Review Article

Evaluation of Fluid Responsiveness: Is Photoplethysmography a Noninvasive Alternative?

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Received 29 September 2011; Revised 29 November 2011; Accepted 21 December 2011

Academic Editor: Ronald G. Pearl

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Background. Goal-directed fluid therapy reduces morbidity and mortality in various clinical settings. Respiratory variations in photoplethysmography are proposed as a noninvasive alternative to predict fluid responsiveness during mechanical ventilation. This paper aims to critically evaluate current data on the ability of photoplethysmography to predict fluid responsiveness. *Method*. Primary searches were performed in PubMed, Medline, and Embase on November 10, 2011. *Results*. 14 papers evaluating photoplethysmography and fluid responsiveness were found. Nine studies calculated areas under the receiver operating characteristic curves for ΔPOP (*>*0.85 in four, 0.75–0.85 in one, and *<*0.75 in four studies) and seven for PVI (values ranging from 0.54 to 0.98). Correlations between ΔPOP/PVI and ΔPP/other dynamic variables vary substantially. *Conclusion*. Although photoplethysmography is a promising technique, predictive values and correlations with other hemodynamic variables indicating fluid responsiveness vary substantially. Presently, it is not documented that photoplethysmography is adequately valid and reliable to be included in clinical practice for evaluation of fluid responsiveness.

1. Introduction

Whether or not to administer intravenous (iv) fluid is a common, difficult, and controversial challenge in clinical practice. The main aim of fluid therapy during surgery or critical illness is to provide adequate tissue perfusion by increasing stroke volume (SV) or cardiac output (CO). Goal-directed fluid therapy aiming to increase oxygen $(O₂)$ delivery reduces morbidity and mortality in various clinical settings [1–8]. Fluid therapy is guided by clinical variables, as well as static and dynamic variables. Clinical variables include blood pressure, heart rate, capillary refill time, skin turgor and diuresis, mixed venous oxygen saturation (SvO2), lactate, pH, electrolytes, and creatinine/urea. Conventional static variables include central venous pressure (CVP) and pulmonary artery wedge pressure (PAWP), but these variables have proven less reliable than initially assumed to evaluate fluid responsiveness [8–10]. Dynamic variables include both SV-dependent and non-SV-dependent methods. The ideal new method should be accurate [11],

easy to use, noninvasive, and widely available with minimal risk of complications. Potential clinical value also depends on reproducibility and predictive values compared to established methods.

Photoplethysmography (more specifically pulse oximetry plethysmographic waveform analysis) as a noninvasive tool in evaluation of fluid responsiveness was first described by Partridge [12] and has been extensively investigated. A pulse oximeter is a standard equipment for measuring arterial $O₂$ saturation, and further analysis of the photoplethysmographic signal can easily be implemented in clinical monitoring. This paper aims to critically evaluate current data on the ability of photoplethysmography to predict fluid responsiveness.

2. Methods

This paper is based on searches performed in PubMed, Medline, and Embase on November 10, 2011 with the following search criteria: "(pulse oximetry OR plethysmographic OR Pleth variability index OR PVI) AND ((fluid responsiveness) OR (volume status))." The searches generated 217 hits. Papers were checked for relevant references and 22 [13-34] papers met the following inclusion criteria:

- (1) reporting predictive values of ΔPOP and/or PVI after fluid challenges and/or reporting correlations between ΔPOP, PVI, and ΔPP,
- (2) mechanically ventilated patients,
- (3) written in English.

3. Results

3.1. Predictive Values of Δ*POP and PVI.* 14 studies performed fluid challenges and these are summarized in Table 1. Patients were mechanically ventilated with tidal volumes of 6–10 mL/kg and investigated preoperatively $(n = 6)$ [23, 26, 28, 30–32], perioperatively (*ⁿ* ⁼ 3) [21, 33, 34], postoperatively $(n = 2)$ [25, 27], and in the intensive care unit (ICU) $(n = 2)$ [22, 24]. One study included different groups of patients [29]. The pulse oximeter was placed on a finger in all papers, and in two papers it was also placed on the earlobe [30, 34]. Different types of pulse oximeters were used, summarized in Table 2. The number of patients included in each study varied substantially $(n = 8-43)$. Registration periods were, with some exceptions [22, 33], short (*<*1 min). Six studies did not indicate duration of the registration period [24, 28–31, 34]. Patients with arrhythmias were excluded in all papers except one, in which this was not expliticitly stated [34]. Patients receiving vasoactive medication were included in four papers [24, 27, 29, 33] and excluded in four [23, 26, 31, 32]. Six papers did not indicate use of vasoactive medication [21, 22, 25, 28, 30, 34]. These data are summarized in Table 3. Fluid challenges were given as HES 6% (*ⁿ* ⁼ 9) [22–26, 28–31], "colloid fluid" $(n = 3)$ [21, 33, 34], and NaCl 0.9% $(n = 2)$ [27, 32]. Fluid volumes ranged from 250 mL to 1000 mL. Fluid responsiveness was defined as increased CO *>* 15% (*ⁿ* ⁼ 2) [25, 29], increased CI *>* 15% (*ⁿ* ⁼ 5) [22–24, 26, 30], ^ΔPP *>* 13% (*ⁿ* ⁼ 1) [27], increased SVI *>* 10% (*ⁿ* ⁼ 1) [21], increased SVI *>* 15% (*ⁿ* ⁼ 2) [28, 31], increased SV *>* 10% (*ⁿ* ⁼ 1) [34], increased SV *>* 15% (*ⁿ* ⁼ 1) [33], and aortic velocity-time integral $(AVTI) > 15\%$ $(n = 1)$ [32]. Best cut-off values ranged from 8.8 to 15% for ΔPP, 9.5 to 15% for ΔPOP, and 9.5 to 17% for PVI. CO was measured with thermodilution $(n = 5)$ [21–23, 26, 30], echo Doppler (*ⁿ* ⁼ 6) [24, 29, 31–34], FloTrac/Vigileo (*ⁿ* ⁼ 1) [28], and intermittent thermodilution by pulmonary artery catheter (Vigilance monitor) $(n = 1)$ [25].

