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RESEARCH ARTICLE

Pulse-oximetry Derived Perfusion Index as a Predictor of the Efficacy of Rescue Analgesia After Major Abdominal Surgeries

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Abstract:

Study Objective:

The use of an easy to apply reliable tool is essential to assess pain in patients in intensive care units. This study aimed primarily to evaluate perfusion index usefulness as an objective indicator of pain.

Methods and Measurements:

Data were collected from 40 non-intubated adult patients admitted to the surgical intensive care unit postoperatively. The Masimo pulse co-oximetry perfusion index (PI) probe was attached to the patient. At the time of the first request for analgesia (T1), the Behavioural pain scale non-intubated scoring system (BPS-NI) was recorded with the PI and patients' haemodynamics following which rescue analgesia was given. Thirty minutes thereafter (T2), second measurements for the mentioned parameters were taken.

Main Results:

There was a statistically significant reduction in the BPS-NI score, blood pressure and heart rate after analgesic administration (P-values, <0.001, 0.039 and 0.001, respectively), together with a significant increase in the PI (P-value, 0.004). This means that the PI increases with adequate relief from pain, as indicated by a decrease in BPS-NI score and haemodynamics, but the correlation was not statistically significant between their changes.

Conclusion:

There was no statistically significant correlation between the PI and the pain score or other clinical indicators of pain either before or after the administration of analgesic.

Keywords: Behavioural pain scale non-intubated, Major abdominal surgery, Masimo, Perfusion index, Postoperative pain, Pulse oximetry.

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1. INTRODUCTION

In the Intensive care unit (ICU), pain is usually underestimated due to the difficulty of its assessment in critically ill patients. It can evolve from many sources, for *e.g.*, postoperative surgical incisions, penetrating chest tubes, and even ICU procedures as bedside debridement. It was shown that alleviating pain effectively in both intubated and non-intubated ICU patients has been associated with improved outcomes [1]. Scales such as the Visual analogue scale (VAS) and numeric rating scale (NRS) are used to assess pain intensity postoperatively. In order to use these scales, patients need to be able to understand what is said to them and express themselves. But this cannot be carried out for individuals with communication problems [2]. Also, the use of haemodynamic changes has been demonstrated to be neither valid nor reliable as it is affected by many other aetiologies, and guidelines recommend that vital signs should not be used to evaluate pain in ICU patients [3]. This phenomenon has led to the construction of categorical and numerical methods of pain assessment in critically ill patients. The behavioural pain scale (BPS) -whether intubated or non-intubated forms- has been reported as a valid and reliable tool for pain assessment in ICU patients with recommendations of its use to assess the presence

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of pain in adult ICU patients when self-reporting is not possible [4]. But unfortunately, the use of Behavioural pain scale non-intubated scoring system (BPS-NI) scale requires sustained efforts to educate and train the ICU team regarding the scale because of its subjective nature [5]. Also, BPS-NI is time-consuming with multiple points of assessment, making it non-practical [6]. The need for simple, non-invasive, rapid, and objective tools for pain evaluation represents a present gap in the literature. The Masimo device could be a promising indirect tool for pain assessment. The Masimo set pulse oximetry system can measure the perfusion index (PI) at the monitored site by calculating the relation between pulsatile and static blood in peripheral tissues. In contrast to the conventional pulse oximeter which measures O2 saturation, Masimo Signal Extraction Technology depends upon the amount of blood at the monitoring site, not upon blood oxygenation. Therefore, PI is considered as an indirect, non-invasive, and continuous measure of peripheral perfusion. It ranges from 0.02% (very weak pulse strength) to 20% (very strong pulse strength) [7]. Pain induces vasoconstriction due to sympathetic nervous system stimulation with a subsequent decrease in PI [8]. This direct relation between pain and sympathetic stimulation raises the hypothesis that the PI can be used as an indirect objective tool for pain assessment. The current study aimed primarily to evaluate the correlation between perfusion index and other clinical indicators of pain after rescue analgesia administration and so detecting its usefulness as an objective indicator of pain assessment in ICU.

