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Surgical pleth index: prediction of postoperative pain in children?

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Abstract

Background. Surgical Pleth Index (SPI) is a non-invasive, dimensionless score (0–100) aimed to allow an estimate of intraoperative nociception. Thus, it may be a useful tool to guide intraoperative analgesia. However, no optimum SPI target range for the use in children has yet been defined. It was the aim of this study to define a clinically appropriate SPI target to predict moderate-severe postoperative pain in children.

Methods. After ethics approval 105 children (2–16 yr) undergoing elective sevoflurane/opioid-based anaesthesia were included. SPI was recorded directly before the end of surgery and compared with acute postoperative pain (age appropriately assessed on different pain scales in the age groups two to three yr, four to eight yr and nine to16 yr) in the postoperative acute care unit (PACU).

Results. Data of 93 children were analysed. A significant negative correlation was found between age and SPI ($r=-0.43$; $P=0.03$). The SPI cut-off value with the highest sensitivity (76%) and specificity (62%) in all children combined was 40. The negative predictive value for SPI ≤ 40 to predict the absence of moderate-severe pain in PACU was 87.5%. The commonly used SPI cut-off (50) published in all related studies had neither any clinically relevant sensitivity nor specificity to predict the presence or absence of acute pain in PACU.

Conclusions. The results suggest that a lower (≤ 40) than previously published (50) target for SPI may be more appropriate in studies investigating SPI guided anaesthesia in children, if the avoidance of moderate-severe postoperative pain is the main goal.

Clinical trial registration. ACTRN12616001139460.

Key words: children; postoperative pain; surgical pleth index

The surgical pleth index (SPI, GE Healthcare, Helsinki, Finland) is a dimensionless, normalized score (0–100) which is based on the photoplethysmographic analysis of the pulse wave and the heart beat interval.[1] Though a gold standard for the assessment of nociception does not exist, SPI scores have been reported to reflect different intraoperative stimuli and different levels of autonomous nervous system activation with some accuracy.[2–4]

Several studies in adult patients have shown that SPI-guided administration of opioids may be beneficial,[3 5 6] but only one

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Editor's key points

- Reliably measuring nociception intraoperatively to optimise analgesia could usefully improve postoperative pain in children.
- Paediatric use of the Surgical Pleth Index (SPI) to monitor nociception has not been validated.
- This study evaluates the predictive value of the SPI for moderate to severe postoperative pain.
- A lower SPI target than previously suggested is required to avoid significant postoperative pain.

trial has investigated this matter in children.[7] In contrast to the studies in adults, in children SPI guided administration of analgesics resulted in higher postoperative pain scores compared with standard intraoperative management.

Of note, all previous studies have uniformly but arbitrarily utilized a target value of SPI ≤ 50, though there is little or no validation of this specific cut-off value. A recent study in adult patients described a significantly lower cut-off value (SPI ≤ 30) as a more reliable intraoperative target to predict the presence *vs* absence of significant acute postoperative pain.[8]

Based on the latter trial in adults, we hypothesised that the SPI target of ≤ 50 utilized in the only available study about SPI guidance and postoperative pain in children,[7] could also have been too high. Thus, it was the aim of this study to investigate the relationship between SPI at the end of surgery and acute postoperative pain in children of three different age groups, with the goal of possibly identifying a more age-appropriate SPI target for future trials.

Methods

After registration of the protocol with the Australian New Zealand Clinical Trials Registry (ACTRN12616001139460), and approval by the Ethics Committee of the Princess Margaret Hospital for Children (EP2016085) and the University of Western Australia (RA/4/1/8634), 105 children undergoing non-emergency surgery under general anaesthesia with sevoflurane and opioids were included in the study. As the standards of assessing postoperative pain in our institution are age-specific (see below), 35 children each were recruited in one of three age groups: two to three yr, four to eight yr and nine to16 yr, respectively.

Exclusion criteria for recruitment included: age<two>16 yr, diabetes, severe peripheral or cardiac neuropathy, pacemaker, use of a surgical tourniquet (unless already deflated before time of measurements), treatment (infusion) with vasoactive medication, any pre or intraoperative treatment until after the five min observation period with ketamine, beta-receptor blockers, clonidine (as premedication, intraoperative use, or regional adjunct), beta-receptor agonists (i.e. Ventolin) or any other drug suspected to interact with the sympatho-vagal balance. Neuromuscular blocking agents antagonism using neostigmine, atropine or glycopyrrolate was only permitted after the six min observation period.

