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Clinical Study

A New Monitor to Measure Dermal Blood Flow in Critically Ill Patients: A Preliminary Study

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Background. Conditions of reduced perfusion are characterized by redistribution of blood flow away from the skin to more vital organs. *Objectives*. To assess the efficacy of a noninvasive, dermal blood flow (DBF) monitor in detecting changes in perfusion in critically ill patients. *Methods*. Eleven adult, critically ill patients in a general ICU were studied. DBF, finger plethysmography, and invasive mean arterial pressure (MAP) were recorded over an 8-hour period. DBF was measured using the DermaFlow DBF monitor via a skin probe placed on the anterior chest wall. Sensitivity was evaluated by visual inspection during active states, either induced, for example, fluid administration, or spontaneous, for example, altered hemodynamics, while specificity was evaluated during stable states. Data are expressed in terms of standard deviation of the difference (SDD) between the MAP and each of the tested methods. *Results*. The DBF detected all true changes detected by MAP while plethysmography detected fewer of these events. Based on SDD, the specificity of the DBF was found to be better than that of plethysmography and close in value to the MAP. *Conclusions*. This preliminary study suggests that the DBF monitor may be a useful noninvasive method for detecting changes in perfusion in critically ill patients.

1. Introduction

Many conditions necessitating admission to an intensive care unit are characterized during their course by hypovolemia and decreased cardiac function. The result is decreased organ perfusion, which, if not corrected, may result in organ dysfunction and even death. Early recognition of these states is therefore essential for timely and appropriate intervention. The methods presently available for detecting such changes are typically invasive and/or expensive, including the measurement of intra-arterial blood pressure, cardiac output, and other hemodynamic variables and gastric tonometry.

Conditions of reduced perfusion are characterized by redistribution of blood flow away from the skin and gastrointestinal tract to more vital organs, such as the heart and brain [1]. The skin therefore provides a potentially, readily accessible organ to detect changes in perfusion.

We report on a preliminary study on the use of a novel noninvasive monitor, the dermal blood flow (DBF) monitor (DermaFlow, USA), for the detection of altered dermal blood flow and its comparison with another noninvasive monitor, namely, finger plethysmography derived from pulse oximetry, and with an invasive monitor, namely, mean intra-arterial blood pressure, in critically ill ICU patients.

2. Methods

2.1. Study Design. Eleven consecutive patients in the ICU were included in the study. The local ethics committee waived the requirement for informed consent as no invasive procedures or data beyond that routinely collected were required. All patients were ventilated and sedated during an 8-hour period of measurement. All patients were monitored for vital

signs including pulse rate, body temperature, respiratory rate (Datex, Ohmeda), and urine output. Mean arterial blood pressure (MAP) was continuously measured via a catheter inserted in the radial artery. A pulse oximeter probe (Datex, Ohmeda) was attached to the index finger of the left hand. The area under the curve of the finger plethysmographic waveform (FPW) was obtained from the monitor. The plethysmographic gain factor of the monitor is held constant once the probe is applied. The MAP and FPW data were continuously recorded and stored in a computerized data system (Metavision, Israel).

2.2. Dermal Blood Flow Measurements. Dermal blood flow was measured with the dermal blood flow (DBF) monitor (DermaFlow, USA), which consists of a skin probe and a measuring and control feedback unit. DBF is measured using the hot-wire principle of thermal balance of a heater cooled by a moving medium according to the following formula: $V = kP/(T2 - T1)$, where V is the rate of the relative movement of a medium, in this case, dermal blood flow, k is a proportional coefficient which depends on the physical properties of the heater and the medium, P is the electrical steady state power dissipated by a heater, $T1$ is the temperature of the medium, and $T2$ is the temperature of the heater. The probe, which has an area of measurement of $3\,\text{mm}^2$, consists of a microheater coupled with a thermosensor placed on the skin surface and thermally insulated from air surroundings. The measuring unit measures the heat energy dissipated by the microheater into the blood flow necessary to maintain a constant temperature difference ($T2 - T1$) between the microheater and a reference skin temperature signal, which is acquired and stored before the heating process is started. A control feedback unit maintains the constant temperature difference between the microheater and the skin surface. DBF, that is, the heat energy, is the electrical steady-state power, measured in milliwatts and in real time, dissipated by the microheater. Thus as DBF increases, more energy will be required to maintain the temperature difference, while less energy will be required when DBF decreases.

In this context we note the linear relationship between the value of the measured parameter (DBF) and the energy required (output voltage); this is an intrinsic feature of the DermaFlow device.

