

PAIN

# Surgical pleth index-guided remifentanyl administration reduces remifentanyl and propofol consumption and shortens recovery times in outpatient anaesthesia

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## Editor's key points

- Rational titration of any drug requires an objective measure of clinical effect.
- Opioid doses are typically determined by a combination of intuition and observation of haemodynamic responses.
- The surgical pleth index (SPI) is proposed as an objective measure of the nociception–anti-nociception balance.
- The current study investigated the influence of SPI-based titration of remifentanyl on drug doses and recovery times.

**Background.** The surgical pleth index (SPI) is an index based on changes in plethysmographic characteristics that correlate with the balance between the sympathetic and parasympathetic nervous system. It has been proposed as a measure of the balance between nociception and anti-nociception. The goal of this study was to test whether it could be used to titrate remifentanyl in day-case anaesthesia.

**Methods.** A total of 170 outpatients were given total i.v. anaesthesia with propofol and remifentanyl. The patients were randomized to have the remifentanyl dose either adjusted according to the SPI (SPI group) or to clinical parameters (control group). The propofol dose was adjusted according to entropy in both groups. The consumption of anaesthetic drugs, recovery times, and complications were compared.

**Results.** The mean [standard deviation (SD)] remifentanyl and propofol infusion rates in the SPI and control groups were 0.06 (0.04) vs 0.08 (0.05)  $\mu\text{g kg}^{-1} \text{min}^{-1}$  and 6.0 (2.1) vs 7.5 (2.2)  $\text{mg kg}^{-1} \text{h}^{-1}$ , respectively (both  $P < 0.05$ ). The mean (SD) times to eye opening were –0.08 (4.4) and 3.5 (4.3) min and to extubation were 1.2 (4.4) and 4.4 (4.5) min in the SPI and control groups, respectively (both  $P < 0.05$ ). There was no difference between the groups with regard to satisfaction with the anaesthetic or intensity of postoperative pain. No patient reported intraoperative awareness.

**Conclusions.** Adjusting the remifentanyl dosage according to the SPI in outpatient anaesthesia reduced the consumption of both remifentanyl and propofol and resulted in faster recovery.

**Keywords:** anaesthesia, depth; EEG; SPI/surgical pleth index; stress; surgery, day-case; sympathetic nervous system

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The number of outpatient operations has increased in recent years.<sup>1</sup> An ideal outpatient anaesthetic should provide adequate anaesthesia but be associated with rapid recovery and mobilization, and few side-effects. Optimal hypnotic dose titration may avoid insufficient dosage (and thus awareness) and also excessive anaesthetic doses, since the latter can prolong surgical process times and duration of hospitalization, and can increase costs.<sup>2–3</sup> Similarly, optimal analgesic titration is desirable, since intraoperative stress resulting from inadequate analgesia (anti-nociception) can influence postoperative outcome.<sup>4–9</sup>

There is broad inter-individual variability in pharmacokinetics and pharmacodynamics, and thus standardized

anaesthetic regimes, even when using age and weight-adapted dosages, can lead to under- or overdosage.<sup>10–11</sup> The use of EEG-based monitors of hypnosis such as the bispectral index or spectral entropy (SE)<sup>12–14</sup> may help to optimize hypnotic administration. These monitors have been shown to reduce anaesthetic doses, achieve greater haemodynamic stability, reduce the incidence of intraoperative awareness, and shorten recovery times.<sup>12–15</sup> EEG-based monitors are not suitable for monitoring analgesia<sup>16–17</sup> because the anatomic regions in the central nervous system differ for analgesia and hypnosis, and thus these systems, which assess EEG activity in the frontal cortex, are not good for predicting spontaneous movements in response to painful stimuli.

For optimal titration of analgesic drugs, a monitor of the nociception–anti-nociception balance is desirable. Studies have shown a correlation between the activity of the sympathetic nervous system and nociception.<sup>18</sup> The surgical pleth index (SPI), first introduced in 2007, uses pulse plethysmography (HBI) and photoplethysmography (PPG), both obtained from pulse oximetry monitoring, to provide an index of the nociception–anti-nociception balance. It correlates with surgical stimuli and dosage of analgesic<sup>19 20</sup> and predicts the effect of pain stimuli and analgesic therapy with greater certainty than common clinical parameters.<sup>19 21</sup>

The aim of our study was to test the hypothesis that the combination of SPI with entropy monitoring reduces the consumption of propofol and remifentanyl and allows recovery times to be shortened, compared with entropy monitoring alone.