All children received a standard anaesthetic with sevoflurane and opioid (opioid dosage as per attending anaesthetist). As per clinical requirement and the attending anaesthetists' preferences, the children were permitted to receive nitrous oxide, regional/neuraxial blocks and a laryngeal mask airway or tracheal tube. After anaesthesia induction, all children received standard anaesthesia monitoring and monitoring of SPI and state entropy (SE) (both GE Healthcare, Helsinki, Finland). SE was kept between 40–60, whereas no specific target was prescribed for SPI.

At the end of surgery (defined as the time of skin closure or wound dressing), but before SE > 60, SPI was recorded six times (T0, T1, T2, T2.5, T4, T5) during a five min observation interval. The highest and the mean SPI of this series were both recorded (only the highest SPI score was used in the final analysis). Thereafter, anaesthesia was terminated and, once appropriate, the patients were discharged from the operating theatre. On arrival, and once the patient was conscious and deemed non-delirious in the postoperative acute care unit (PACU), acute postoperative pain was recorded every five min for 15 min, and the mean and the highest pain scores noted (with the highest pain score used in the final analysis). Pain was rated as per the guidelines of the Princess Margaret Hospital for Children on three different age-appropriate pain scales (all 0–10): two to three yr aged children were assessed with the FLACC (Face, Legs, Activity, Cry, and Consolability) score, the group of four to eight yr old children with the Revised Faces Pain Scale (FPS-R) and the group of nine to16 yr by means of a Numeric Rating Scale. Treatment of pain was as per our institution's PACU standards.

The primary study outcome parameter was the definition of the optimum (highest combined sensitivity and specificity, Youden's point) cut-off value for SPI to distinguish between no to mild (≤ 3/10) *vs* moderate to severe (>3/10) postoperative pain in children. The secondary outcome parameter was the assessment of a potential variation in SPI in children depending on their age undergoing surgery under general anaesthesia.

Statistics

As no related study was available as guidance, we aimed to gather data from at least 30 patients in each age group in a pilot trial design. As a certain loss of data because of technical difficulties, consent withdrawal or protocol violations was expected, we included 105 patients (35 per group) in total.

All data were tested for normal distribution (K-S test). As appropriate, further analysis (IBM SPSS Statistics Version 20 [IBM Australia, ST Leonards, NSW]) of continuous data was performed via ANOVA or Mann-Whitney*U*-test, correlations were tested using Pearson correlation coefficient or Spearmans' rho, positive and negative predictive values of SPI cut offs were calculated using a χ^2 test and the predictive value (sensitivity and specificity) of SPI cut-offs for acute postoperative pain scores was computed with receiver-operating characteristics (ROC). For the description of a "best-fit" cut-off for SPI, the Youden's point (highest combined sensitivity and specificity) was used. Data are displayed as either mean (SD) or median (quartiles), as appropriate.

Results

105 patients were included in the study. However, data from 12 patients were excluded as a result of protocol violations and thus 93 complete data sets were analysed.

Patient characteristics are displayed in Table 1.

Across all age groups, SPI at the end of surgery was significantly higher when the highest pain rating in PACU was rated moderate to severe (pain score>3) *vs* nil or mild (pain score ≤3): 39 (31–46) *vs* 47 (40–51); P=0.009. In all children combined, the area under the ROC curve (testing whether SPI may predict

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Table 1 Patient Characteristics. Number of patients in each age group for ASA risk score, gender, the use of regional/neuraxial or local anaesthesia, the use of nitrous oxide, and the highest pain score (0–10) within the first 15 min after admission to PACU

Age group	*n*	ASA (*n*)	Gender (*n*)	Regional anaesthesia (*n*)	Nitrous oxide (*n*)	Highest pain score (*n*)
2–3 yr	31	1: 19 2: 10 3:2	Male: 23 Female: 8	No: 6 Epidural: 3 Regional: 3 Local: 19	Yes: 14 No: 17	0: 15 1–3: 7 4–5: 6 6–10: 3
4–8 yr	28	1: 19 2: 9 3: 0	Male: 18 Female: 10	No: 3 Epidural: 4 Regional: 1 Local: 20	Yes: 17 No: 11	0: 10 1–3: 14 4–5: 1 6–10: 3
9–16 yr	34	1: 22 2: 11 3: 1	Male: 16 Female: 18	No: 3 Epidural: 0 Regional: 1 Local: 30	Yes: 22 No: 12	0: 8 1–3: 14 4–5: 5 6–10: 7

