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ORIGINAL ARTICLE

Assessment of postoperative pain intensity by using photoplethysmography

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Abstract
Purpose Timely assessment of acute postoperative pain is very important for pain management. No objective and reliable method to assess postoperative pain intensity exists till now. The aim of the study was to investigate the feasibility of photoplethysmography (PPG) signals in postoperative pain assessment.
Methods Thirty patients scheduled for elective abdominal surgery under general anesthesia were examined. Finger PPG signals and visual analogue scale (VAS) score were acquired before and 5, 10, 20, and 30 min after sufentanil administration when the patients were awake and transferred to the post-anesthesia care unit (PACU). During each pain rating, the patient's blood pressure, heart rate, and pulse oxygen saturation were recorded. The amplitude of alternating current (AC) and direct current (DC) extracted from finger PPG signals were analyzed, and the ratio of AC and DC (AC/DC) was calculated. Receiver operating characteristic (ROC) curves were built to assess the performance of AC and AC/DC to detect patients with VAS >4 in the PACU.
Results After administration of sufentanil, VAS scores decreased significantly ($p < 0.05$), as did blood pressure and heart rate. Simultaneously, both values of AC and AC/DC increased significantly. The VAS score had significant correlations with AC ($r = -0.477$; $p < 0.01$), AC/DC ($r = -0.738$; $p < 0.01$) and heart rate ($r = 0.280$; $p < 0.01$). In contrast, no statistical correlations between VAS score and blood pressure were found. Further analysis found significant differences in both AC and AC/DC among different pain levels, but no obvious differences in blood pressures and heart rate. The area under the ROC curves were 0.754 for AC and 0.795 for AC/DC, respectively.
Conclusion The finger PPG signal can be used in acute postoperative pain assessment. Both AC/DC and AC had significant correlations with the pain rating levels, while blood pressure and heart rate were unreliable in pain assessment.

Keywords Photoplethysmography · Pain intensity · Vital sign

P. Ling and Y. Siyuan have contributed equally to this work.

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Introduction

Effective pain management can reduce complications, improve recovery and shorten hospital stay [1–3]. Timely and accurate assessment of postoperative pain is a key factor for successful pain management [4]. However, pain

is a subjective experience, and series of pain evaluation approaches, such as the visual analogue scale (VAS), numeric rating scale (NRS), and verbal descriptor scale (VDS), are designed according to patients' subjective feelings and reporting. Thus, pain assessment almost entirely depends on the cooperation of patients [5–8]. In clinical practice, vital signs such as blood pressure, heart rate, or respiration rate are often used as surrogate indicators for pain assessment in some uncooperative patients, but the published studies showed that vital signs were unreliable for pain assessment [9–12]. Recently the value of skin conductance in pain monitoring was also questionable [12, 13]. Photoplethysmography (PPG) was regarded as a sensitive indicator in reflecting blood volume change [14, 15]. The decreased amplitude of PPG waveform was found when systematic vascular resistance was higher [16–18] or when the subjects' fingers grew cold [19]. Postoperative acute pain could increase resistance and reduce perfusion in the peripheral vascular bed due to the increased sympathetic tone. However, the values of PPG in pain monitoring are rarely reported. The aim of this study was to investigate the feasibility of using PPG signals in postoperative pain assessment.

