CASE REPORT

Paradoxical increase in the photoplethysmography amplitude in response to nociceptive stimulation induced by tracheal intubation : A case report

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Abstract : Background : Although an increase in sympathetic nerve activity is generally associated with a decrease in the photoplethysmography (PPG) amplitude, the present case study demonstrates that nociceptive stimuli, such as tracheal intubation, paradoxically induce an increase in PPG amplitude. To the best of our knowledge, this is the first study to capture an increase in the PPG amplitude in response to sympathetic nerve activation. Case presentation : A 73-year-old woman underwent open surgery. Following anesthesia induction, tracheal intubation was performed, which resulted in increased heart rate and raised blood pressure. While nociception usually decreases the PPG amplitude, the opposite was found. Conversely, the vascular stiffness K value, our research group's unique monitoring method to quantify the strength of sympathetic activity, increased reflecting increased peripheral vascular resistance. Conclusions : We report a paradoxical case of increased PPG amplitude following tracheal intubation. It is important to note that the PPG amplitude does not always decrease with nociceptive stimuli. J. Med. Invest. 68 : 383-385, August, 2021

Keywords **:** *Photoplethysmography, sympathetic response, vascular stiffness*

BACKGROUND

Nociceptive stimuli are known to provoke sympathetic responses, resulting in increased inotropic and chronotropic effects (cardiac index), systemic vascular resistance (SVR), and blood pressure (BP). Thus, it is important to accurately evaluate these sympathetic responses to estimate the intensity of nociceptive stimuli. However, although heart rate (HR) and BP are simple monitoring methods of sympathetic responses, they are greatly influenced by cardioactive agents and changes in circulating blood volume in addition to nociception. On the other hand, photoplethysmography (PPG) is a widely used technique to quantify the nociceptive stimulus, as increase in SVR decreases skin blood flow and amplitude (1). Therefore, recently proposed monitoring devices for quantifying nociception during surgery, such as the Surgical Pleth Index and Nociception Level, often use SVR measurement based on the PPG amplitude as an index of peripheral sympathetic nerve activity (2, 3). The PPG amplitude can be easily measured with a pulse oximeter, which is indispensable in anesthesia management, and can be used as a simple method to monitor SVR. Nociceptive stimuli theoretically increase SVR and decrease the PPG amplitude. However, nociceptive stimuli may increase the PPG amplitude when the magnitude of the stroke volume increase overcomes that of the vascular constriction increase (4). There have been several reports of cases where increased SVR increases the cardiac output (CO) (5). However, to the best of our knowledge, no case has been reported in which nociceptive stimuli actually increased the PPG amplitude. Here, we present a paradoxical increase in the PPG amplitude in response to noxious stimuli, i.e., tracheal intubation in a patient scheduled to undergo open hepatectomy under general anesthesia. In addition, we simultaneously recorded the changes in PPG and SVR (or vascular stiffness) and compared them. Prior written consent was obtained from the patient whose case is reported in this study. This study fully adheres to the CARE guidelines.

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VASCULAR STIFFNESS VALUE K

Previously, our research group succeeded in quantifying SVR using the vascular stiffness value (K) by fitting the beat-to-beat PPG and Lissajous curves of invasive arterial BP (ABP) waveforms to a mechanical impedance model (6). Details of the calculation of K have been reported previously (7). K is the coefficient of a function in which the arterial waveform is estimated from the function of the PPG waveform, and calculated by a least square fitting of all waveforms in each heartbeat. K is adopted only when the coefficient of determination of the fitting is ≥ 0.95 ; therefore, it has a high reliability. K is more sensitive to changes in peripheral vascular resistance than PPG, as it is not affected by stroke volume. Furthermore, K was reported to quantitatively measure pain and reflect sympathetic nerve activity (8, 9). K is calculated by using the data from electrocardiography (ECG), ABP, and PPG. In our hospital, ECG, ABP, PPG, and other data are recorded not only numerically, but also as waveform data for all patients. Because of the rare phenomenon of a paradoxical increase in the PPG during tracheal intubation, we analyzed these waveform data postoperatively.

