Non-Calibrated Pulse-Contour Analysis for Monitoring Adequacy of Tissue Perfusion in Major Abdominal Surgeries in Perioperative Period

Thesis

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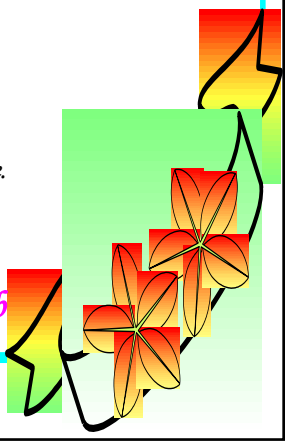

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$CaCo_2$	Arterial carbon dioxide content
CaO_2	Arterial oxygen content
CI	Cardiac index
CO	Cardiac out-put
CvO_2	Venous carbon dioxide content
CvO_2	Venous oxygen content
LIDCO	Lithium Dilution Cardiac Output
NICO	Non-invasive carbon dioxide rebreathing
O_2ER	Oxygen extraction ratio
PAC	Pulmonary artery catheter
PICCO	Pulse induced continuous cardiac output monitor
PPV	Pulse pressure variation
PRAM	pressure recording analytical method
SID	Strong ion difference
SV	Stroke volume
SVI	Stroke volume index
$SvcO_2$	Mixed venous oxygen saturation
SVV	Stroke volume variation
TOD	Trans-esophageal Doppler
TTD	Trans-Thoracic Doppler
VO_2	Oxygen uptake

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Introduction

During major abdominal surgeries, incidence of major blood loss as well as major fluid loss is an acute risk factor. If the fluid is not replenished in the perioperative period, can lead to increased risk of complications, including cardiac and respiratory failure, cognitive impairment and physiologic reaction to the infection due to lack of the oxygenation and organ perfusion. Underlying disease and co morbidities, anesthetic use and nature and duration of the surgery also associated with the development of these complications which often lead to poor patient outcome (**Green** *et al*, **2012).**

Major abdominal surgery generates a strong inflammatory response that leads to increase in the oxygen requirement from an average 110 ml/min/m^2 at rest to an in average of 170 ml/min/m^2 in the post operative period. The substantial increase in the oxygen demand is normally met by increase in the cardiac output and tissue oxygen extraction (**Davies** *et al*, **2004).**

To potentially improve outcomes and reduce complications, monitoring modalities that reflect the patient's dynamic intra vascular physiology in real time should be employed. Increasingly, clinicians have turned to haemodynamic assessment to measure cardiac output to guide vasopressor support for oxygen delivery, organ perfusion, blood pressure, as well as the use of appropriate anesthetic. Data has shown that using haemodynamic assessment to guide fluid management leads to reduce hypovolemia and hypoperfusion. Using measurement of stroke volume, stroke volume variation and pulse pressure variation. Over other volume indicators like central venous

pressure have been effective in reducing complications and improving outcomes via goal directed therapy protocols (**Green** *et al,* **2012).**

Primary research efforts over the past 2 decades have highlighted the emergence of goal-directed therapies (GDT), a spectrum of fluid management strategies that use patient-specific hemodynamic outcomes to optimize physiologic stability, cardiovascular volume, tissue oxygenation, nutrient delivery, microvascular flow, and end organ perfusion while minimizing the long-term sequelae associated with perioperative fluid volume depletion or overload (**Trinooson** *et al, **2013).***

Functional Hemodynamic Monitoring

Recent interest in functional hemodynamic monitoring for the bedside assessment of cardiovascular insufficiency has heightened. Functional hemodynamic monitoring is the assessment of the dynamic interactions of hemodynamic variables in response to a defined perturbation, **(Garcia** *et al*, **2011).**

Current hemodynamic monitoring is mainly focused on monitoring of pressure-derived hemodynamic variables related to systemic circulation. Increasingly, oxygen transport pathways and indicators of the presence of tissue dysoxia are now being considered. In addition to the microcirculatory parameters related to oxygen transport to the tissues, it is becoming increasingly clear that it is also important to gather information regarding the functional activity of cellular and even subcellular structures to gain an integrative evaluation of the severity of disease and the response to therapy. Crucial to these developments is the need to provide continuous measurements of the physiological and pathophysiological state of the patient, in contrast to the intermittent sampling of biomarkers. As technological research and clinical investigations into the monitoring of the patients have progressed, an increasing amount of information is being made available to the clinician at the bedside. This complexity of information requires integration of the variables being monitored, which requires mathematical models based on physiology to reduce the complexity of the information and provide the clinician with a road map to guide therapy and assess the course of recovery, **(Donati** *et al.*, **2013).**