## Methods

The study had the approval of our institutional review board and was conducted exactly according to the methods in the study protocol approved by the ethics committee. After written informed consent, 170 patients were recruited for the study. Inclusion criteria were ASA I–III physical status, age between 18 and 75 yr, and scheduled outpatient orthopaedic surgery in a supine or beach-chair position, such as arthroscopy of knee, shoulder, or ankle. Exclusion criteria were intended position change during surgery and cardiac arrhythmias.

After randomization using a computer-generated list, the patients were assigned to one of the two study groups. In the SPI group, the remifentanyl dose was adjusted according to the SPI, while in the control group, it was administered according to standard clinical criteria. The propofol dose was adjusted according to SE entropy in an identical manner in both groups. All anaesthetics were given by the same two consultant anaesthetists, who were both experienced in the use of SPI.

The SPI is a dimensionless number between 0 (low stress) and 100 (high stress) that is calculated from the heart rate (HR) and the pulse wave amplitude obtained with a finger clip, which simultaneously measures transcutaneous oxygen saturation, HR, and pulse-induced volume changes (PPG). The individual patient's heartbeat index (HBI) and photoplethysmogram (PPG) are normalized ( $HBI_{norm}$ ;  $PPG_{norm}$ ) to the corresponding data distribution determined in a large group of adult patients and used in the equation:

$$SPI = 100 - (0.33 \times HBI_{norm} + 0.67 \times PPG_{norm})$$

The precise description and calculation of the algorithm is provided elsewhere.<sup>22</sup> SPI has not been validated for irregular heartbeats and patients with pre-existing cardiac arrhythmia were excluded.

## Induction and maintenance of general anaesthesia

All patients were given i.v. midazolam in the operating theatre (1–3 mg), titrated to provide an anxiolytic effect. Monitoring for ECG, non-invasive arterial pressure (AP),

pulse oximetry (CARESCAPE Monitor B650, GE Healthcare Finland Oy, Finland), and entropy (CARESCAPE Monitor B650) was established, and a peripheral venous cannula was inserted. The SPI sensor was attached to the patients in the SPI group (CARESCAPE Monitor B650). The baseline values for AP, HR, SPI, and SE/RE were recorded before induction after the patient had relaxed from instrumentation. Further defined measuring points were immediately after intubation, after incision, and after eye opening. SPI, SE, AP, and HR were registered continuously during the procedure and averaged over the time period.

The anaesthetic was a total i.v. technique with remifentanyl (Ultiva®, GlaxoSmithKline, Germany) and propofol. It was induced with a bolus injection of remifentanyl ( $1 \mu\text{g kg}^{-1}$ ) followed by a continuous infusion at an initial rate of  $0.2 \mu\text{g kg}^{-1} \text{min}^{-1}$ . The infusion rate was adjusted continuously according to the criteria described below. Propofol was injected at a rate of  $2 \text{ mg kg}^{-1} \text{min}^{-1}$  for a maximum of 2 min with continuous entropy monitoring. The injection was stopped when the entropy SE value had decreased below 60. The propofol infusion was then continued at an initial rate of  $4 \text{ mg kg}^{-1} \text{h}^{-1}$ . The rate was adjusted intraoperatively to keep the entropy SE value in the target range between 40 and 60. The infusion rate was reduced 10 min before the expected end of the operation and the SE value was allowed to increase to between 60 and 65. The airway was secured whenever possible with a laryngeal mask airway for lower limb surgery, and with a tracheal tube for shoulder operations. The patient was given mivacurium ( $0.2 \text{ mg kg}^{-1}$ ) to facilitate tracheal intubation. If necessary, AP was lowered with titrated 5 mg i.v. doses of urapidil. Haemodynamic stability was defined as the absence of hypotension or bradycardia. Intraoperative hypotension was defined as a decrease in the systolic AP by more than 20% from the initial value. It was treated with the injection of 0.2 ml of a theodrenaline/cafedrine combination preparation (Akrinor®, AWD Pharma, Germany; 1 ml contains 100 mg cafedrine/5 mg theodrenaline) and by increasing the infusion rate of i.v. fluids and also by reducing the remifentanyl infusion rate. Bradycardia was defined as an HR under  $50 \text{ beats min}^{-1}$ . It was only treated (atropine 0.5 mg, repeated if necessary) if hypotension was simultaneously present.