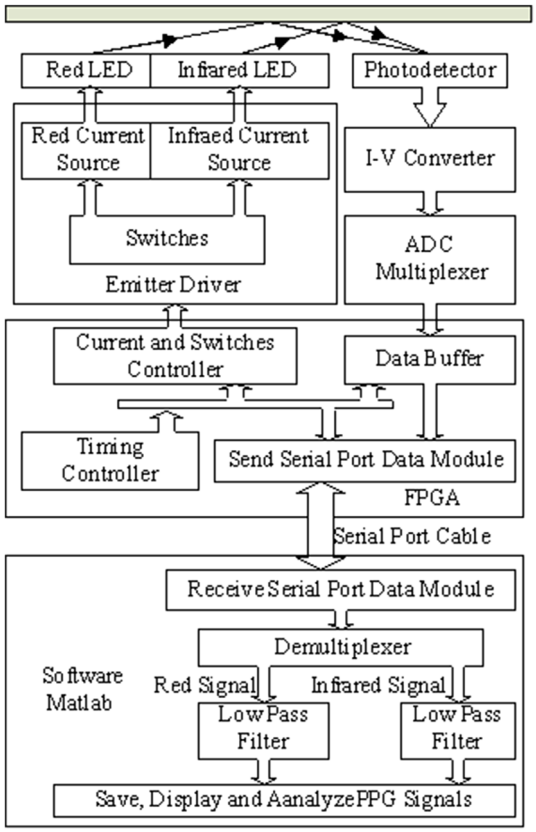

Fig. 1 A schematic diagram of the custom-made pulse oxygen saturation signal acquisition and processing system (APS)

Methods

This prospective observational study was approved by the Ethics Committee (West China Hospital, Sichuan University) and the trial was registered with the Chinese Clinical Trials Register (ChiCTR-ONC-12002300). Written informed consents were obtained before the study. Thirty adult patients (aged 18–60 years, ASA physical status I–II) who entered the post-anaesthesia care unit (PACU) after elective abdominal surgery were enrolled. Individuals of uncooperative status, receiving beta blockers, anticholinergic agents, or any vasoactive substance, and/or having a first VAS score lower than 4 were excluded. Anaesthesia was induced with midazolam 0.05 mg/kg, fentanyl 3–5 μg/kg, rocuronium 0.6 mg/kg, propofol 2–4 mg/kg and maintained with inhaled 1–2 % sevoflurane and infused 0.1–0.15 μg/kg/min remifentanil. The postoperative patient was transferred rapidly to the PACU after the trachea tube was removed.

In the PACU, patients were asked to rate their pain on a 0–10 VAS scale (T_0), with 0 representing 'no pain' and 10 the 'worst possible pain' after they were able to answer questions. Then, an analgesic dose of 0.1 μg/kg sufentanil was given, and the pain rating was asked after 5 min (T_5), 10 min (T_{10}), 20 min (T_{20}), and 30 min (T_{30}), respectively. The PPG signals were detected by the oximetry probe (Nellcor Puritan Bennett Division, Pleasanton, CA, USA) placed on the index finger without an intravenous catheter in that side. Finger PPG signals were monitored continuously by a custom-made PPG signal acquisition and processing system (APS) that was connected to a personal computer (ph pavilion dv2500). The schematic diagram of the APS is shown in Fig. 1 [20]. During each pain rating, the 60 s PPG waveform was saved as a "txt" file for alternating current (AC) and direct current (DC) measurement, and blood pressure including systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), as well as heart rate and pulse oxygen saturation (SpO_2) were recorded simultaneously. The room temperature was controlled at 20–25 °C throughout the observational period.

Matlab version R2007b (The MathWorks, Ins. Natick, MA, USA) software was used to analyze the metrics extracted from the PPG waveform (Fig. 2), and the filter (FIR, Bandpass, 20th order) was applied to remove the motion artifacts of the raw signals. The amplitudes of AC and DC were averaged over 10 optimal PPG waveforms, and the ratio of AC and DC (AC/DC) was calculated. The quantitative analysis of the PPG waveform was performed by another observer who was blind to the sufentanil treatment.