2. METHODS AND MEASUREMENTS

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The work was approved by the Ethics committee of Ain Shams University hospital (FMASU R 05/ 2019) on 23/1/2019. The study was prospectively registered with Pan African Clinical Trial Registry (PACTR) with Registration Number PACTR201901839969911 in accordance with WHO and ICMJE standards. Written informed consent was obtained from all subjects or their legal surrogate.

This is a prospective observational study that was conducted in Ain Shams university hospital intensive care unit through the period from January 2019 to October 2019. The study comprised 40 patients. Eligibility criteria for this study included patients with American Society of Anaesthesiologists (ASA) physical status I to III, of either sex, 18-80 years of age, non-sedated non-intubated patients that were admitted postoperatively to ICU after major abdominal surgery. We categorized the participants into two “age groups” according to age: an elderly group (> 60 years) and a young group (< 60 years). Then we further classified each “age group” into a male group and a female group. Now we had a total of 4 groups: an elderly male group (> 60 years) = OM group, an elderly female group (> 60 years) = OF group, a young male group (< 60 years) = YM group and a young female group (< 60 years) = YF group. Exclusion criteria involved patients with fever, hypothermia, history of a neurological, psychiatric, dementia or chronic pain disorder. Patients with unstable haemodynamic status and unconscious patients were also excluded. Patients who had combined general epidural anaesthesia or Transversus abdominis plane block were also excluded.

2.1. Patients’ Postoperative Interventions and Management

After extubation and full recovery, patients were admitted to ICU. Standard monitors were applied: an Electrocardiogram, pulse oximeter, and non-invasive arterial blood pressure monitor, and all baseline readings were recorded. All patients received nasal oxygen (4 L/min). The oximeter probe (Radical-7®, Masimo Corporation, Irvine, CA, USA) used to monitor the PI was attached to the middle fingertip of the hand and was wrapped in a towel to decrease heat loss. The patients were kept warm with wool blankets, warm i.v. fluids, and a warm air-forced device. All patients were observed until they asked for rescue analgesia. Sedation was assessed by Richmond agitation-sedation scale score (RASS) that was recorded at specific timings: on arrival to ICU, and after 1 and 2 hours from arrival to ICU [9]. The RASS is a 10- point validated sedation scale with 4 levels for agitation, 5 levels for sedation, and 1 level for calm, awake patients. The scale’s anchor is centered at 0 (alert and calm) [9]. Our intensive care unit analgesia protocol in general is 1 g i.v. paracetamol repeated every 6 h and 5 mg Nalbuphine increments upon patients’ request or if Behavioural pain scale non-intubated scoring system (BPS-NI) ≥ to 5, to whatever 1st occurred. Pain assessment in this study was achieved by Behavioural pain scale non-intubated scoring system [6]. The BPS-NI evaluates three behavioural domains (*i.e.*, facial expression, movements of upper limbs and vocalization). Each domain contains four descriptors that are rated on a 1–4 scale, and the total BPS value can range from 3 (no pain) to 12 (most pain). The procedure for using the BPS is estimated to take minimal time (2–5 minutes). Because each domain of the BPS-NI contains four descriptors, it has the advantage of avoiding a possible observer bias that is described as when an observer rates preferentially the middle item of a three-point scale [6]. At the time of the first request for analgesia (T1), Behavioural pain scale non-intubated scoring system (BPS-NI) was recorded together with the PI, heart rate (HR), mean arterial blood pressure (MAP), peripheral oxygen saturation, and axillary temperature, following which 5 mg Nalbuphine and 1 gram paracetamol were given. Thirty minutes after postoperative analgesia (T2), second measurements for the mentioned parameters were taken. We considered the following criteria as indicators of pain relief: a 100% increase of PI value from baseline.