In the early 1960s, -Weil- realized the importance of continuous monitoring of physiological parameters coupled with calculations to provide real-time information on the hemodynamic status of

patients at the bed side **(Weil** *et al.,* **1966)**. One can argue that this characteristic – namely, the continuous monitoring and support of physiological variables – defines the health of the patients. The introduction by Weil and Safar of monitors attached to digital computers to continuously monitor respiratory and hemodynamic measurements was a defining moment in the development of critical care medicine. This technology, used in conjunction with the pulmonary artery catheter introduced by Swan, provided the intencivist with a powerful platform to semi continuously monitor the functional state of the heart as the main motor driving systemic circulation. By including measurements of arterial and mixed venous gas analysis, the arterial oxygen content and the mixed venous oxygen content could easily be calculated. Consequently, oxygen delivery and oxygen consumption could be calculated from known formulae, and a target for titration therapy was formulated, **(Donati** *et al.,* **2013).**

Shoemaker was the main proponent of driving systemic circulation by targeting high values of cardiac output, oxygen delivery and oxygen consumption **(Shoemaker** *et al.,* **1988)**. The basic idea behind this approach was that maximizing the oxygen delivery of the systemic circulation would ensure ample oxygen for the organ beds at risk. In initial studies, Shoemaker utilized the hemodynamic data obtained from the pulmonary artery catheter in high-risk adult surgical patients before, during and after surgical procedures. From these observational data, he established a protocol using super normal values for cardiac output, oxygen delivery and oxygen consumption as the therapeutic goals. Indeed, this approach seemed to be favorable in surgical patients because it resulted in improved outcomes. Donati and colleagues demonstrated that this approach was also

successful in reducing morbidity and the length of hospital stay in high-risk surgical patients (**Donati** *et al.*, **2013)**. However, the effectiveness of this strategy in other critically ill patients remains controversial. Gattinoni and colleagues, for example, found no difference between patients who were treated with a protocol that targeted normal values for cardiac output, oxygen delivery and oxygen consumption, super normal values or mixed venous saturation >70% **(Gattinoni** *et al.,* **1995)**. Hayes and colleagues found an increased mortality in patients who were treated using the supranormal values protocol. The condition of normal or reduced oxygen extraction seemed to be a key hemodynamic component that contraindicated targeting supranormal values of oxygen delivery. Vincent suggested that the application of a dobutamine challenge to identify the effect of increasing systemic oxygen delivery was an effective strategy to achieve hemodynamic optimization for the critically ill patient, **(Donati** *et al,* **2013).**

Cardiac function monitoring:

Systolic cardiac function results from the interaction of four interdependent factors: heart rate, preload, contractility, and afterload. Heart rate can be quantified easily at the bedside, while preload estimation has traditionally relied on invasive pressure measurements, both central venous and pulmonary artery wedge. Heart rate Heart rate is the easiest parameter to measure at the bedside. Cardiac output can be adversely affected by extreme sinus tachycardia (for example, with hypovolaemia or excessive inotrope use), bradycardia, or any arrhythmia producing loss of atrioventricular synchrony, **(Tibby** *et al.*, **2013).**

A- Preload:

Preload encompasses the variety of factors resulting in ventricular end diastolic volume. It is important to appreciate that the preload of the right and left heart are not necessarily the same. The two commonly used measures of preload, namely central venous pressure (right heart) and pulmonary artery occlusion pressure (left heart) both have clinical limitations. This is because many factors affect the ability of a pressure measurement to act as a marker of volume status, including venous capacitance, cardiac chamber compliance, valve competence, pulmonary artery pressures, and the ability of the lung to function as a Starling resistor with positive pressure ventilation, to name a few. However it is probably reasonable to assume that a low central venous pressure may represent under filling, and this parameter may be useful for trending. Two new volume based measures, intrathoracic blood volume and right ventricular end diastolic volume, have been evaluated favourably as preload indicators. Both are calculated from modifications of a thermodilution technique; however, neither has been adequately evaluated in children. Analysis of variation in arterial pulse pressure waveform shows great promise, and can easily be incorporated into routine invasive blood pressure monitoring on a continuous basis. Several transoesophageal Doppler derived parameters have been explored; one has been used successfully in adults to guide intraoperative volume replacement. Two echocardiographic indicators of preload have been suggested. The functional preload index requires specialised software and a series of calculations, thus limiting its clinical use, while interpretation of mitral inflow velocity profiles is often beset by confounding variables. Diastolic dysfunction also affects preload, although controversy exists regarding the interpretation of echocardiographic

parameters of diastolic function in certain clinical scenarios, **(Wiesenack** *et al*, **2001).**

B- Contractility:

An adequate bedside measure of contractility does not exist. The echocardiographic stress velocity index has provided insight into pathophysiology, but requires the same technical specifications as the functional preload index. Recently one of the assumptions on which this parameter is based, namely the linear relation between stress velocity (contractility) and end systolic wall stress (afterload) has been questioned, suggesting a reappraisal of its clinical interpretation. Stoke work index represents the area enclosed by the ventricular pressure-volume loop; however, this may be estimated at the bedside from stroke index and arterial pressure measurements (figure 1). Although not a true measure of contractility, it allows some insight into cardiac reserve, namely how stoke index (volume) is adjusted in the face of changing afterload, **(Tibby** *et al*, **2013).**