Nine studies calculated areas under receiver operating characteristics curves (ROC curves) for ΔPOP [21–27, 32, 33]. It was calculated to *>*0.85 in four studies [24–27], 0.75– 0.85 in one [23], and *<*0.75 in four [21, 22, 32, 33]. In five studies values for ΔPOP were as good as, or better than, values for ΔPP [23, 24, 26, 27, 33]. In one of these studies, predictive value of ΔPOP was defined as a certain change in ΔPP, thus presuming that ΔPP is a good indicator [27]. One study found poor values for both ΔPP and ΔPOP [33]. Four

studies reported lower predictive values for ΔPOP than for ΔPP [21, 22, 25, 32]. Thus, only two of nine studies reported high predictive values for ΔPOP [24, 26]. The ROC curves for ΔPOP and ΔPP were not found to be significantly different in any of the nine studies. The best ΔPOP cut-off value for identifying responders ranged from 9.5 to 15%.

Seven studies calculated ROC curves for PVI [26, 28– 32, 34], with values ranging from 0.54 to 0.98. Although correlations between PVI and other parameters vary, predictive values remain relatively good in stable conditions. In one study, the predictive value of PVI decreased from 0.96 at baseline to 0.71 perioperatively [34]. The best PVI cut-off value for identifying responders ranged from 9.5 to 17%.

3.2. Correlations between Δ*POP, PVI, and* Δ*PP.* ΔPP is considered to be a good predictor of fluid responsiveness [6]. Thus, other variables should correlate with ΔPP. 11 of the included papers reported correlations between ΔPP and ΔPOP. Six of these papers reported relatively good correlations (*r >* 0*.*84) [13, 15, 17, 23, 24, 27]. However, five papers reported relatively poor correlations (*r <* 0*.*78) [14, 16, 18, 32, 33]. One of these investigated children preoperatively [32]. Landsverk et al. [16] concluded that there are poor correlations between ΔPOP and ΔPP in ICU patients due to sympathetic oscillations in skin circulation, which lead to larger variation in ΔPOP than in ΔPP during registrations over longer time periods. These findings are supported by Hoiseth et al. [33] who also found larger variation in ΔPOP than in ΔPP during ongoing open major abdominal surgery. Four papers examined correlations between PVI and ΔPP. Three of them found relatively poor correlations (*^r* ⁼ ⁰*.*72, 0.46 and 0.78) [17, 20, 32], whereas one reported better correlations ($r = 0.85$) [29]. Three papers investigated correlations between PVI and ΔPOP [17, 26, 32]. One study reported poor correlations $(r = 0.39)$ [32], whereas two studies reported relatively good correlations (*^r* ⁼ ⁰*.*92) [17, 26]. These data are presented in Table 2.

4. Discussion

Photoplethysmography is applicable on most patient categories and is noninvasive, simple, widely available, and without risk of complications. Several physiological, clinical, and practical factors must be taken into account when evaluating whether or not it is a noninvasive alternative to evaluate fluid responsiveness.

Firstly, there are several physiological prerequisitions for using dynamic variables.

Mechanical ventilation provides the stable and predictable variations in intrathoracic pressure required for photoplethysmography to be accurate. A large mechanical tidal volume will influence intrathoracic pressure to a greater extent than a small tidal volume. It is presumed that the influence of tidal volume reaches significance at *>*8 mL/kg. It is a challenge that the accuracy of photoplethysmography increases with larger tidal volumes, whereas it is clinically desirable to minimize the tidal volume. The accuracy of

TABLE 1: Papers in which APOP and/or PVI have been evaluated and fluid challenges performed. Table 1: Papers in which ΔPOP and/or PVI have been evaluated and fluid challenges performed.