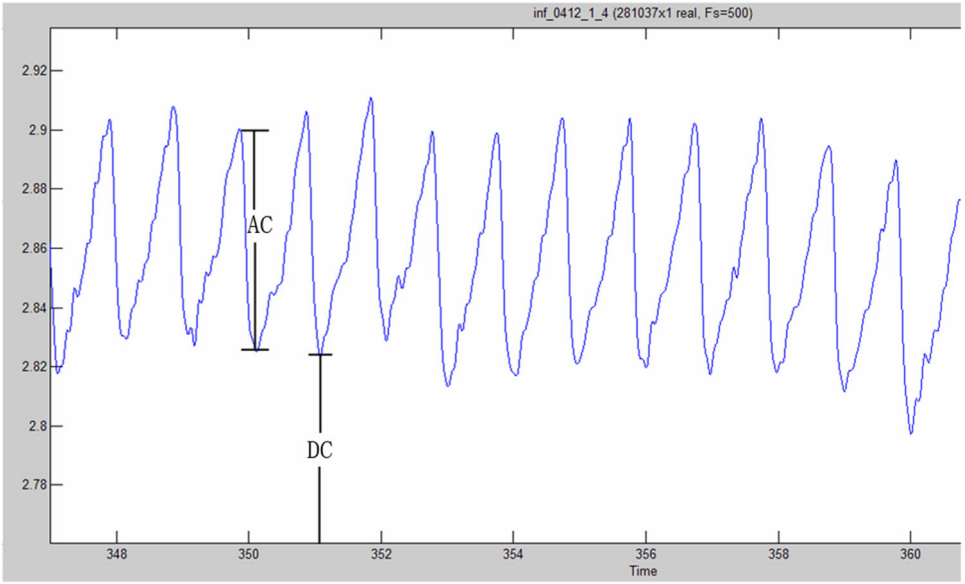

Fig. 2 Filtered infrared component during metrics extraction are shown. Ten continual stable PPG waveforms were selected to analyze, and the voltage of the peak and trough were obtained from the average of the 10 waveforms. DC was equal to the trough voltage, and AC was equal to peak voltage minus trough voltage. *AC* alternating current, *DC* direct current

All data were tested for normal distribution using the Kolmogorov–Smirnov test and presented as mean ± SD. The variances of different time points and different pain levels were analyzed using one-way analysis of variance (ANOVA). Post-hoc pairwise comparisons were made using the LSD test for multiple comparisons. Pearson's correlation coefficient (r) was used to describe the relationship between the VAS score and the values of PPG metrics (AC, AC/DC), blood pressure (SBP, DBP, MAP), and heart rate. A receiver operating characteristics curve (ROC) was built by plotting the sensitivity as a fraction of 100-specificity to evaluate the predictive performance of AC and AC/DC in moderate to severe pain (VAS >4). Statistical analysis was performed using the SPSS package (version, 17.0). A value of $p < 0.05$ was considered statistically significant.

Results

Satisfactory finger PPG signals were detected successfully from all patients, and the characteristic of patients were shown in Table 1. After sufentanil administration, the reporting VAS score dropped significantly in 30 min. Simultaneously, AC increased significantly in about 20 min, and then dropped to baseline at 30 min. The significant increase of AC/DC lasted 30 min after analgesic treatment (Fig. 3). Blood pressure (SBP, DBP, MAP) and heart rate increased significantly, but lightly in 10 min (Table 2). The blood pressure and heart rate decreased by nearly 10 % and 12 %, respectively, while the AC and AC/DC increased by more than 150 % in 10 min after injection of analgesic agent (Table 3). Significant negative correlations existed between VAS score and AC, AC/DC. The correlation coefficients between VAS and AC, AC/DC were −0.477 and 0.738, respectively (Fig. 4). Meanwhile, VAS score only showed a weak correlation with heart rate ($r = 0.280$; $p < 0.01$), and no significant correlation with blood pressure (SBP, DBP, MAP) (Fig. 5). According to pain intensity level, the PPG metrics and vital signs under mild (VAS 1–3), moderate (VAS 4–6), and severe (VAS 7–10) pain were further analyzed. The significant differences of both AC and AC/DC were found among different pain levels, but there were no obvious differences in blood pressures and heart rate (Table 4). The area under the ROC curves (AUC) were 0.754 for AC and 0.795 for AC/DC, respectively. The optical threshold values of AC and AC/DC in predicting VAS >4 were 36.4 mv (sensitivity, 66.3 %; specificity, 81.0 %) and 1.33 % (sensitivity, 82.6 %; specificity, 67.2 %) (Fig. 6). The average patient temperature was 36.6 ± 0.5 °C (35.5–37.0 °C) and the SpO_2 was above 95 % throughout the observational procedure.

