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ORIGINAL RESEARCH

Evaluation of perfusion index as a tool for pain assessment in critically ill patients

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Abstract Pain is a common and undertreated problem in critically ill patients. Pain assessment in critically ill patients is challenging and relies on complex scoring systems. The aim of this work was to find out the possible role of the perfusion index (PI) measured by a pulse oximeter (Masimo Radical 7; Masimo Corp., Irvine, CA, USA) in pain assessment in critically ill patients. A prospective observational study was carried out on 87 sedated non-intubated patients in a surgical intensive care unit. In addition to routine monitoring, a Masimo pulse oximeter probe was used for PI measurement. The sedation level of the patients was assessed by using the Richmond Agitation-Sedation Scale (RASS). The pain intensity was determined by applying the behavioral pain scale for non-intubated (BPS-NI) patients. The PI, arterial blood pressure, heart rate, RASS, and BPS-NI values before and after the application of a standard painful stimulus (changing the patient position) were reported. Correlation between the PI and other variables was carried out at the two measurements. Correlation between changes in the PI (delta PI) and in the hemodynamic variables, RASS, and BPS-NI was also done. Changing the patient position resulted in a significant increase in SBP (128 ± 20 vs 120.4 ± 20.6, $P = 0.009$), DBP (71.3 ± 11.2 vs 68.7 ± 11.3, $P = 0.021$), heart rate (99.5 ± 19 vs 92.7 ± 18.2, $P = 0.013$), and BPS-NI (7[6–8] vs 3[3–3], $P < 0.001$) values and a significant decrease in the PI (1[0.5–1.9] vs 2.2[0.97–3.6], $P < 0.001$) value compared to the baseline readings. There was no correlation between the values of the PI and the ABP, BPS-NI, and RASS at the two measurements. A good correlation was found between the delta PI and delta BPS-NI ($r = -0.616$, $P < 0.001$). A weak correlation was observed between the PI and heart rate after the patient positioning ($r = -0.249$, $P < 0.02$). In surgical critically ill non-intubated patients, the application of a painful stimulus was associated with decreased PI. There was a good correlation between the change in the PI and the change in BPS-NI values after the application of painful stimulus.

Keywords Perfusion index · Pain · Critically ill patients

1 Introduction

Pain is a common and undertreated problem in critically ill patients [1, 2]. Unrelieved pain in critically ill patients activates the sympathetic nervous system, increases stress hormones causing vasoconstriction, increases oxygen demands, alters glycemic control, and impairs immune system function [3]. Pain can develop from numerous sources, e.g. surgical incisions, invasive procedures, penetrating tubes, and intensive care unit (ICU) procedures [4].

Pain is usually underestimated in critically ill patients because of the difficulty of its assessment [3, 5]. The methods of pain assessment in critically ill patients include categorical and numerical tools. The behavioral pain scale (BPS) has been reported as a valid and reliable tool for pain assessment in patients with artificial airway [3, 6, 7]. The BPS has the advantage of being calculated by using three components that are not dependent on a cooperative

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patient: facial expression, movement of upper limbs, and ventilator compliance with painful stimuli [6, 7]. The behavioral pain scale–non-intubated (BPS-NI) is an adaptation of the BPS for use in non-intubated critically ill patients [8]. Although the aforementioned pain scales have shown good performances in critically ill patients, more subjective and simple tools are still needed.

The perfusion index (PI) is the ratio of the pulsatile blood flow to the non-pulsatile flow in peripheral tissue as measured by a special pulse oximeter [9]. The PI allows the measurement of peripheral perfusion noninvasively and continuously [9]. The pulse oximetry waveform has been used to monitor changes in sympathetic response to noxious stimuli [10, 11]. The PI has also been used to determine the success of peripheral nerve blocks [12–14].

The direct relation between pain and sympathetic stimulation [15] raises the hypothesis that the PI can be used as an indirect tool for pain assessment. This study aimed to investigate the usefulness of the PI in pain assessment in sedated surgical ICU patients by examining the relationship between the PI and the BPS-NI after the application of a painful stimulus (changing the patient position).

