Evaluation of perfusion index as an objective tool to assess analgesia during laparoscopic surgeries under general anaesthesia

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ABSTRACT

Background and Aims: Changes in the sympathetic nervous system by pain can impact smooth muscle tone and can alter perfusion. This can be monitored by perfusion index (PI). It is a non-invasive, indirect, and continuous measure of peripheral perfusion. This study investigates the changes in PI due to painful stimuli under general anaesthesia. Methods: Twenty patients between the ages of 20 and 45 years, with informed consent, who were undergoing elective laparoscopic procedure, and belonging to the American Society of Anesthesiologists (ASA) physical status class I were connected with standard monitors along with SEDLINE, pulse oximetry (Root, Masimo Corporation®, Irvine, CA, USA) to monitor PI and Pleth-Variability Index (PVi). General anaesthesia was administered. PI, PVi, heart rate (HR), and non-invasive blood pressure were recorded pre-induction, during induction, before and after intubation, at the time of pneumoperitoneum (P0), and first laparoscopic port insertion (P1). Later, intravenous injection of fentanyl 0.5 µg/kg was administered and values were recorded at the second (P2) and third (P3) port insertion. The aforementioned parameters were recorded for up to 30 minutes. Statistical confirmation was done through paired t-tests. Results: PI values after fentanyl increased from 5.33 ± 2.67 (P1) to 5.99 ± 2.8 (P2) (P < 0.001), and to 6.3 ± 2.88 (P3) (P < 0.001). This increase correlated with a decrease in HR, from 101.42 ± 12.53 (P1) to 87.93 ± 10.98 (P2) (P < 0.001), and to 83 ± 10.82 (P3) (P < 0.001). Conclusion: PI can be a tool to monitor the nociception in anaesthetised patients when administering analgesia.

Key words: Analgesia, nociception, perfusion index, plethysmography

INTRODUCTION

Anaesthesia is a state of analgesia, unconsciousness, and muscle paralysis.[1] Quantification of nociception under anaesthesia is difficult, and therefore, reaction to nociception is used for monitoring it through increased sympathetic activity or the corresponding decreased parasympathetic stimulation (i.e., increased heart rate (HR)).[2]

Perfusion index (PI) is a non-invasive and continuous measure of peripheral perfusion.[3] The changes in sympathetic tone affect smooth muscle tone and can alter the perfusion, but are not affected by saturation and HR variability.[4]

Limited literature is available on the correlation between PI and intraoperative nociception under general anaesthesia. In this study, we aimed at investigating the changes in PI corresponding to painful stimuli under general anaesthesia.

METHODS

This prospective, non-randomised, single-blind study was conducted from April to June 2021.
in a general hospital after institutional ethics committee approval and Clinical Trials Registry-India registration [CTRI/2021/04/033195]. Twenty patients of either sex, aged 20–45 years, belonging to the American Society of Anesthesiologists (ASA) class I, and scheduled for laparoscopic cholecystectomy were included. Patient refusal, those with neurological or psychiatric illness, chronic pain disorder, peripheral vascular disease, hypertension, diabetes mellitus, ischaemic heart disease, autonomic dysfunction or on drugs which affect autonomic dysfunction, allergy to any drug used in the study, and unstable haemodynamic status were excluded.

The primary outcome of the study was to compare the change in PI to pain stimulus (laparoscopic port insertion) and its variability to subsequent pain stimulus after intravenous (IV) administration of 0.5 µg/kg injection of fentanyl. The secondary outcome was to compare PI with haemodynamic parameters such as HR and mean arterial pressure (MAP).

The sample size was calculated using the standard deviation of PI as 0.9, which was obtained from results by Mohamed et al. With a significance level of 5% and power of 80%, the sample size was calculated to be 14. Adding a safety factor to account for drop-offs, 20 participants were considered for this study.

On the day of surgery, all the monitors were attached: an electrocardiogram, non-invasive blood pressure (NIBP) monitor, and SedLine pulse oximetry (Root, Masimo Corporation®, Irvine, CA, USA) was placed on the index finger contralateral to the side of the blood pressure cuff. Pre-induction values of PI, Pleth-Variability Index (PVi), HR, NIBP, and MAP were noted. Observations were single-blinded to eliminate bias at the observer level.