If the depth of anaesthesia was considered insufficient, the remifentanyl infusion rate was increased in  $0.05 \mu\text{g kg}^{-1} \text{min}^{-1}$  increments. It could also be carefully decreased in the same decrements if the depth was considered more than adequate (i.e. continuing lack of response to unchanging stimulus intensity or SPI values lower than 20). Adequate depth was assessed clinically in the control group. Adequate 'depth' was equated with adequate analgesia (with documented adequate SE levels) in the SPI group and assessed according to the SPI values, which were to be between 20 and 50. If the SPI value changed suddenly by more than 10, the remifentanyl infusion rate was also increased by  $0.05 \mu\text{g kg}^{-1} \text{min}^{-1}$ , even if the SPI were still within the target range. The maximum allowed remifentanyl infusion rate was  $0.5 \mu\text{g kg}^{-1} \text{min}^{-1}$  in both groups.

The propofol infusion was stopped as soon as the surgical trocar was removed from the joint. The remifentanyl infusion was stopped at the end of surgery, defined as the completion of all surgical procedures (e.g. sterile wound dressing, leg bandages, Gilchrist sling). At the end of the operation, the surgeon instilled 5 ml bupivacaine 0.5% (Carbostesin<sup>®</sup>, Astra-Zeneca, Germany) and 4 mg dexamethasone-21-palmitate (Lipotalon<sup>®</sup>, Merckle Recordati, Germany) into the joint.

Recovery times were defined as the periods of time between the end of surgery to eye opening and to extubation, respectively, and were documented as such. SPI, entropy, AP, and HR were measured directly before induction of anaesthesia, directly after tracheal intubation, directly after incision, and immediately at eye opening. Haemodynamic parameters, volumes of infused fluids, and doses of administered drugs were also documented. The patients were monitored after operation in the post-anaesthesia care unit (PACU) by a nurse who was blinded to study group assignment. The patients were given 600 mg oral ibuprofen for postoperative pain therapy on admission to the PACU. Criteria for discharge to home were stable vital signs within normal limits, no postoperative nausea or vomiting (PONV), and tolerable pain under treatment with minor analgesics. On discharge, the patients were given ibuprofen tablets (600 mg) to be taken every 6 h. Metamizole (1 g every 6 h) was prescribed as standard rescue medication, and tramadol (100 mg every 8 h; Tramal<sup>®</sup>, Grünenthal, Germany) was given in the case of severe pain. The patients were given the telephone numbers of the surgeon and the anaesthesiologist. An appointment was made for follow-up 2 days after the operation at the latest. Telephone interviews were conducted on the evening after the operation, and on the first and second postoperative days. The patients were questioned about pre-existing and postoperative pain on a scale of 0–10, the amount of analgesics consumed. They were also asked about intraoperative awareness, satisfaction with the anaesthesia, and whether or not the patient had suffered from PONV.

The primary endpoints of the study were differences between the groups in the recovery times and the consumption of anaesthetic drugs. Secondary endpoints were the occurrence of complications such as intraoperative awareness, nausea and vomiting, postoperative pain, patient satisfaction with the anaesthesia, shivering, and haemodynamic stability.

### Statistical analysis

Statistical analysis was performed with a spreadsheet program (Microsoft Office Excel 2003) and a statistics program (StatSoft Europe). The data were tested for normal distribution with the Kolmogorov–Smirnov test. Ordinally scaled data were described by mean and standard deviation (sd) if normally distributed. Categorical data were given as percentages. Student's *t*-test for unpaired samples was used to test for differences between the groups for ordinally scaled, normally distributed data. Categorical data were analysed by Pearson's  $\chi^2$  or Fisher's exact test depending on the number of categories. For all tests,  $P < 0.05$  was considered significant.