CASE PRESENTATION

The patient described here was a 73-year-old woman (height : 144 cm ; weight : 44 kg) who was scheduled to undergo hepatic S7 subsegment resection due to hepatocellular carcinoma secondary to hepatitis C and gallbladder resection. Her medical history included thrombocytopenia (83,000 / μL), hypertension, and diabetes. Her indocyanine green retention

rate at 15 minutes was 14.6%, and Child-Pugh classification was grade A, indicating that liver damage was relatively mild. Oral medications included omega-3-acid ethyl esters, nicardipine hydrochloride, sitagliptin phosphate hydrate, and teprenone. Without premedication, laxatives were administered on the day before surgery as preoperative treatment, which caused a reaction stool. The patient had her last meal and drink 14 hours and 12 hours, respectively, before entering the operating room. In the operating room, the equipment was attached and monitoring was started. This included : a photoplethysmography probe (TL-271T, Nihon Kohden, Tokyo, Japan) was placed on her left middle finger ; ECG and electroencephalogram probes (EEG ; Entropy, GE Healthcare UK Ltd., Buckinghamshire, UK) were placed on her chest and anterior forehead, respectively ; a neuromuscular blockade monitoring device (NMT- Neuromuscular Transmission, GE Healthcare UK Ltd., Buckinghamshire, UK) was placed on the ulnar side of her right forearm ; and a non-invasive blood pressure cuff was placed on her right upper arm. A preoperative dosing plan was developed to achieve a predicted effect-site concentration of 2 ng/mL remifentanil. Minto's pharmacokinetic model (10) was used to calculate predicted effect-site concentrations. Before anesthesia induction, her HR was 52 bpm, BP was 139/58 mmHg, oxygen saturation (SpO_2) was 100%, axillary temperature was 35.8℃, and she had cold extremities. Remifentanil was administered as per the dosing plan, and propofol was used to induce anesthesia using a target-controlled infusion (TCI) pump with built-in 'Diprifusor' (TE-371, Terumo, Tokyo, Japan). After the patient became unconscious, 50 mg of rocuronium were administered, and a 22 G catheter was secured in the left radial artery for measuring arterial blood pressure (ABP). ECG, ABP, and PPG waveform data were monitored by a bedside patient monitor (BSS-9800, Nihon Kohden, Tokyo, Japan), and outputted to a personal computer for the calculation of K. When the target blood concentrations of propofol and predicted effect-site concentration of remifentanil reached a steady state at 2.2 μg/mL and 2 ng/mL, respectively, the patient's ABP decreased (58/35 mmHg). This was promptly followed by tracheal intubation using a Macintosh laryngoscope. Figure shows the waves and trends of each parameter during tracheal intubation. Briefly, significant increases in the patient's HR and ABP were observed in response to tracheal intubation, and K increased as a normal response to noxious stimuli, reflecting vasoconstriction. However, despite the noxious stimuli, her PPG amplitude paradoxically reached a peak, which was several seconds behind the ABP and K value peaks and continued even after those returned to their basal values.

DISCUSSION

Here, we reported the case of a patient scheduled to undergo open hepatectomy under general anesthesia who showed paradoxical increase in the PPG amplitude in response to noxious stimuli. Previous literature suggests that an unpleasant stimulus produces a sympathetic response that increases SVR, resulting in an increase in BP and a decrease in the PPG amplitude (4). Many of the currently proposed nociceptive monitoring methods utilize this phenomenon and are designed so that the index of nociception decreases with increase in the PPG amplitude (2, 3). Therefore, it should be noted that nociceptive monitors using the PPG amplitude as the primary signal will provide erroneous readings in cases that show paradoxical changes in the PPG amplitude, as observed here.

In the present case, a cold sensation in the periphery of the patient's extremities was observed before anesthesia induction. In addition, her BP was extremely low after anesthesia induction. These findings suggest that the patient's circulating blood volume was very low. In addition, the vasodilator action and heart deterrent effect of propofol may have contributed to the hypovolemia before tracheal intubation. Based on the change in K after tracheal intubation, SVR is likely to have increased because of tracheal intubation in this patient. However, the PPG amplitude paradoxically increased. Similar to studies showing that elevated SVR during hypovolemia increases venous return and CO (5), sympathetic responses associated with tracheal intubation likely caused the increase in SVR, venous return, and CO. The PPG amplitude is determined by the balance of the forces between the blood supply (CO) and SVR (11). When comparing the increase in the cardiac index and SVR due to tracheal intubation, the former may have had a greater effect, resulting in an increase in the PPG amplitude. It is important to note that nociceptive stimuli may paradoxically increase the PPG amplitude under conditions of reduced circulating blood volume.

In contrast to PPG, K displayed a normal response and increased with the noxious stimulus. Given that K is the coefficient of the first derivative of the displacement of the vascular wall against the force applied on the vascular wall itself, it is less affected than PPG by the change in blood volume and accurately reflects changes in SVR. In our previous studies, the direction of the response to tracheal intubation of the K value and PPG were often the same (12). However, the amount of change in K was larger than that in the PPG amplitude. This may be because the increased PPG amplitude due to the increased CO induced by nociception offsets the effect of increased SVR.

