CONTINUOUS MONITORING OF INTRAVASCULAR VOLUME STATUS DURING RENAL REPLACEMENT THERAPY IN THE CRITICALLY ILLS USING PLETHYSMOGRAPHY VARIABILITY INDEX (PVI)

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Tajuk: Kesesuaian Penggunaan Plethysmographic Variability Index(PVI) Dalam Penilaian Berterusan Status Hidrasi Pesakit Kritikal Ketika Menjalani Rawatan Hemodialisis

Later Belakang: Walaupun terdapat pelbagai jenis modaliti untuk menilai status hidrasi pesakit kritikal, penilaian status hidrasi secara berterusan terutama bagi pesakit kritikal yang menjalani hemodialysis masih rumit dan mencabar. Kajian ini bertujuan untuk mengkaji tahap persetujuan di antara teknik penilaian dinamik Plethysmographic variability index(PVI) pada dua tempat ukuran, iaitu dahi dan hujung jari dengan a) teknik penilaian dinamik , seperti variasi tekanan nadi (PPV) dan tekanan darah arteri invasif (IABP), dan b) teknik penilaian statik seperti tekanan pusat vena (CVP) di kalangan pesakit kritikal yang menjalani rawatan hemodialisis.

Metodologi: Kajian ini adalah 'prospective observational comparative study' dan dijalankan secara dua fasa: Fasa pertama-kajian rintis, dan fasa kedua- kajian berterusan. Seramai 30 orang pesakit (10 kajian rintis, 20 kajian berterusan) yang dimasukkan ke unit rawatan rapi, diintubasi dan menjalani hemodialisis serta memenuhi kriteria kajian telah direkrut dengan kebenaran bertulis dari waris. Set data yang diperoleh dari 30 pesakit adalah sebanyak 250 set. Pengiraan sampel yang diperlukan adalah sekurang-kurangnya 109 set data. PVI (dahi dan hujung jari), CVP, IABP, PPV dicatat selang 5 minit untuk jangka masa 30 minit sebelum permulaan hemodialisis dan selang 30 minit dari masa permulaan sehingga tamat hemodialisis. Data demografik seperti umur, jantina, skor APACHE II dan diagnose utama dicatatkan. Analisis Cohen Kappa diggunakan untuk penilaian tahap persetujuan antara

bacaan data. Data berangka dinyatakan dalam kekerapan dan peratusan dan data berkategori dinyatakan dalam purata and sisihan piawai. Nilai $p<0.05$ dianggap signifikan secara statistik. Semua analisa statistik berdasarkan SPSS versi 22.

Keputusan :250 set data diperolehi daripada 20 pesakit untuk fasa 2. Purata umur pesakit kajian adalah 60 ± 9. 70% pesakit adalah lelaki manakala 30% pesakit adalah perempuan. Nilai APACHE secara purata adalah 25.8±10.0. Nilai 'PVI' dari hujung jari dengan dahi menunjukkan persetujuan yang hamper sempurna($r= 0.98$, CI= 95% 0.98±0.01, $p<0.01$). PVI menunjukkan persetujuan yang memuaskan dengan CVP (hujung jari: $r= 0.27$, CI= 95% 0.27±0.11, $p<0.01$, dahi: $r= 0.27$, CI= 95% 0.27±0.11, $p<0.01$) dan juga MAP (hujung jari: $r =0.22$, CI= 95% 0.22±0.11, $p<0.01$, dahi: $r=0.21$, CI= 95% 0.21±0.10, $p<0.01$). PVI menunjukkan persetujuan yang sederhana dengan PPV (hujung jari: $r= 0.56$, CI= 95% 0.56±0.09 , $p<0.01$dahi: $r= 0.53$, CI= 95% 0.53±0.09, $p<0.01$).

Kesimpulan : Berdasarkan kajian rintis ini menunjukkan persetujuan dengan PVI antara dua tempat ukuran(kuat), PPV(sederhana), CVP(lemah) dan IABP(lemah).