moderate-severe pain scores in PACU) was 0.68 (95% confidence interval 0.56–0.80; $P=0.008$). The SPI with the highest combined sensitivity (76%) and specificity (62%) to predict moderate to severe pain in PACU was 40. A SPI>40 had a positive predictive value (PPV) for moderate-severe pain in PACU of only 42%, however, a SPI ≤40 had a relatively high (87.5%) negative predictive value (NPV) to exclude significant postoperative pain. The association between SPI and pain scores (all children combined) is shown in Figure 1. The cut-off value (≤50) for SPI used in the previously published trial about SPI guided anaesthesia in children[7] had in our cohort a sensitivity for moderate-severe pain of only 24% (specificity 85%).

The use of nitrous oxide did not significantly influence the area under the ROC curve. Though some children received a regional or neuraxial block, there were insufficient numbers to meaningfully calculate differences in SPI scores or ROC characteristics between children who did *vs* children who did not receive a block.

Investigating the three age groups separately, SPI at the end of surgery was found to be significantly higher if pain in PACU was moderate-severe in the younger age groups: two to three yr. SPI 47 (45–52) *vs* four to eight yr SPI 48 (48–60) *vs* nine to16 yr SPI 42 (29–51); $P=0.04$. In children with moderate-severe pain in PACU, there was a significant negative correlation between age and SPI (pearsons r: -0.43; $P=0.03$).

Table 2 displays the area under the ROC curve, the SPI cut-off with the highest sensitivity + specificity, and the corresponding PPV and NPV for each age group.

Discussion

The "best-fit" cut-off value for SPI to distinguish between no-mild *vs* moderate-severe pain in PACU was approx. 40, with slightly higher values in very young (two to three yr) *vs* older (nine to 16 yr) children. The SPI cut-off value utilized in previous studies (50) did not have any significant sensitivity or specificity for the prediction of moderate-severe pain in PACU. These results are very similar to the ones recently published for adult patients[8] ("best-fit" SPI 30) and underline concerns for the use of inappropriately high SPI target values (50) previously published for SPI guided anaesthesia studies in adult and paediatric cohorts. Though the uniform use of SPI 50 as target value in adult patients still resulted in a slightly beneficial[3 6 9] or at least neutral[10] outcomes in adult patients, its use in children produced a catastrophically bad outcome with significantly more postoperative agitation and fentanyl consumption.[7] The latter result cannot be seen as proof that SPI *per se* may fail in a paediatric population, with our current study, in line with our previous adult study, demonstrating associations between intraoperative stimuli, SPI and postoperative pain scores.[11] However, the fact that the previously published SPI target of 50 would have had neither any clinically relevant sensitivity nor specificity to predict the presence or absence of moderate-severe pain in PACU and the "best fit" SPI of 40 (all paediatric age groups) found by us strongly suggest that the target of 50 may have been too high. This appears even more true for older children as SPI values in the presence of acute postoperative pain showed a significant negative correlation with age. This is not surprising as it is long known that autonomic cardiac control (one of the main parameters within the SPI equation) is strongly influenced by age.[12]

Interestingly, and in contrast to a recent study in adults,[8] SPI values equal or below 40 had very high NPV for the absence of significant pain in PACU, however very low PPVs for the prediction of moderate-severe pain. In children it appears thus most useful to exclude significant postoperative pain. In a clinical context that means that only 6/48 (12.5%) children found to have no-mild pain (≤3 on the pain scales) on admission to PACU would have been under-treated with opioids, had the low SPI (≤40 as defined by us) been used to guide opioid administration towards the end of surgery. However, 26/45 children with high SPI scores (>40) indicating higher levels of postoperative pain (>3) would have been over-treated, despite their actual pain levels in PACU being low.

Though over-treatment with opioids is for obvious reason undesirable, it appears, at least in the view of the authors, to be less undesirable than under-treatment.