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TABLE 2: Papers in which correlations between APOP PVI. and APP have been investigated. Table 2: Papers in which correlations between ΔPOP, PVI, and ΔPP have been investigated.

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photoplethysmography relies on a continuous beat-to-beatanalysis. Thus, patients need to have stable heart rate. Additionally, decreased RV ejection fraction can lead to falsepositive variations in pulse pressure [35]. These requisitions also apply for other dynamic variables [36–39].

Secondly, the complex network of correlations between ΔPOP/PVI and ΔPP/other hemodynamic variables varies greatly between different studies. The best correlations are found in studies where short registration periods (3–5 respiratory cycles) have been used and in patients under stable pre- and postoperative conditions. These conditions do not reflect genuine intraoperative instability, the setting where precise guidance of fluid therapy is perhaps most important. The correlations are poorer with longer periods of registration [16], in heterogeneous patient groups in ICUs [16], and during ongoing open abdominal surgery [21, 33]. The best predictive values for ΔPOP and PVI were found in papers in which patients were investigated preoperatively [26, 28]. The poorest predictive values $(0.51-0.72)$ were found during ongoing open major abdominal surgery [21, 33], on sedated patients in ICU [22], and on children preoperatively [32]. In one paper, the predictive value of PVI decreased from 0.96 at baseline to 0.71 during surgery [34]. This indicates that photoplethysmography shows best results in standardized conditions, during short registration periods, and in homogenous groups of pre- and postoperative patients. Importantly, it has been demonstrated that PVI reduces both lactate levels and volumes of fluid administered in surgical patients [40]. This is interesting evidence. However, the study does not report improvement in terms of the number of complications. Further studies are needed to clarify the very important aspect of improved outcome.

Finally, a number of additional factors must be considered. Variations in total peripheral resistance and vasomotor tone increase under the influence of general anesthesia [41, 42], with vasoactive drugs, with site of measurement, and with physiological responses such as inflammation, pain, fear, and body temperature. This may lead to inaccuracy of the photoplethysmography signal. The papers included suggest that ΔPOP is less reliable in ICU patients. This may be explained by the above-mentioned factors. Hemodynamics of patients in the OR or in ICUs changes rapidly and continuously. In most papers which good predictive values for photoplethysmography have been found, short registration periods are used. In papers with longer registration periods, poorer predictive values have been reported.

A threshold value refers to a value of ΔPOP, ΔPP, or PVI that separates responders from nonresponders. Failure to agree upon a threshold value in clinical settings does not necessarily make the parameters (i.e., PVI or POP) less valuable. Different patient groups may well present with different threshold values. A septic patient may have a threshold value different from that of a hemodynamically stable patient undergoing surgery. In the same way, threshold values may also change pre-, peri-, and postoperatively. Cannesson et al. [43] discussed the very interesting notion of a gray-zone approach to fluid responsiveness and found that an intermediate zone of pulse pressure variation could

not predict fluid responsiveness. Future studies should grade responses instead of dividing responses in two categories.

Cut-off values for increases in SV/CO/CI are defined to separate reponders and nonresponders. These thresholds are based on the variability and errors in the chosen measuring technique as well as what change is believed to be clinically important. These thresholds may be more or less arbitrarily chosen and differ between the studies.

Level of intra-abdominal pressure may influence ΔPP and ΔPOP and is relevant in three of the articles included [21, 28, 33]. Results are not coherent. Animal studies have shown that increased intra-abdominal pressure leads to an increase in ΔPP [44]. Studies investigating the influence of these fluctuations during laparoscopic surgery are currently running.

In theory, a number of potentially confounding factors exist. Different pulse oximeter-technology, errors due to software autogain features which filter and amplify the raw signal (thus making it unreliable for quantitative analysis), atherosclerosis, type of fluid, skin pigmentation, saturation, movement artefacts, statistical weaknesses, variations in pleural and transpulmonary pressures, and venous components of the pulsatile signal may affect measurements.

5. Conclusion

We conclude that although photoplethysmography is a promising technique, predictive values and correlations with other hemodynamic variables indicating fluid responsiveness vary substantially. Based on studies using short registration periods photoplethysmography might seem promising for evaluation of volume status. However, in studies using longer registration periods it has been shown that intraand interindividual variability for ΔPOP is greater than for ΔPP, leading to poor agreement between ΔPOP and ΔPP. Thus, it is not presently evident that photoplethysmography is adequately accurate, valid, and reliable to be included in clinical practice for evaluation of volume status. In future studies it is important to evaluate new hemodynamic methods in clinically relevant settings and to test their reproducibility in clinically relevant time frames. Relatively poor predictive values during ongoing major surgery further underscore this point and results vary in different patient groups. The greatest potential for photoplethysmography in evaluation of volume status might be in settings where invasive monitoring is not indicated.

Conflict of Interests

There is no conflict of interests for any of the authors.

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