during general anaesthesia," *British Journal of Anaesthesia*, 96(3), 2006, 367–376,
8. M. Huiku, K. Uutela, M. van Gils *et al*., "Assessment of surgical stress during general anaesthesia," *British Journal of Anaesthesia*, 98(4), 2007, 447–455,
9. J. Wennervirta, M. Hynynen, A. M. Koivusalo, K. Uutela, M. Huiku, and A. Vakkuri, *et al*., "Surgical stress index as a measure of nociception/antinociception balance during general anesthesia," *Acta Anaesthesiologica Scandinavica*, 2008, 52(8), 1038–1045,
10. M. Gruenewald, P. Meybohm, C. Ilies *et al*., "Influence of different remifentanil concentrations on the performance of the surgical stress index to detect a standardized painful stimulus during sevoflurane anaesthesia," *British Journal of Anaesthesia*, 103(4), 2009, 586–593,
11. W. D. Smith, R. C. Dutton, and N. T. Smith, *et al*. "Measuring the performance of anesthetic depth indicators," *Anesthesiology*, 84, 1996, 1,38–51,
12. W. D. Smith, R. C. Dutton, and N. T. Smith, *et al*., "A measure of association for assessing prediction accuracy that is a general- ization of non-parametric roc area," *Statistics in Medicine*,15, 1996, 1199–1215,
13. X. Chen, C. Thee, M. Gruenewald *et al.,* "Comparison of surgical stress index-guided analgesia with standard clinical practice during routine general anesthesia: a pilot study,"*Anesthesiology*, 112(5), 2010, 1175–1183,
14. T. Schricker, F. Carli, M. Schreiber *et al*., "Propofol/sufentanil anesthesia suppresses the metabolic and endocrine response during, not after, lower abdominal surgery," *Anesthesia and Analgesia*, 90(2), 2000, 450–455,
15. M. F. Roizen, R. W. Horrigan, and B. M. Frazer, *etal*.,"Anes- thetic doses blocking adrenergic (stress) and cardiovascular responses to incision-MAC BAR," *Anesthesiology*, 54(5), 1981,390–398,.