Premedication was done with 0.05 mg/kg of injection midazolam, 0.004 mg/kg of injection glycopyrrolate and 2 µg/kg of injection fentanyl intravenously, and induction with injection propofol at 2 mg/kg, along with muscle relaxation using injection vecuronium 0.1 mg/kg given intravenously. PI, PVi, HR, NIBP, and MAP were noted soon after induction. Endotracheal intubation was confirmed with capnography and a nasopharyngeal temperature probe was applied. The patient was ventilated with a tidal volume of 6–8 ml/kg, and the ventilatory rate was adjusted to maintain end-tidal carbon dioxide (ETCO₂) between 35 and 40 mmHg. Injection paracetamol 15 mg/kg IV was given post-intubation over 15 minutes. Anaesthesia was maintained with isoflurane and top-up doses of injection vecuronium (0.05 mg/kg). The intraoperative MAP was maintained between 60–65 mmHg, and patient state index (PSI) was maintained between 35–50. The thermoneutrality was maintained by keeping the room temperature at 25°C and by providing a warming mattress and warmed IV fluids.

PI, PVi, HR, NIBP, and MAP were noted before intubation, after intubation, and at the time of pneumoperitoneum (P0). Later, the values were recorded at the time of insertion of the first laparoscopic port (P1), following which a 0.5 µg/kg injection of fentanyl IV was administered, and the values were recorded at the time of insertion of second (P2) and third (P3) laparoscopic port. After the insertion of the third laparoscopic port, the PI, PVi, HR values were recorded every minute up to 10 minutes and later every five minutes until 30 minutes of surgery. However, the NIBP and MAP values were recorded every five minutes until 30 minutes of surgery. The residual neuromuscular blockade was reversed at the end of surgery by using an injection of neostigmine 0.05–0.07 mg/kg and an injection of glycopyrrolate 0.05 mg/kg.

All values observed were on the continuous scale. Since each value was repeated several times for the same patient before administration of anaesthesia, pairs of values were taken and tested for statistical significance in their difference. The null hypothesis was that the difference between these pairs of values was 0, and a 95% confidence interval (CI) was used to determine deviation from the null hypothesis. Paired t test calculations were conducted using data analysis tool in Microsoft Excel (version 15.12.3 ©2015 Microsoft). Pearson’s correlation coefficients were also computed when comparing PI to MAP and HR using the correlation function in Microsoft Excel.

**RESULTS**

A total of 20 patients were enrolled for the study out of which twelve were females and eight were males with a mean age of 36.5 ± 8.3 years, and all participants who enrolled completed the study. All tests were conducted with a degree of freedom 19 and a confidence level of 95%. PI values after administering fentanyl between P1 and P2 increased from 5.33 ± 2.67 to 5.99 ± 2.8 with a P value less than 0.001 [Table 1]. Similarly, these values saw a significant increase between P1 and P3, with P3 at 6.3 ± 2.88 (P < 0.001) [Table 1]. The
heart rate (HR) decreased from 101.42 ± 12.53 at P1 to 87.93 ± 10.98 at P2 \((P < 0.001)\), and to 83 ± 10.8 at P3 \((P < 0.001)\) [Table 1], whereas the changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), and MAP were not significant [Tables 2 and 3]. A Pearson’s correlation \((r)\) test was also run on the difference in PI, HR, and MAP values between P2 and P1, and P3 and P1 [Table 4]. The increase in PI values between both these port insertions correlated to the decrease in HR and MAP and was found to be statistically significant \((r = -0.734, P < 0.001)\) [Figures 1 and 2].