ABSTRACT

Title: Continuous Monitoring Of Intravascular Volume Status During Renal Replacement Therapy In The Critically Ills Using Plethysmographjc Variability Index (PVI)

Background: Intravascular volume status monitoring in the critical care setting remains a big challenge to intensive care providers especially in the groups of patients who receives renal replacement therapy despite the abundance of choices available to assist physicians. This pilot study aims to investigate the degree of agreement of plethysmographic variability index (PVI) of two different sites(digits and forehead) with a) dynamic modality of pulse pressure variation (PPV) and intraarterial blood pressure (IABP) and b) static modality of central venous pressure measurement(CVP) in the assessment intravascular volume status in critically ill patients who requires renal replacement therapy.

Methods: This was a prospective observational comparative study conducted in 2 phases (phase 1- pilot study, phase 2 -continuous study). A total of 30 patients (phase 1- 10, phase 2- 20) who were admitted to critical care facilities, intubated and prescribed with renal replacement therapy and fulfilled study criteria were recruited in this study after consented by the legal guardian. The PVI (digit and forehead), CVP, PPV, and intra-arterial blood pressure(IABP) values were collected at an interval of 5 minutes 30 minutes pre-dialysis and at an interval of 30 minutes till completion of dialysis. Categorical variables were expressed in frequency and percentage with 95% confidence interval while numerical variables were expressed in mean and standard deviation. Agreement analysis between set of data was done

using the Cohen's Kappa analysis. P value of < 0.05 is considered statistically significant. All data were analysed using SPSS version 22.0.

Results: A total of 250 sets of data were obtained from 20 study subjects from phase 2. The mean age for patients included this study was 60 ± 9. There were 70% male and 30% female. The mean APACHE score of the participants was 25.8±10.0. PVI showed statistically almost perfect agreement between measurements from digits and forehead(r= 0.98, CI= 95% 0.98±0.01, p<0.01). PVI was shown to have a fair agreement with CVP (digit: r= 0.27, CI= 95% 0.27±0.11, p<0.01 forehead: r= 0.27, CI= 95% 0.27±0.11, p<0.01) as well as MAP (digit: r =0.22, CI= 95% 0.22±0.11, p<0.01 forehead: r=0.21, CI= 95% 0.21±0.10, p<0.01). However, PVI shows moderate agreement with PPV (digit: r= 0.56, CI= 95% 0.56±0.09 , p<0.01forehead: r= 0.53, CI= 95% 0.53±0.09, p<0.01).

Conclusion: This study demonstrates almost perfect agreement of PVI taken at digits and forehead, a moderate agreement between PVI and PPV and a fair agreement between PVI, CVP and MAP.

LIST OF ABBREVIATION

ΔPOP	Changes in the amplitude of the pulse oximeter plethysmographic waveform
BP	Blood pressure
CI	Cardiac index
CVP	Central venous pressure
HD	Hemodialysis
IABP	Intra-arterial blood pressure
IASBP	Intra-arterial systolic blood pressure
ICU	Intensive care unit
MAP	Mean Arterial Pressure
PI	Perfusion index
PAOP	Pulmonary artery occlusion pressure
PPV	Pulse pressure variability
PVI	Plethysmographic variability index
RRT	Renal replacement therapy
SVV	Stroke volume variability

Chapter 1

1.1 Introduction

In the intensive care setting, it has always been a challenge to accurately predict patient's fluid volume status, more so in patient that requires dialysis therapies which is about 5% of the critical care population.(1) However, despite the challenges presented, it is imperative that intensivist and anesthetist try to ascertain the fluid status of the patient in order to provide optimal care to the patient, as under resuscitation results in inadequate organ perfusion and worsening organ dysfunction while at the same time it has been proven that a positive balance is an important negative prognosticating factor that worsens the outcome of critically ill patients(2-5). Thus, it is of utmost importance to have an accurate assessment of a patient's fluid volume status so that an optimum fluid resuscitation regime can be tailored made for each patient in order to provide a better outcome.

Recently, there are a lot of studies looking into the accuracy of relating fluid volume status of a patient to static clinical variables. And it has been suggested that there is little correspondence of static clinical variables to fluid volume status(6) Comparison studies on static clinical variables and dynamic clinical variables has been done and results have been in favour of dynamic clinical variables for predicting fluid volume status(7). However, most methods present significant limitations and inaccuracy in patient who are critically ill. Thus, a continuous, non-invasive and accurate hemodynamic parameter should be most ideal in guiding fluid optimization and allowing treatments to be administered and titrated towards the patient's requirements.