2 Materials and methods

A prospective observational study was carried out on sedated postoperative patients who were admitted to the surgical ICU at Cairo University Teaching Hospital. After obtaining approval from the research ethical committee of the hospital, written informed consent to participate in the study was obtained from the patients' next-of-kin.

2.1 Inclusion criteria

Sedated non-intubated patients between 18 and 70 years old were included in this study. All participants were surgical ICU patients on first two postoperative days.

2.2 Exclusion criteria

Patients with a history of neurologic disorder (hemiparesis, quadriparesis, and neuropathy), an epidural catheter, peripheral vascular disease, fever, hypothermia, and hemodynamic instability needing vasopressor support were excluded from the study.

2.3 Monitoring

All patients were monitored with the use of basic monitoring tools: electrocardiogram, pulse oximetry, and automated noninvasive blood pressure (NIBP). In addition, a pulse oximeter probe (Masimo Radical 7; Masimo Corp., Irvine, CA, USA) was attached to the index finger of the patient during the positioning. This pulse oximeter was connected to the Masimo monitor and shielded to prevent outside light from interfering with the signal.

2.4 Assessment of sedation and pain

Sedation was assessed by using the Richmond Agitation-Sedation scale (RASS) as follows: (+4) combative, violent, immediate danger to staff; (+3) very agitated, removes tubes or catheters, aggressive; (+2) agitated, non-purposeful movement, fights ventilator; (+1) restless, anxious but movements not aggressive, vigorous; (0) alert and calm; (−1) drowsy, eye opening/eye contact to voice >10 s; (−2) light sedation, eye contact to voice <10 s; (−3) moderate sedation, movement or eye opening to voice; (−4) deep sedation, movement or eye opening to physical stimulation; (−5) unarousable, no response to voice or physical stimulation [16].

Pain assessment was achieved by using the behavioral pain scale for non-intubated patients, as presented in Table 1.

2.5 Sedation and analgesia protocol

Sedation and analgesia were guided by the BPS-NI and RASS. The patients received 0.05–0.2 mg/kg morphine sulfate as a loading dose, followed by 2–10 mg/h infusion to keep the BPS or BPS-NI between 1 and 3. If the pain score was more than 5, a rescue dose of 3–5 mg was given, and then the pain was reassessed after 5 min. If the patient received more than 2 boluses/h, the infusion dose was increased by 2 mg/h.

For sedation, the patients received midazolam i.v. at a loading dose of 0.02–0.08 mg/kg, followed by continuous infusion of 1–10 mg/h to achieve a RASS sedation score of

Table 1 Behavioral pain scale non-intubated (BPS-NI)

Component	Grade	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Vocalization	Vocalization	1
	Moaning ≤3/min	2
	Moaning >3/min	3
	Verbal complain or breath hold	4

0 to 3. A rescue dose of 0.01 mg/kg was given if the RASS score was more than 3. If the patient received more than 2 boluses/h, the infusion dose was increased by 2 mg/h.

2.6 Data collection

- Demographic data: age, sex, body mass index (BMI), and types of surgeries
- Assessment of pain (BPS-NI) and sedation (RASS)
- Hemodynamic assessment: heart rate, systolic blood pressure (ABP), and diastolic blood pressure (DBP)
- PI
- The BPS-NI, RASS, PI, and hemodynamic variables were evaluated twice.
  - T1: under adequate sedation (BPS-NI <3 and RASS between 0 and 3) before the application of a standard painful stimulus (changing of position)
  - T2: after changing of patient position from supine to lateral position during patient care
- The delta PI was calculated as: PI before positioning—PI after positioning. The delta BPS-NI was calculated as: BPS-NI before positioning—BPS-NI after positioning.
- The data were manually recorded in paper sheets and the delta PI an delta BPS-NI were calculated during data analysis.

2.7 Statistical analysis

Sample size was calculated using Medcalc software. In observational studies designed for correlation between two variables, sample size calculation requires the presence of: the power of the study, alpha error, and correlation coefficient (r). In our study, we set a study power of 80 % and alpha error of 0.05. As there are no previous data for the correlation of PI and BPS-NI, we used a conservative approach by assuming (r) of 0.3 to detect the presence of any correlation even if weak. Based on the aforementioned assumption, a minimum number of 84 patients was calculated.