**DISCUSSION**

PI is the ratio of pulsatile blood flow to non-pulsatile blood flow in a person’s peripheral tissue such as finger tip or ear lobes. The finger photoplethysmographic waveform relies on red and infrared light absorption which includes two components. The first component is the constant amount of light, which is absorbed by the skin, bone, tissue, pigment, and non-pulsatile blood.\(^6\) The second component is said to be a variable amount of light. It is measured by pulsatile arterial blood flow. For PI calculation, the infrared pulsatile signal is indexed against the non-pulsatile infrared signal and expressed as a percentage.\(^7\) It ranges from 0.02% (very weak pulse strength) to 20% (very strong pulse strength).\(^8\)

Pain induces vasoconstriction due to sympathetic stimulation which also results in a decrease in PI.\(^9\) This direct relation between pain and sympathetic nervous stimulation raises the hypothesis that PI can be used as a tool for pain assessment.\(^10\)

Lee et al.\(^{11}\) reported that parameters derived from finger photoplethysmography appear to be suitable for monitoring autonomic nervous system activation. Tapar et al.\(^{12}\) evaluated the usefulness of PI values for assessing postoperative pain and responses to analgesics in the recovery room. Taking the conclusions from Lee et al.\(^{11}\) and Tapar et al.,\(^{12}\) this study was designed to assess the changes in PI response to painful stimuli in patients under general anaesthesia. To achieve this, laparoscopic cholecystectomy surgeries were chosen with the piercing of the abdominal wall to insert a port as the painful stimulus. P2 and P3 showed lower values of PI compared to P1. The analgesic effect of fentanyl blunted the painful stimuli to the subsequent port insertion which was reflected in the decrease in PI value and this decrease was statistically significant.

The findings of our study could be further confirmed by the findings of another study in which it was concluded that the PI may be of clinical value.

### Table 1: Haemodynamic changes (Mean±SD)

| Time of Reading | PI      | PVi     | HR         |
|----------------|---------|---------|------------|
| Pre-induction  | 5.71±2.62| 15.53±5.41| 106.27±15.21|
| Induction      | 6.49±2.32| 15.57±4.74| 90.44±14.81  |
| Before intubation| 6.63±2.34| 17.66±5.99| 89.65±13.56  |
| After intubation| 6.36±1.74| 15.68±5.13| 104.85±14.78 |
| P0             | 5.04±2.59| 20.75±7.42| 101.59±12.98 |
| P1             | 5.33±2.67| 23.74±7.12| 101.42±12.53 |
| P2             | 5.99±2.82| 23.32±4.1 | 87.93±10.98  |
| P3             | 6.3±2.88 | 24.69±7.32| 83±10.82    |
| 1 min          | 5.54±3.57| 20.36±8.04| 84.64±13.54 |
| 2 min          | 5.69±3.58| 26.48±15.89| 85.43±11.88 |
| 3 min          | 5.15±3.24| 21.14±7.21| 89.24±15.4  |
| 4 min          | 5.99±3.1 | 19.98±6.72| 91.06±16.87 |
| 5 min          | 5.71±3.18| 19.25±7.81| 91.42±14.89 |
| 6 min          | 5.79±3.01| 18.85±7.95| 94±16.29    |
| 7 min          | 5.78±2.92| 19.98±7.85| 93.34±11.74 |
| 8 min          | 5.75±2.65| 19.56±7.25| 95.28±12.72 |
| 9 min          | 5.66±2.54| 19.78±5.85| 93.64±11.74 |
| 10 min         | 5.89±2.53| 20.01±5.57| 95.84±12.21 |
| 15 min         | 5.89±2.31| 19.14±7.64| 95.58±10.15 |
| 20 min         | 5.98±1.99| 20.71±7.2 | 94.58±9.58  |
| 25 min         | 6.02±2.2 | 19.26±7.17| 92.24±8.22  |
| 30 min         | 6.26±2.19| 18.34±7.28| 94.69±11.41 |

Data expressed as Mean±Standard Deviation; PI=Perfusion Index; PVi=Pleth-Variability Index; HR=Heart Rate measured per minute; SD=Standard Deviation

**Figure 1:** Changes in PI in comparison to heart rate at various time points. PI = Perfusion Index; HR = Heart Rate measured per minute