The aim of the study is to examine the feasibility of the plethysmographic variability index as a predictor of fluid volume status in comparison to the other common dynamic and static measurements in the critically ills who requires renal replacement therapy.

1.2 Problem statement

Fluid volume status has been one of the biggest concerns of the anesthetic practice as under resuscitation results in impaired organ perfusion and subsequent organ dysfunction while at the same time over resuscitation have been proven to increase the mortality rate of patients. Therefore, fluid volume status assessment plays a big role in improving the general outcome of these groups of patients. For a long time, CVP has been the most commonly used measurement for fluid volume status. Other parameters such as heart rate, blood pressure, pulmonary artery occlusion pressure and also inferior vena cava assessment using ultrasound have also been used. However, most methods have its own problem, for example, for CVP measurements, an invasive insertion of the central venous assess in required and it is affected by numerous factors influencing its accuracy. The same goes for PAOP which requires an even more invasive line insertion. While ultrasound assessment using the IVC diameter is noninvasive, there is a dependent on the operator for the accuracy of the assessment.

1.3 Justification

Recent studies show promising result that PVI is the way forward as it correlates well with fluid responsiveness(8-11). The PVI measurement is also a continuous, non-invasive, non-operator dependent and easy to use method in assessing fluid responsiveness. Comparing the pulse oximeter plethysmographic waveform against the arterial pressure waveform, it is noted that the pulse oximeter plethysmographic waveform measures volume rather than pressure changes in both the arterial and venous vessels. Dynamic changes of the peak and amplitude of the pulse oximeter plethysmographic waveform have been used to predict fluid responsiveness and shows a significant correlation with the PPV as well as accurately predicting fluid responsiveness in patients under anesthetic care.(8-11,13)

At the same time, renal replacement therapy is one of the most common occurring procedures in the intensive care units for a variety of indication with acute kidney injury being the most common of the indication (1). It is therefore our aim to investigate the changes of PVI value in the peri-dialytic periods in comparison to other static and dynamic measurements such as CVP, intra-arterial pressures as well as the clinical parameters.

Chapter 2

GENERAL OBJECTIVES

To evaluate the clinical utility and degree of agreement/disagreement of non-invasive continuous monitoring and measurement with Pleth Variability Index algorithm (PVI) and standard monitoring devices of central venous pressure (CVP), mean arterial pressure (MAP) and pulse pressure variation (PPV) as a surrogate in determining intravascular volume status in critically ill patients during renal replacement therapy (RRT).

2.2 SPECIFIC OBJECTIVES

2.2.1 To determine the degree of agreement between PVI values measured at two different sites; digital and forehead during RRT.

2.2.2 To evaluate the degree of agreement of intravascular volume status during RRT obtained concomitantly from PVI and central venous pressure (CVP)

2.2.3 To evaluate the degree of agreement of intravascular volume status during RRT obtained concomitantly from PVI and mean arterial pressure (MAP) and pulse pressure variation (PPV)

2.3HYPOTHESIS

2.3.1 H0: There is no agreement between PVI values measured at two different sites: digital and forehead during RRT

2.3.2 H0: There is no agreement of intravascular volume status during RRT between PVI and CVP obtained concomitantly

2.3.3 H0: There is no agreement of intravascular volume status during RRT between PVI and MAP and PPV obtained concomittantly

Title

Article Title: Continuous Monitoring of Intravascular volume Status during Renal Replacement Therapy in the Critically Ills using Plethysmography Variability Index (PVI)

Running Head:

1. To determine the degree of agreement between PVI values measured at two different sites; digital and forehead during RRT.
2. To evaluate the degree of agreement of intravascular volume status during RRT obtained concomitantly from PVI and central venous pressure (CVP)
3. To evaluate the degree of agreement of intravascular volume status during RRT obtained concomitantly from PVI and mean arterial pressure (MAP) and pulse pressure variation (PPV)

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ABSTRACT

Title: Continuous Monitoring Of Intravascular Volume Status During Renal Replacement Therapy In The Critically Ills Using Plethysmographic Variability Index (PVI)