## Results

One hundred and fifty-one of the 170 recruited patients were included in the final analysis. Nineteen patients were excluded due to incomplete data sets or retraction of consent. The anthropometric data are shown in Table 1. Seventy-six patients were in the group with SPI-guided remifentanyl administration and 75 patients in the control group. The groups did not differ with regard to age, height, weight, BMI, gender distribution, ASA classification, or calculated PONV risk. In none of the patients was it necessary to replace the laryngeal mask airway with a tracheal tube.

Recovery was more rapid in the SPI group (Table 2). The mean (sd) times from 'end of surgery' to 'eye opening' were  $-0.08$  (4.4) vs 3.5 (4.3) min and from 'end of surgery' to 'extubation' were 1.2 (4.4) vs 4.4 (4.5) min in the SPI and control groups, respectively ( $P < 0.001$ ). The duration of anaesthesia and time in the PACU did not differ between the groups ( $P < 0.05$ ). Figure 1 shows the time to 'eye opening' as a Kaplan–Meier diagram.

Patients in the SPI group required both less remifentanyl and less propofol (Table 2). Remifentanyl consumption was 0.06 (0.04) and 0.08 (0.05)  $\mu\text{g kg}^{-1} \text{min}^{-1}$  in the SPI and control groups, respectively ( $P = 0.006$ ). Propofol consumption was 6.0 (2.1) and 7.5 (2.2)  $\text{mg kg}^{-1} \text{h}^{-1}$  in the SPI and control groups, respectively ( $P < 0.001$ ).

SPI and SE values at the defined times are given in Table 2. SE entropy values were higher in the SPI group at the time of eye opening [89.4 (12.0) vs 73.3 (9.4);  $P < 0.001$ ], but the groups did not differ at the other measuring times.

**Table 1** Characteristics of the study populations

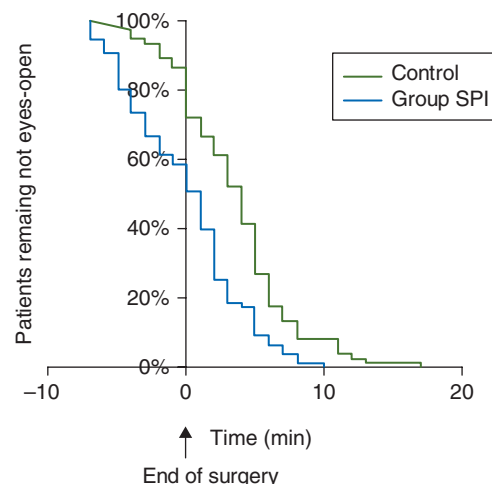
	SPI group (n = 76) (%)	Control (n = 75) (%)	P-value
Height (m)	1.76 (9)	1.77 (11)	0.53
Weight (kg)	85 (16)	86 (15)	0.60
BMI ( $\text{kg m}^{-2}$ )	27 (4)	28 (4)	0.74
Male (%)	66	72	0.21
Age (yr)	48 (18–69)	44 (18–74)	0.07
Type of surgery (%)			
Shoulder	36	17	0.04
Knee	62	79	
Ankle	2	4	
Tendency to PONV			
APFEL score (%) <sup>33</sup>			0.91
0	0 (15.8)	0 (18.7)	
1	1 (46.1)	1 (50.7)	
2	2 (22.4)	2 (18.7)	
3	3 (6.6)	3 (5.3)	
4	4 (9.1)	4 (6.7)	
ASA I–III (%)			0.96
I	47.4	49.3	
II	47.4	45.3	
III	5.2	5.3	

**Table 2** Recovery times, anaesthetic drugs, and SPI and SE entropy values. 'During surgery' data represent the average over the entire duration of the procedure

