〈Original Article〉

Experimental validation of blood flow derived from pulse oximeter wave signals in beagles

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ABSTRACT *Purpose* Pulse oximeter wave reflects blood volume changes in tissue, suggesting the possibility of monitoring changes in tissue blood flow. Thus, our aim was to examine the correlation between tissue blood flow derived from pulse oximeter wave signals (Q_{pulse}) at a toe and the arterial flow measured by a Doppler probe at the femoral artery ($Q_{Doppler}$).

Methods Six beagles under general anesthesia were studied. A 24-G catheter was placed in the proximal femoral artery for drug infusion and an ultrasonic transit-time flow probe applied to the artery to measure $Q_{Doppler}$. The pulse oximeter signals from the right toe were processed with in-house−developed software to obtain Q_{pulse}. Three saline solutions containing respectively the vasodilators isosorbide dinitrate (20 μg/mL), adenosine (20 μg/mL), and nicardipine (10 μg/mL) were infused at increasing rates of 0, 2.5, 5.0, 10, or 20 mL/h for 8 minutes into the femoral artery with a syringe pump.

Results Both $Q_{Doppler}$ and Q_{pulse} increased fourfold with increasing rates of infusion of the three vasodilators. Plotting of $Q_{Doppler}$ and Q_{pulse} across the three vasodilators in each animal revealed linear correlations (R^2 = 0.17−0.76). Overall regression analysis showed a less strong but still statistically significant linear relation ($y=3.68x + 18.5$, $R^2 = 0.25$, $P < 0.01$).

Conclusions We found a linear correlation between $Q_{Doppler}$ and Q_{pulse} in a wide range of femoral arterial blood flow measures induced by different vasodilators in each animal. Arterial flow wave derived from pulse oximetry was quantitatively validated.

doi:10.11482/KMJ-E41(1)1 *(Accepted on January 26, 2015)*

Key words: **Pulse oximetry, Blood flow, Monitor**

INTRODUCTION

Although pulse oximeter is an essential monitor during anesthesia and critical care for patient safety, the information obtained from pulse oximeter wave signals is underused. Cook developed a method to obtain an arterial blood flow wave from pulse oximetry wave signals and demonstrated that a close similarity exists between the Doppler flow

This study was presented at the annual meeting of American Society of Anesthesiologists, October 18, 2009, in New Orleans.

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waveform at the radial artery and the waveform derived from the pulse oximeter at the finger tip[1,2]. However, whether the derived arterial flow quantitatively reflects actual blood flow remains to be determined. In this study, we experimentally investigated the correlation between blood flow derived from pulse oximetry wave signals at a toe (Q_{pulse}) and the arterial flow measured by a Doppler probe at the femoral artery ($Q_{Doppler}$) in beagles.

MATERIALS AND METHODS

After obtaining the approval of our institutional ethical committee (#03-098), we performed the study using six beagles (11.4 ± 2.5 kg). The animals were premedicated with intramuscular ketamine (100 mg). After induction of anesthesia with thiopental (50 mg), the trachea was intubated and the lungs ventilated with a ventilator at 20 bpm with a tidal volume adjusted to maintain normocapnia. Anesthesia was maintained with inhalation of 1.5% halothane in a gas mixture of 60% nitrous oxide and 40% oxygen and intravenous fentanyl (0.15 mg). Body temperature was maintained at 37－38℃ with a heated water blanket throughout the experiment.

The right femoral artery was exposed, and a 24-G indwelling catheter was placed in the artery for drug infusion. An ultrasonic transit-time flow probe (T-206, Transonic System, USA) was applied to the artery 3 cm distal to the indwelling catheter to measure its flow ($Q_{Doppler}$). Arterial pressure (P_{po}) was measured via another 24-G catheter inserted into a branch of the right popliteal artery. A disposable pulse oximeter probe was attached to the right toe and connected to the pulse oximeter (OLV-3100, Nihon Kohden, Japan). Electrocardiography, P_{po}, $Q_{Doppler}$, and Q_{pulse} results were transferred to a PC via a 16-bit AD interface at 1 kHz and processed using our in-house software.