Background: Intravascular volume assessment of the critically ill patients remains challenging in the intensive care units especially with renal replacement therapy. Recent evidence shows good correlation between plethysmography variability index with PPV and SVV which is a fair reflection of a patient's fluid volume status while being noninvasive and easy to use, making PVI an interesting option to assist in fluid volume status assessment. This pilot study aims to investigate the degree of agreement of plethysmographic variability index (PVI) of two different sites (digits and forehead), with a) dynamic monitoring of pulse pressure variation (PPV) and intraarterial blood pressure(IABP) and b) static measurement of central venous pressure (CVP) in the assessment intravascular volume status in critically ill patients who requires renal replacement therapy.

Methods: This was a prospective observational comparative study conducted in 2 phases. A total of 30 patients who were admitted to critical care facilities, intubated and prescribed with renal replacement therapy were recruited. The PVI (digit and forehead), CVP, PPV, and intra-arterial blood pressure(IABP) values were collected at an interval of 5 minutes 30 minutes pre-dialysis and at an interval of 30 minutes till completion of dialysis. Categorical variables were expressed in frequency and percentage with 95% confidence interval while numerical variables were expressed in mean and standard deviation. Agreement analysis between set of

data was done using the Cohen's Kappa analysis. P value of < 0.05 is considered statistically significant. All data were analysed using SPSS version 22.0.

Results: A total of 250 sets of data were obtained from 20 study subjects from phase 2. The mean age for patients included this study was 60 ± 9. There were 70% male and 30% female. The mean apache score of the participants was 25.8±10.0. PVI showed statistically almost perfect agreement between measurements from digits and forehead (r= 0.98, CI= 95% 0.98±0.01, p<0.01). PVI was shown to have a fair agreement with CVP (digit: r= 0.27, CI= 95% 0.27±0.11, p<0.01 forehead: r= 0.27, CI= 95% 0.27±0.11, p<0.01) as well as MAP (digit: r =0.22, CI= 95% 0.22±0.11, p<0.01 forehead: r=0.21, CI= 95% 0.21±0.10, p<0.01). However, PVI shows moderate agreement with PPV (digit: r= 0.56, CI= 95% 0.56±0.09, p<0.01forehead: r= 0.53, CI= 95% 0.53±0.09, p<0.01).

Conclusion: This study demonstrates almost perfect agreement between PVI taken at digits and forehead, a moderate agreement between PVI and PPV and a fair agreement between PVI and CVP, PVI and MAP.

INTRODUCTION

Various studies have been conducted to look into the accuracy to measure the relationship between intravascular volume status and both static and dynamic clinical variables with studies favouring the dynamic clinical variables as a predictor of intravascular volume status.(14) However, most methods present significant limitations and inaccuracy. Despite the challenges presented, it is imperative that clinicians try to ascertain the fluid status of the patient in order to provide optimal care as inadequate resuscitation results in impaired organ perfusion and worsening organ dysfunction while at the same time it has been proven that a positive balance is an important negative prognosticating factor that determines the outcome of critically ill patients.(15-17) Thus, a continuous, non-invasive and accurate hemodynamic parameter should be most ideal in guiding fluid optimization and allowing treatments to be administered and titrated towards the patient's requirements.

Plethysmographic Variability Index (PVI)- Advancement In Fluid Volume Status Determination In Anesthetic Practice

Traditionally, the central venous pressure(CVP) has been the most frequently used parameter in guiding fluid resuscitation in critically ill patients.(18) However, most of the recent studies have demonstrated that there is no relationship between CVP or the change in CVP and fluid responsiveness. At the same time, studies have shown that pulse pressure variation (PPV) and stroke volume variation (SVV) which correlates well with the variation of the amplitude of the pulse oximeter plethysmographic waveform to be highly predictive of fluid responsiveness(19)

Comparing the pulse oximeter plethysmographic waveform against the arterial pressure waveform, it is noted that the pulse oximeter plethysmographic waveform measures volume

rather than pressure changes in both the arterial and venous vessels. Dynamic changes of the peak and amplitude of the pulse oximeter plethysmographic waveform have been used to predict fluid responsiveness and shows a significant correlation with the PPV as well as accurately predicting fluid responsiveness in patients under anesthetic care. (20-23) PVI is an automated measure of the dynamic changes in the PI that occurs during a respiratory cycle. The PI is the infrared pulsatile signal indexed against the non-pulsatile signal and reflects the amplitude of the pulse oximeter waveform.