2.2. Data Collection

The required sample size was calculated using the G*Power software v. 3.1.9.4 [10]. The primary outcome measure was the correlation between the change in PI and the change in pain score as assessed using the BPS-NI. We considered that a correlation coefficient of 0.45 would be of clinical value. So, assuming an alpha error of 0.05, we calculated that a sample size of 40 patients would be required to achieve a power of 85% to detect statistical significance for a correlation coefficient of 0.45 between the change in PI and change in pain score. Data were analysed using IBM© SPSS©

Statistics version 23 (IBM© Corp., Armonk, NY). Categorical variables were presented as number and percentage. Normally distributed numerical variables were presented as mean and standard deviation and intergroup differences were compared using the unpaired t-test. The paired t-test was used to compare normally distributed paired data. Non-normally distributed numerical variables were presented as median and interquartile range and intergroup differences were compared using the Mann-Whitney U-test. The Wilcoxon signed ranks test was used to compare non-normally distributed paired data. Correlations were tested using the Spearman rank correlation. Multivariable linear regression was used to examine the effect of age or sex on the change in PI after analgesic administration. The PI was subjected to logarithmic transformation prior to entry into regression because of marked skewness of its frequency distribution. Two-sided P-values <0.05 were considered statistically significant.

3. RESULTS

We studied 40 age-matched patients, 20 males and 20 females, with a mean ± SD age of 48 ± 19 years. The characteristics of the study population and operative details are shown in Table **1**.

Table **2** shows a comparison of pain score, PI and other indicators of pain before and after analgesic administration. There was a statistically significant reduction in the BPS-NI score, MAP and heart rate after analgesic administration (P-values, <0.001, 0.039 and 0.001, respectively). On the other hand, there was a statistically significant increase in the PI after analgesic administration (P-value, 0.004). Regarding the difference in axillary temperature, there was no statistically significant difference between the measured axillary temperature at T1 and that at T2 (P-value, 0.442). There was no statistically significant correlation between the PI and the pain score or other clinical indicators of pain either before or after administration of analgesic. There was no statistically significant correlation between the change in PI and the change in pain score or other clinical indicators of pain (Table **3**). Studying the correlation of PI with other clinical variables before and after administration of analgesic showed a weak inverse correlation between the PI after administration of analgesic and the RASS score at 1 h (rho, -0.378; P-value, 0.016) and moderate inverse correlation between the change in PI and the RASS score at 1 h (rho, -0.409; P-value, 0.009). There was no statistically significant relationship between the age or sex and the PI either before or after the administration of analgesic. Neither there was a statistically significant relationship between the change in PI and the age or sex (Table **4**).

Table 1. Characteristics of the study population.

Variable	Value
Sex	
F	20 (50.0%)
M	20 (50.0%)
Age (years)	48 ± 19
Age category	
≤60 yr.	20 (50.0%)
>60 yr.	20 (50.0%)
Weight (kg)	73 ± 15
ASA-PS	
ASA-PS I	6 (15.0%)
ASA-PS II	18 (45.0%)
ASA-PS III	16 (40.0%)
Surgical procedure	
Abdominal wall debridement	2 (5.0%)
Aortobifemoral bypass	1 (2.5%)
Appendectomy	6 (15.0%)
Bariatric surgery	1 (2.5%)
Colon resection	2 (5.0%)
Drainage of renal abscess	1 (2.5%
Exploration laparotomy	16 (40.0%)
Intestinal resection and anastomosis	2 (5.0%)
Pancreatic resection with triple bypass	1 (2.5%)
Perforated DU repair	1 (2.5%)
Radical cystectomy	1 (2.5%)
Rectovesical fistula repair	1 (2.5%)
Splenectomy	2 (5.0%)
Strangulated hernia repair	2 (5.0%)
Open prostatectomy	1 2.5%

(Table 1) contd.....

