Photoplethysmographic characterization of vascular tone mediated changes in arterial pressure: an observational study

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Abstract

To determine whether a classification based on the contour of the photoplethysmography signal (PPGc) can detect changes in systolic arterial blood pressure (SAP) and vascular tone. Episodes of normotension (SAP 90–140 mmHg), hypertension (SAP > 140 mmHg) and hypotension (SAP < 90 mmHg) were analyzed in 15 cardiac surgery patients. SAP and two surrogates of the vascular tone, systemic vascular resistance (SVR) and vascular compliance (Cvasc = stroke volume/pulse pressure) were compared with PPGc. Changes in PPG amplitude (foot-to-peak distance) and dicrotic notch position were used to define 6 classes taking class III as a normal vascular tone with a notch placed between 20 and 50% of the PPG amplitude. Class I-to-II represented vasoconstriction with notch placed > 50% in a small PPG, while class IV-to-VI described vasodilation with a notch placed < 20% in a tall PPG wave. 190 datasets were analyzed including 61 episodes of hypertension [SAP = 159 (151–170) mmHg (median 1st–3rd quartiles)], 84 of normotension, SAP = 124 (113–131) mmHg and 45 of hypotension SAP = 85(80–87) mmHg. SAP were well correlated with SVR ($r = 0.78$, $p < 0.0001$) and Cvasc ($r = 0.84$, $p < 0.0001$). The PPG-based classification correlated well with SAP ($r = -0.90$, $p < 0.0001$), SVR ($r = -0.72$, $p < 0.0001$) and Cvasc ($r = 0.82$, $p < 0.0001$). The PPGc misclassified 7 out of the 190 episodes, presenting good accuracy (98.4% and 97.8%), sensitivity (100% and 94.9%) and specificity (97.9% and 99.2%) for detecting episodes of hypotension and hypertension, respectively. Changes in arterial pressure and vascular tone were closely related to the proposed classification based on PPG waveform. *Clinical Trial Registration* NTC02854852.

Keywords Arterial pressure · Photoplethysmography · Vasodilation · Vasoconstriction · Vascular tone

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Episodes of hypertension or hypotension during anesthesia are common and when important are associated to postoperative complications and can thus have an impact on patient's outcome [1–5]. A tight intraoperative control of arterial blood pressure is therefore mandatory for the conduction of a safe anesthesia. The invasive monitoring of blood pressure through an indwelling arterial catheter is the reference method in high-risk patients whereas automated cuff oscillometric noninvasive blood pressure (NIBP) is the most widely used method for monitoring normal or low-risk anesthetized patients [6]. These monitoring systems do not provide information regarding the mechanism/s behind hyper or hypotensive episodes so that interpretation, and hence decisions on potential therapeutic interventions, must be done according to the clinical context. As one of the principal mechanisms of hyper and hypotension during anesthesia is related to changes in systemic arterial vascular resistance induced by

anesthetic drugs [7–9], the possibility of monitoring vascular tone would be of clinical interest.

The pulse oximetry photoplethysmographic (PPG) signal provides non-invasive beat-by-beat information related to the characteristics of the vascular system [10]. The association between PPG, arterial blood pressure and systemic vascular resistance (SVR) has been previously described [11–13]. Such relationship is based on the fact that the PPG waveform represents the change of blood volume in a tested tissue (commonly the finger) during one beat [14, 15]. This pulse *flow* wave is strongly influenced by ventricular-vascular interactions in a similar way as the forward and backward pulse *pressure* waves [16, 17]. As opposed to the positive returning backward pressure wave, the backward flow wave returns to the heart as an inverse negative wave after reflecting back from the peripheral arterial tree bifurcations [18]. This leads to marked changes in the contour of the PPG waveform (PPGc) anytime the arterial compliance is affected by modifications in the peripheral vascular tone.

Based on the dynamic changes observed in the PPGc in response to alterations in vascular tone we recently proposed a classification in which we identified six differentiated patterns (Fig. 1) [19]. This classification stems from close clinical observations and is supported by some published evidences [20–23] but has not properly been tested or validated in anesthetized mechanically ventilated patients before.

We believe that the changes observed in PPGc recorded at the finger level are related to modifications on the arterial blood pressure induced by changes in vascular tone. We used the previously described PPGc classification system to test this hypothesis. For this purpose we compared the PPGc with invasive arterial blood pressure and two surrogates of vascular tone in anesthetized patients undergoing cardiac surgery.

1 Methods

This prospective observational pilot study was performed in the operating theater of a community hospital with the corresponding local IRB approval (Clinical Trial Registration NTC02854852). After obtaining signed informed consent, we studied mechanically ventilated patients aged ≥ 18 years undergoing cardiac surgery. We excluded emergency surgery and patients with baseline arrhythmias. Patients who developed intraoperative hypothermia (naso-pharyngeal temperature ≤ 36 °C), arrhythmias and a total bleeding ≥ 350 mL were also excluded to avoid any source of changes in the PPG signal.

