Type of the Paper (Systemic Review)

Excessive Variations in The Plethysmographic Waveform During Controlled Ventilation; An Important Pain Indicator

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Abstract:

Introduction: Despite advancements in anesthetics and operations, pain intensity following surgery has not significantly decreased over the past two decades, as shown by the surgical pleth index (SPI).

Aim of the study: To assess the efficacy of SPI as a predictor for immediate pain following the operation and the number of opioids required within the first two days after surgery, by measuring the surgical pleth index before the patient wakes up from general anesthesia.

Methods: We conducted a thorough search on Google Scholar, PubMed, Embase, and the Cochrane Library. The investigation utilized both text terms and medical subject headings, such as anesthesia, monitoring during surgery, pain after surgery, nociception, and pulse wave analysis. In addition, we conducted a thorough investigation on ClinicalTrials.gov and examined the references cited in selected materials and reviews to discover any more pertinent observational research.

Results & Conclusion: Before arousal, the values of action of the SNS, as assessed using the Skin Conductance Response, could serve as a predictor for both following surgery pain levels in the recovery room and the number of opioids consumed by patients who have undergone the operation. This thorough investigation can be utilized to measure pain after surgery individually, with the need for additional research on different anesthetic procedures. It also highlights the practicality of using the SPI to anticipate postoperative pain following the operation.

Keywords: Anesthesia; Nociception; Monitoring Intraoperative; Pulse Wave Analysis; Postoperative Pain.

1. Introduction

Severe acute pain following surgery is related to reduced case satisfaction, delayed ability to walk after surgery, the development of chronic pain after operation, and a higher occurrence of pulmonary adverse events [1, 2].

Despite attempts have been made to decrease pain following an operation, a significant number of cases (20-40%)

continue to suffer intense pain right following the operation [3]. distinguishing immediate pain following surgery from following surgery agitation and delirium might be challenging. Insufficient anti-nociceptive medication can result in excessive pain following surgery because of this misinformation, while overtreatment may contribute to respiratory suppression and hormonal, inflammatory, as well as immunologic imbalances [4, 5].

Thus, it is necessary to have comprehensive standardized and validated tools that can aid in regularly assessing and documenting pain severity for personalized evaluation of pain following surgery. The effectiveness of pain management after surgery protocols depends on their capacity to utilize proven best practices in the during-surgery setting, restore normal physiological functions, and enhance case engagement to enhance the process of healing [6].

The SPI is a method that uses 2 parameters to evaluate the photo-plethysmographic waveform and analyze the heart rate beat-to-beat [7].

The pre-arousal surgical pleth index score after the conclusion of general anesthesia exhibits a tenuous connection with acute pain following surgery in the recovery room [8].

We postulated that the surgical pleth index value may be utilized not only to predict acute pain following an operation but also to evaluate the quantity of opioids needed throughout the first forty-eight hours after surgery. Confirming that assumption could aid in the advancement of techniques for managing acute pain following an operation.

This systematic review aimed to assess the effectiveness of measuring the SPI before awakening from general anesthesia in predicting immediate pain after the procedure and the need for opioids in the forty-eight hours after the operation.

2. Methods

2.1. Search strategy

We performed a thorough search on Google Scholar, PubMed, Embase, and Cochrane Library. The investigation utilized both textual terms and medical subject titles, such as monitoring during operation, anesthesia, nociception, pain after surgery, and pulse wave analysis. In addition, we conducted a thorough search on ClinicalTrials.gov and examined the references cited in selected publications and reviews to discover more relevant observational research.

Inclusion criteria

Researchers were eligible if they met the inclusion criteria:

- Population: Adult individuals undergoing surgical procedures, irrespective of the specific method of operation.
- Intervention: the surgical pleth index levels before becoming alert at the final stage of the surgical procedure; The study aims to examine three specific outcomes: the severity of pain following surgery in the PACU, which will be determined by reliable methods such as the numeric rating scale (NRS); and observational investigations that provide data on true-positive (TP), false-positive (FP), false-negative (FN) and true-negative (TN) values.

Exclusion criteria:

- Non-surgical population.
- No outcomes available.
- Pediatric population.
- SPI values not available at the end of surgery.