In clinical setting, it is difficult to measure the PPV as well as changes in the amplitude of the pulse oximeter plethysmographic waveform (ΔPOP) through visual assessment. Thus recently, Masimo Corp has developed a non-invasive, continuous and easy-to-use commercial device that automatically calculates the respiratory variation in pulse oximeter waveform amplitude. The data collected through the pulse oximetry sensor were used to formulate physiologic indices, perfusion index (PI) and pleth variability index (PVI). The PVI was found to be correlated with PPV. (24) Infrared pulsatile signal is indexed against the non-pulsatile infrared signal and expressed as a percentage [PI = (AC/DC) x 100%] reflecting the amplitude of the pulse oximeter waveform in the calculation of PI. Using PI, PVI is calculated, PVI = [(PImax–PImin)/ PImax] x100% and is displayed continuously. The lower the PVI number the less variability is in PI over a respiratory cycle, and thus more likely the patient is not a fluid responder. The higher the variability, the more likely the patient will be a fluid responder.

Modalities Of Fluid Status Monitoring

Numerous modalities of fluid status monitoring are available for use in the ICU. They are mainly divided into the static parameters as well as the dynamic parameters. Central venous

pressure, pulmonary artery occlusion pressure are examples of static parameters that are invasive while inferior vena cava(IVC) diameter , IVC distensibility index, end-diastolic volume, corrected flow time are examples of non-invasive static parameters. As for the dynamic parameters, the examples are pulse pressure variation, plethysmographic variability index(non-invasive) and stroke volume variation(invasive). There are also modified fluid challenge method to assess fluid responsiveness namely the passive leg raising test and mini fluid bolus.(30)

Physiology Changes Of Fluid During Renal Replacement Therapy

Dialysis hypotension is estimated to occur in about 20% of haemodialysis(HD) sessions with potentially debilitating complications such as cerebral infraction and cardiac and mesenteric ischaemia (33). It may also contribute to chronic overhydration due to an inability to reach patient's dry weight and may lead to under-dialysis. It is believed that dialysis hypotension is caused by a decrease in blood volume that is resulted from the imbalance between the ultrafiltration rate and the plasma refilling rate. Frank dialysis hypotension only occurs when the cardiovascular compensatory mechanisms has been overwhelmed by the loss of blood volume. The major compensation mechanisms are a reduction of the venous capacity by venoconstriction of the capacitance vessels, active increases in arterial tone and increases in heart rate and contractility. Venous return is promoted by the venous constriction which helps to maintain the systemic filling pressure, whereas arteriolar vasoconstriction helps to maintain blood pressure as well as lower capillary pressure, facilitating vascular refill. Cardiac underfilling can also lead to activation of the sympaticoinhibitory cardiopressor reflex and sudden hypotension. The compensatory mechanisms are affected by multiple patient and treatment factors and thus may vary between HD sessions even in the same patient.(31)

Methodology

Study Design: A single center, prospective observational comparative study

This study was conducted in 2 phases:

Phase 1- Pilot study to determine standard deviation and calculation of sample size

Phase 2- Continuation study

Inclusion criteria:

1. Critically ills, intubated and ventilated adults (> 18 years old) receiving standard of critical care monitoring (arterial line and central venous pressure, CVP)

2. Prescribed for RRT (Intermittent mode: IHD, SLEDD continuous mode: CVVH)

Exclusion criteria:

1. Echocardiogram evidence of right ventricular dysfunction

2. Abnormalities in cardiac rhythm

3. Inability to place PVI electrodes at digital / forehead (eg: severe burn)

4. Thoracic compliance less than 30 ml/cmH2O

5. Heart rate/Respiratory rate ratio less than 3.6

6. Clinical abdominal hypertension

7. Pregnant

Recruitment

Study Population:

All adult patients admitted to critical care facilities (general ICU, Surgical ICU, Neurosurgical ICU) in Hospital USM.