Operative time (hr)	2.5 ± 1.1
Volume of transfused blood (ml)	0 (0 to 350)
Intraoperative opioid dosage (mg of morphine equivalent)	15 (15 to 20)
TFA request (min)	35 (10 to 60)

Data are number (%), mean ± SD or median (interquartile range).
ASA-PS; American Society of Anaesthesiologists - physical status, DU; Duodenal ulcer, F; female, M; Male, TFA; Time of the first request of analgesia.

Table 2. Comparison of pain score, PI and other indicators of pain before and after analgesic administration.

Variable	Before analgesia	After analgesia	P-value*
BPS-NI score	6 (4 - 7)	4 (3 - 5)	**<0.001**
PI	1.15 (0.64 - 2.05)	1.45 (0.99 - 3.45)	**0.004**
MAP (mmHg)	86 (62 - 99)	79 (61 - 95)	**0.039**
HR (bpm)	100 (84 - 116)	96 (75 - 116)	**0.001**
Axillary temperature (°C)	37.1 ± 0.5	37.1 ± 0.5	0.442§
SpO_2 (%)	98 ± 2	98 ± 3	0.107§

Data are median (interquartile range) or mean ± SD.
*Wilcoxon signed ranks test unless otherwise indicated.
§Paired-samples t-test.
BPS-NI; Behavioral pain scale non-intubated scoring system, HR; Heart rate, MAP; Mean arterial blood pressure, PI; Perfusion index, SpO2; Oxygen saturation.

Table 3. Correlation of PI with pain score and other clinical indicators of pain before and after administration of analgesic.

Before analgesic		PI	
	Variable	*rho*	*P-value*
	BPS-NI	0.177	0.276
	MAP	0.198	0.221
	HR	0.261	0.104
	Axillary temperature	0.101	0.536
	SpO_2	-0.088	0.596
After analgesic		PI	
	Variable	*rho*	*P-value*
	BPS-NI	-0.002	0.989
	MAP	0.049	0.763
	HR	0.291	0.069
	Axillary temperature	-0.215	0.188
	SpO_2	-0.061	0.713
Change		Δ PI	
	Variable	*rho*	*P-value*
	Δ BPS-NI	-0.130	0.425
	Δ MAP	-0.116	0.474
	Δ HR	0.285	0.075
	Δ Axillary temperature	-0.248	0.128
	Δ SpO_2	-0.103	0.534

Rho = Spearman rank correlation coefficient.
BPS-NI; Behavioral pain scale non-intubated scoring system, HR; Heart rate, MAP; Mean arterial blood pressure, SpO2; Oxygen saturation, Δ means change in parameter

Table 4. Relationship between PI and age category or sex.

			PI		
Before analgesic	Variable		Median	Interquartile range	P-value*
	Age category	≤60 yr.	1.30	0.70 to 3.45	0.323
		>60 yr.	0.93	0.64 to 1.35	
	Sex	M	1.10	0.79 to 1.65	0.924
		F	1.25	0.58 to 3.10	

(Table 4) contd.....

			PI		
After analgesic	Variable		Median	Interquartile range	P-value*
	Age category	≤60 yr.	1.75	0.85 to 4.50	0.675
		>60 yr.	1.30	1.05 to 2.60	
	Sex	M	1.60	1.10 to 2.30	0.925
		F	1.40	0.85 to 4.20	
			Δ PI		
Change	Variable		Median	Interquartile range	P-value*
	Age category	≤60 yr.	0.30	-0.25 to 1.30	0.695
		>60 yr.	0.38	0.05 to 0.89	
	Sex	F	0.38	-0.01 to 1.30	0.797
		M	0.35	-0.05 to 0.74	

*Mann-Whitney test.
F; female, M; Male

Table 5. Multivariable regression analysis for the effect of age or sex on the change in PI (Δ PI) with adjustment for other confounding factors.