Calculation of blood flow from pulse oximeter wave signals

The algorithm for extracting arterial blood flow (Q_{pulse}) from pulse oximeter wave signals is described elsewhere[1]. In brief, three assumptions were made for processing: 1) the pulse oximeter wave represents volume change against time; 2) changes in volume represent total flow, comprising arterial inflow and venous outflow; and 3) venous outflow from the arteriolar bed is proportional to the volume within it. If the venous outflow is subtracted from the total flow, the remaining sum

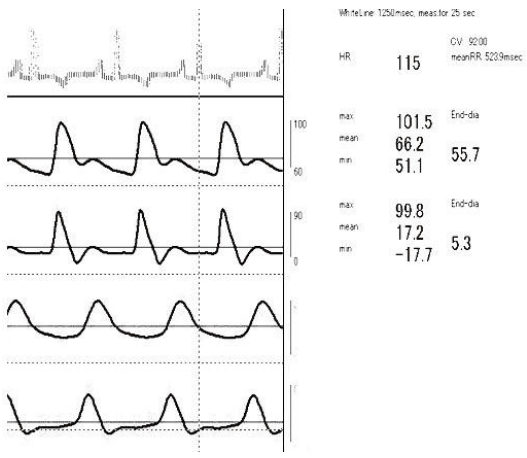

Fig. 1. An example of a PC display during measurement.
From top to bottom, electrocardiogram recording, P_{po}, $Q_{Doppler}$ (arterial blood flow measured by transit-time flow meter at the femoral artery), pulse oximeter wave signal, and Q_{pulse} (tissue blood flow derived from pulse oximeter signal at the toe of the same limb). All signals were transmitted to a PC via a 16-bit AD interface and processed to calculate Q_{pulse}.

is the Q_{pulse} (Fig. 1). One of the authors (Y.F.) wrote the computer program.

Drug administration

Three saline solutions containing the vasodilators isosorbide dinitrate (20 μg/mL), adenosine (20 μg/mL), and nicardipine (10 μg/mL), respectively, were infused at increasing rates of 0, 2.5, 5.0, 10, and 20 mL/h for 8 minutes into the femoral artery with a syringe pump (STC-521, Terumo, Japan) via the catheter. The order of drug administration was randomized. Before the start of each drug administration, maximum vasoconstriction was achieved by infusion of 20 μg phenylephrine into the artery for 2 minutes. A period of 10 minutes was allowed for hemodynamic stabilization after each drug administration. Hemodynamic measurements including P_{po}, heart rate (HR), $Q_{Doppler}$, and Q_{pulse} were carried out at the end of each vasodilator infusion.

Statistics and data analysis

All data were presented as means ± SD. The level of statistical significance was $P < 0.05$. Linear regression analysis was performed to compare the relation of $Q_{Doppler}$ and Q_{pulse} across the three drugs in each animal and then in all animals.

RESULTS

The mean P_{po} and HR remained unchanged regardless of infusion rate for each drug (Table 1). $Q_{Doppler}$ and Q_{pulse} values during infusions of the three vasodilators into the femoral artery are presented in Table 2. Both $Q_{Doppler}$ and Q_{pulse} increased with increasing rates of infusion of each vasodilator. Plotting $Q_{Doppler}$ and Q_{pulse} across the three vasodilators in each animal revealed linear correlations between the two measures ($R^2 = 0.17 - 0.76$) (Fig. 2). Overall regression analysis showed a less strong but still statistically significant linear