Patients were anesthetized using standard procedures. Routine monitoring included ECG, time-based capnography, pulse oximetry and naso-pharyngeal temperature (S5, Datex-Ohmeda, Helsinki, Finland). Anesthesia was induced with propofol 1–1.5 mg kg^{-1}, vecuronium 0.08 mg kg^{-1} and fentanyl 10 μ kg^{-1} and maintained with propofol 80 μ kg^{-1} min^{-1} and remifentanil 0.5 μ kg^{-1} min^{-1}. Lungs were ventilated in volume-controlled ventilation using the Advance workstation (GE Healthcare, Madison, WI, US) with a tidal volume of 8 mL kg^{-1} of predicted body weight, respiratory rate 15 breaths min^{-1}, PEEP 5 cm H_2O, I:E ratio 1:2 and FIO_2 0.5.

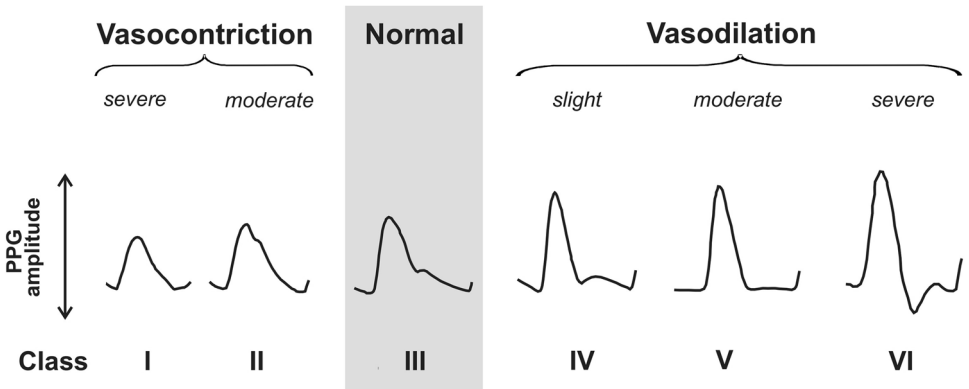

Fig. 1 Classification of the vascular tone based on the visual inspection of the photo-plethysmography waveform shape. The classification is based on the photoplethysmography (PPG) amplitude and on the positioning of the dicrotic notch. Normal PPG shape (class III) presented the dicrotic notch between 20 and 50% of the total PPG amplitude. Vasodilation increases PPG amplitude because the finger receives more blood flow (more infrared light absorbance). In PPG class IV the notch reaches baseline although the backward wave is still evident. Class V shows a flat phase without notch and in the class VI the notch becomes negative. Vasoconstriction shows less PPG amplitude than normal meaning that blood flow decreases (less infrared light absorbance). The notch ascends and fuses with the systolic pulse peak (classes II and I, respectively)

1.1 Hemodynamic monitoring

A femoral artery 5F catheter (Pulsion Medical Systems, Munich, Germany) and an internal jugular 8F catheter were inserted before anesthesia induction. Pressure transducers were placed and zeroed at the phlebostatic level before data recording. Invasive systolic (SAP), mean (MAP), diastolic (DAP) and pulse (PP = SAP − DAP) arterial pressures were obtained beat-by-beat. Normotension was defined as a SAP between 90 and 140 mmHg, hypertension as a SAP > 140 mmHg and hypotension as a SAP < 90 mmHg [4, 24].

Cardiac output (CO) was continuously monitored by pulse wave contour analysis after calibration with 3 stable transpulmonary thermodilutions every 20 min (PICCO Science, Pulsion Medical Systems, Munich, Germany). Stroke volume (SV) was calculated as CO/heart rate. Central venous pressure (CVP) was continuously measured by the central venous catheter connected to the PICCO monitor. We thus calculated SVR and arterial vascular compliance (Cvasc) as surrogates of systemic vascular tone in a beat basis [25]. SVR was derived from the standard formula:

$$\mathrm{SVR} = (\mathrm{MAP} - \mathrm{CVP})/\mathrm{CO} \times 80$$

Cvasc was calculated as SV/PP as described previously [26].

Pulse pressure variation (PPV) was calculated as [27].

$$\mathrm{PPV}(\%) = 100 \times \left[\left(\mathrm{PP}_{\max} - \mathrm{PP}_{\min}\right)/\left(\mathrm{PP}_{\max} + \mathrm{PP}_{\min}\right)/2\right]$$

were $\mathrm{PP}_{\max}$ and $\mathrm{PP}_{\min}$ are the maximal and minimal pulse pressure values determined over a single respiratory cycle. The stroke volume variation (SVV) was calculated as [27]:

$$\mathrm{SVV}(\%) = 100 \times \left[\left(\mathrm{SV}_{\max} - \mathrm{SV}_{\min}\right)/\left(\mathrm{SV}_{\max} + \mathrm{SV}_{\min}\right)/2\right]$$

The global end-diastolic volume index (GEDI) is a volumetric preload parameter related to the volume of blood within the heart, derived from the transpulmonary thermodilution (TPTD) curve as [28]:

$$\mathrm{GEDI} = \text{Cardiac index} \times (\text{mean transit time} - \text{downslope time})$$

Extravascular lung water index (ELWI) was calculated as [29]:

$$\mathrm{EVLWI} = (\mathrm{ITTV} - \mathrm{ITBV})/\text{predicted body weight}$$

where the intrathoracic thermal volume (ITTV = CO × mean transit time × 1000/60) and intrathoracic blood volume (ITBV = GEDV × 1.25).

