

# Most Care<sup>®</sup>: a minimally invasive system for hemodynamic monitoring powered by the Pressure Recording Analytical Method (PRAM)

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## ABSTRACT

Invasive hemodynamic monitoring is a cornerstone of the care of critically ill and hemodynamically unstable patients in both intensive care units and operating rooms. The assessment of cardiac output by means of the pulmonary artery catheter has been considered the clinical gold standard. Nevertheless, several concerns have been raised regarding its invasiveness, usefulness, and associated complications. These disadvantages have led to the development, during the last years, of a number of less invasive technologies for cardiac output determination. Among them, those based on the analysis of a peripheral arterial waveform have become commonly used. Most Care<sup>®</sup> is a minimally invasive arterial pressure based monitor powered by the Pressure Recording Analytical Method (PRAM), the only algorithm that does not require prior calibration or pre-calculated parameters and which is based of flow. PRAM provides the measurement of the main factors of hemodynamics, such as systemic blood pressures, stroke volume, cardiac output, and vascular resistances. Moreover, dynamic indices of fluid responsiveness are continuously displayed. In the present paper, we reviewed the current literature focusing on advantages and limitations of PRAM.

**Keywords:** *most care, PRAM, cardiac output, hemodynamic monitoring.*

## INTRODUCTION

The maintenance of adequate organ perfusion is one of the main targets in anesthesia and intensive care settings since it is mandatory for anesthesiologists and intensivists to meet the tissue oxygen and metabolites need in their patients in any clinical condition (1).

As a consequence, physicians need to continuously monitor hemodynamics in order to optimize pre-load, after-load, and contractility by titrating fluids, diuretics, inotropes, and vasoactive drugs, as to achieve the adequate delivery of oxygen and metabolites to tissues (1). Thermodilution (ThD) by means of the pulmonary artery catheter (PAC) has always been considered the clinical gold standard for the measurement of cardiac output (CO) (2).

Nevertheless, pulmonary artery catheterization is associated with considerable risk of morbidities and mortality (arrhythmias,

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**Table 1** - *Main characteristics of PCMs (3).*

	<b>PiCCO (Pulsion Medical Systems, Munich, Germany)</b>	<b>LiDCO (LiDCO Group Plc, London, UK)</b>	<b>VIGILEO (Edwards Lifesciences Corporation, Irvine, CA, USA)</b>	<b>Most Care® PRAM (Vytech Health, Padova, ITALY)</b>
Source of the signal (Artery)	Femoral or Brachial	Radial	Radial	Femoral or Radial
Need of dedicated material	Yes	Yes	Yes	No
External calibration or preloaded data	Yes	Yes	Yes	No

valvular lesions, rupture of the pulmonary artery) and its use is declining (2). Currently, various less invasive technologies based on the analysis of the peripheral arterial waveform (Pulse Contour Methods, PCMs) are gaining popularity in critical care settings and operating rooms (3, 4).

They are based on the principle of predicting a flow from an arterial pressure waveform. In fact, the arterial pressure waveform derives from the interaction between stroke volume (SV), ejected by the left ventricle, and the physical characteristics of the systemic vascular system during each cardiac beat. Thus, ventricle contractility, resistance, compliance, and arterial impedance (dynamic physical properties of the vascular system) are simultaneously considered when assessing SV and CO (SV × heart rate, HR). The theory of PCMs, goes back to the classic Windkessel (air chamber) model described by Otto Frank in 1899 (5). During the XX century, the researchers attempted the measurement of dynamic arterial impedance by means of calibrations and/or tests carried out both *in vitro* and *in vivo* (6).

These studies led to unsatisfactory and conflicting results (6). Today the most PCMs use direct calibration by means of ThD for the estimation of SV (7-10) and

fittings, obtained *in vitro*, are used to follow the modifications over time (7-10). According to the PCMs, SV can be estimated dividing the integral of the change in pressure over time (from the beginning of systole to the diastolic notch) by the value of aortic impedance. SV is then adjusted taking into account HR, mean arterial pressure, and age. The SV measured by PCM is then corrected with that measured by the reference method (e.g. ThD; EXTERNAL CALIBRATION; *Table 1*).