In preliminary studies with 5 patients, we tested various sites for placement of the skin probe, including the foot, forearm, hand, anterior chest, and forehead. Results were most consistent, with minimal artifacts due to patient movement, when the probe was applied to the chest site (anterior chest, 4th intercostal space in the midclavicular line) so that all further studies were performed at this site. Data from the DBF monitor was collected and stored every minute using a Data Logger (EasyLog, Lascar Electronics, UK).

2.3. Statistical Considerations. All therapeutic interventions and any changes in MAP which provoked an active intervention by the attending medical staff were noted by a dedicated observer. For statistical purposes, the MAP data obtained was separated into 3 possible states: (1) a stable state, in which fluctuations of MAP values were relatively stable, that is, with no spikes or specific trend; this corresponded to a clinical state during which no active interventions were applied or required; (2) an active state, which was either induced by an intervention (e.g., sedation, fluid bolus) or spontaneous state (i.e., related to the patient's underlying state); and (3) a disturbed state, which was characterized by abrupt or large fluctuations in MAP which could not be explained on a medical basis. These changes were considered the result of technical problems. Analyses were focused on evaluating the sensitivity and specificity of the DBF and FPW in the first two states.

The sensitivity of each of the tested methods was evaluated according to the detection of a change in the trend of the values observed during active states. For induced states, this reflects the extent of the response whereas for spontaneous states this reflects the probability that the medical staff would be alerted when a medical decision would be required, that is, a true alarm. In the absence of clearly defined criteria for the expected pattern of the values responding to a medical intervention or spontaneous event, the sensitivity of each method was evaluated according to similarity between the tested and the MAP curves as judged by visual inspection.

The results during the stable states were used to provide estimates of the specificities of the tested methods. During this state, fluctuations around a common baseline are to be expected. However, since the three methods measure different parameters, the observed values may not necessarily follow the same pattern and/or intensity. While the pattern of the fluctuations does not affect the sensitivity of the method, the intensity of the fluctuations might, as with large fluctuations only an extremely large change would be considered an active state. The data were therefore analyzed in order to assess the "jitteriness" of the curve of each tested method relative to the MAP curve. For this purpose, the results of each tested method were rescaled so as to match the MAP results. This rescaling was done for each stable state by multiplying the DBF or the FPW values by the ratio between the means of the two series (i.e., MAP/DBF or MAP/FPW). Assuming normal distribution, the mean difference and the standard deviation of the difference (SDD) were calculated. Since by definition, the mean difference during each stable period is 0, the SDD reflects the "jitteriness" of the DBF or the FPW curve relative to that of the MAP. Assuming that part of the fluctuations reflects biological changes in the blood flow, the SDD (rather than the SD) was used so that fluctuations that originated from common sources are controlled.

3. Results

3.1. Demographics. The demographic data of the 11 patients is shown in Table 1. There were 7 males and 4 females, with a mean age of 54.2 ± 15.3 years. All patients were receiving mechanical ventilation at the time of the study.

3.2. Comparison of MAP, DBF, and FPW. Sensitivity could be assessed in 4 patients and these are discussed in detail with corresponding figures. The start and the end of active

Table 1: Demographic data.

Patient no.	Age (years)	Sex	Diagnosis	Mechanical ventilation
1	54	M	Severe intra-abdominal sepsis	Yes
2	61	M	Pneumonia, severe sepsis	Yes
3	72	F	Sepsis, acute renal failure	Yes
4	69	M	COPD exacerbation	Yes
5	51	M	Multitrauma	Yes
6	19	F	Multitrauma	Yes
7	38	F	Postpartum hemorrhage, shock	Yes
8	52	M	Pneumonia	Yes
9	54	F	Urinary tract infection, sepsis	Yes
10	70	M	Bowel perforation, after surgery	Yes
11	56	M	Head trauma, multiple fractures	Yes

COPD: chronic obstructive pulmonary disease; ARDS: acute respiratory distress syndrome.