						95% CI for B	
variable	B	SE	Beta	t	P-value	Lower Bound	Upper Bound
(Constant)	-0.750	0.567		-1.322	0.200	-1.927	0.427
Male sex (=1) †	0.176	0.246	0.169	0.716	0.482	-0.334	0.685
Age >60 yr.‡	-0.337	0.297	-0.322	-1.135	0.269	-0.953	0.279
ASA-PS II (=1) §	0.037	0.333	0.035	0.110	0.913	-0.654	0.727
ASA-PS III (=1) §	0.034	0.445	0.030	0.077	0.939	-0.888	0.956
Operative time (h)	-0.006	0.120	-0.012	-0.048	0.962	-0.255	0.244
Intraoperative opioid dosage (mg morphine equivalent)	0.039	0.034	0.311	1.134	0.269	-0.032	0.110

B = unstandardized regression coefficient, SE = standard error, Beta = standardized regression coefficient, 95% CI = 95% confidence interval.
† Referenced to female sex (=0).
‡ Referenced to age ≤60 yr. (=0).
§ Referenced to ASA-PS I (=0).
ASA-PS American Society of Anaesthesiologists physical status

Table **5** shows the results of multivariable regression analysis for the effect of age or sex on the change in PI (Δ PI) with adjustment for other confounding factors. After adjustment for the effect of American Society of Anaesthesiologists - Physical Status, operative time and intraoperative opioid consumption, there was no statistically significant relationship between the change in PI and the patient's age (P-value, 0.269) and sex (P-value, 0.482).

4. DISCUSSION

In our study, there was a statistically significant increase in the PI after analgesic administration. Also, there was a statistically significant reduction in the BPS-NI score, MAP and heart rate after analgesic administration. But, we did not find any statistically significant correlation between the absolute value of "PI and other examined clinical pain indicators (the BPS-NI, MAP, and HR)" before or after rescue analgesia administration as well as with their changes. The relationship between analgesia and PI is the basis of our hypothesis in this study. The PI is a non-invasive and easy method that can be used for evaluating pain and monitoring the effectiveness of analgesia. It can also eliminate psychological factors such as fear, anxiety, depression, and anger [11]. This benefit can be more valid in patients suffering from cognitive impairment and dementia especially because common pain behaviour scales are very difficult, require training of the ICU staff and are time-consuming [11]. There are multiple studies exploring the relationship between PI and pain, whether in awake patients [12, 13] or those under general anaesthesia [8]. And they all proved that PI decreased due to painful stimulus. On the other hand, other studies explored the relationship between PI and analgesia whether under general anaesthesia [2, 11, 14] or epidural analgesia [15] or transforaminal block [16]. And they all proved that PI increased after analgesic administration. All of these studies explored different types of pain as postoperative surgical pain [2, 11, 14, 15], intensive care procedural pain [13], electric stimulation pain [8, 12] and finally, chronic radicular pain [16].

In agreement with the current study, Tapar and colleagues [2] showed that there was a statistically significant difference between pre-analgesic and post-analgesic PI, VAS scores and haemodynamics with no correlation between PI absolute values & VAS scores absolute values at pre- and post-analgesic measurements. Also, there was a detected weak negative correlation between the change in PI and the change of pain score (VAS score). It was a prospective observational study that was done on 89 patients that had undergone minor to moderate surgical procedures and were observed in Post Anesthesia Care Unit (PACU) postoperatively. They used