	SPI group (n=76)	Control (n=75)	P-value
Recovery times (min)			
End of surgery-eye opening	-0.08 (4.4)	3.5 (4.3)	<0.001
End of surgery-extubation	1.2 (4.4)	4.4 (4.5)	<0.001
Duration of anaesthesia	46 (19)	38 (16)	0.38
Arrival recovery room-discharge	66 (29)	63 (27)	0.46
Consumption of anaesthetic drugs			
Propofol (mg kg <sup>-1</sup> h <sup>-1</sup> )	6.0 (2.1)	7.5 (2.2)	<0.001
Remifentanyl (µg kg <sup>-1</sup> min <sup>-1</sup> )	0.06 (0.04)	0.08 (0.05)	0.006
SPI			
Before induction	57 (22)		
After intubation	36 (19)		
After incision	31 (18)		
During surgery	31 (15)		
At eye opening	50 (21)		
SE entropy			
Before induction	84 (26)	79 (23)	0.31
After intubation	40 (13)	39 (13)	0.8
After incision	42 (11)	42 (13)	0.86
During surgery	45 (20)	43 (21)	0.89
At eye opening	89 (12)	73 (9)	<0.001
AP <sub>MAP</sub> (mm Hg)			
Before induction	103 (13)	97 (17)	0.06
After intubation	72 (18)	81 (14)	0.005
After incision	76 (13)	77 (10)	0.6
Eye opening	85 (22)	82 (10)	0.3
Heart rate (beats min <sup>-1</sup> )			
Before induction	76 (14)	73 (11)	0.13
After intubation	67 (13)	66 (10)	0.36
After incision	65 (12)	65 (10)	0.72
Eye opening	76 (15)	69 (12)	0.005

The mean AP was lower in the SPI group at intubation [72 (18) vs 81 (14) mm Hg,  $P=0.005$ ], but did not differ at the other times. HR was higher in the SPI group at eye opening [76 (15) vs 69 (12) beats min<sup>-1</sup>].

The haemodynamic outcome parameters only included patients on whom an intraoperative change of position was not performed (e.g. shoulder operation in the beach-chair position). One hundred and eleven patients in both groups (49 patients in the SPI group; 62 patients in the control group) were operated on in the supine position without an operation-related change of position occurring intraoperatively. There were no significant differences here between the groups with regard to AP behaviour and the dose of the administered medications acting on the cardiovascular system and infused volume ( $P>0.05$ ).



**Fig 1** Eye opening at the end of surgery as the Kaplan-Meier survival curve. Some patients opened their eyes before dressing and bandaging was completed. (Patients in the SPI group are represented by a blue line; patients in the control group are represented by a green line.) The difference between the groups was significant ( $P<0.001$ ).

Hypertension requiring treatment did not occur in any patient. Initially, the maximum and mean HRs did not differ nor did the relative increase from the mean. However, there were differences in the minimum HR and the percentage increase of the HR ( $P<0.05$ ). These results are summarized in Table 3.

The groups did not differ with regard to the intensity of post-operative pain, incidence of nausea and vomiting, or the length of stay in the PACU. The results of the postoperative telephone survey revealed no differences between the groups with regard to pain on the day of surgery or during the first two postoperative days. They did not differ with regard to the incidence of postoperative nausea and vomiting or satisfaction with the anaesthesia. None of the patients reported intraoperative recall or awareness. Table 4 shows the data from the survey.

## Discussion

In this study, we found that using SPI to guide the administration of remifentanyl during general anaesthesia for orthopaedic operations performed on an outpatient basis reduced mean remifentanyl consumption by 25% and propofol consumption by 20%, while shortening the time to eye opening by an average of 3.5 and the time to extubation by 3.2 min.

EEG-based parameters such as BIS or entropy can help ensure equihypnotic propofol doses in study groups, while avoiding excessive propofol doses in a total i.v. anaesthesia (TIVA) regimen or the inherent risk of intraoperative awareness, although the latter benefit has not been demonstrated conclusively for entropy.<sup>23 24</sup> Propofol was infused at a rate