This study has some clear limitations: firstly, it was designed as a pilot study, with no formal sample size calculation performed. Secondly, the prevalence of no-mild *vs* moderate-severe pain on PACU admission was not identical between the three age groups, with less patients in significant pain in the four to eight yr old group. Though the distribution of pain scores across all children appears clinically acceptable, the lower prevalence of pain amongst four to eight yr old children may have affected the analysis of ROC, PPV and NPV data. As the assessment of pain in young children does naturally present a challenge, it is also conceivable that in some children post-arousal agitation may have confounded the rating of pain, and by this means the ROC analysis

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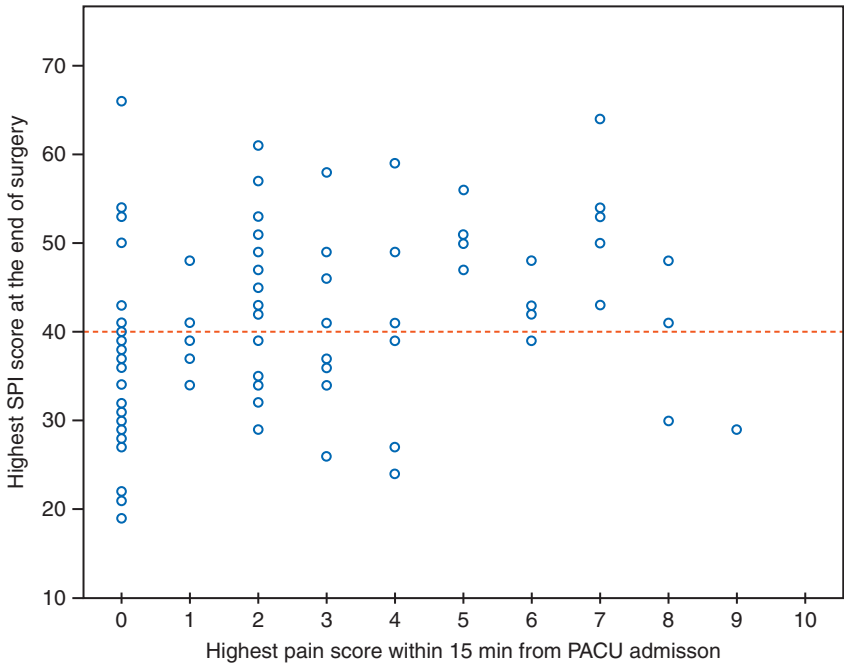

Fig 1 Highest Surgical Pleth Index (SPI) at the end of surgery and highest pain scores (0–10) in the postoperative acute care unit (PACU) in all children (two to16 yr.). The dotted line depicts the SPI cut-off value with the highest combined sensitivity and specificity to predict pain ≤3 *vs*>3.

Table 2 Area under the receiver operating curve (ROC AUC) for a cut-off value of SPI to predict moderate-severe pain during the first 15 min in the postoperative acute care unit (PACU), calculated "best fit" SPI cut-off (highest combined sensitivity + specificity), positive predictive value (PPV) and negative predictive value (NPV) of the SPI cut-off to predict/exclude moderate-severe pain in PACU

Age group	ROC AUC (95% confidence interval)	SPI cut off	Sensitivity/specificity%	PPV%	NPV%
All children	0.68 (0.56–0.80)	40	76/62	42	87.5
2–3 yr	0.83 (0.68–0.98)	40	100/73	60	100
4–8 yr	0.71 (0.48–0.95)	39	100%/52	19	91.7
9–16 yr	0.63 (0.43–0.83)	38	67%/70	50	75

of the value of SPI. Thirdly, the selection of children into three predefined groups may have somewhat hindered a more detailed analysis of the association between SPI and age. However, as three very different methods for the assessment of pain in the differently aged children are standard in our (and other) institutions, we felt that it was more robust to analyse the data separately.

In conclusion, SPI in children from two to16 yr was found to have a significant negative correlation with age, and SPI "best-fit" cut-off values were markedly lower than the target values used in previously published studies about SPI guided anaesthesia. Based on our results it appears likely that previously published studies may have used too high SPI targets. The latter may explain the published significantly worse outcome of children after SPI guided anaesthesia.[7]

Authors' contributions

Study design/planning: T.L., D.S., L.S., B.v.U.S.
Study conduct: D.S., L.S., J.C., B.v.U.S.
Data analysis: T.L.
Writing paper: T.L., D.S., L.S., B.v.U.S.
Revising paper: all authors

Declaration of interest

T.L. and B.v.U.S. have previously received speaker honoraria from GE Healthcare. However, GE Healthcare had neither influence on planning, data collection nor data analysis of this trial.

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