Table 1 Characteristics of subjects

Gender (M/F)	19/11
Age (year)	42 ± 5
Weight (kg)	58.5 ± 8.0
Operation time (min)	192 ± 48
Total fentanyl dose (mg)	0.13 ± 0.06
Total remifentanil dose (mg)	1.10 ± 0.3

Discussion

Postoperative acute pain can evoke the excitability of sympathetic nerves and cause a rise in blood pressure or heart rate [12, 21]. The increases in blood pressure and heart rate usually indicate that the anesthetized patient had insufficient analgesia. In our study, after a bolus of 0.1 μg/kg sufentanil administration, the reported VAS score obviously decreased from about 6 to 4. Simultaneously, heart rate and blood pressure (SBP, DBP, MAP) showed statistical decreases of about 10 % in 10 min due to the analgesic effect of sufentanil. However, further analysis found no obvious differences in both blood pressure and heart rate under different pain levels. Only heart rate had a statistical but slight difference between mild and severe pain. In Ledowski's studies [11, 12], neither blood pressure nor heart rate had any correlation with the reported level of pain in postoperative patients. Although a significant correlation between heart rate and VAS score was found in our study, the correlation was very weak. Some antihypertensive agents can suppress the response of blood pressure and heart rate to postoperative pain stimulation. For example, β blockers can suppress the increase of heart rate relative to pain stimuli, whereas perioperative β blocker administration has became the effective prevention method for cardiac and cerebral vascular complications in high-risk patients [22–24]. Therefore, it is unreliable to monitor

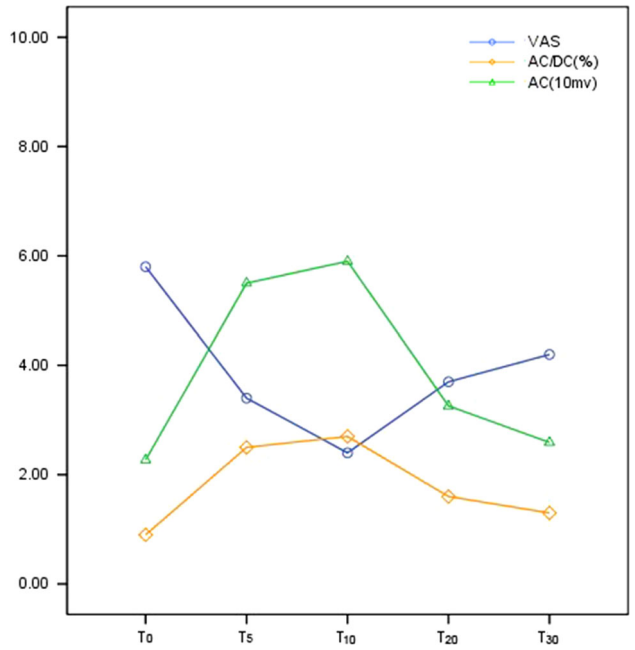

Fig. 3 Showed the variation trend of VAS, AC, and AC/DC at 30 min after sufentanil administration. The reporting VAS score dropped significantly by 30 min after analgesic treatment, while AC and AC/DC increased significantly. *VAS* visual analogue scale, T_0 the time point before sufentanil administration, T_5, T_{10}, T_{20}, T_{30} the time point of 5, 10, 20, and 30 min after sufentanil administration

Table 3 The percentage changes of blood pressure, heart rate, AC, and AC/DC after sufentanil administration