**Table 3** Intraoperative course of HR and AP, infusions, drugs acting on the cardiovascular system

	SPI group (n=49)	Control (n=62)	P-value
Adjunct drugs and infusions			
Atropine (mg)	0.02 (0.1)	0.11 (0.34)	0.07
Theodrenaline+cafedrine (mg)	3.9 (7.4)+78 (148)	3.8 (9.1)+76 (181)	0.96
Crystalloid infusion (ml)	690 (280)	68 (300)	0.99
Colloid infusion (ml)	41 (140)	32 (120)	0.73
Mean arterial pressure			
Baseline (mm Hg)	103 (12)	97 (17)	0.03
Maximum (mm Hg)	106 (12)	104 (12)	0.33
Minimum (mm Hg)	74 (10)	74 (8)	0.72
Mean value (mm Hg)	88 (9)	87 (8)	0.41
Decrease from baseline (%)	29 (11)	27 (9)	0.25
Decrease from mean (%)	16 (9)	14 (7)	0.15
Heart rate			
Baseline (beats min <sup>-1</sup> )	74 (13)	75 (13)	0.69
Maximum (beats min <sup>-1</sup> )	78 (13)	78 (12)	0.99
Minimum (beats min <sup>-1</sup> )	65 (11)	60 (10)	0.02
Mean (beats min <sup>-1</sup> )	70 (11)	68 (8)	0.2
Increase from baseline (%)	22 (23)	31 (25)	0.04
Increase from mean (%)	11 (14)	16 (13)	0.07

**Table 4** Postoperative complications and pain

	SPI group (n=76)	Control (n=75)	P-value
Postoperative complications			
Nausea (%)	4	3	0.80
Vomiting (%)	0	0	
Shivering (%)	10	10	0.93
Patients requiring analgesics (%) and perceived pain severity of those patients (numeric rating scale NRS 0–10)			
Pain severity on discharge from PACU	2.4 (2.0)	2.3 (2.2)	0.75
On evening after surgery (%)	47	47	0.47
Pain severity in these (NRS 0–10)	3.9 (2.1)	4.0 (1.8)	0.82
On Postoperative day 1 (%)	41	34	0.46
Pain severity in these (NRS 0–10)	3.3 (1.3)	3.0 (1.1)	0.36
On Postoperative day 2 (%)	37	27	0.30
Pain severity in these (NRS 0–10)	3.3 (1.4)	2.8 (1.0)	0.27
Satisfaction (NRS 1–6)	1.2 (0.5)	1.3 (0.5)	0.74

adjusted to keep SE values in the range of 40–60 considered to indicate an adequate hypnotic state.<sup>12</sup>

We used SPI to guide remifentanyl administration as it reflects the autonomic nervous system's response to stressful stimuli and correlates better with clinical surrogate parameters for adequacy of analgesia (AP and HR) than does entropy.<sup>19 20 22 25 26</sup> The SPI target range of 20–50 chosen for this study was based on the results of previous studies

by Struys and colleagues<sup>19</sup> and Chen and colleagues.<sup>26</sup> We added an additional dynamic criterion by prescribing an increase in the remifentanyl infusion rate if a rapid increase in the SPI occurred, even if it remained within the target range.

SPI was high before induction with an average of 56.8 (21.9). This high mean value in the absence of painful stimuli may be related to the preoperative stress experienced by the un-premedicated patient. The only investigation of SPI in awake subjects studied the effect of hot and cold thermal pain on SPI with contradictory results.<sup>27</sup> There are, however, no data on the effect of anxiety on SPI and one may therefore have to interpret the pre-induction values bearing this in mind. The SPI value immediately after securing the airway was 36.2 (19.4), which is lower than the mean SPI of 59 described by Chen and colleagues.<sup>26</sup> This difference could be explained by the fact that remifentanyl was given as a bolus injection of 1 µg kg<sup>-1</sup> followed by an SPI-adapted infusion rate in the present study, while Chen and colleagues administered it as a target-controlled infusion, which would result in lower maximal plasma concentrations. A further factor could be that in the present study, the airway was usually managed with a laryngeal mask airway, while all patients in the study of Chen and colleagues were intubated, which is a stronger stimulus. After induction, the patients in the SPI group had lower mean AP values than control patients, which correlates with the lower SPI values at that time and is evidence of better management of analgesia for the stimulus of inserting the airway. The difference between the groups could possibly be explained by the fact that in the SPI group, the remifentanyl infusion rate had already been increased to maintain SPI within the target range.

Maintaining a constant level of analgesia would help prevent or, at least, attenuate the breakthrough events described by Chen and colleagues that required repeated bolus injections of remifentanyl. This oscillating effect would explain the lower minimum HR and also the larger HR increase from baseline seen in the control group.

