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Comparison between respiratory pulse oximetry plethysmographic waveform amplitude and arterial pulse pressure variations among patients with and without norepinephrine use

Comparação entre as variações respiratórias da amplitude de onda pletismográfica da oximetria de pulso e do pulso arterial em pacientes com e sem uso de norepinefrina

ABSTRACT

Objectives: Arterial pulse pressure respiratory variation is a good predictor of fluid response in ventilated patients. Recently, it was shown that respiratory variation in arterial pulse pressure correlates with variation in pulse oximetry plethysmographic waveform amplitude. We wanted to evaluate the correlation between respiratory variation in arterial pulse pressure and respiratory variation in pulse oximetry plethysmographic waveform amplitude, and to determine whether this correlation was influenced by norepinephrine administration.

Methods: Prospective study of sixty patients with normal sinus rhythm on mechanical ventilation, profoundly sedated and with stable hemodynamics. Oxygenation index and invasive arterial pressure were monitored. Respiratory variation in arterial pulse pressure and respiratory variation in pulse oximetry plethysmographic waveform amplitude were recorded simultaneously in a beat-to-beat evaluation, and

were compared using the Pearson coefficient of agreement and linear regression.

Results: Thirty patients (50%) required norepinephrine. There was a significant correlation ($K = 0.66$; $p < 0.001$) between respiratory variation in arterial pulse pressure and respiratory variation in pulse oximetry plethysmographic waveform amplitude. Area under the ROC curve was 0.88 (range, 0.79 – 0.97), with a best cutoff value of 14% to predict a respiratory variation in arterial pulse pressure of 13. The use of norepinephrine did not influence the correlation ($K = 0.63$, $p = 0.001$, respectively).

Conclusions: Respiratory variation in arterial pulse pressure above 13% can be accurately predicted by a respiratory variation in pulse oximetry plethysmographic waveform amplitude of 14%. The use of norepinephrine does not alter this relationship.

Keywords: Hemodynamic; Oximetry; Blood pressure; Plethysmography; Respiration, artificial; Norepinephrine

INTRODUCTION

Cardiovascular shock is a condition that results from inadequate blood flow. The standard therapeutic approach is venous hydration, which has proven to alter mortality in patients with septic shock when initiated early.⁽¹⁾ However, a substantial number of patients with shock are non-responsive to fluid replacement therapy,⁽²⁾ and the excess fluids can generate pulmonary and peripheral edema, which can negatively affect prognosis, particularly in patients with increased pulmonary permeability.⁽³⁾

Fluid responsiveness is determined by the change in cardiac output caused by volume infusion. By definition, a patient responds to a fluid challenge when the cardiac output rises 15% after infusion of 500 ml of colloid solution.⁽⁴⁾ Historically,

studies have attempted to demonstrate fluid responsiveness with different hemodynamic monitoring methods. However, measurements of venous central pressure, pulmonary capillary wedge pressure, or their variations, did not forecast responsiveness to volume.⁽⁵⁾ On the other hand, measurements of respiratory variations in systemic pulse pressure (ΔPP) has proven to be a reliable method for predicting the outcome of fluid challenge, with a predictive cutoff value of 13%.⁽⁶⁾ However, in order to measure ΔPP , invasive monitoring of the mean arterial pressure is necessary, which is associated with complications inherent to the procedure itself. In addition, most patients do not have an intra-arterial catheter in place when hemodynamic instability manifests.

Pulse oximetry is a useful and universal tool at all intensive and emergency care units. The use of this curve as an instrument of hemodynamic analysis has been reported in previous studies,⁽⁷⁻⁹⁾ and a recent study has reported a relationship between ΔPP and the pulse oximetry curve.⁽¹⁰⁾ Therefore, we wanted to evaluate the relationship between ΔPP and respiratory variations in pulse oximetry plethysmographic waveform amplitude (ΔPOP), and to determine the influence of norepinephrine infusion on this relationship.

METHODS

The ethics committee of Casa de Saúde São José, Rio de Janeiro, Brazil, approved the protocol used in this study. Inclusion criteria were profoundly sedated patients or those under the effects of neuromuscular blockers in controlled mechanical ventilation, sinus rhythm, hemodynamic stability during the 15 minutes preceding the measurements, and pre-established invasive arterial pressure monitoring. The tidal volume for all patients was set to 8 mL/kg, according to Michard et al.⁽⁶⁾

Exclusion criteria were spontaneous ventilation, cardiac arrhythmia, and an inadequate pulse oximetry signal. POP waveform quality was considered suitable when the curve amplitude was superior to the minimum size for reliable SpO₂ value (Figure 1). According to our protocol, the pulse oximeter was placed on the fourth finger of the left hand and patients were positioned supine, with a zero degree incline.