Nowadays, several algorithms have been elaborated and the measurements of SV and CO have become part of daily practice in several clinical settings such as major surgery, emergency department, and Intensive Care Units (ICU) (11, 12).

The major concern about PCMs lies in the measurement of the total vascular impedance (a dynamic physical property of the whole arterial tree), key factor for the calculation of SV from the arterial pressure waveform (13).

Until now, as stated above, PCMs overtake this important issue by means of an external calibration with an indicator dilution technique (ThD or dye-dilution methods) or uploading other pre-estimated parameters such as age, sex, and anthropometric data (13, 14).



**Figure 1** - Most-Care®

Most Care® (Figure 1, powered by *Pressure Recording Analytical Method, PRAM*; Vytech Health®, Padova, Italy) is the only PCM that measures SV without any form of external calibration and/or pre-loaded data (4, 15-19).

The purpose of this paper is to review the current literature in order to focus on advantages and limitations of *PRAM* in various clinical settings.

### **Most Care® (PRAM)**

*PRAM* is a method designed for arterial pressure-derived continuous CO and it is the only methodology that does not need any starting calibration, central venous catheterization, or any adjustments based on experimental data (15).

As a consequence, *PRAM* needs only an arterial line (radial, brachial, femoral) for working.

*PRAM* is based on the principle that, in any given vessel, volume changes occur mainly because of radial expansion in response to pressure variations (15, 16).

This process involves the dynamic interplay among a number of physical parameters including the force of left ventricular ejection, arterial impedance counteracting the pulsatile blood inflow, arterial com-

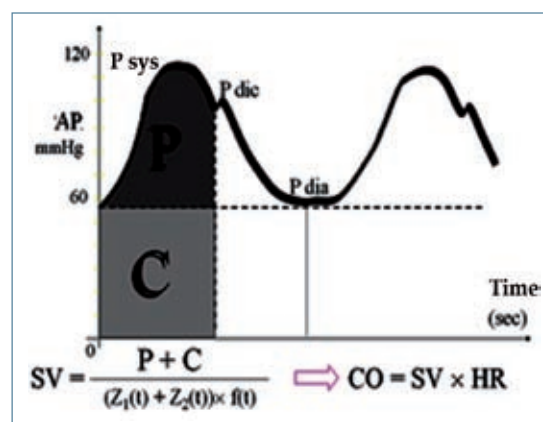
pliance, and peripheral small vessel resistance.

These variables are closely interdependent and simultaneously evaluated by *PRAM* (15). Thus, any kind of flow that is perceived at the peripheral arterial level, whether pulsatile and continuous, is evaluated by *PRAM*. According to pulse contour methodology (7) changes in the area under the pulsatile systolic portion of the pressure waveform reflect changes in SV.

In *PRAM*, otherwise from other PCMs, the area is computed taking into account both pulsatile and continuous contributions of the physical forces underlying the relationship between pressure curve morphology and blood flow (Figure 2) (15-17).

The entire concept behind *PRAM* represents the practical application of a theoretical model totally developed *a priori* differently from other PCMs (15-18). SV is calculated by pulsatile and continuous area divided by a factor, system impedance  $Z(t)$ , determined by the physical characteristics of the circulatory system of the subject under study (Figure 2).

Using *PRAM*, it is possible for each subject to compute  $Z(t)$  directly from the analysis of his/her pressure recording signal (15).



**Figure 2** - Basic algorithm of the *PRAM* system (14). See text.

Another peculiar and fundamental characteristic of the PRAM methodology is the frequency sampling of 1000 Hz whereas the other PCMs usually use a sampling rate of 100 Hz (3). A so high frequency sampling allows a high degree of precision which is of primary importance for the calculation of the arterial impedance, and the correct measure of systolic, diastolic, mean, and dicrotic pressure.