1.2 Photoplethysmography

Core temperature was maintained ≥ 36 °C using a warming mattress. PPG was obtained by a conventional pulse oximeter (FluxMed, MBMED, Buenos Aires, Argentina) placed at the index finger of the tested hand. Data was recorded at 100 Hz via a laptop using a customized data collecting system. The PPG signal is the amount of light absorbed by the finger. In order to improve the visualization and have a comprehensive range, the dimensionless PPG signal is presented in an arbitrary scale 0–100% by the Fluxmed device. Any improvement in blood flow at the finger increases PPG amplitude because more light is absorbed by a crescent amount of blood. The opposite is true when finger's blood flow decreases, making PPG amplitude small.

The contour of the PPG was classified according to six patterns related to different vascular tone conditions as previously described [19]. This classification is based on (1) the position of the dicrotic notch and (2) the amplitude of the PPG waveform defined as the foot-to-peak PPG distance [14, 16–18]. The classification is then described as follows (Fig. 1):

- Class I: decreased PPG amplitude and dicrotic notch fusion with the systolic peak. Meaning: decrease in blood flow due to a significant increase in vascular tone secondary to severe vasoconstriction.
- Class II: decreased PPG amplitude and notch positioning at the upper 50% of the PPG waveform maximal amplitude. Meaning: decrease in local blood flow due to a moderate increase in vascular tone.
- Class III: the PPG amplitude of this class was arbitrarily taken as the reference amplitude because in our experience class III is related to normal blood pressure. The dicrotic notch is commonly located between 20 and 50% of PPG's maximum amplitude in this class
- Class IV: increased PPG amplitude and notch positioning at 20% of the PPG's waveform maximal amplitude. Meaning: increase in blood flow due to a reduced vascular tone caused by mild vasodilation.
- Class V: increased PPG amplitude where notch and diastolic wave are flat, located at the foot of the PPG. Meaning: increased blood flow due to moderate vasodilation.
- Class VI: increased PPG amplitude and the notch becoming negative. Meaning: increase in blood flow caused by severe vasodilation.

1.3 Protocol and data manipulation

Data was continuously recorded 45 min before sternotomy and within 1 h after closing the chest with patients placed in supine position during the whole protocol. These moments were chosen to avoid any interference from surgical manipulations and to minimize the risk of surgical bleeding. Patients received a bolus of 3 mL kg^{-1} of crystalloids during the induction of anesthesia and a maintenance infusion of 4 mL kg^{-1} h^{-1} for the remaining surgical time.

Intraoperative hemodynamic management was based on standard care guidelines used at our institution. Arterial blood hypotension related to a pulse pressure variation (PPV) > 12% was treated by a 2 mL kg^{-1} bolus of a crystalloid solution [25]. Any bleeding < 350 mL was immediately compensated by a bolus of crystalloid at a 1:3 ratio. Arterial blood hypotension associated to vasodilation according to low SVR (SVR values below 15% of the one observed during normal arterial blood pressure) was treated by norepinephrine (NE) infusion between 0.01 and 0.15 μ kg^{-1} min^{-1} until reach normal arterial blood values. Arterial blood hypertension was treated increasing the doses of anesthetic drugs (propofol bolus of 20 mg together an increment in its infusion to 90 μ kg^{-1} min^{-1} + fentanyl bolus of 150 μ + increment in remifentanyl infusion to 0.6–0.8 μ kg^{-1} min^{-1}). If SAP remained high after adjusting anesthetics doses, a nitroglycerine infusion of 0.01–0.10 μ kg^{-1} min^{-1} was then administered until its normalization.

The clocks from S5, PICCO and Fluxmed devices were synchronized and data simultaneously recorded. Analysis of the recorded files was performed off-line. We selected episodes of arterial blood normotension, hypertension and/or hypotension according to their definition based on SAP values [4, 24]. We arbitrarily choose those episodes in a sequential way, from the beginning to the end of the file, as depicted with arrows in Fig. 2. We selected 20 beats at each moment (arrows) and obtained mean values for each of the studied variables. A mean value of each studied variable build the final database. As no automated detection routines exist, one of the investigators allocated the PPGc to the corresponding class by visual inspection (Fig. 1).

Radial arterial blood pressure was recorded in two additional patients using the S5 device, which simultaneously collected the coordinated arterial blood pressure and PPG raw data. This information was not provided by the PICCO monitor and was only used to build Figures showing examples of our results.