Systolic and diastolic arterial pressures were measured using a standard monitor (IntelliVue™ Patient Monitor MP60, Phillips®) on a beat-to-beat basis, and PP was calculated as the difference between systolic and diastolic pressures. Maximal and minimal values for systolic PP (PP_{max} and PP_{min}) were determined over a single respiratory cycle. ΔPP was calculated as follows⁽⁶⁾: $\Delta PP = 100 \Delta (PP_{max} - PP_{min}) / [(PP_{max} + PP_{min})/2]$. POP waveforms were obtained using the oxymeter module of the same monitor. POP waveform amplitude was mea-

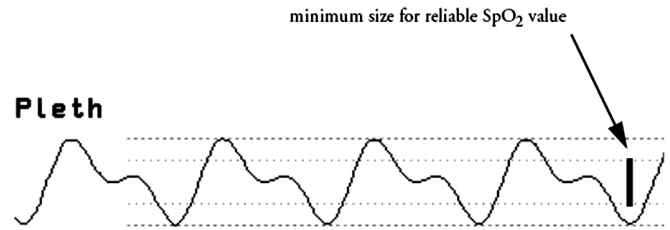


Figure 1 - The Pleth wave. The vertical bar indicates the minimum size for reliable peripheral oxygen saturation (SpO₂) value.

sured on a beat-to-beat basis as the vertical distance between the peak and the preceding valley trough in the waveform, and was expressed in millimeters (mm). Maximum POP (POP_{max}) and minimum POP (POP_{min}) were determined over the same respiratory cycle. The plethysmographic gain factor was constant throughout the procedure. ΔPOP was calculated using a formula similar to that for ΔPP : $\Delta POP (\%) = 100 \times (POP_{max} - POP_{min}) / [(POP_{max} + POP_{min})/2]$. PP and POP waveforms were printed and ΔPP and ΔPOP were evaluated over three consecutive respiratory cycles.

Statistical analysis

Continuous variables were expressed as the median \pm standard deviation (SD) and categories were expressed as percentages. For comparison of continuous variables, we used the Student's t-test and the Mann Whitney test. The correlation between ΔPP and ΔPOP was analyzed using the Pearson coefficient of agreement and linear regression. ROC curves were constructed to determine the best ΔPOP cutoff for a ΔPP of 13%. Kappa coefficient of agreement⁽¹¹⁾ (K) was estimated for the correlation between $\Delta PP > 13\%$ and the ΔPOP above the best cutoff value. The diagnostic utility was determined according to this value. K was calculated for one subgroup according to the use of norepinephrine.

RESULTS

The study group consisted of sixty patients with a mean age of 65 ± 17 years, who were on mechanical ventilation (Table 1). Among them, 30 patients (50%) required norepinephrine infusion (doses ranged from 0.01 $\mu\text{g}/\text{kg}/\text{min}$ to 1.6 $\mu\text{g}/\text{kg}/\text{min}$).

Respiratory variation in pulse oximetry plethysmographic waveform amplitude ΔPOP accurately predicted ΔPP with a sensitivity of 83.3%, a specificity of 85.7%, a positive predictive value (PPV) of 71.4, and a negative predictive value (NPV) of 92.3. Area under the ROC curve

Table 1 - Demographic data and baseline values of hemodynamic, plethysmographic, and respiratory parameters

Parameter	Value	Range
Age (year)	65 ± 17	18 - 94
Weight (kg)	63 ± 13	45 - 85
Height (cm)	165 ± 10	150 - 182
Mean arterial pressure (mmHg)	83 ± 12	59 - 118
Heart beats/min	89 ± 18	51 - 145
ΔPP (%)	12 ± 11	0 - 52
ΔPOP (%)	12 ± 11	0 - 66

ΔPOP - respiratory variations in pulse oximetry plethysmographic waveform amplitude; ΔPP - respiratory variations in pulse pressure. Results are expressed in mean ± standard deviation and range.

Table 2- Agreement between respiratory variations in pulse pressure and respiratory variations in pulse oximetry plethysmographic waveform amplitude among all patients and different subgroups

Patients subgroups	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Kappa index	P value
All patients	60	83.3	85.7	71.4	92.3	0.66	p < 0.001
Patients receiving norepinephrine	30	71.4	91.3	71.4	91.3	0.63	p < 0.001
Patients not receiving norepinephrine	30	90.9	78.9	71.4	93.8	0.66	p < 0.001

N - number of patients; ΔPOP - respiratory variations in pulse oximetry plethysmographic waveform amplitude; ΔPP - respiratory variations in pulse pressure; PPV - positive predictive value; NPV - negative predictive value.

was 0.88 (range, 0.79 – 0.97) with a best cutoff value of 14% to predict a ΔPP of 13%. Kappa index of agreement was 0.66 ($p < 0.001$). Nineteen (31%) patients had ΔPP above 13% and 21 (35%) showed ΔPOP above 14%.