It is noteworthy that the PPG amplitude trend during tracheal intubation was different from that of K. Specifically, vasoconstriction, represented by K, increased and returned to baseline after intubation, while PPG continued to increase. As a result, the timing of PPG amplitude maximization lagged behind ABP by approximately 40 seconds, with K reaching maximum values (Fig. 1). This temporal change in the PPG amplitude is similar to the report that phenylephrine causes an increase in venous return and CO approximately 20–30 seconds after the rise in BP (5). When a nociceptive stimulus is applied, the PPG amplitude is susceptible to changes in SVR (4). However, it seems likely that the PPG amplitude in this case showed a change that was more greatly influenced by the change in CO than SVR. Conversely, K increased quickly after tracheal intubation and was a more accurate estimate of SVR change than the PPG amplitude.

LIMITATIONS

First, considering that the effective circulating blood volume was not measured, determining the change in CO before and after anesthesia induction was not possible. Therefore, we assumed that CO was at a decreased level after anesthesia induction with the given standard clinical signs (e.g., bowel preparation, cold skin, and hypotension). Second, atropine was not administered, as it may modify the sympathetic response. Although the vagal reflex caused by tracheal intubation should be considered, it was thought to be less likely, since the HR did not change and BP was increased by intubation. Finally, we performed tracheal intubation at an effect-site concentration of 2 ng/mL of remifentanil. Our research group has previously reported that this concentration of remifentanil suppresses some sympathetic responses to tracheal intubation in a subset of patients (12). In addition, we did not increase the dose to avoid exacerbating hypotension. While it is possible that the low remifentanil concentration resulted in a strong sympathetic response, in light of the actual changes in HR and BP, it is unlikely that the sympathetic response was stronger than the ones in

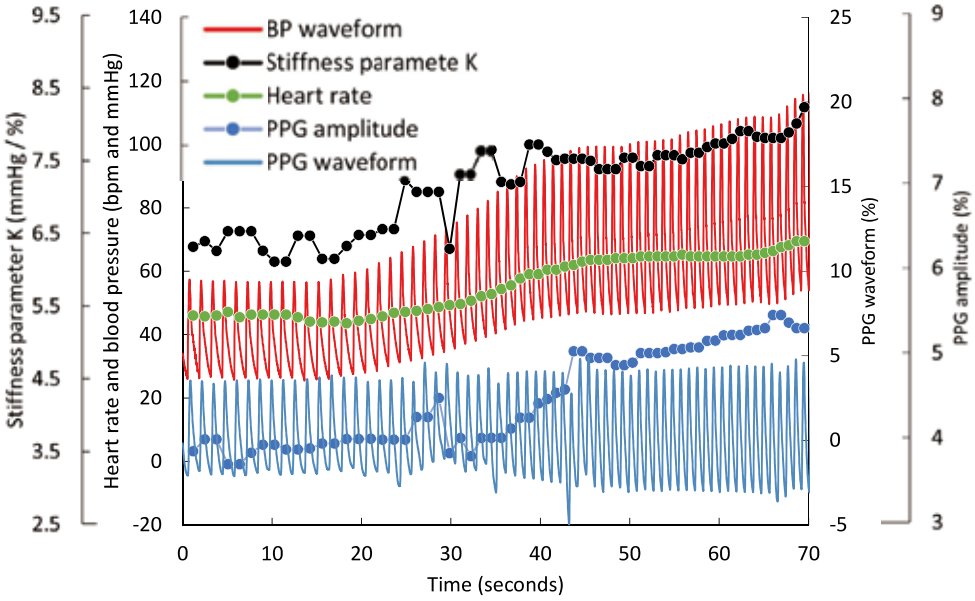

Figure 1. Changes in parameters before and after the tracheal intubation.
The measured values of K, HR, PPG amplitude, and raw waveforms of PPG and ABP are presented. The time at the start of tracheal intubation was set to zero. While the HR and ABP increased following tracheal intubation, PPG also simultaneously increased.
HR, heart rate ; PPG, photoplethysmography ; ABP, arterial blood pressure

routine clinical practice.

CONCLUSION

We suggest that the PPG amplitude does not always correctly reflect changes in peripheral vascular resistance when special circulatory dynamics occur, e.g., when the effective circulating blood volume is extremely low. In the present case, K was found to be more accurate for reflecting changes in SVR due to nociceptive stimuli, as it correctly showed an increase in vascular tone.

CONFLICTS OF INTEREST

Satoshi Kamiya declares no conflict of interest associated with this manuscript.

Ryuji Nakamura declares no conflict of interest associated with this manuscript.

Noboru Saeki declares no conflict of interest associated with this manuscript.

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