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PII: S0104-0014(23)00094-5
DOI: https://doi.org/10.1016/j.bjane.2023.08.004
Reference: BJANE 744460

To appear in: *Brazilian Journal of Anesthesiology (English edition)*

Received date: 17 April 2023
Accepted date: 20 August 2023

Please cite this article as: Suzana Margareth Lobo , João Manuel da Silva Junior , Luiz Marcelo Malbouisson , Improving perioperative care in low-resource settings with goal-directed therapy: a narrative review, *Brazilian Journal of Anesthesiology (English edition)* (2023), doi: https://doi.org/10.1016/j.bjane.2023.08.004

BJAN-D-23-00190_Narrative Review

Improving perioperative care in low-resource settings with goal-directed therapy: a narrative review

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Received 17 April 2023; accepted 20 August 2023

KEYWORDS
Perioperative care;
Early goal-directed therapy;
Surgery; hemodynamic monitoring

Abstract

Perioperative Goal-Directed Therapy (PGDT) has significantly showed to decrease complications and risk of death in high-risk patients according to numerous meta-analyses. The main goal of PGDT is to individualize the therapy with fluids, inotropes, and vasopressors, during and after surgery, according to patients' needs in order to prevent organic dysfunction development. In this opinion paper we aimed to focus a

discussion on possible alternatives to invasive hemodynamic monitoring in low resource settings.

The burden of postoperative complications

Epidemiological studies suggest that 4.8 billion people are unable to access safe surgical treatments.[1] According to estimations, an expansion of surgical services to address unmet needs would increase total global deaths to 6.1 million annually, of which 1.9 million deaths would be in Low- and Middle-Income Countries (LMIC). Perioperative complications are common in high-risk patients undergoing moderate or major surgeries and are associated with longer ICU stays, mortality, and higher costs.[2] Many qualities improvement programs have been proposed to face the challenges of perioperative complications.[3]

Goal-directed perioperative therapy

Perioperative Goal-Directed Therapy (PGDT) has been always about individualization of treatment according to patients' needs and has significantly shown to decrease complications and risk of death in selected high-risk patients, if applied at the right time.[4] Many RCT and meta-analyses, including network meta-analysis have demonstrated consistently that the most effective goals of therapy are those using accurate methods to evaluate fluid responsiveness and therapeutic goals that include improving flow, therefore Cardiac Output (CO), and Oxygen Delivery (DO2).[5-9]

A continuum of treatment with fluids and hemodynamic management takes place before, during and after surgery. There is still large variability in the amounts of fluids given to these patients. In a large study in patients undergoing colon and orthopedic surgeries, the authors found increased morbidity and costs for both the highest and the lowest 25 percentiles of fluids given.[10] An observational study conducted in ICUs around the world indicated that in 43% of the cases no hemodynamic variable was used to guide fluid resuscitation and safety limits were rarely used.[11]

The aim of goal-directed therapy is to prevent an imbalance between DO_2 and oxygen consumption in order to avoid the development of multiple organ dysfunctions.[2] Cardiac output, the product of Stroke Volume (SV) and heart rate, is an important determinant of DO_2. SV depends on ventricular end-diastolic volume (preload) and contractility. If hypoperfusion or hypotension is present, the clinician must decide whether intravenous fluid will augment CO. The safest approach is to test SV response to fluid boluses (bolus-induced increase in SV > 10%) or to predict responsiveness when CO monitoring is not available. If these derangements are not solved after initial fluid resuscitation, the next step is to decide whether further intravenous fluid will augment CO or if other measures (such as vasopressors or inotropes) should be used to adjust the hemodynamic management.

The utilization of CO monitoring In the perioperative period has been shown to improve outcomes if integrated into a GDT strategy, particularly in adult non-cardiac surgical patients undergoing major abdominal surgery.[5-9] International Societies Guidelines do recommend PGDT, however the adoption is still very poor.[12] Possible causes for that are lack of knowledge regarding monitoring techniques, costs and lack of available equipment, or problems with reimbursement. Therefore, a discussion about possible alternatives to invasive hemodynamic monitoring in low resource settings is extremely essential.

Nothing less than central venous and arterial lines

In low-resource hospital settings, CO monitoring is not available and commonly used hemodynamic variables in the perioperative period are heart rate, diuresis, arterial pressure, lactate, and blood gas. The problem is the lack of accuracy of these measures in the case of more complex patients. As we know well, in surgical patients, it is all about delivering oxygen to the tissues. We can do better by integrating and interpreting a set of data provided from central and arterial lines in place along with point-of-care blood gases and lactate. These tools would provide measures of Mean Arterial Pressure (MAP), Pulse-Pressure Variation (PPV), Central Venous Pressure (CVP), Central-Venous Oxygen Saturation ($ScvO_2$), Oxygen Extraction Rate (O_2ER), that is the difference between arterial Oxygen Saturation (SaO_2) and SvO_2/over SaO_2, and venoarterial carbon dioxide difference (CO_2-gap), the difference between venous and arterial PCO_2. In addition, a simple Foley catheter in our set of tools adds intra-abdominal pressure. By targeting MAP and these indices we are able to manage fluids[13] and other supportive treatments with greater safety (Fig. 1).