In patients receiving norepinephrine, the ΔPOP cutoff of 14% had a sensitivity of 71.4%, a specificity of 91.3%, a PPV of 71.4%, and an NPV of 91.3%, to predict ΔPP above 13% ($K = 0.63$; $p = 0.001$). In the group of patients who did not receive norepinephrine, sensitivity was 90.9%, specificity was 78.9%, PPV was 71.4%, and NPV was 93.8% ($K = 0.66$; $p < 0.001$). Results are summarized in table 2.

DISCUSSION

Michard et al.⁽⁶⁾ showed that in profoundly sedated patients on controlled mechanical ventilation, with sinus rhythm, a ΔPP above 13% predicts responsiveness to fluid challenge, defined as a raise in the cardiac output of 15% after the infusion of 500 ml of colloid solution, with a sensitivity of 94% and a specificity of 96%. However, fluid responsiveness does not necessarily imply hypovolemia, so not all patients who can respond to fluid infusion actually need volume.

The rationale for fluid challenge is based on the physiological consequences of the respiratory cycle in the venous return during mechanical ventilation. When inspiration begins, the intra-thoracic pressure rises, causing venous return to the right atrium to decrease.⁽¹²⁾ Cardiac output of the right heart decreases so less blood reaches

the left heart. As a result, left heart output decreases, but this happens during expiration because inspiration ends when the blood ejected through the right ventricle is still in the pulmonary circulation.⁽¹³⁾

One advantage of using the ΔPP measurement is that it is minimally invasive. Patients in circulatory shock usually have arterial pressure monitored by an invasive means; however, patients who develop shock rapidly or unexpectedly may not have an arterial line in place yet, despite already being in an intensive care environment. The predictive value of ΔPP can be very valuable when deciding the therapeutic course of action for these patients. Our study demonstrated a significant correlation between ΔPP and ΔPOP. The best value of ΔPOP to predict a ΔPP of 13% was 14%. Since pulse oximetry is in widespread use in intensive care centers, no additional costs are incurred when seeking the relevant information to predict fluid responsiveness.

One limitation to this method is that it depends on a good quality oximetry curve, which is not always possible, especially in patients with compromised peripheral perfusion. However, when an adequate oximetry signal is obtained, the infusion of norepinephrine does not influence the agreement between ΔPP and ΔPOP.

Moreover, although current technologies do not provide for direct determination of ΔPOP, which might limit its use, the simple calculations required to determine ΔPOP are an easy and effective means for predicting fluid responsiveness.

CONCLUSION

In intensive care patients, a Δ POP value of 14% can effectively predict a Δ PP value of 13%. This method could be useful for evaluating patients without an arterial catheter in place. Norepinephrine administration does not affect the relationship between Δ PP and Δ POP, preserving the predictive value of Δ POP in patients who have received norepinephrine.

RESUMO

Objetivos: A variação respiratória da pressão arterial é um bom preditor da resposta a fluidos em pacientes ventilados. Foi recentemente demonstrado que a variação respiratória na pressão arterial de pulso se correlaciona com a variação da amplitude da onda pletismográfica da oximetria de pulso. Nossa intenção foi avaliar a correlação entre a variação respiratória da pressão arterial de pulso e a variação respiratória na amplitude da onda pletismográfica da oximetria de pulso, e determinar se esta correlação foi influenciada pela administração de norepinefrina.

Métodos: Estudo prospectivo de sessenta pacientes com rit-

mo sinusal normal sob ventilação mecânica, profundamente sedados e hemodinamicamente estáveis. Foram monitorados o índice de oxigenação e pressão arterial invasiva. A variação respiratória da pressão do pulso e a variação respiratória da amplitude da onda pletismográfica na oximetria de pulso foram registradas simultaneamente batimento a batimento, e foram comparadas utilizando o coeficiente de concordância de Pearson e regressão linear.

Resultados: Trinta pacientes (50%) necessitaram de norepinefrina. Ocorreu uma correlação significativa ($K=0,66$; $p<0,001$) entre a variação respiratória na pressão arterial de pulso e a variação respiratória na amplitude de onda pletismográfica na oximetria de pulso. A área sob a curva ROC foi de 0,88 (variando de 0,79-0,97) com melhor valor de corte de 14% para prever uma variação respiratória na pressão arterial de pulso de 13. O uso de norepinefrina não influenciou esta correlação ($K=0,63$; $p=0,001$, respectivamente).

Conclusões: Uma variação respiratória na pressão do pulso arterial acima de 13% pode ser prevista com precisão por meio de uma variação respiratória da amplitude de onda pletismográfica na oximetria de pulso de 14%. O uso de norepinefrina não modifica este relacionamento.

Descritores: Hemodinâmica; Oximetria; Pressão arterial; Pletismografia; Respiração artificial; Norepinefrina

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