1.4 Statistical analysis

Statistical analysis was performed using IBM SPSS Statistic 19.0.0 (IBM Company, USA) and Matlab® (Mathworks, Natick, MA, USA). Lilliefors test described a no normal distribution of data. Wilcoxon rank sum test and Spearman rank correlations coefficient were used for comparisons between studied variables. Due to the high inter-individual variability in studied parameters, correlations were done after normalizing them by the following formula:

$$x_{norm} = \frac{x - x_{min}}{x_{max} - x_{min}}$$

where x is the absolute value of one parameter and $x_{min} - x_{max}$ the minimum and maximum value of this parameter,

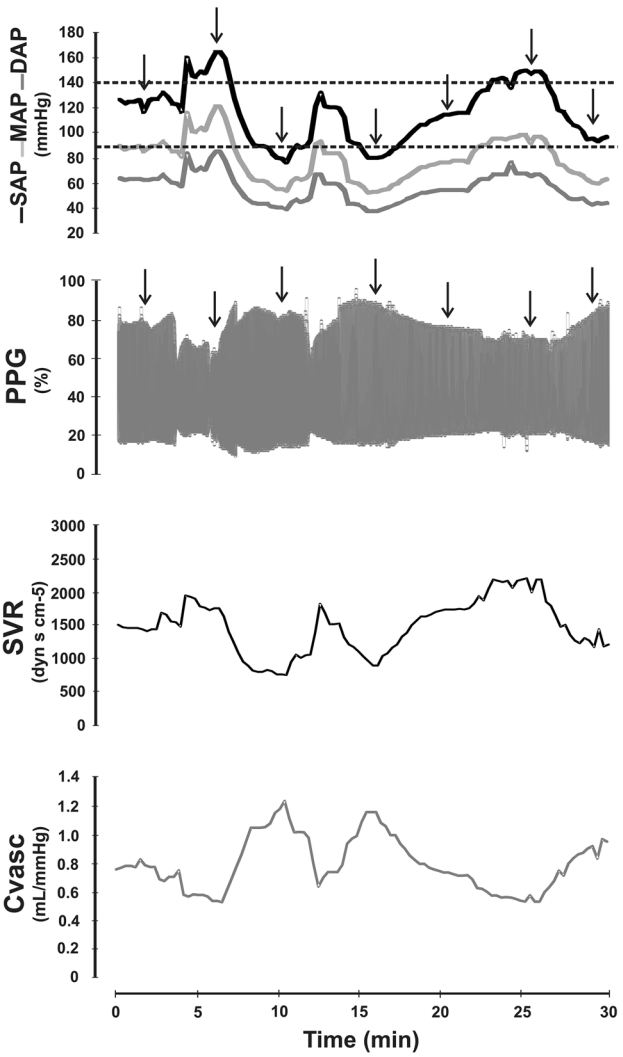

Fig. 2 Example of data analysis. Systolic (SAP), mean (MAP) and diastolic (DAP) arterial blood pressures, photoplethysmography (PPG), systemic vascular resistance (SVR) and vascular compliance (Cvasc) are depicted in one patient. Horizontal broken lines in arterial blood pressure showed the cut off value of SAP for the diagnosis of arterial blood hypertension (> 140 mmHg) and hypotension (< 90 mmHg). The arrows indicate the moment selected arbitrarily in this particular patient to build the database according to the changes in SAP. Note the simultaneous modifications observed in PPG amplitude and in the surrogates of vascular tone (SVR and Cvasc) during data collection

calculated for each patient. Thus, normalized value lies in an interval between 0, 1 for proper global correlation analysis. Results are expressed as mean ± standard deviation (SD) or median and 1st–3rd quartiles as appropriated. A p value < 0.05 was considered statistically significant.

A diagnostic test 2 × 2 table was used for the assessment of sensitivity = [TP/(TP + FN)] × 100; specificity = [TN/(TN + FP)] × 100; positive predicted value = [TP/(TP + FP)] × 100; negative predicted value = [TN/(TN + FN)] × 100 and diagnostic accuracy = [(TP + TN)/

(TP + TN + FP + FN)] × 100; where *TP* is true positive, *TN* is true negative, *FP* is false positive and *FN* is false negative. The test was applied to determine the ability of our classification to detect arterial blood hypertension or hypotension caused by changes in vascular tone; where the "disease" defined abnormal blood pressure according to known cut-off values [4, 24] and "healthy" is represented by normotension.

2 Results

In this analysis we studied 16 patients submitted to coronary artery bypass graft (CABG) surgery (Table 1). No patient developed new arrhythmias nor needed pacemaker when collecting the data. One patient was excluded due to acute bleeding of > 350 mL and data from the remaining 15 patients were analyzed. This patient presented a medical coagulopathy after cardiopulmonary bypass that needed more i.v. fluids, platelets and red cells transfusion.