2.2. Data extraction

Two researchers (KKT and HWH) conducted separate assessments of the titles and abstracts of all the papers generated to determine their relevance. We thoroughly examined each trial that was discovered and decided whether to include it or not. Researchers also independently extracted the data into a standardized data extraction form. The two reviewers established a consensus on decisions about the inclusion of research and data extraction. The 3rd researcher (JJS) would have the final authority to determine trial eligibility and extract data where discrepancies have been discovered.

3. Results

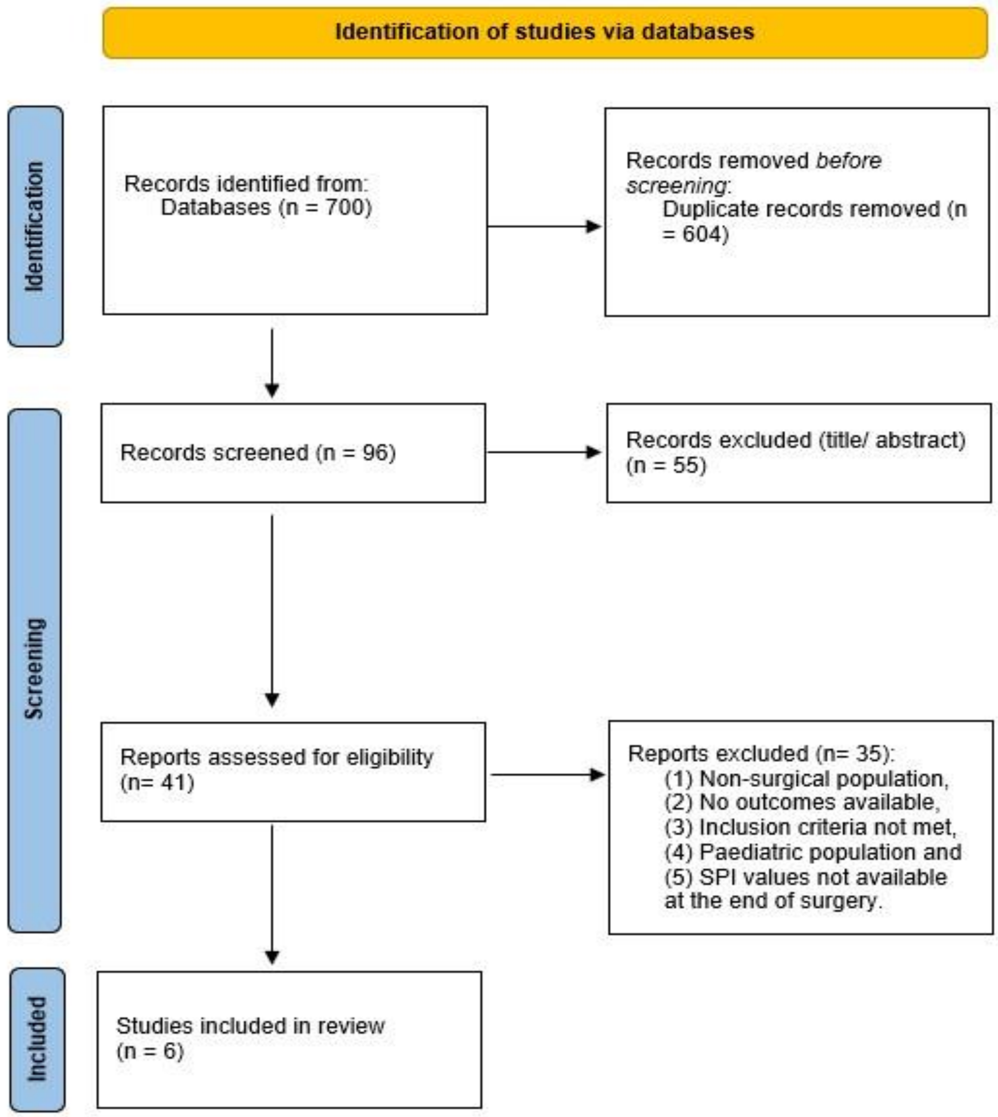

Figure 1. Flow chart for exclusion and inclusion of studies (9-13).