Parameters	T_5	T_{10}	T_{20}	T_{30}
SBP (mmHg)	9.87↓	9.55↓	2.67↓	0.34↓
DBP (mmHg)	7.635↓	7.01↓	0.78↑	2.47↑
MAP (mmHg)	8.57↓	8.01↓	0.74↓	1.22↑
HR (bmp)	12.62↓	12.08↓	3.27↓	0.09↓
AC (mv)	142.95↑	159.46↑	43.49↑	13.82↑
AC/DC (%)	166.67↑	177.00↑	63.00↑	35.48↑

"↑" increase compared with T_0, "↓" decrease compared with T_0

Table 2 The changes of vital signs, photoplethysmographic metrics, and visual analogue scale scores

Parameters	T_0	T_5	T_{10}	T_{20}	T_{30}
SBP (mmHg)	126.1 ± 11.6	113.6 ± 10.2#	114.0 ± 9.8#	122.7 ± 12.7	125.6 ± 12.5
DBP (mmHg)	80.9 ± 6.2	74.7 ± 5.7#	75.2 ± 6.4#	81.5 ± 7.0	82.8 ± 6.7
MAP (mmHg)	95.7 ± 7.3	87.5 ± 6.8#	88.0 ± 7.0#	95.0 ± 8.5	96.9.1 ± 8.3
HR (bmp)	79.5 ± 9.4	69.5 ± 8.2#	69.9 ± 7.8#	76.9 ± 9.2	79.4 ± 8.2
SpO_2 (%)	99 ± 1	98 ± 1	98 ± 3	99 ± 2	99 ± 1
AC (mv)	22.7 ± 5.3	55.0 ± 15.2#	59.0 ± 14.6#	32.6 ± 11.9*	25.9 ± 8.7
AC/DC (%)	0.9 ± 0.4	2.5 ± 0.6#	2.7 ± 0.6#	1.6 ± 0.5*	1.3 ± 0.5*
VAS	5.8 ± 1.0	3.4 ± 1.2#	2.4 ± 1.3#	3.7 ± 1.4*	4.2 ± 1.4*

T_0, before administration of sufentanil; T_5, T_{10}, T_{20}, T_{30} represent the 5, 10, 20, and 30 min after administration of sufentanil, respectively

SBP systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial pressure, *HR* heart rate, SpO_2 pulse oxygen saturation, *AC* alternating current, *DC* direct current, *VAS* visual analogue scale