According to the pre-defined blood pressure groups we studied 84 normotensive, 61 hypertensive and 45 hypotensive episodes. A total of 190 complete dataset was analyzed with an average of 13 ± 5 measurements per patient. SAP ranged from 65 to 197 mmHg.

Table 2 presents the recorded parameters of the different arterial blood pressure groups. CVP, PPV and SVV remained at normal values during the protocol. Mean GEDI was 742 ± 88 mL m^{-2} and EVLWI 8.2 ± 1.4 mL kg^{-1} during the protocol. These last two variables are not included in Table 2 because they were not continuously recorded only during thermodilutions.

The SVR increased and Cvasc decreased during arterial hypertension and changed in opposite direction during hypotensive episodes ($p < 0.0001$ both compared to normotension). Changes in SAP were correlated with these vascular tone related variables: SAP versus SVR ($r = 0.78$, $p < 0.0001$) and SAP versus Cvasc ($r = -0.84$, $p < 0.0001$).

PPGc class allocation adequately discriminated hypertensive and hypotensive from normotensive episodes (Table 2). We found a good correlation between PPGc class and SAP ($r = -0.90$, $p < 0.0001$), MAP ($r = -0.88$, $p < 0.0001$), DAP ($r = -0.85$, $p < 0.0001$), and PP ($r = -0.87$, $p < 0.0001$). PPGc class was also well correlated with SVR and Cvasc [−0.72 ($p < 0.0001$) and 0.77 ($p < 0.0001$) respectively] the chose surrogates of systemic arterial impedance.

As expected PPGc amplitude decreased during hypertension and increased during hypotensive episodes when compared to normotension (Table 2, all $p < 0.0001$). This parameter was also well correlated with SAP ($r = -0.79$, $p < 0.0001$), MAP ($r = -0.76$, $p < 0.0001$), DAP ($r = -0.75$, $p < 0.0001$), PP ($r = -0.77$, $p < 0.0001$), SVR ($r = -0.66$, $p < 0.0001$) and Cvasc ($r = 0.82$, $p < 0.0001$).

Figure 3 presents examples of the performance of the PPGc classification in one patient during changes in arterial blood pressure. Figure 4 illustrates how PPG dynamically changes in response to treatment of hypertensive and hypotensive episodes.

The PPG-based classification system failed in 7 out of the 190 measurements. Three episodes of normal arterial blood

Table 1 Patient's data

Cardiac surgery patients ($n = 15$)	
Age (years)	67 ± 19
Gender (% females)	33
Weight (kg)	85 ± 24
Height (cm)	169 ± 43
BMI (kg/cm^2)	29 ± 8
Type of surgery (number of patients)	Aorto-coronary bypass (13) Aortic valvular replacement (stenosis) + bypass (2)
EF (%)	58 ± 17
LV function (number of patients)	Normal systolic (10)–slight systolic dysfunction (5)–normal diastolic (9)–slight diastolic dysfunction (6)
RV function -Tapse (mm)	25 ± 3
Chronic diseases (number of patients)	Arterial hypertension (12) Smokers (8)–diabetes (3)–chronic renal failure (1)–obesity (3)–hypotiroidism (2)–stroke (1)
Preoperatory drugs (number of patients)	B-blockers (10) Vasodilators (7) Diuretics (1)–T4 (2)–statins (3) Oral hypoglycemic agents (3)

Data is presented as mean ± SD

BMI body mass index, *EF* ejection fraction left ventricle (LV), *RV* right ventricle

Table 2 Main studied parameters

Parameter	Hypertension (n = 61)	p value	Normotension (n = 84)	p value	Hypotension (n = 45)
SAP (mmHg)	159 (151–170)	< 0.001	124 (113–131)	< 0.001	85 (80–87)
MAP (mmHg)	100 (94–109)	< 0.001	77 (72–85)	< 0.001	53 (47–59)
DAP (mmHg)	67 (61–74)	< 0.001	53 (49–59)	< 0.001	37 (33–42)
PP (mmHg)	93 (86–104)	< 0.001	70 (60–77)	< 0.001	47 (40–51)
CO (L min^{-1})	4.6 (3.4–6.4)	0.030	4.2 (3.7–6.1)	0.026	3.8(2.9–5.4)
HR (bpm)	52 (47–60)	0.354	51 (48–62)	0.407	54 (48–65)
PPV (%)	4 (3–6)	0.406	6 (4–8)	< 0.001	9 (5–12)
SVV (%)	3 (3–4)	0.512	5 (3–7)	0.066	7 (6–10)
CVP (mmHg)	10 (6–12)	0.004	8 (4–11)	0.016	7 (3–9)
SVR (dyn s cm^{-5})	1766 (1165–2105)	< 0.001	1381 (962–1711)	< 0.001	1075 (750–1252)
Cvasc (mL $mmHg^{-1}$)	0.97 (0.64–1.25)	< 0.001	1.17 (0.80–1.59)	< 0.001	1.39 (1.10-2.00)
PPG class	2 (1–2)	< 0.001	3 (3–3)	< 0.001	5 (5–6)
PPG amplitude (%)	43 (38–52)	< 0.001	56 (44–66)	< 0.001	71(61–79)