Source of sampling: All intubated and ventilated critically ill patients (general ICU, Surgical ICU, Neurosurgical ICU) in Hospital USM and prescribed for RRT.

Statistical Analysis

Cohen's kappa statistic was used to measure the degree of test agreement between two different independent results. Interpretation of kappa agreement analysis are as follows: ≤ 0.20 = poor agreement, 0.21– 0.40 = fair agreement, 0.41–0.60 = moderate agreement, 0.61–0.80 = substantial agreement; and 0.81–0.99 = almost perfect agreement (McHugh, 2012). . Categorical variables were expressed in frequency and percentage with 95% confidence interval while numerical variables were expressed in mean and standard deviation. All data were analysed using SPSS version 22.

RESULTS

Based on the pilot study of ten participants after RRT:

A. PVI (Digital) versus PVI (Forehead)

Based on 5% Type I error rate, 20% Type II error rate, and the expected correlation coefficient of 0.980, the required sample size for correlational study between PVI digital and forehead was 4 sets of data.

B. PVI (Digital) versus MAP

Based on 5% Type I error rate, 20% Type II error rate, and the expected correlation coefficient of 0.556, the required sample size for correlational study between PVI digital and MAP was 23 sets of data.

C. PVI (Digital) versus CVP

Based on 5% Type I error rate, 20% Type II error rate, and the expected correlation coefficient of 0.266, the required sample size for correlational study between PVI digital and CVP was 109 sets of data.

D. PVI (Digital) versus PPV

Based on 5% Type I error rate, 20% Type II error rate, and the expected correlation coefficient of 0.626, the required sample size for correlational study between PVI digital and PPV was 18 sets of data.

Overall, the minimum sample size for fulfilment of the study objective was 109, based on the largest calculated sample size.

We decided to collect a sample of 20 patients with each patient yielding 10-15 sets of data which will yield more than the minimum requirement of 109 sets of data.

Power of study was calculated to be 0.95 retrospectively.

Phase 2 results

A total of 250 data sets were obtained from 20 study subjects (Table 1). Their mean age was 60±9 years old. There were 70% male and 30% female. The mean apache score of the participants was 25.8±10.0.

There was almost perfect correlation between the PVI values measured at two different sites. (r= 0.98, CI= 95% 0.98±0.01, $p<0.01$)(Figure 1).

There were also a fair correlations between MAP and PVI values measure at two different sites. (digit: r =0.22, CI= 95% 0.22±0.11, $p<0.01$ forehead: r=0.21, CI= 95% 0.21±0.10,

p<0.01)(Figure 3) The correlations between PPV and PVI values measured at two different sites were moderate. (digit: r= 0.56, CI= 95% 0.56±0.09 , p<0.01forehead: r= 0.53, CI= 95% 0.53±0.09, p<0.01)(Figure 4)

The correlation between CVP and PVI values measured at two different sites were fair(digit: r= 0.27, CI= 95% 0.27±0.11, p<0.01 forehead: r= 0.27, CI= 95% 0.27±0.11, p<0.01)(Figure 2).

PVI values measured at two different sites showed significant correlations regardless of the prescription of vasoactive drug (Table 2). However, there were only significant moderate associations between CVP and PVI values measured at the two different sites in the present of vasoactive drug prescription. On the other hand, there were only significant moderate associations between MAP and PVI values measured at the two different sites in the absent of vasoactive drug prescription. Nonetheless, there were significant moderate associations between PPV and PVI values measured at two different sites regardless of the prescription of vasoactive drug.

PVI values measured at two different sites showed significant correlations regardless of the prescription of diuretic drug (Table 3). However, there were only significant moderate associations between CVP and PVI values measured at the two different sites in the present of diuretic drug prescription. On the other hand, there were only significant moderate associations between MAP&PPV and PVI values measured at the two different sites in the absent of vasoactive drug prescription.

There was a significant almost perfect agreement between PVI values measured at two different sites for determination of intravascular volume status (Table 4). There were no significant agreements between intravascular volume status during RRT obtained concomitantly from digital and forehead PVI and central venous pressure (CVP), as shown in Tables 5 and 6. There were significant fair agreements between intravascular volume status during RRT obtained concomitantly from digital and forehead PVI and mean arterial pressure (MAP) and pulse pressure variation (PPV), as shown in Tables 7 and 8.