**Figure 2:** Changes in PI in comparison to MAP at various time points. PI = Perfusion Index; MAP = Mean Arterial Pressure measured as mmHg
in assessing pain in the anaesthetised state by applying electrical current to the anterior thigh in two healthy individuals anaesthetised with propofol and maintained with sevoflurane at different concentrations (1%, 1.5%, 2%, 2.5%). The painful stimulus produced an increase in HR and MAP with a decrease in PI. In a study on 50 children scheduled for inguinal herniorrhaphy, anaesthesia was induced with nitrous oxide-oxygen-sevoflurane via mask and four Masimo SET radical pulse oximeters were attached, one on each limb. Patients received a one-shot lumbar epidural block with 0.2% ropivacaine (0.7 ml/kg). Four minutes after receiving the lumbar epidural injection shot, the PI values of both lower limbs of the patients were significantly increased compared to upper limbs. The patients who had symptoms of a failed epidural block showed a lower average PI of the lower limbs and concluded that PI was a useful tool to evaluate the effect of epidural block and that also showed the effect of analgesia on PI in anaesthetised patients. In the present study, there was a significant increase in PI and decrease in HR, but not a significant decrease in MAP after administration of analgesia. The increase in PI correlated with a decrease in HR and MAP post-administration of analgesia.

In a prospective observational study on 87 sedated, non-intubated patients in a surgical intensive care unit, it was concluded that the application of a painful stimulus was associated with a decreased PI. Additionally, arterial blood pressure, HR, Richmond Agitation-Sedation Scale (RASS), and Behavioural Pain Scale for Non-Intubated (BPS-NI) values before and after the application of a standard painful stimulus (changing the patient position) were recorded in this study. The authors reported that changing the patient’s position resulted in a significant increase in SBP, DBP, HR, and BPS-NI values and good correlation was found between the change in the PI and the change in BPS-NI values after the application of a painful stimulus. In the current study, there was a good correlation between the increase in PI and decrease in HR after administration of IV injection of fentanyl.

The literature available on the effects of painful stimulus on the PI under general anaesthesia is limited. But there are studies that have proven that there is an increase in PI after administration of analgesia in the post-operative care unit. One such study was conducted on 70 ASA class I patients who underwent lumbar discectomy, in a post-operative room with Masimo pulse oximetry connected. At the time of the first request for analgesia (T1), visual analogue scale (VAS), PI, HR, MAP, peripheral oxygen saturation, and axillary temperature were noted, following which analgesia was given. Thirty minutes thereafter (T2), second measurements were taken. The PI was significantly higher at T2 than at T1, and this increase was associated with a statistically significant increase in VAS, HR, MAP, leading to a conclusion that PI can be added to other indicators of pain assessment in the post-analgesia care unit. Similar results were reported in a study on 80 patients in the postoperative anaesthesia care unit. HR, MAP, VAS, and PI were recorded at the baseline and post-administration of IV

### Table 2: Haemodynamic changes (Mean±SD)

| Time of Reading | MAP | SBP | DBP |
|-----------------|-----|-----|-----|
| Before induction | 84.95±10.67 | 116.7±13.08 | 68.9±10.73 |
| Induction       | 85.23±9.86  | 118.3±14.74  | 68.8±8.28  |
| After intubation| 84.2±14.55  | 109.05±18.3  | 71.7±12.99 |
| P0              | 86.35±13.29 | 113.65±14.53 | 72.55±13.79 |
| P1              | 85.5±16.7   | 116.95±15.09 | 69.8±19.28 |
| P2              | 86.5±9.86   | 115.5±13.53  | 72.1±9.1   |
| P3              | 83±10.72    | 106.3±13.07  | 71.4±9.97  |
| 5 min           | 83.9±11.14  | 112.55±13.21 | 69.65±11.07 |
| 10 min          | 87.05±11.59 | 115.35±13.29 | 72±11.7   |
| 15 min          | 85.4±13.41  | 115.4±15.21  | 70.15±13.13 |
| 20 min          | 88.35±10.99 | 118.15±13.85 | 73.5±10.33 |
| 25 min          | 86.95±11.43 | 118.4±14.01  | 71.25±11.06 |
| 30 min          | 87.2±11.32  | 118.85±14.75 | 72.95±10.94 |