Statistical calculations were done by using the Statistical Package for the Social Sciences (SPSS) software version 15 for Microsoft Windows (SPSS Inc., Chicago, IL, USA). Data were checked for normality using Shapiro–Wilk test. Continuous data were described as means ±SD for normally distributed data, and as medians and ranges for abnormally distributed data. Categorical data were expressed as frequencies (%). Data analysis was preformed using paired t tests for normally distributed data and Wilcoxon rank test for abnormally distributed data. Correlation between variables was carried out by applying the Pearson correlation equation for linear relations and spearman correlation equation for non-linear correlation. A P value of <0.05 was considered statistically significant. Receiver operating characteristic curve was constructed for the ability of PI to detect a change more than three points in BPS-NI. The best cutoff value for PI was calculated.

3 Results

During a period of 6 months, 240 patients were admitted to our ICU. Of these patients, 105 were non-intubated and sedated. Thirteen patients were excluded because of hypothermia, and five patients due to hemodynamic compromise. A total of 87 patients were included in the analysis. Table 2 shows the patient demographic characteristics and the types of surgical procedures done.

There was a significant increase in the SBP (128 ± 20 vs 120.4 ± 20.6, $P = 0.009$), DBP (71.3 ± 11.2 vs 68.7 ± 11.3, $P = 0.021$), heart rate (99.5 ± 19 vs 92.7 ± 18.2, $P = 0.013$), and BPS-NI (7 [6–8] vs 3 [3–3], $P < 0.001$) values at T2 (post-positioning) compared with T1 (pre-positioning). A significant decrease in PI was also observed at T2 compared with T1 (1[0.5–1.9] vs 2.2[0.97–3.6], $P < 0.001$) (Table 3).

No correlation was found between the PI values and any other variable (heart rate, SBP, DBP, PI, and BPS-NI) before or after the patient positioning. A weak correlation was observed between the PI and heart rate after positioning ($r = -0.24$; $P = 0.02$). The delta BPS-NI showed a good correlation with the delta PI ($r = -0.61$; $P < 0.001$) (Table 4).

Area under receiver operating characteristic (AUROC) curve for delta PI to detect a change of three points in BPS-NI was 0.846. The best cutoff value for delta PI was >0.7 with a sensitivity of 69 % and specificity was 85 %. (Fig. 1)

Table 2 Demographic data and patient characteristics

Patients	n = 87
Age (years)	49 ± 15
Male gender	40(46 %)
BMI (kg/m^2)	28 ± 8
Operation	
Radical cystectomy	13 %
Colectomy	17 %
Aorto-bifemoral bypass	10 %
Gastrojejunostomy	9 %
Orthopedic procedures	10 %
Abdominal exploration	26 %
Partial gastrectomy	15 %

BMI Body mass index

Table 3 Changes in BPS-NI, PI, heart rate, SBP, and DBP after painful stimulus (positioning)

	At rest	After positioning	*P* value
BPS-NI	3(3–3)	7(6–8)	<0.001*
PI	2.2(0.97–3.6)	1(0.5–1.9)	<0.001*
HR (bpm)	92.7 ± 18.2	99.5 ± 19	0.013*
SBP (mmHg)	120.4 ± 20.6	128.09 ± 20.1	0.009*
DBP (mmHg)	68.7 ± 11.3	71.3 ± 11.2	0.021

Data are presented as mean ± standard deviation and median (quartiles)

BPS-NI Behavioral pain scale non-intubated, *PI* perfusion index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

*Denotes statistical significance ($P < 0.05$)

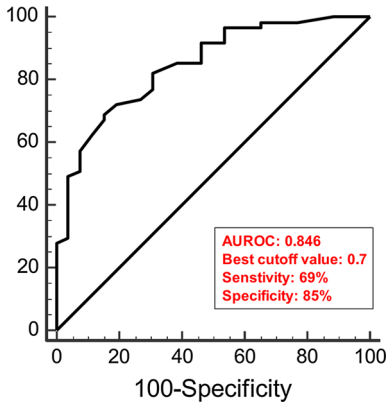

Fig. 1 Area under receiver operating characteristic (AUROC) curve, sensitivity and specificity for the ability of PI to detect a three point change in BPS-NI