SAP systolic arterial pressure, *MAP* mean arterial pressure, *DAP* diastolic arterial pressure, *PP* pulse pressure, *CO* cardiac output, *HR* heart rate, *PPV* pulse pressure variation, *SVV* stroke volume variation, *CVP* central venous pressure, *SVR* systemic vascular resistance, *PPG* photoplethysmography. p value = Wilcoxon rank sum test compared with normotension. Data is presented as median and 1st–3rd quartiles

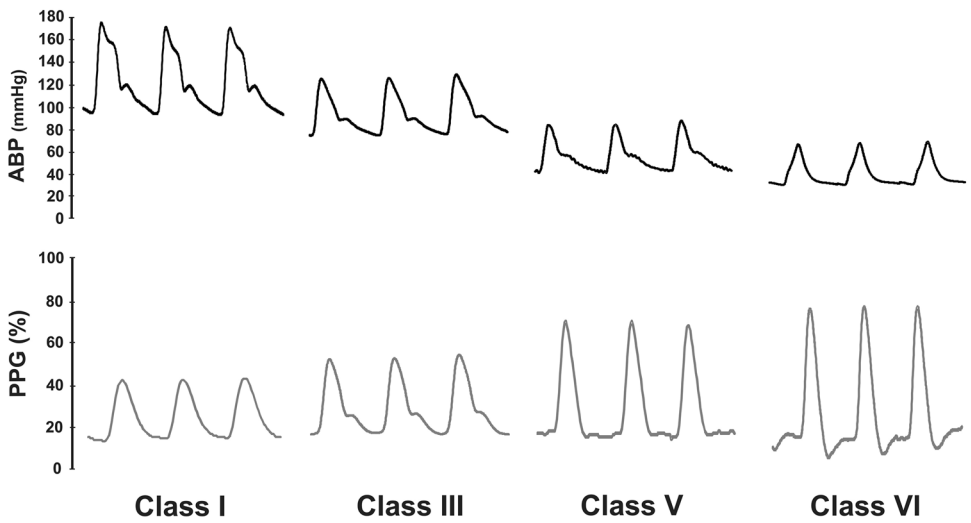

Fig. 3 Example of the PPG classification in one patient. Arterial blood pressure (ABP) and photoplethysmography (PPG) at different hemodynamic states in patient #9. Note the inverse relationship between PPG and pulse pressure amplitude

pressure were misclassified as arterial blood hypotension and one as hypertension (false positives). The other 3 episodes of arterial blood hypertension were misclassified as normotension because patients presented a class III pattern at SAP above 140 mmHg (false negatives). The corresponding analysis of accuracy, sensibility and specificity of the PPGc-based classification to detect hypo and hypertensive episodes are depicted in Table 3. The diagnostic test 2 × 2 table showed high accuracy of PPGc to diagnose arterial blood hypotension (98.4%) and hypertension (97.8%).

3 Discussion

In this observational pilot study we have found that a classification system based on the simple visual inspection of the photoplethysmography waveform's morphology was closely related to episodes of arterial blood hypertension or hypotension mediated by changes in vascular tone.

During surgery patients go through different phases in a dynamic way. Intraoperative hemodynamic alterations,