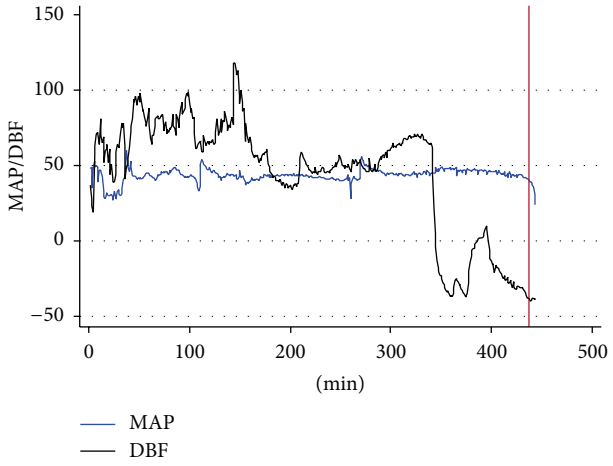

Figure 1: Patient with severe septic shock due to intra-abdominal sepsis resulting in death. The DBF curve shows a dramatic decrease at 345 minutes, which preceded the decrease in MAP by 93 minutes. Due to severe peripheral vasoconstriction the FPW was unrecordable so that no FPW data was available. DBF: dermal blood flow; MAP: mean arterial pressure.

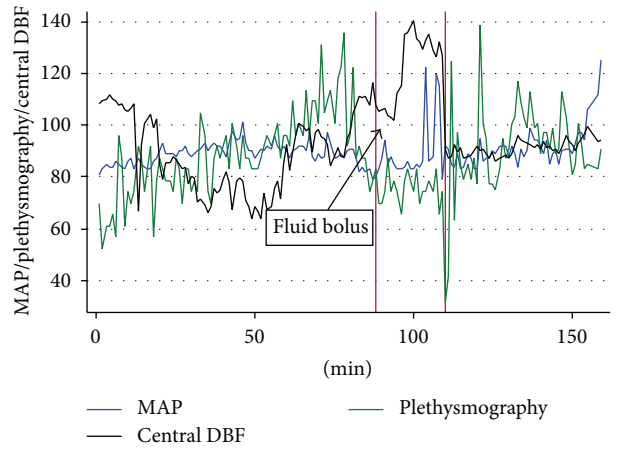

Figure 2: Patient with pneumonia and severe sepsis. Between two stable states the dose of noradrenaline was reduced and the patient received a fluid bolus. During this time the pattern of the DBF curve, but not the FPW, is similar to that of the MAP. The change in the trend of the DBF curve occurs several minutes earlier than in the MAP curve. DBF: dermal blood flow; MAP: mean arterial pressure.

and disturbed states are each marked by 2 red perpendicular lines. It should be noted that as the scales of the figures are affected by the presence of large spikes, comparing the stable states of the curves of different patients by visual inspection rather than by the SDD may be misleading. In addition, since rescaling was carried out after each active or disturbed state, an abrupt superficial change may be observed in the curves at the beginning of a stable state that follows an active or disturbed state.

Patient 1. This patient had severe septic shock due to intra-abdominal sepsis and was receiving large doses of noradrenaline (Figure 1). The data comprise a single stable state until death after 438 minutes of monitoring. The DBF curve showed a dramatic decrease at 345 minutes, which preceded the decrease in MAP by 93 minutes. Due to severe peripheral vasoconstriction the FPW was unrecordable so that no FPW data was available.

Patient 2. This patient, suffering from severe sepsis, was stable during the first 87 minutes of the recording and again after the 100th minute (Figure 2). Between two stable states the dose of noradrenaline was reduced and the patient received a fluid bolus. These interventions plus a short disturbed state were considered as a single active state. During this time the pattern of the DBF curve, but not the FPW, was similar to that of the MAP. The change in the trend of the DBF curve occurred several minutes earlier than in the MAP curve.

Patient 3. This patient had two stable states and two active states, each following an intervention (Figure 3). In the first active state, haemodialysis was performed and then fluids

Table 2: Standard deviation of the difference (SDD) between MAP and DBF and between MAP and FPW results observed during stable states.

Patient no.	State 1		State 2		State 3		State 4	
	DBF	FPW	DBF	FPW	DBF	FPW	DBF	FPW
1	40.05	Not possible						
2	10.23	24.20						
3	8.45	37.13						
4	17.66	15.12	6.83	18.97				
5	7.72	13.91	2.93	10.47	15.91	8.06		
6	22.80	28.34	4.53	18.22				
7	17.69	26.04	10.80	43.51	9.57	61.12	6.73	8.75
8	9.17	10.80	6.93	21.30				
9	4.75	6.64	3.93	8.19	4.75	6.96		
10	5.62	60.79	12.84	87.87				
11	10.82	10.37	4.33	23.24				

DBF: dermal blood flow; FPW: finger plethysmographic waveform.