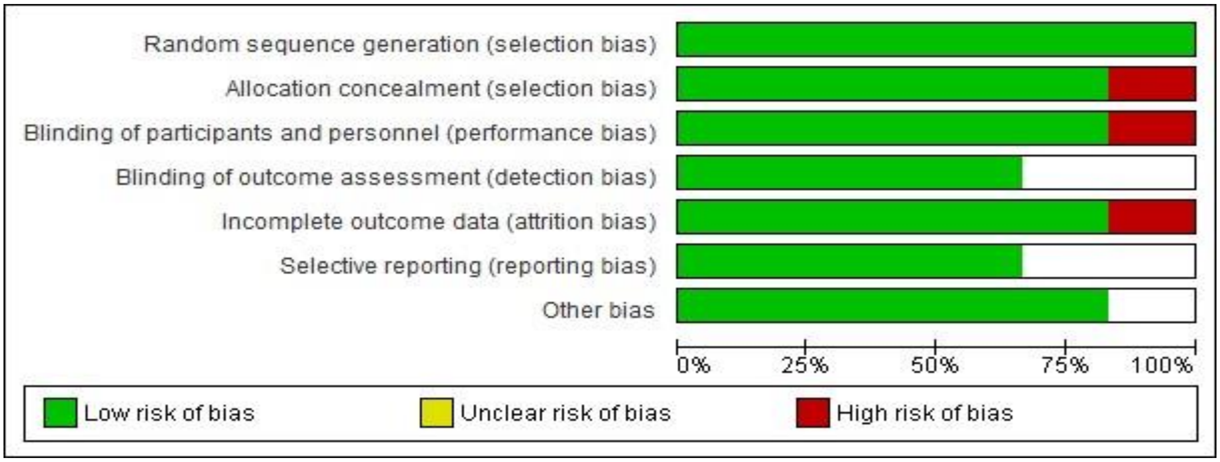

Figure 2. Risk of bias graph.

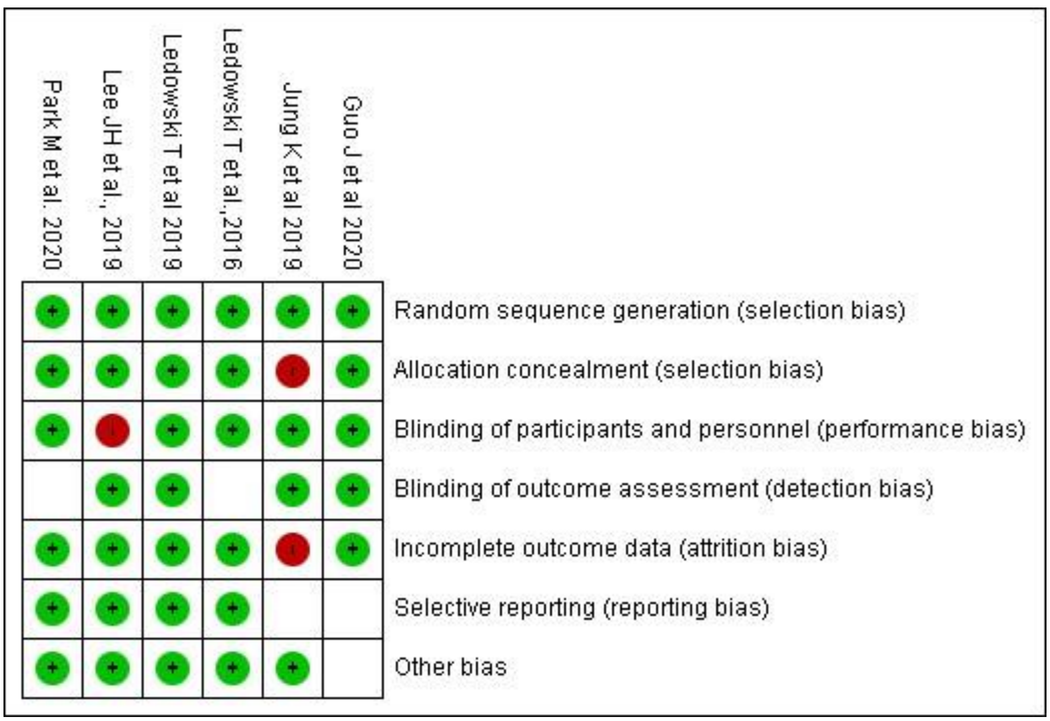

Figure 3. Risk of bias summary.

The investigative descriptions are shown in **Table 1**. The investigations were done prospectively and have been published throughout the time frame of 2016 to 2020. A group of 610 individuals, ranging in age from eighteen to eighty-seven years, were accepted for surgical procedures. All the studies included in the analysis had a greater number of female cases in comparison to male cases., except for one study [13]. The primary discoveries of the papers that were involved are elucidated in **Table 2**.