morphine increments for post-operative analgesia and the subjective pain score used was VAS score. Another study confirming our findings was carried out by Mohammed and colleagues [11], in which a Masimo pulse co-oximetry perfusion index was attached to 70 American Society of Anaesthesiologists-Physical Status I adult patients at PACU, who underwent lumbar spine discectomy. The PI was significantly higher at post-analgesic timing than at pre-analgesic timing. This increase was associated with a statistically significant decrease in other measured parameters. This means that the PI increases with adequate relief from pain, as indicated by a decrease in VAS, HR, and MAP. A decrease in VAS was associated with an increase in PI, but the correlation was not statistically significant. Also, the correlation between change in PI and change in VAS score & change in MAP was not statistically significant and this is consistent with our study. It is to be noted that there was a statistically significant negative correlation between change in HR and change in PI. For all patients, analgesia was achieved with i.v. morphine and i.v. 1 g paracetamol and subjective pain scale used was the VAS score. In correspondence to the current study, Nishimura and colleagues [12] studied the changes in perfusion index in response to noxious electrical stimulation in awake healthy subjects. They measured the PI and pulse rate in 70 healthy volunteers exposed to increasing electrical stimulation until they reached their pain tolerance threshold. They observed a significantly decreased PI in response to electrical stimulation but with no increase in the pulse rate due to its very small intensity. They concluded that the PI may be an independent parameter reflecting the perception of noxious stimuli and offers a non-invasive option for objectively evaluating pain perception. Finally, in a study done by Hasanin and colleagues [13], they reported a difference between PI values, Systolic blood pressure, Diastolic blood pressure, HR, and pain intensity before and after the pain created by positioning in ICU patients. BPS-NI has been used for subjective pain assessment especially as all patients were sedated (but not-intubated), which might affect their communication with the medical staff. There was a significant increase in the Systolic blood pressure, Diastolic blood pressure, heart rate and BPS-NI post-positioning values compared with pre-positioning values. Also, a significant decrease in PI was also observed at post-positioning values compared with pre-positioning values. Also, no correlation was found between the PI values and any other variable (Systolic blood pressure, Diastolic blood pressure, HR, and BPS-NI) before or after the patient positioning. Hasanin's study differs from the current study in that the change in BPS-NI showed a good correlation with the change in PI. On the other hand, there are two studies which showed a weak correlation between different parameters. In a retrospective observational study done by Chu and colleagues [14], the correlation between the PI and VAS score together with their delta change and their percentage change showed weak correlations. They enrolled 80 female patients postoperatively, with a different age range, who were observed in PACU before and after intravenous morphine analgesic administration. The second study was done by Kupeli & Kulhan [15]. They investigated the relationship between labour pain level and PI in 30 women undergoing spontaneous vaginal delivery under epidural analgesia. They noticed that upon activation of the epidural blockade with 10 mL 0.25% bupivacaine, the PI increased. Also, they noticed a gradual decrease in PI with a fade of epidural analgesia (manifested by a gradual increase in labor pain). They concluded that PI could offer a non-invasive option to objectively assess pain perception and this is in accordance with our study findings. But in opposition, there was a significant negative association between PI and VAS absolute values at the 10th, 30th, 60th minutes and 2nd hour after epidural blockade activation. Also, there was a significant negative association between PI and HR absolute values before the procedure and at the time of administration of epidural analgesia and 5 minutes later. They noted that perfusion index had no significant correlation with both systolic and diastolic blood pressures.

Few studies had explored the effect of age or sex on the change in PI after analgesic administration or painful stimulation. In the current study, there was no statistically significant relationship between the age or sex and the PI either before or after the administration of analgesic. Neither was there a statistically significant relationship between the change in PI and the age or sex. Supporting our findings, Chu and colleagues [14] stated the same findings in their study. On the other hand, Nishimura and colleagues [12] observed that the old women group did not show any changes in PI before or after electrical stimulation when compared to other age and sex groups that showed a decrease in PI.

5. LIMITATION

PI measurements are very sensitive to patients' movements. The rapid fluctuation and sensitivity of PI are its weakness as well as strength in the clinical field. To compensate for this limitation, PI monitoring should be done after ensuring position stability.

CONCLUSION

Perfusion index can be added to other indicators of pain assessment in ICU. It is easy, non-invasive, free of subjective interpretation, less time-consuming and finally, not affected by age or sex related factors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The work was approved by the Ethics committee of Ain Shams University hospital (FMASU R 05/ 2019) on 23/1/2019. The study was prospectively registered with Pan African Clinical Trial Registry (PACTR) with Registration Number PACTR201901839969911 in accordance with WHO and ICMJE standards.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the

Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all subjects or their legal surrogate.

AVAILABILITY OF DATA AND MATERIAL

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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