# $p < 0.01$ compared with T_0, * $p < 0.05$ compared with T_0

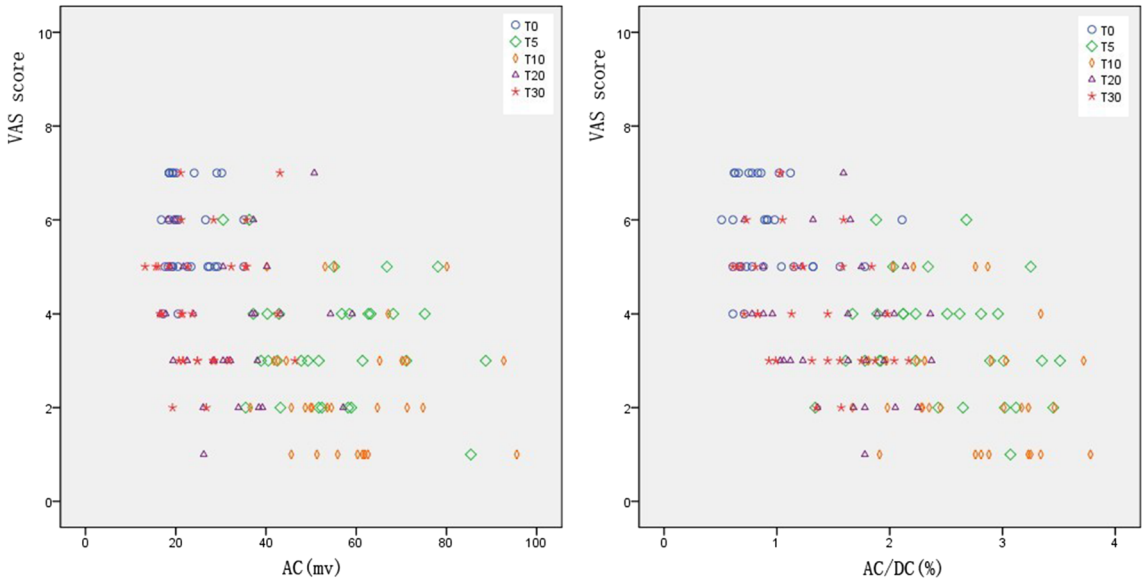

Fig. 4 Significant correlations were found between VAS score and AC amplitude, AC/DC value. The correlation coefficients were −0.477 ($p < 0.01$) and −0.738 ($p < 0.01$)

postoperative pain according to the changes in heart rate or blood pressure.

Finding an objective and reliable method to assess levels of pain has always been the key point in the pain research field. However, until now, no universal, reliable pain monitoring method has been recognized by most physicians. Skin conductance has been reported as a reliable and objective parameter to assess postoperative pain intensity [11, 25]. The rationale for this method is that the filling of the sweat gland could change the electrogalvanic properties of the skin when acute pain excites the sympathetic nerve [26]. However, the reliability of this parameter in pain assessment has been queried with a lower sensitivity and specificity [12, 27, 28]. A recent research reported that skin conductance did not change at different remifentanil infusion rates for children undergoing ear surgery [29]. In addition, the pupillary dilatation reflex (PDR) was suggested to be a useful objective index reflecting analgesia [30], although it needed the patient's cooperation and was affected by opioids and anticholinergic agents. Recently, the analgesia/nociception index (ANI), a noninvasive parameter calculated from heart rate variability, was proven to have a higher sensitivity and specificity in the assessment of immediate postoperative pain [31]. However, ANI can be easily influenced by many factors such as β-blockers, anticholinergic agents, age, awareness, hemodynamic condition, and inspired oxygen fraction.

As a potential pain monitoring index, the changes of PPG signals can in a timely and sensitive manner detect variations in local blood perfusion caused by pain stimuli. Surgical stress index (SSI) is calculated from PPG amplitude and heart beat interval to assess the balance of nociception and anti-nociception [32–34]. The SSI ranges from 0 to 100, and a higher value is associated with a higher noradrenalin levels [35] and a lower remifentanil concentration in patients under general anesthesia [36]. In contrast, the value of SSI in postoperative pain assessment can be discounted for the effects of residual anesthesia, β-blockers, and anticholinergic agents on heart beat interval. In the present study, both values of AC and AC/DC extracted from PPG signals increased significantly after sufentanil administration, and the reported pain levels decreased at the same time. The reported levels of pain had significant correlations with both AC and AC/DC. ROC analysis also showed that AC and AC/DC work well in predicting pain intensity for adult patients in PACU. AC represents the maximal light absorption value in each heart rate, and is correlated positively with the pulsatile arterial blood component in the monitoring site [37]. DC is the constant light absorption value including non-pulsatile blood and tissue components [37]. AC/DC has been used to monitor the peripheral perfusion, and a higher AC/DC represents a better perfusion [38]. Pain stimuli could excite sympathetic nerves and result in a decrease of peripheral perfusion. Then, the strength of peripheral PPG signals would become weak and the AC and AC/DC decreased as well. On the other hand, the values of AC and AC/DC would increase after analgesic treatment in postoperative patients. Our results