SPI group patients had higher HRs and entropy values at eye opening, which could reflect the reduced consumption of remifentanyl and propofol, and could be related to the more rapid recovery.

The use of SPI not only reduced the total remifentanyl dose but somewhat surprisingly also reduced propofol consumption. There is no obvious pharmacokinetic or pharmacodynamic explanation for this, since reducing the analgesic component of general anaesthesia normally requires an increase in the hypnotic component to maintain equipotency. This has been shown for numerous combinations of anaesthetic drugs.<sup>28 29</sup>

One possible explanation for the observed reduced dosage requirements for both drugs might be related to the fact that remifentanyl directly affects the EEG entropy parameters resulting in lower SE readings for equihypnotic states.<sup>30 31</sup>

Another possibility could be that administering remifentanyl according to clinical parameters might lead to alternating phases of break-through nociceptive stimulation requiring higher doses of remifentanyl and propofol, and phases with excessive remifentanyl and propofol doses. This hypothesis is supported by the study of Chen and colleagues which showed that the total intraoperative dose of remifentanyl was lower when remifentanyl administration was guided by SPI, but that there were more incidents of hypertension and movement in their group without SPI, despite a larger total dose of remifentanyl. *Post hoc* analysis of the SPI data in their control group, which had been concealed from the attending anaesthetist, showed that the SPI values had varied widely during the operation, indicating phases of significant remifentanyl under- and over-dosing.<sup>26</sup>

A similar reduction in opioid and propofol requirements as that observed in our study was seen during an entropy-guided TIVA for cardiac surgery, but our study is the first to show that SPI can also reduce the consumption of hypnotic drugs.<sup>32</sup>

The more rapid recovery seen with SPI in the present study was not described by Chen and colleagues.<sup>26</sup> This may be due to a different definition of 'end of surgery', or to the fact that Chen and colleagues continued the propofol infusion, albeit at a reduced rate, to their defined end of surgery, whereas we stopped the propofol infusion several minutes before our defined end of surgery.

Rapid recovery can reduce turnover times, which is especially meaningful for surgical procedures of short duration as is typical for outpatient cases. In this study, an average of 15 outpatient operations were performed per study day, and the use of SPI resulted in an average daily saving of 49 min. With a typical operation lasting an average of 45 min, one additional operation could be performed with the same resources. In addition to reducing turnover time, faster patient recovery

means that less personnel is bound in the operating theatre and PACU. We did not actually detect any difference between the groups with regard to the duration of stay in the PACU, but we attribute this to the fact that our institutional guidelines stipulate a minimum stay of 60 min.

Our groups were similar with regard to haemodynamic stability, and in that respect, confirmed the results of Chen and colleagues,<sup>26</sup> but in contrast to their study, we did not observe a single instance of spontaneous movements in our patients.

### Limitations

AP was measured every 3 min so that extremely transient episodes of hypertension or hypotension might not have been detected. The distribution of shoulder and knee/ankle operations differed significantly between the groups. However, all operations were performed arthroscopically, so that we expected the same intraoperative nociceptive stimulation level. In addition, patients were tracheally intubated for shoulder operations, while a laryngeal mask airway was used during operations of the lower limb. Despite this, consumption of propofol and remifentanyl was lower in the SPI group, with tracheal intubation and a higher percentage of shoulder operations (propofol 6.0 vs 7.5 mg kg<sup>-1</sup> h<sup>-1</sup>; remifentanyl 0.06 vs 0.08 µg kg<sup>-1</sup> min<sup>-1</sup>, respectively). If shoulder operations were associated with a significantly stronger nociceptive stimulus, one would have expected higher propofol and remifentanyl consumption in the SPI group, which was not the case. However, we cannot absolutely exclude the possibility that the results might have been influenced by the type of surgery.

It is not possible to exclude with certainty the possibility that haemodynamic changes, the volumes of infused fluids, or the use of vasoactive or circulatory drugs might have an effect on SPI values. However, the groups in our study did not differ in any of these possibly confounding factors (Table 3).

### Conclusion

Using the SPI to adjust the remifentanyl dose in outpatient anaesthesia reduces the consumption of both remifentanyl and propofol. The patients awaken faster and can be extubated sooner.

### Declaration of interest

None declared.

### Funding

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