**Other parameters provided by Most Care®**

*Pulse Pressure Variation (PPV)*

*Stroke Volume Variation (SVV)*

*Systolic Pressure Variation (SPV)*

Most clinicians optimize intravascular volume with the use of fluid loading guided by blood pressure, central venous pressure, or pulmonary artery occlusion pressure. Fluid responsiveness is considered to be present when an increase in cardiac index of at least 15% after a volume loading can be documented.

However, several recent lines of evidence (19) strongly suggest that these markers of cardiac preload, independently of the methodologies used for their measurement, are poor predictors of fluid responsiveness.

There is a growing interest, especially on a clinical ground, in the measurements of the variations in blood pressure and SV that result from the interaction between the heart and the lungs during controlled mechanical ventilation.

Positive pressure ventilation, when applied to a patient at rest and with no spontaneous respiratory effort, is associated with a cyclic increase in right atrial pressure during the inflation. It follows that, since right atrial pressure is the back-pressure to venous return, if upstream venous pressures do not simultaneously increase, right ventricular (RV) filling will also decrease in a cyclic fashion.

In presence of RV and left ventricle (LV)

preload responsiveness, this cyclic variation in RV filling will induce a cyclic variation in left ventricular (LV) filling. The latter phenomenon will induce a cyclic variation in LV SV and Pulse Pressure (systolic arterial pressure *minus* diastolic arterial pressure) in presence of preload responsiveness. Therefore, Stroke Volume Variation (SVV), Pulse Pressure Variation (PPV), and Systolic Pressure Variation (SPV), are useful predictors of volume responsiveness when exceeded 10-15% if some conditions of cardiac rhythm and ventilator pattern are respected (19, 21).

Most Care® displays SVV, PPV, SPV, and Dicrotic PV (DicPV), calculated according to the operator's needs (default every 15 seconds).

*Maximal Pressure/Time ratio ( $dP/dT_{MAX}$ )*

With a sampling rate of 1000 Hz, PRAM displays the exact value of  $dP/dT_{MAX}$  (the maximal slope of the systolic portion of the arterial pressure waveform).

This parameter depends on the relationship between left ventricular function and arterial tone and stiffness.

The velocity of transmission and the reflected waves depend on the arterial vessel characteristics (stiffness, tone, stenosis, and so on).

Thus, an accurate value of  $dP/dT_{MAX}$  contemporary to the other hemodynamic parameters, helps in depicting the cardiovascular status of the patient.

*Systemic Vascular Resistance (SVR)*

Systemic Vascular Resistance is calculated in Dynes\* sec/cm<sup>5</sup> with the standard formula:  $SVR = (\text{mean arterial pressure} \textit{ minus} \textit{ central venous pressure}) / CO \times 80$ . The central venous pressure can be measured by means of a second auxiliary cable. Otherwise the operator can set a value of pressure if a central venous catheter has not been placed.

### Cardiac Cycle Efficiency (CCE)

CCE (adimensional value) describes the cardiac hemodynamic performance in terms of the ratio between hemodynamic work performed and the energy expenditure (23).

CCE shows the ability of the cardiovascular system to maintain homeostasis at different energy levels.

The clinical significance of this parameter is still under evaluation.

### Validation studies

In 2002, Romano et al. (15), simultaneously estimated CO by direct-oxygen Fick method, PAC-ThD, and PRAM applied to pressure signals recorded either invasively from an aortic catheter (PRAMa) or non-invasively, at the finger level, by photoplethysmography (PRAMf) in 22 adult hemodynamically stable cardiac patients submitted to cardiac catheterization.

A good correlation between PRAM and both Fick method and ThD were found (Fick method vs. PRAMf,  $r^2=0.94$ ; Fick method vs. PRAMa,  $r^2=0.88$ ; ThD vs. PRAMf,  $r^2=0.77$ ; ThD vs. PRAMa,  $r^2=0.77$ ).