Table 1. Hemodynamics during infusion of vasodilators

Infusion rate	0 mL/h	2.5 mL/h	5 mL/h	10 mL/h	20 mL/h
Nitrol (20 μg/mL)					
HR (mL/min)	109.0 ± 48.2	108.2 ± 46.9	111.7 ± 47.5	115.0 ± 49.3	116.7 ± 48.8
Mean P_{po} (mmHg)	82.7 ± 33.5	83.3 ± 32.9	84.9 ± 33.3	85.8 ± 33.1	86.2 ± 33.5
Adenosine (20 μg/mL)					
HR (mL/min)	110.8 ± 46.5	111.5 ± 46.2	114.8 ± 47.9	114.5 ± 48.6	117.7 ± 49.3
Mean P_{po} (mmHg)	85.1 ± 33.5	88.0 ± 34.4	87.7 ± 34.3	87.4 ± 34.8	87.0 ± 34.2
Nicardipine (10 μg/mL)					
HR (mL/min)	114.5 ± 47.3	123.0 ± 52.3	118.7 ± 48.8	122.7 ± 49.2	121.7 ± 49.9
Mean P_{po} (mmHg)	87.1 ± 34.4	87.3 ± 36.5	88.5 ± 34.1	89.2 ± 34.2	86.4 ± 33.0

Mean P_{po}, mean arterial pressure measured at the right popliteal artery. Nitrol, isosorbide dinitrate. Vasodilators including isosorbide dinitrate and nicardipine were infused directly into the right femoral artery in a randomized sequence. There were no significant changes in heart rate (HR) or the mean P_{po} during infusion of vasodilators. Data are presented as means ± SD; n = 6.

Table 2. Comparison of $Q_{Doppler}$ and Q_{pulse} during infusion of vasodilators

Infusion rate	0 mL/h	2.5 mL/h	5 mL/h	10 mL/h	20 mL/h
$Q_{Doppler}$ (mL/min)					
Nitrol (20 μg/mL)	10.7 ± 4.8	17.9 ± 6.6	22.5 ± 5.3	32.4 ± 7.7	43.0 ± 5.3
Adenosine (20 μg/mL)	15.4 ± 5.4	22.9 ± 4.9	29.8 ± 6.8	38.8 ± 12.4	55.3 ± 13.0
Nicardipine (10 μg/mL)	13.1 ± 3.3	19.0 ± 3.8	22.7 ± 6.5	32.8 ± 7.5	48.3 ± 21.1
Q_{pulse} (volts/s)					
Nitrol (20 μg/mL)	0.72 ± 0.57	1.90 ± 0.29	2.17 ± 0.39	3.17 ± 1.50	4.84 ± 3.19
Adenosine (20 μg/mL)	1.33 ± 1.07	2.48 ± 1.34	2.85 ± 1.58	3.93 ± 2.13	4.62 ± 2.71
Nicardipine (10 μg/mL)	1.65 ± 1.14	2.48 ± 1.09	2.71 ± 2.45	3.06 ± 2.42	3.67 ± 2.74

$Q_{Doppler}$ was measured by a Doppler flow meter at the femoral artery, and Q_{pulse} was calculated from the signal of the pulse oximeter wave signals at the toe of the same limb. Nitrol, isosorbide dinitrate. Data are presented as means ± SD; n = 6.

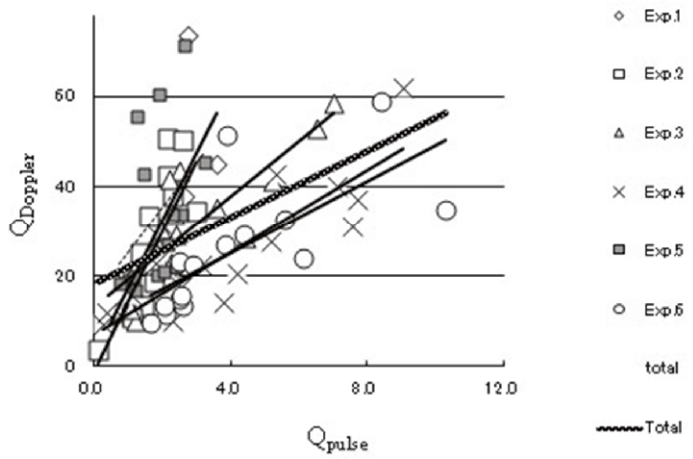

Fig. 2. When $Q_{Doppler}$ and Q_{pulse} were plotted across the three vasodilators in each animal, relatively good linear correlations (R^2 = 0.17 − 0.76) were obtained. Abbreviations: $Q_{Doppler}$, arterial blood flow measured by transit-time flow meter (mL/min); Q_{pulse}, tissue blood flow derived from pulse oximeter signal (volts/s).

relation ($y = 3.68x + 18.5$, $R^2 = 0.25$, $P < 0.01$).