Data expressed as Mean±Standard Deviation; MAP=Mean Arterial Pressure measured as mmHg; SBP=Systolic Blood Pressure measured as mmHg; DBP=Diastolic Blood Pressure measured as mmHg; SD=Standard deviation

### Table 3: P values from paired t test

|       | P1 vs P2* | P1 vs P3* |
|-------|-----------|-----------|
| PVI   | 0.37      | 0.29      |
| SBP   | 0.18      | <0.001    |
| DBP   | 0.23      | 0.29      |
| MAP   | 0.35      | 0.14      |

*: P<0.05; Not Significant, degree of freedom=19; Confidence level=95%; MAP=Mean Arterial Pressure; SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; PVI=Pleth-Variability Index; P1=First Laparoscopic Port Insertion; P2=Second Laparoscopic Port Insertion; P3=Third Laparoscopic Port Insertion; P value=Probability value

### Table 4: Correlation between change in PI with change in heart rate and mean arterial pressure before and after administration of intravenous injection Fentanyl 0.5 μg/kg

|               | ΔPI vs ΔHR | ΔPI vs ΔMAP |
|---------------|------------|-------------|
| ΔPI vs ΔHR    |            |             |
| Pearson Correlation | -0.30      | -0.734      |
| n (sample size) | 20         | 20          |
| Degree of freedom | 19         | 19          |
| t-stat         | 1.586      | 4.585       |
| P-value        | <0.001     | 0.084       |

ΔHR=Difference in Heart Rate measured per minute; ΔPI=Difference in Perfusion Index; ΔMAP=Difference in Mean Arterial Pressure measured as mmHg

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In the current study, there was a good correlation between the increase in PI and decrease in HR after administration of IV injection of fentanyl.
injection of 3 mg morphine at 10-, 20- and 30-minute intervals. It was observed that there was an increase in PI post administration of analgesia and a weak correlation with the VAS score. It was concluded that a 12% increase in PI can be used as a discharge criterion in postoperative anaesthesia care units. Such an increase in PI to analgesia was observed post administration of 0.5 µg/kg IV injection of fentanyl. This was supported by a significant decrease in HR, and these changes in PI had a correlation with HR.

Further studies done with regional anaesthesia showed that an increase in PI from baseline proved the onset of epidural action. One such study investigated the relationship between labour pain level and PI in 30 women undergoing spontaneous vaginal delivery under epidural analgesia. It was noticed in the study that upon activation of the epidural blockade with 10 mL of 0.25% bupivacaine, the PI increased. Also, a gradual decrease in PI with a fade of epidural analgesia was noted. Similar results were obtained in a study where a PI monitor was applied to the limb to which the supraclavicular block was given with a local anaesthetic, and there was an increase in PI following the block compared to the baseline and the PI in the blocked limb was higher compared to the unblocked limb. This showed that PI was a useful tool for the evaluation of a successful supraclavicular nerve block.

In the above mentioned studies, there was a significant correlation between increased PI and decrease in HR, MAP, VAS, SBP, and DBP post administration of analgesia and vice-versa on painful stimulus, and in our study, the increase in PI and decrease in HR post-administration of analgesia was significant \( (P < 0.001) \). The decrease in SBP, DBP, MAP was not statistically significant \( (P > 0.05) \) post administration of analgesia, unlike other studies.

In a study conducted on 65 patients undergoing upper limb surgery under ultrasound-guided supraclavicular block, it was found that the increase in PI from baseline at subsequent time intervals was high in a successful block compared to a minimal change in PI in a failed block, indicating the ability of PI to assess the painful stimulus.

One limitation of this study is that with the use of several exclusion criteria, there is a limited utility in using ASA grade I or II cases with surgeries that do not involve fluid shifts since it becomes a confounding factor. Another limitation is the small sample size of the study. A larger sample size may provide more evidence to support the preliminary results found here.

**CONCLUSION**

From the conducted study, it was found that the change in PI could be a surrogate monitoring tool to determine the nociception intraoperatively after excluding the confounding factors in relatively fit (ASA physical status class I and II) surgical patients.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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