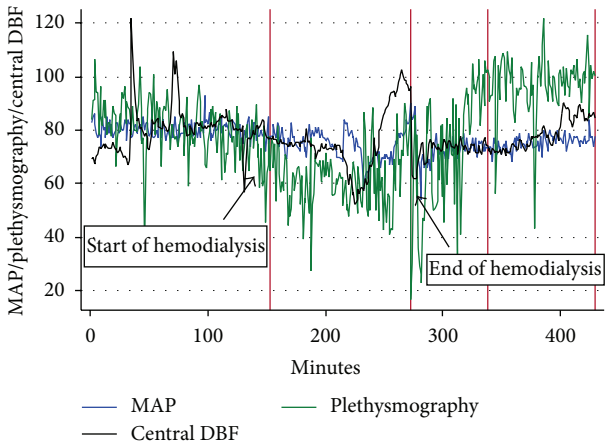

Figure 3: Patient with severe sepsis undergoing hemodialysis. Both the MAP and the DBF curves follow the same pattern, showing a clear decrease at the onset and an increase at the end of dialysis; the FPW curve vaguely follows the MAP pattern but was very "jittery." DBF: dermal blood flow; MAP: mean arterial pressure.

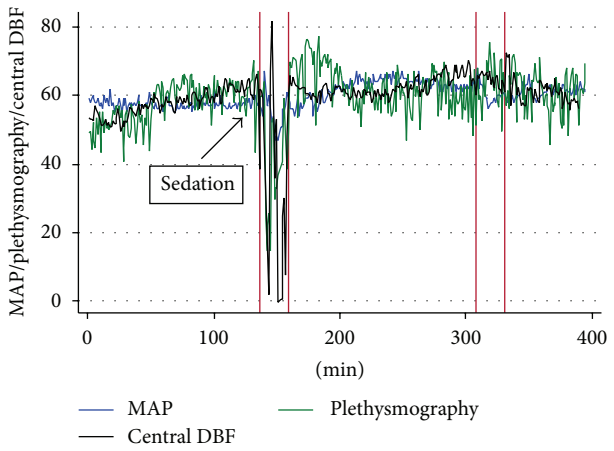

Figure 4: Patient requiring mechanical ventilation for COPD exacerbation. MAP, the DBF, and plethysmography curves show a trend towards a decline during the active state (in which a sedating drug was administered). DBF: dermal blood flow; MAP: mean arterial pressure.

administered. These two treatments plus a short disturbed state were considered as a single active state. Both the MAP and the DBF curves followed the same pattern, showing a clear decrease at the onset and an increase at the end of dialysis; the FPW curve vaguely follows the MAP pattern but was very "jittery." The second active state was induced by the administration of fluids and sedation (IV midazolam). A clear change in the MAP curve during this state was not noted. The DBF curve ran close to that of the MAP for most of the time, but was elevated at its end, whereas the trend of the FPW curve was stable, jittery, and remote from the MAP curve. This increase in the DBF may well reflect the effect of fluid administration. However, since no change in pattern was observed for the MAP, it is difficult to evaluate the sensitivities of the methods in this active state.

Patient 4. There were three stable, one disturbed and one active states (Figure 4). The MAP, the DBF, and plethysmography curves show a trend towards a decline during the active state (in which a sedating drug was administered).

In the remaining 7 patients there were no defined active states.

3.3. Standard Deviation of the Difference (SDD). The results of the SDD analysis during stable periods for the entire group are shown in Table 2. The SDD of the DBF was lower than that of FPW and close in value to that of the MAP. SD of FPW values were much larger than those of the corresponding MAP or DBF methods. The SD of the DBF and the MAP were quite close in values, except for the first stable state of each

patient. The SD of DBF in the first stable state tended to be larger than those of other stable states in the same patient. With stabilization of the DBF measurements, the SD of the DBF matched more closely that of the MAP.

4. Discussion

The results of this preliminary study suggest that the DBF was at least as sensitive as MAP and more sensitive and specific than FPW in detecting changes in perfusion in critically ill ICU patients.

The cutaneous circulation, which participates actively in blood pressure regulation, is normally about 250 mL/min and is regulated by sympathetic neural control via the noradrenergic vasoconstrictor and sympathetic active vasodilator systems [2]. The mechanism controlling dermal blood flow in response to a challenge in blood pressure appears to depend on the degree of unloading of cardiopulmonary and sinoaortic baroreceptor populations [3]. Thus it has been shown that during simulated orthostasis (induced by lower body negative pressure), dermal blood flow is significantly reduced [4]. The skin therefore provides a readily accessible organ to detect changes in perfusion.