Table 1: The characteristics of the studied groups.

Authors	Country	Type of the study	Sample size	Age (year)	Sex
Ledowski et al., 2016 [8]	Australia	Observational study	65	43 ±15	Females: 46 Males: 19
Ledowski et al., 2019 [9]	Australia	Prospective trial study	196	18–87	Females: 84 Males: 112
Park et al., 2020 [10]	Korea	Prospective observational study	49	68 ±2	Females: 15 Males: 34
Lee et al., 2020 [11]	Korea	Observational study	192	54 ±12	Females: 108 Males: 84
Jung et al., 2020 [12]	Korea	Prospective observational study	46	20–80	Females: 14 Males: 32
Guo et al., 2021 [13]	China	Prospective, randomized and controlled study	62	18–65	Females: 35 Males: 27

Table 2: The main findings of the studied groups.

Authors	Type of surgery	Main findings
Ledowski et al., 2016 [8]	Patients underwent non-emergency surgery; the surgery has been conducted by general (n= 48), plastic (n= 5), orthopaedic (n= 2), and other (n= 10) surgical specialties.	An examination of the receiver operating characteristic curve showed that a surgical pleth index value of thirty during surgery is the best level for distinguishing among numerical rating scale scores of zero to three and four to ten. The positive and negative predictive values for distinguishing among numerical rating scale scores of zero to three and four to ten were 50% and 89.7%, respectively. Arousal had a substantial impact on the SPI, and the SPI scores acquired during this period did not serve as a reliable predictor of pain following surgery.
Ledowski et al., 2019 [9]	Patients underwent non-emergency surgery; the operations have been done by general (n= 77), plastic (n= 38), orthopaedic (n= 40), urology (n= 11), and other (n= 30) surgical specialties.	The examination of the receiver-operating curve demonstrated that a surgical pleth index value of 29 is the most effective threshold during surgery to differentiate between NRS 0e3 and 4e10. This validates the previously disclosed 'best fit' threshold for SPI. While the SPI was still better than HR and MAP, its specificity and sensitivity were only low. The prediction accuracy of the surgical pleth index was not affected by age.
Park et al., 2020 [10]	Patients underwent laparotomy or laparoscopic liver resection.	A ROC curve has been utilized to assess the accuracy of SPI in predicting NRS≥5. The surgical pleth index value showed a strong correlation with the greatest pain score in the recovery room (r=0.63, p <0.001). A post hoc analysis defined a surgical pleth index value of 60 as the cut-off for moderate-severe pain (NRS≥5), which demonstrated the greatest sensitivity and specificity. When comparing cases with a surgical pleth index value above sixty to those without, there was a significant variance in the amount of fentanyl consumed over the forty-eight hours after surgery (1093 ±406 µg vs. 766 ±369 µg, p =0.014; SPI≥60 vs. SPI<60). The pre-arousal surgical pleth index measurement during inhalation anesthesia is correlated with both immediate pains following surgery levels and the number of opioids consumed following surgery.
Lee et al., 2020 [11]	Patients after elective	The surgical pleth index value results

	surgery (thyroid, breast, or abdominal).	exhibited a significant variation between conscious cases who did not experience pain (NRS=0) and those who did (NRS>0). The receiver operating curves for the surgical pleth index have an area of 0.73, p <0.0001. The cut-off values for the surgical pleth index for pain prediction after surgery have been determined to be 44, with a sensitivity of 84% and specificity of 53%. These values differ from the recommendations provided by the manufacturers for usage during general anesthesia in the surgery condition.
Jung et al., 2020 [12]	Patients underwent laparotomy	The average of the highest surgical pleth index values recorded throughout the surgical incision was 56 ±12 and a range of 26-85. The investigation involved cases who had a surgical pleth index >50 (Group H) or between 20-50 (Group L). There significant variance was observed in the Numeric Rating Scale scores between both groups throughout their recovery room stay and 24 hours after surgery (5 [5, 6] versus 7 [6, 8], for Group L (p =0.007) and 3.5 [3, 5] versus 5 [5,6], for Group H (p =0.006)). Group H administered a greater amount of fentanyl by patient-controlled analgesia in the 24 hours following surgery (573 (253) µg versus 817 (305) µg, p =0.008). The pre-incision and post-incision surgical pleth index values that had the best sensitivity (67%) and specificity (68%) were retrospectively determined to be the threshold for fentanyl use throughout the 24 hours following surgery, with a value of ≥1000 µg.