C- Afterload:

Afterload is defined as the force opposing left ventricular fibre shortening during ventricular ejection, in other words left ventricular wall stress. Wall stress can be measured at various points throughout cardiac ejection, although it is thought that calculation at end systole provides the best measure of afterload. Calculation of wall stress requires measurement of end systolic transmural ventricular pressure, and echocardiographic measurement of left ventricular end systolic dimension and wall

thickness. Here transmural pressure equals the difference between intra- and extraventricular (or intrathoracic) pressures. While intraventricular pressure can be estimated from the mean arterial pressure, accurate estimation of extraventricular/intrathoracic pressure is difficult and may involve measurement of oesophageal or pleural pressures. Using this approach it is easy to understand how factors that increase intrathoracic pressure, such as positive pressure ventilation, result in a reduction in afterload. A recent publication has suggested that the clinical contribution of extracardiac pressure when calculating indices of systolic function may in fact be minimal; however, whether this is so for calculation of afterload remains to be seen.

The commonest clinical measure of afterload is systemic vascular resistance. This parameter is analogous to Ohm's law, treating the heart as a "DC" (constant) rather than an "AC" (pulsatile) generator of flow, by measuring the ratio of mean pressure drop across the systemic vascular bed to the flow (table 1). Seen in this light, the limitations of this calculation are obvious; however, it provides the clinician with a single figure that has prognostic value. The importance of minimizing afterload in the failing myocardium is well documented. However, the clinical dilemma is usually one of balancing afterload reduction against maintaining perfusion pressure (blood pressure); in reality this can only be optimised if CO is measured, **(Haney** *et al.,* **2001).**

Measurement of contractility and afterload is difficult; thus in clinical practice the bedside assessment of cardiac function is represented by cardiac output. Cardiac output (CO) is defined as the volume of blood ejected by the heart per minute. As such, CO represents the clinical manifestation of cardiac function, which can be measured at the bedside, **(Tibby** *et al,* **2013).**

Interpretation of the CO:

Integration of CO into a global metabolic assessment necessitates an appreciation of the contribution of CO to oxygen delivery, and an understanding of the balance between oxygen delivery and consumption, **(Tibby** *et al*, **2013).**

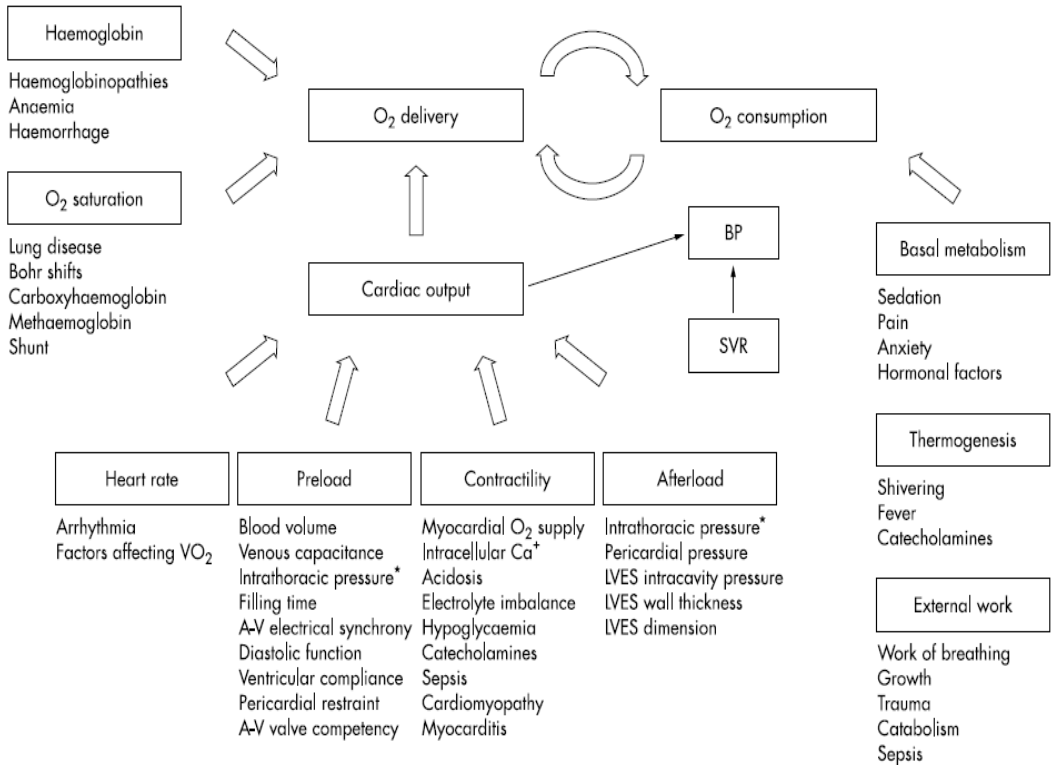

Figure 1: Factors affecting oxygen delivery and consumption, **(Tibby** *et al*, **2013).**