DISCUSSION

We identified a linear correlation between $Q_{Doppler}$ and Q_{pulse} across a wide range of femoral arterial blood flow values resulting from infusion of different vasodilators into each animal. The pulse oximeter wave reflects blood volume changes at the site of the finger. Cook[1] developed a computer program to extract an arterial flow wave from pulse oximeter wave signals and showed a waveform similar to that of a radial arterial blood flow[2]. However, a quantitative analysis has not been performed previously.

In this study, we evaluated the correlation of the Q_{pulse} with $Q_{Doppler}$ as a surrogate parameter rather than with tissue blood flow of the toe directly because of the lack of a reliable continuous tissue blood flow measuring method. We believe that $Q_{Doppler}$ closely reflected toe tissue blood flow in our carefully performed and controlled experiment. As is well known, sympathetic activity affects blood flow in the skin and tissue profoundly and is mainly controlled by thermoregulation and stress. We therefore maintained a constant anesthetic depth with halothane and minimized pain stress with fentanyl during the operative procedure. Body temperature was also kept in a narrow range throughout. In addition, during measurements, we avoided systemic hemodynamic changes from local infusion of vasodilators by using systemic administration instead. Our inference, therefore, is that sympathetic activity did not change significantly during measurements and that the tissue blood flow at the toe was closely proportional with $Q_{Doppler}$.

For this reason, the demonstrated linear correlation of Q_{pulse} and $Q_{Doppler}$ appears to apply to the relationship between Q_{pulse} and toe tissue blood flow. On the other hand, the plotted lines did not cross the zero point. This feature may be explained by the possibility that Q_{Pulse} contains not only arterial blood flow but also a venous blood flow component. Thus, modification might be needed of the third assumption that venous flow is proportional to the blood volume in the arterial bed.

We induced vasodilation by means of drugs with different action sites. Adenosine acts primarily on small arterioles[3], isosorbide dinitrate on venous sites, and nicardipine on greater arterioles[4]. All three drugs induced significant increases in the

femoral arterial flow. Despite the different sites of action, a relatively good linear correlation between Q_{pulse} and $Q_{Doppler}$ was found in a wide range of arterial blood flow measures. However, we may also need to test the validity of the tissue blood flow measurement using a pulse oximeter in pathologic conditions such as sepsis, hypovolemia, and heart failure.

Limitations

Although the Q_{pulse} was considered to closely reflect tissue blood flow in this study, it is measured in units of volts/s and cannot yield tissue blood flow (mL/kg/min). To convert the Q_{pulse} into physical values requires calculating the attenuation coefficients of the pulse oximeter lights in the finger tissue, including the nail, soft tissue, and finger bone, measuring the distance between light-emitting and -receiving elements of the pulse oximeter probe. Although the latter can be measured when the probe is attached, the former must be experimentally determined. If the former does not vary substantially among patients, the Q_{pulse} may be converted into tissue blood flow with acceptable limits of confidence, suggesting the possibility that we can measure tissue blood flow with a pulse oximeter in clinical practice.

In conclusion, this study demonstrated that Cook's idea of extracting arterial flow wave from pulse oximeter waves can be quantitatively validated by comparison with femoral arterial flow in experimental animals. Thus, it is theoretically possible that pulse oximeter can be developed to monitor tissue blood flow at the fingertip.

ACKNOWLEDGMENTS

This work was partly supported by JSPS Kaken Grant Number 24592367.

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