Discussion

The PVI is one of the many modes of examining a patient's fluid volume status. It provides a modality which is simple to use, non-invasive, continuous and is an automated dynamic measurement of the changes in pulse oximetry plethysmographic waveform amplitude that correlates well with a patient's fluid responsiveness(10). PVI has been noted to have a sensitivity of 95% and specificity of 91% in predicting fluid responsiveness in patients who are mechanically ventilated with those who are fluid responsive having a value of >13% while those who are not fluid responsive having a value of 13% or less(10,12). PVI correlates well with respiratory induced variation in both the arterial pressure waveforms and also the plethysmographic waveforms.

Demographic Data

It is observed that the majority of patients admitted to the ICU requiring renal replacement therapy from our study are male patients. The patients recruited in our study has a mean APACHE II score of 25.8 and has a similar finding to other literatures on mean APACHE II score of patients requiring dialysis (mean APACHE score of 26.1) (32). The higher the APACHE II score the higher the mortality rate with no patient surviving with a score of more than 40 while APACHE II score of 10-19 has a survival rate of 40% (32). Another literature showed that the mean APACHE II score for patients requiring dialysis as 22.03±6.92 with the mean APACHE II score on the first day of dialysis significantly higher in nonsurvivors than survivors, 23.79 ± 6.92 vs. 17.72 ± 4.74. (33)

PVI Digit Vs PVI Forehead

Despite recent evidence showing that there is a threshold difference in terms of measurement of PVI from different sites (26), we noted that the PVI readings that were obtained from digits and the forehead had an almost perfect (r= 0.98) agreement in the critically ill patients during the peri-dialytic periods. This agreement does not change even with the prescription of vasoactive drugs differing from the evidence prior to this (28). This phenomena is most probably caused by the different dosage as well as different types of vasoactive drugs used, as the differences of the agents and drug dose would likely have a different degree of effect towards the peripheral perfusion which will subsequently influence the accuracy of the digital PVI values. Other factors such as difference in the underlying pathology, would have a variable influence to the patient's peripheral vasomotor tone as well- for example in the case of neurogenic shock secondary to spine injury requiring vasoactive agents in comparison to septic shock patients requiring pressors to reduce the distributive shock. As such, we believe there is a necessity to conduct further studies to look into the effect of different doses of specific vasoactive drugs such as norepinephrine and epinephrine towards PVI readings obtained from the digits as well as forehead for fluid volume status assessment. Diuretics did not alter the agreement between PVI readings from the digits and forehead as well.

PVI vs Dynamic Measurement (MAP, PPV)

MAP showed a fair agreement towards PVI values during the peri-dialytic periods. MAP is more of an indicator of perfusion pressure rather than a good indicator for fluid volume status. Meanwhile, PPV showed a moderate agreement with PVI values taken over both the digits and forehead during the peri-dialytic periods. This shows that PVI is a good

indicator for fluid responsiveness as recent evidence shows that PPV as well as SVV are good indicators for fluid responsiveness (29). Both PPV and PVI correlate closely with respiratory induced variation in the plethysmographic and arterial pressure waveform. However, in the intensive care unit setting, PVI would be more accurately obtained as PPV is dependent on manual calculation unless special equipment is obtained. As a result, this further demonstrates the potential role of PVI as a fluid volume status monitoring in the critical care setting.

PVI vs Static Measurement (CVP)

CVP was noted to have a fair agreement to PVI values obtained from the patients during the peri-dialytic periods. Single CVP reading has been proven to be misleading in terms of fluid volume status (27), and as such, it does not come as a surprise that the agreement between PVI and CVP were not strong. However, we believe that further evaluation regarding agreement of PVI with CVP trend should be assessed as CVP trend is still one of the most commonly used clinical parameters guiding fluid management in the intensive care unit rather than the single reading of CVP reading.

In conclusion, with PVI being a simple to use, non-invasive, continuous and non-operator dependent, it appears to be an ideal hemodynamic monitoring device to be used in tandem with other clinical parameters in order to guide fluid management in the critically ill patients who requires meticulous management of fluids given to them in order to provide the best outcome in terms of patient care.

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