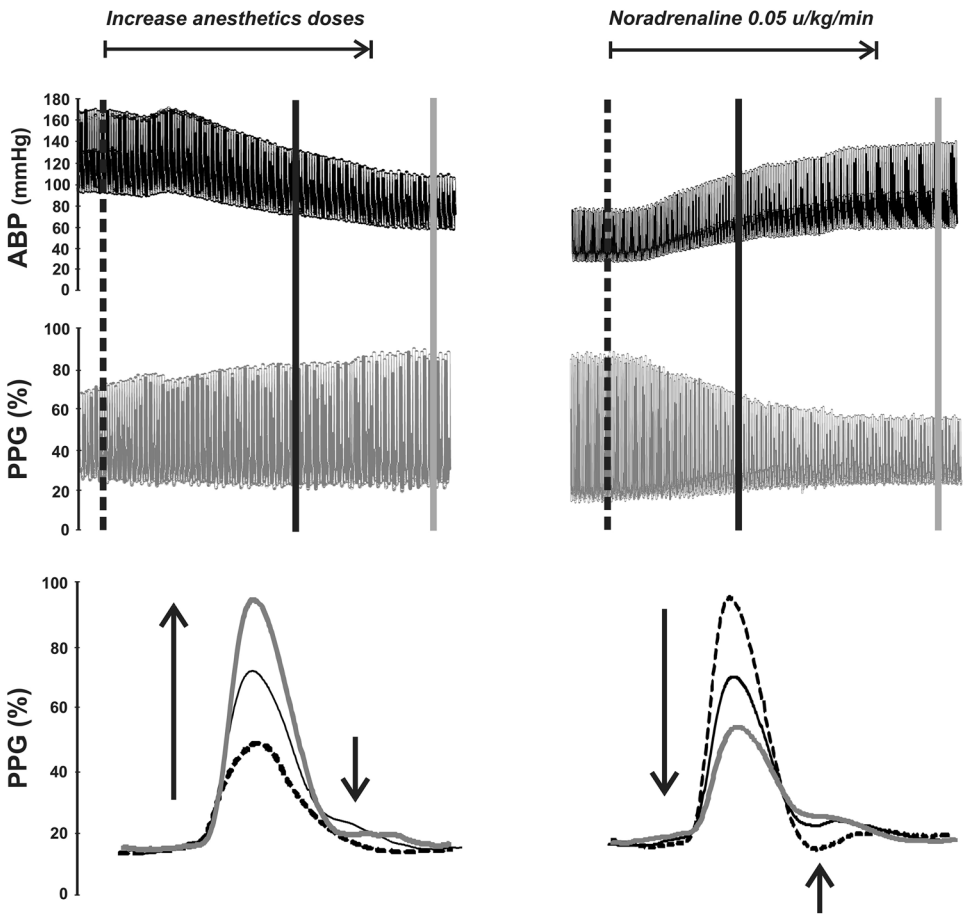

Fig. 4 Example of Arterial blood pressure and photoplethysmography recordings in two patients. Arterial blood pressure (ABP) and photo-plethysmography (PPG) continuous beat-by-beat recordings. Black-dotted, black and gray lines indicate the moments when PPG was analyzed with the corresponding waves presented at the bottom of the figure. Left: arterial blood hypertension episode treated by increasing anesthetic-drug doses as described in methods. As a result the initial low PPG amplitude increases and the position of the dicrotic notch descends progressively as blood pressure decreases. Right: a hypotensive episode corresponded to a PPG class V with an almost flat diastolic wave (black dotted-line wave). Noradrenaline infusion was administered until PPGc changed from class V to class III. Noradrenaline was discontinued once the normal PPGc target was reached. The direction of change in PPG amplitude and dicrotic notch position correspond to the long and short arrows marks, respectively

Table 3 Performance of the PPGc-based classification for diagnosing arterial blood hypotension and hypertension

ABP	Sensitivity	Specificity	Accuracy	PPV	NPV
Hypotension	1	0.979	0.984	0.938	1
Hypertension	0.949	0.992	0.978	0.982	0.977

Diagnostic test 2 × 2 table for the assessment of sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predicted value (NPV) of the PPG classification of hypotensive and hypertensive episodes

in the form of hyper or hypotensive episodes, are common and caused by surgical manipulations, bleeding, the interaction of the anesthetic agents and previous patient's chronic diseases. The standard blood pressure routine monitoring is based on NIBP systems that intermittently asses blood pressure at regular preselected periods. This implies that many of such hemodynamic episodes that appear suddenly may go undetected [6]. Depending on the measurement rate set, routine NIBP monitoring leaves "blind" periods between cuff compressions of variable duration in which, sometimes important changes in the hemodynamic status occur. Furthermore, the performance of NIBP is often impaired in situations of severe hypertensive or hypotensive episodes, manipulations in the surgical field affecting the monitored arm (i.e. external cuff compression) or in morbid obese patients among others [30–33]. Early detection of changes in the vascular tone and its effect on blood pressure by simple PPGc analysis could therefore facilitate the early diagnosis of circulatory instability and allow for an early proactive corrective therapeutic intervention when needed.

The PPGc classification would also help to interpret the pathophysiologic mechanisms behind arterial blood pressure changes during anesthesia and intensive care management. Changes in arterial blood pressure induced by alterations in vascular tone are common for most anesthetic and many sedative drugs [7–9]. Thus, medical therapies for intraoperative blood pressure changes could be better targeted to one of its main pathophysiologic causative mechanisms.

The clinical use of the arterial pulse pressure waveform for monitoring hemodynamics has been well described [16–18]. The same is true for the PPG contour analysis, which has been used for the assessment of fluid responsiveness [34, 35] and for studying the effect of aging and diseases on the vascular system [36, 37]. Previous publications have highlighted the relationship between PPG and arterial blood pressure. PPG has been used to estimate blood

pressure using different approaches like the pulse wave velocity analysis [38], the artery clamp method [39, 40], reappearance of the PPG waveform during cuff deflation [41, 42] or the analysis of different PPG features among others [43, 44]. The association between the PPGc and arterial wall compliance has also been described. Lopez-Beltrán et al. and Jagomägi et al. calculated beat-by-beat vascular compliance in a non-invasive way using PPG and finger blood pressure (Peñaz's method) [45, 46]. These authors demonstrated that vascular compliance derived from PPG quickly changes with the cold-pressure test and during arm elevation, respectively. Awad et al. and Middleton et al. have already studied the correlation between PPGc derived-parameters and SVR [11, 13]. Dawber et al. focused on the upward position of the dicrotic notch of the PPGc for the screening of hypertensive patients [20]. This notch's position shift reflects the early return of backward waves during cardiac systole and was related to arterial blood hypertension. However, they did not describe any PPGc changes to characterize arterial blood hypotension.