The Bland-Altman analysis confirmed the agreement between the Fick method and PRAM, and ThD and PRAM.

In 2004, Giomarelli et al. (18) measured CO in 28 patients undergoing coronary artery bypass grafting at 15 min after anesthesia induction, 30 min after weaning from extracorporeal circulation, 1 and 3 h after arrival in the ICU comparing PAC-ThD and PRAM. CO ranged from 2.3 to 7.4 l/min.

A good correlation between methods was indicated by  $r^2=0.78$ . The Bland-Altman analysis demonstrated that the overall estimates of CO measured by PRAM closely agreed with CO measured by PAC (mean difference, 0.027; standard deviation, 0.43; limits of agreement, -0.83 and +0.89). In

2005, Scolletta et al. (17) compared PRAM with electromagnetic flowmetry (EM-CO) and ThD (ThD-CO) during various hemodynamic states (dobutamine and hemorrhage) in a swine model. CO ranged from 1.8 to 10.4 l/min.

The authors found close agreement between the techniques. Mean bias between EM-CO and PRAM-CO was -0.03 l/min (precision 0.58 l/min). The 95 % limits of agreement were -0.61 to +0.55 l/min. Similar results between ThD-CO and PRAM-CO were found.

Romano et al. in 2006 (16) compared PRAM-CO and ThD-CO in 50 cardiac patients. PRAM-CO was measured invasively in ascending aorta (PRAMa) and non-invasively at the finger (PRAMf). PRAMa and PRAMf resulted to be accurate when compared with the gold standard (ThD vs. PRAMf,  $r^2=0.76$  and mean bias 0.05 l/min/m<sup>2</sup>; ThD vs. PRAMa  $r^2=0.73$  and mean bias 0.03 l/min/m<sup>2</sup>).

In 2008, CO measured by PRAM was compared with CO measured by Doppler echocardiography in 48 pediatric patients (20) showing a good agreement between methods also in children.

Patients with low cardiac output syndrome treated with inotropic drugs or with Intra Aortic Balloon Pump do not represent a limitation for PRAM as Maj et al. (22) recently observed in a prospective study comparing cardiac index measured with PRAM and ThD in 20 patients who underwent cardiac surgery.

We recently published an experimental study comparing the CO measured by means of PRAM (PRAM-CO) with that measured with two different methods: thermodilution-PAC (ThD-CO) and Transesophageal Echocardiography (TEE-CO) in a swine model (4).

Dobutamine, vasoconstriction, hemorrhage, and volume resuscitation were induced step-by-step. The Bias resulted from

the comparison between PRAM-CO and ThD-CO was  $-0.006$  l/min and the Percentage Error was 22.8%. The comparison between PRAM-CO and TEE-CO resulted in: Bias =  $-0.007$  l/min and Percentage Error = 22%. Sub-group analysis revealed disagreement between methods during the last two steps of hemorrhage ( $-35$  and  $-50$  % of the theoretical volemia): PRAM-CO vs ThD-CO: Bias =  $-0.37$  l/min, and Percentage Error = 45%; PRAM-CO vs. TEE-CO: Bias =  $0.4$  l/min and Percentage Error = 62%. We concluded that PRAM proved to be accurate in measuring CO during hemodynamic stability, tachycardia, and vasoconstriction. When volemia was reduced more than 35 %, disagreement between methods was observed.

Further larger clinical studies are needed to confirm the reliability of PRAM in measuring hemodynamic parameters during conditions of hemodynamic instability.

Moreover, studies focusing on the influence of hemodynamic monitoring, by means of minimally-invasive tools, on outcome are still lacking.