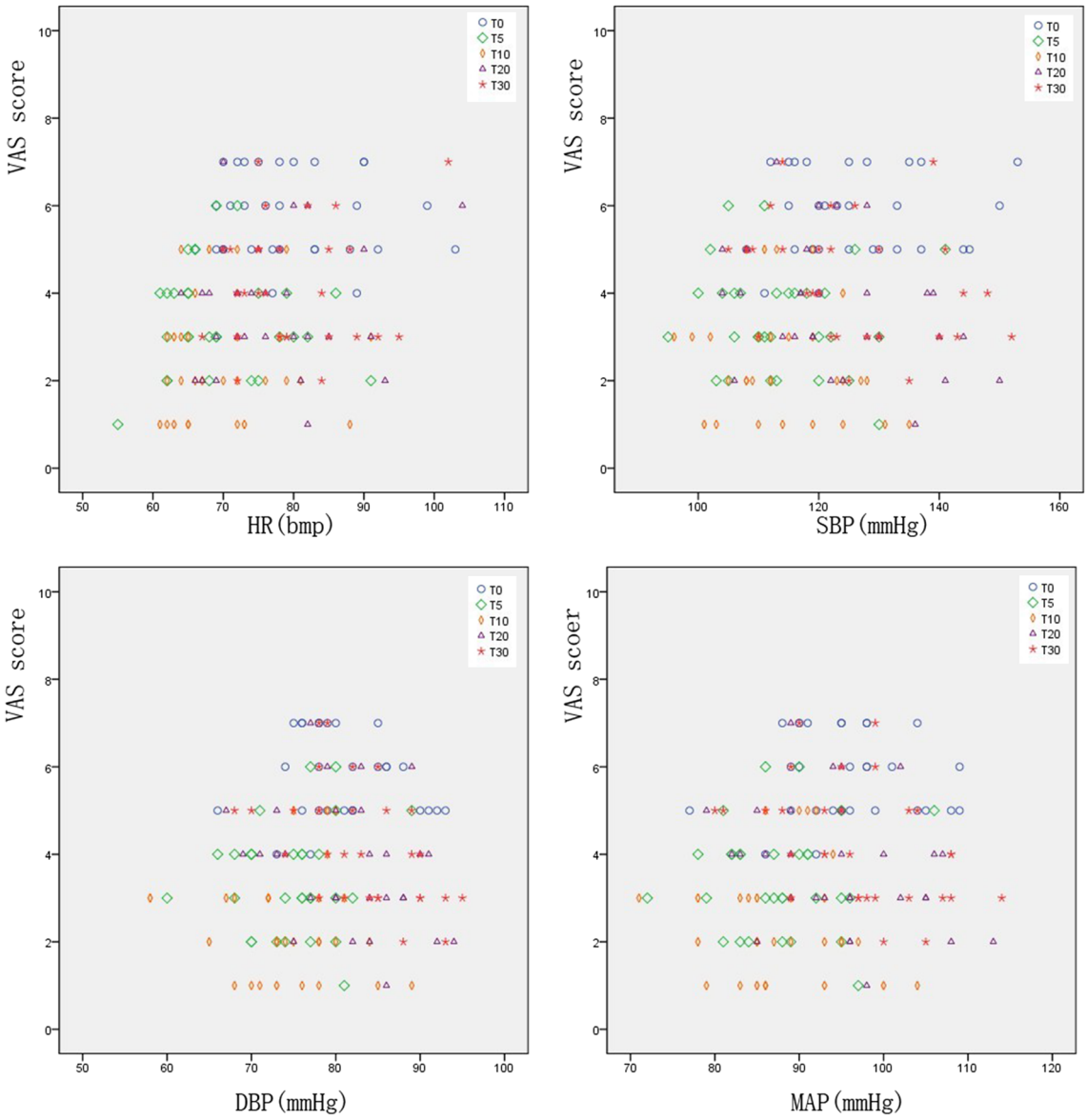

Fig. 5 Correlations were studied between the VAS score and general vital signs; VAS score only showed a weak correlation with heart rate ($r = 0.280$; $p < 0.01$), and no significant correlation with blood pressure (SBP, DBP, MAP). *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial pressure

demonstrated the above theory and suggested that PPG signals have advantages in postoperative pain monitoring over blood pressure or heart rate, and that AC/DC might be more valuable. Lower AC amplitude or AC/DC may help to evaluate the pain intensity in unconscious patients. However, its pain monitoring value in anaesthetized patients should merit further confirmation.