Our results are in line with these studies. We observed a good correlation between the PPGc class and SAP at blood pressure levels ranging from 65 to 197 mmHg. We also found good correlations between SAP and surrogates of vascular tone such as SVR and Cvasc. Taking all this information together, our findings support and raise the interest of the use of PPGc as a non-invasive hemodynamic monitoring option [47].

The effect on the PPGc of vasodilation induced by alcohol, nitrites or heat has been previously studied by several authors [21–23, 34]. In our daily practice we also observed that arterial hypotension induced by anesthetic drug induced vasodilation had a clear effect on the PPGc; effect that is reversed by an intravenous infusion of a vasoconstrictor like noradrenaline [48–50]. Similar to arterial hypertension, the changes on PPGc during vasodilation-induced arterial hypotension could be explained by ventricular-vascular interaction. During hypotension the vascular tree is more compliant and the backward wave returns slowly and late in diastole, delaying and moving the dicrotic notch downwards. If vasodilation is moderate-to-severe we observed that the notch became flat and then negative.

We believe our findings are of clinically interest because most of severe postoperative complications, like acute myocardial infarction, intracranial hemorrhage or kidney failure are related not only with the degree of intraoperative arterial blood hyper/hypotension but also with the duration and number of such episodes [1–5]. The proposed classification can help to quickly suspect an arterial hyper/hypotensive episode in patients where invasive arterial blood pressure or advanced hemodynamic monitoring is not indicated. Besides, the classification could be potentially helpful to differentiate the pathophysiological mechanisms that caused the changes in arterial blood pressure, guiding the treatment as observed in Fig. 4. We did not test the potential role of the proposed PPG based classification in the detection of other hemodynamic changes like hypovolemia in the studied patients. Therefore, whether such a classification can differentiate vasoplegic from hypovolemic hypotension must be addressed in future studies.

3.1 Limitations

Despite the protocol was design to avoid occult hypovolemia or hypervolemia, we cannot confirm or discard these conditions using PPV. The changes observed in arterial blood pressure could be affected not only by changes in the vascular tone but also for some degree of hypo/hypervolemia. Thus, the performance of our PPG based classification of the vascular tone could be influenced by a potential change in patient's volemia. We assume that the main changes in arterial blood pressure were caused by changes in the vascular tone in our patients. This assumption is because the fast changes in blood pressure were reversible and related to changes in the surrogates of vascular tone (SVR and Cvasc) and not related to bleeding, fluid deficit or overload. Next studies must be done in controlled experimental environments to test different hemodynamic scenarios.

We only investigated those PPG parameters related to the proposed classification—the amplitude and the position of the dicrotic notch. Other PPG derived variables related to the hemodynamic status like the plethysmographic variation index, the stiffness index, the diastolic-to-systolic ratio (B/A ratio), the PPG second derivative or the PPG width were not tested in this study. The addition of those PPG parameters could improve the sensitivity and specificity of the PPGc method as described by Lee et al. [12].

We did not analyze inter-observer agreement in this study and certainly the automatization of this PPGc-based estimation of the vascular tone, including many other PPG-derived parameters, would eliminate any physician's subjectivity and improve the diagnostic performance of PPGc. Our primary intention at this stage was a preliminary description of a method that can provide clinicians with an easy, fast and simple assessment of vascular tone and its association with arterial blood pressure changes just by observing the standard pulse oximeter's waveform display and not depending on any more complex computational waveform analysis. All detected episodes of arterial blood normo-hyper-hypotension were selected for analysis but, as the investigator was not blinded for the PiCCO tracings (as they were used to detect the episodes), certain subjectivity in the selection could not be ruled out and could induce a bias in our final results.

The studied cohort of cardiac surgery patients is an unstable population with vascular disease and endothelial

dysfunction, which results in common and frequent fluctuations in blood pressure. Different cohorts like elderly or children or patients with different hemodynamic conditions such as heart failure and/or acute bleeding could affect the performance of a PPGc-based estimation of the vascular tone. Future studies will be needed to test the accuracy of the proposed method in a broader population of patients.

3.2 Conclusions

Changes in arterial blood pressure mainly mediated by alterations in the vascular tone were closely related to a classification based on the shape of the photo-plethysmographic waveform. The proposed non-invasive classification has potential monitoring, diagnostic and therapeutic applications.

Compliance with ethical standards

Conflict of interest No potential conflicts of interest exist except for Matías Madorno who is partner and manager of MBMed S.A; a company that produce respiratory monitoring equipments.

Informed consent Informed consent was obtained from all individual participant included in the study.

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