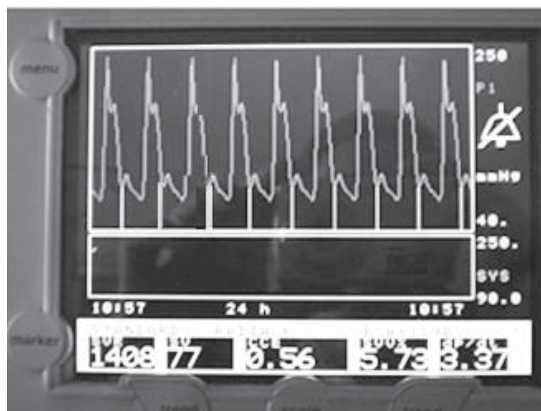
#### Limitations

A primary concern about PCMs reliability is related to the *quality of the recorded arterial pressure signal*.

The signal can be inadequate for *patient-related* and *technical-related* reasons.

*Patient-related* causes of inappropriate signal acquisition may be due to aortic valve regurgitation or abnormal transmission of the signal itself such as during aortic dissection or in every vascular condition resulting in obstruction to the transmission of the signal (thoracic outlet syndrome, significant stenosis along the arterial tree from the aortic valve to the sampling site).

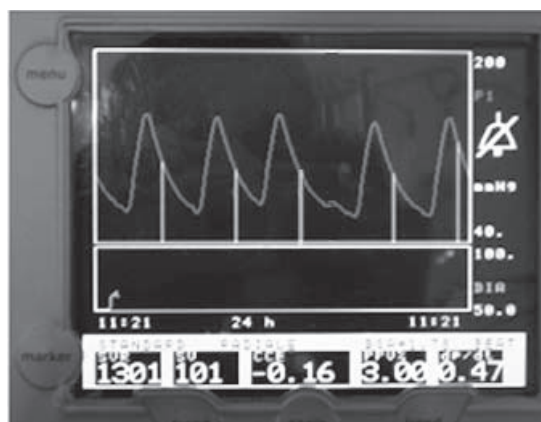
*Technical-related* problems may be due to inadequate dynamic response of the transducer and fluid-filled tubing system cur-



**Figure 3** - Under-damped resonating arterial-signal. Note steep systolic upstroke and narrow systolic peak.

rently used for invasive blood pressure monitoring.

Under-damped waveforms and resonance of the signal (*Figure 3*) are frequently encountered during arterial pressure monitoring in both operating rooms and critical care settings. An inadequate damping of the signal (*Figure 3* and *4*), may lead to an incorrect estimation of arterial impedance and hence an incorrect value of SV. As a consequence, the possibility to correctly employ a minimally-invasive system for hemodynamic monitoring like PRAM is



**Figure 4** - Over-damped arterial signal. Note the loss of evidence of the details.

influenced by the physician after a *careful observation of the arterial waveform*.

The user must be aware that an inadequately damped signal may lead to misinterpretation of hemodynamics, several devices with different degrees of invasiveness are available for monitoring hemodynamics in critically ill patients and none fulfils the criteria of optimal monitor.

In this context, *PRAM* seems to be a feasible and efficient alternative to standard monitoring systems in particular in those settings in which a more invasive and somewhat aggressive monitoring (TEE and/or PAC) appears not justified or disproportionate.

Since *PRAM* does not require any calibration, or any additional invasive procedure, it is not time-consuming and does not expose the patient to potential complications related to central venous catheterization.

Although *PRAM* seems to be easy to use, the understanding of the underlying cardiovascular pathophysiology is of primary importance to avoid misinterpretation of the displayed data. Finally, a careful observation of the arterial wave morphology represents the first and key contribution that the physician has to take into account when an arterial pressure-based hemodynamic monitoring as *PRAM* is used before interpreting the data.

Even a highly sophisticated and accurate methodology as *PRAM* cannot replace the critical mind of the physician.

*Conflict of interests*

*For the potential implications concerning Conflicts of Interest, the authors wish to inform the Editor that Dr. SM Romano is the owner of the patent for the Pressure Recording Analytical Method (PRAM). The other authors declare that they have no competing interests.*

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