The measurement of dermal blood flow has typically been used to assess responses of the microcirculation to various neurotransmitters [5] and to assess the viability of skin grafts [6] and a variety of skin diseases [7]. Various techniques have been described to measure skin blood flow; however, they all appear to have disadvantages. Thus tissue pH measurement using an invasive probe, photoplethysmography, reflects tissue blood volume rather than flow, and capillary microscopy requires an invasive probe and is dependent on the patient remaining still [8].

The aim of the present study was to assess the efficiency of a new monitor, which measures dermal blood, in detecting changes in perfusion. The DBF monitor (DermaFlow, USA) uses the hot-wire anemometer principle of thermal balance and provides a noninvasive and continuous method for obtaining qualitative values of DBF. The device consists of a skin probe, comprising a microheater with a thermosensor, which is insulated from the surroundings, and a measuring unit, which measures the heat energy dissipated by a microheater into the blood flow. DBF is directly proportional to the electrical power. We compared this monitor with another noninvasive monitor, namely, FPW of the pulse signal derived from pulse oximetry, which has been used to provide a qualitative indicator of blood volume changes [9], and with the most widely used invasive monitor of perfusion, namely the MAP as measured via an intra-arterial cannula.

In order to demonstrate equivalence between the values of MAP and each of the tested methods we evaluated parameters assumed to reflect the sensitivity and the specificity. Sensitivity, which is related to the probability of a true alarm, was assessed by the ability of the tested methods to detect responses to both active therapeutic interventions and to spontaneous changes in the patient's condition. As the expected changes in the pattern of the curves to fluid administration or other therapeutic interventions cannot be clearly defined a priori, as, for example, an increase or decrease of at least 20 mmHg for at least 20 minutes, our assessment of sensitivity to therapeutic interventions was based on the similarities between the patterns of the tested methods and the MAP curves as subjectively judged by visual inspection. Although this may be subjective in general, it was apparent that in all active induced states, including after the administration of fluids, sedative agents, and hemodialysis, the results of the DBF are clear in the sense that the expected change, whether an increase or decrease, is quite large relative to the fluctuations observed just before the initiation of the changes. The FPW method was less sensitive, and the pattern of the graphs was quite vague. It should be noted that as active induced states were a priori defined, that is, the administration of a therapy, and that the pattern of the MAP curve was determined as the "true response," the sensitivity of the tested method can only exceed that of the MAP when there is a clear active spontaneous event. This is evident in our study in the patient who died; the DBF showed a dramatic decline well before that shown by the MAP. Due to severe peripheral vasoconstriction, FPW data was unrecordable in this patient.

Evaluation of specificity, that is, during stable states, is important as this provides information about false alarms which may lead to wrong decisions, for example, discharge from an ICU. To do this we assessed the SDD. A small SD may be associated with good specificity if the fluctuations during a stable state are random, that is, stem from random small and irregular "background noises." As the three methods are based on different principles, the results of each method may differ with respect to the level of this "noise." However, assuming that the fluctuations may partly reflect true biological changes in perfusion, the SD is affected by "noise" as well as by true biological variations. If the three methods are almost equally sensitive to biological variations, then the SDD reflects the difference between the "noise" of the MAP and that of the tested method *per se*. As such it is more relevant than the SD in comparing the specificity of the two tested methods. Since on average the difference between the two curves is 0, the SDD reflects the jitteriness of the results. Based on our assumptions, if SDD = 5, for example, the distance between the (rescaled) DBF and the MAP values is within ±8.2 mmHg for 95% of the values. Based on the SDD results, the specificity of the DBF was better than that of FPW. Except for two instances, the SD of FPW values were much larger than those of the corresponding MAP or DBF methods whereas the SD of the DBF and the MAP were close in value.

There are limitations of the present study. Firstly, only 11 patients were included in the study and only 4 of them could be analyzed with respect to sensitivity. However, patients were monitored over 8 hours and data collected every minute so that in fact many data points were available for study. Secondly, the data derived from the DBF monitor is qualitative and was rescaled to provide data corresponding to that of the MAP. In the future absolute values of blood flow, measured in mL/min/gm of tissue, will be incorporated into the monitor.

5. Conclusion

This preliminary study suggests that the DBF monitor may be a useful noninvasive method for detecting changes in perfusion in critically ill patients and that further studies with a larger number of patients and varying clinical conditions are warranted.

Conflict of Interests

J. Cohen, R. Chen, and P. Singer have no conflict of interests to declare. I. Skoletsky is the Chief Technology Officer of DermaFlow and D. Weiss is the Chief Medical Officer of DermaFlow.

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