There are some limitations in this study. First, the accuracy of the VAS ratings may have been influenced by residual sedation in patients who have experienced general anaesthesia before. Second, the skin temperature of the monitoring site was not measured even though the environmental temperature was controlled, so the potential influence of skin temperature cannot be excluded. Fortunately, skin temperatures should undergo little change during the 30 min in which PPG signals are acquired.

In conclusion, it is feasible to assess acute postoperative pain by finger PPG signal. Both AC/DC and AC showed significant correlations with the pain rating levels, and they also performed well in predicting pain intensity for

Table 4 The photoplethysmographic metrics and vital signs at different pain levels

Parameters	Pain level		
	Mild ($n = 66$)	Moderate ($n = 72$)	Severe ($n = 12$)
AC (mv)	46.9 ± 18.7	34.0 ± 17.6[#]	26.0 ± 10.2[#]
AC/DC (%)	2.4 ± 0.6	1.4 ± 0.7[#]	0.8 ± 0.2[#,†]
SBP (mmHg)	119.7 ± 13.1	120.5 ± 11.9	124.3 ± 13.8
DBP (mmHg)	78.7 ± 8.0	79.6 ± 7.0	77.3 ± 2.0
MAP (mmHg)	92.1 ± 9.3	93.0 ± 8.3	92.9 ± 5.3
HR (bmp)	73.7 ± 9.6	75.7 ± 9.3	79.6 ± 9.9[*]

The pain level was divided into mild (VAS score 1–3), moderate (VAS score 4–6), and severe (VAS score 7–10). PPG metrics (AC, AC/DC) and vital signs (SBP, DBP, MAP, HR) were compared among the different pain levels

[#] $p < 0.01$ versus mild pain, [*] $p < 0.05$ versus mild pain, [†] $p < 0.01$ versus moderate pain

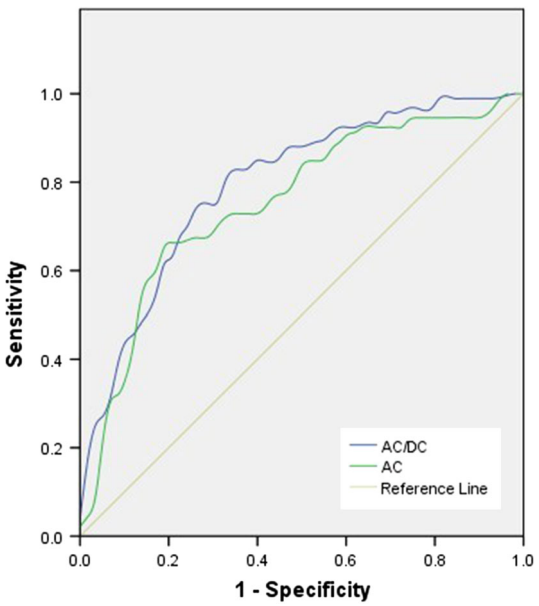

Fig. 6 ROC analysis to assess the predictive performance of AC and AC/DC in postoperative pain intensity. The area under the ROC curves (AUC) were 0.754 for AC and 0.795 for AC/DC, respectively. The optical threshold values of AC and AC/DC in predicting VAS >4 were 36.4 mv (sensitivity, 66.3 %; specificity, 81.0 %) and 1.33 % (sensitivity, 82.6 %; specificity, 67.2 %). *ROC* receiver operating characteristic curve, *AUC* the area under the curve

postoperative patients. Blood pressure or heart rate changes proved to be unreliable indicators for assessing postoperative pain.

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Ethical standards This study was approved by the Ethics Committee's chairman Zeng Yong. Institution: West China Hospital, Sichuan University. Address: No.37 Guo Xue Xiang, Chengdu, Sichuan, 610041. P.R. China Phone: +86 02885422654 Email: huaxilunli@163.com.

Informed consent This study was conducted with written informed consent from the study subjects. The study was registered prior to patient enrollment.

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