4 Discussion

We did not find a significant correlation between the PI and the BPS-NI absolute values; however, the changes in both variables (delta PI and delta BPS-NI) after the application of a painful stimulus showed a significant correlation. A change in PI of 0.7 detected a change of three points in BPS-NI with AUROC of 0.846. Pain is usually associated with increased sympathetic activity [15] leading to a state of vasoconstriction. The PI is well known to increase with vasodilatation and to decrease with vasoconstriction [9].

Previous studies have reported an association between the state of sympathetic stimulation and a decreased PI. The PI decreased with the insertion of airway devices [17] and with the application of painful stimuli in volunteers [18, 19]. The PI increased with different degrees of vasodilatation such as: Induction of general anesthesia [20], successful peripheral nerve blocks [12, 13, 21], stellate ganglion blocks [14], and epidural blocks [22]. The PI has been used to assess the degree of sympathectomy after epidural block with different doses of bupivacaine [23].

Table 4 Correlation between PI and other variables

Variables	r value	*P* value
PI and BPS-NI (before positioning)	0.118	0.27
PI and BPS-NI (after positioning)	0.159	0.14
PI and heart rate (before positioning)	−0.116	0.284
PI and heart rate (after positioning)	−0.23	0.03*
PI and RASS (before positioning)	0.184	0.09
PI and RASS (after positioning)	−0.13	0.23
Delta PI and delta BPS	−0.631	<0.001*

PI Perfusion index, *BPS-NI* behavioral pain scale non-intubated, *RASS* Richmond agitation sedation scale

*Denotes statistical significance ($P < 0.05$)

The PI has also been reported to be an intraoperative indicator of successful thoracic sympathectomy in patients with hyperhidrosis [24]. Moreover, a recent study by our group reported that the PI was an early predictor of vasopressor therapy in patients with severe sepsis [25].

We reported a relation between delta PI and delta BPS-NI values; whilst, we did not find any correlation between the absolute values of both variables. This is most probably to the high skewness in PI values. PI values are usually not normally distributed; this was previously reported by Lima et al. [26] who investigated the use of PI as an index of peripheral perfusion. Lima et al. [26] reported that the changes in PI reflects the changes in core-to-toe temperature difference.

The relation between the PI and pain has been previously reported in two studies. Nishimura et al. [18] found a significant decrease in the PI in response to noxious electrical stimulation in healthy subjects. Høiseth et al. [19] reported a similar finding in volunteers after a cold pressor test (ice water exposure). To the best of our knowledge, no studies have previously reported on the effect of pain on the PI in critically ill patients.

Assessment of pain usually relies on subjective scoring systems and questionnaires which need patients' awareness and education; this is usually feasible in stable and not in critically ill patients. Critically ill patients are usually not cooperative; thus, pain assessment in this population is usually difficult. Scoring systems such as BPS-NI have been developed to enable pain evaluation without the need of patient cooperation; however, these scoring systems are time consuming with multiple points of assessment making them non-practical. The need for simple, rapid, and objective tools for pain evaluation represents a present gap in literature. To the best of our knowledge, there are no reliable available devices for pain monitoring. According to our findings, the Masimo device could be a promising

tool for pain assessment. Future research is warranted to confirm our findings by randomized controlled trials.

Inclusion of a heterogeneous group of surgical patients is considered a potential limitation in our study. Future research should focus on different surgical patient subgroups for more precise results. Future research should also explore the accuracy of the PI in other groups patients such as hypotensive patients, mechanically ventilated patients, and postoperative patients outside the ICU.

5 Conclusions

In surgical critically ill non-intubated patients, the application of a painful stimulus was associated with decreased PI. There was a good correlation between the change in the PI and the change in BPS-NI values after the application of painful stimulus.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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