Guo et al., 2021 [13]	Patients after laparoscopic cholecystectomy	Out of the initial eighty cases, a total of eighteen withdrew from the study due to different reasons. Consequently, the data from the final 62 cases were finally evaluated. The amount of fentanyl used during surgery was significantly less in the surgical pleth index group in comparison to the control group (177.1 ±65.9 vs. 213.5 ±47.5, $p = 0.016$). The duration of extubating after surgery was shorter in the surgical pleth index group compared to the control group (16.1 ±5.2 vs. 22.1 ±6.3, $p < 0.001$). The before-surgery and following-surgery levels of plasma cortisol, and IL-6, blood glucose, as well as during-surgery alterations in hemodynamics, post-surgery VAS scores, remedial analgesic use, and complication of opioids, were similar in both groups.

4. Discussion

The SPI, developed by GE Healthcare in Helsinki, Finland, is a standardized measure obtained by the examination of the pulse wave and heartbeat interval using photoplethysmography [14]. While it is challenging to establish a definitive standard for evaluating pain perception, intraoperative surgical pleth index scores were found to reasonably reflect various surgery and non-surgery stimuli and varying levels of activation in the autonomous nervous system [15, 16].

In recent times, several researchers have examined the results of anesthesia guided by surgical pleth index [8-9]. Nevertheless, although several writers have shown advantages such as expedited healing, others have observed an increased incidence of following surgery agitation and higher levels of pain with surgical pleth index guidance [17]. Unfortunately, the surgical pleth index cut-off values utilized to direct anesthesia procedures in prior investigations seem to have been established with minimal evidence [8].

The study revealed a significant correlation between the surgical pleth index value measured before arousal on BIS<60 and the severity of pain following surgery experienced in the recovery room. A surgical pleth index value of Sixty had a negative predictive value of 63% for NRS≥5 while exhibiting a significantly elevated positive predictive value of 92%. Furthermore, cases with an SPI≥60 exhibited a higher consumption of postoperative opioids within the first forty-eight hours after surgery [9]. Due to the subjective nature of pain, its measurement poses a significant challenge. However, it is crucial to try to quantify it. Currently, no widely accepted and well-tested monitoring tool is considered the most accurate and reliable for assessing the balance between antinociception and nociception during the period following operation. The traditional methods employed for evaluating pain after surgery, such as the Numeric Rating Scale, lack objectivity [18]. Recently, researchers have been using surgical pleth index monitoring as a method for evaluating pain following surgery.

The surgical pleth index values exhibited a modest to moderate association with pain following surgery in conscious cases [19, 20]. During the emerging stage, it is usual to face anesthetic medications, agitation, anxiety, and noise, all of which have been found to elevate sympathetic activity [9].

A prior systematic review and meta-analysis examined the efficacy of surgical plenty-index-guided analgesia in general anesthesia [21]. The findings indicated that SPI-guided analgesia, when in comparison to conventional analgesia, can decrease the number of opioids used during surgery and assist in the process of extubating.

In another detailed meta-analysis and review, it was shown that cases with moderate to severe pain had elevated levels of surgical pleth index compared to those without pain [22]. The pooled data showed a mean variance of 7.82 (95% CI: 3.69 to 11.95, $p = 0.002$, I2 = 46%). Furthermore, a higher Surgical Pain Index after the operation was found to accurately predict the occurrence of moderate-to-severe pain, with a sensitivity of 0.71 (95% CI: 0.65–0.77; I2 = 29.01%) and a specificity of 0.58 (95% CI: 0.39– 0.74; I2 = 79.31%). The accuracy, as determined by the summary receiver operating characteristic (sROC) curve, was 0.72.

5. Conclusion

Consequently, this systematic review determined that pre-arousal surgical plenty-index values can be used to predict pain after an operation level in the recovery room and the number of opioids consumed by patients who have undergone operations. This systematic review can be utilized to evaluate pain following surgery individually, with the need for additional research on different anesthetic procedures. It emphasizes the practicality of using the SPI to anticipate surgery discomfort following the operation.

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