Important endpoints: arterial pressure

The incidence of intraoperative hypotension is very high, with 90% of the patients presenting at least one episode of hypotension during operations and one third of them even before skin incision.[14] Intraoperative hypotension is associated with harm such as myocardial and acute kidney injury, overall organ injury and mortality. In an RCT, the IMPRESS trial demonstrated that targeting an individualized systolic blood pressure within 10% of the reference preoperative value with continuous norepinephrine infusion reduced the risk of postoperative organ dysfunction in moderate and high-risk surgical patients.[15] Arterial lines have been relatively safe and easy to implement. Expert consensus recommends monitoring and optimization of MAP by keeping MAP > 65 mmHg or 10–20% target within preoperative baseline.[16]

Important endpoints: pulse pressure variation

The most frequently asked question daily in our ICUs is “will this patient respond to fluid challenge?”.[17] It means that the bolus of fluids will improve CO and therefore tissue perfusion. In low-resource intraoperative settings, Pulse Pressure Variation (PPV) can be used as an indicator to give fluids.[13] For PPV monitoring we just need the curves obtained from an arterial line and a simple bedside monitor. The conditions in the operating room as well as in the early postoperative period with sedated and mechanically ventilated patients are usually good for its use. In a systematic review of 14 studies a 49% reduction in postoperative morbidity with dynamic monitoring-guided fluid strategies was reported.[18] Nonetheless, attention to the limitations of the method is essential (Fig. 2).[19] According to experts’ opinion it is important to use a “validity criteria checklist” before using PPV (or similar methods) to estimate fluid responsiveness, then to give iterative small fluid boluses to maintain intraoperative PPV below the threshold values that define fluid responsiveness.[20]

PPV is a very reliable predictor of fluid responsiveness as long as we respect the limits of the method. The use of low Tidal Volume (TV) ventilation is a limitation for the use of PPV. Both in the OR and in the ICU, we should use protective ventilation – 6 $mL.kg^{-1}$ of predicted BW. But this limitation can be overcome by using “tidal volume challenge”.[21] The “TV challenge” is a simple test that can be performed easily at the bedside by increasing TV to 8 $mL.kg^{-1}$ PBW, for 1 minute and observing the change in PPV. This test does not require a CO monitor, what makes it especially applicable in low resource settings.

Important endpoints: Oxygen (O_2) and carbon dioxide (CO_2)-derived indices

Oxygen extraction ratio

Oxygen and CO_2 derived indices combined are very helpful in the perioperative period. Point-of-care technologies made these tools even more available and affordable. $ScvO_2$ and O_2ER are parameters related to global perfusion. Trends in $ScvO_2$ can be used to reflect imbalances between DO_2/VO_2, particularly in the ICU. Increase of 2% or more in SvO_2 during fluid loading after major vascular surgery or cardiac surgery indicates fluid responsiveness.[22] In a Randomized Controlled Trial (RCT) from 9 hospitals in Italy the target was to keep O_2ER at values < 27% according to an algorithm of GDT in 135 patients undergoing major abdominal surgeries.[23] They demonstrated decreased number of patients with organ failures, declining from 29.8% to 11.8%.

Serum lactate

Serum lactate, a commonly used marker of global perfusion in the ICU, is an independent predictor of death due to MOF after non-cardiac surgery in high-risk patients.[24] Nonetheless, failure of lactate concentrations to decrease over time is associated with worse outcomes in surgical patients. Lactate-guided therapy after ICU admission improved outcomes in a heterogeneous population in whom half were surgical patients.[25] In spite of well accepted in postoperative care as a marker of hypoperfusion, its use is limited as a therapeutic target during the intraoperative period. Due to anesthesia and possible hypothermia there is a smaller increase in serum lactate levels.[2]

Veno-arterial difference of CO_2 (CO_2-gap)

There is an inverse relationship between CO and CO_2-gap. CO_2-gap increases if systemic blood flow reduces. It is a good indicator of the inadequacy of CO relative to the actual global metabolism. A CO_2-gap higher than 5 or 6 is suggestive of reduced blood flow, either by a low CO, usually the case in the perioperative period, or microcirculatory dysfunction.[26] A CO_2-gap $\geq$ 5.0 mmHg before surgery was associated with more postoperative complications, mainly shock, renal failure and infection, and hospital mortality in adult high-risk patients.[24] A retrospective study evaluated data from 70 patients undergoing major abdominal surgery by measuring CO_2-gap hourly until the end of the surgery. CO_2-gap of 6 or higher was able to predict postoperative complications.[26] Another study in 60 patients undergoing coronary-artery bypass grafting with $ScvO_2 > 70\%$, assuming they would be in an adequate circulatory status, divided patients in High and Low CO_2-gap groups after ICU admission.[27] The High CO_2-gap group had significantly lower DO_2 and mesenteric flow, higher cytokine levels, and more complications. A before/after study reported better outcomes by targeting MAP, PPV, as a parameter of fluid responsiveness, and CO_2-gap as a surrogate for CO, with less complications and lower 90-day mortality rate.[28] One RCT aiming at SvO_2 of > 75% and CO_2-gap < 6 mmHg found improved oxygen-derived parameters, lower length of ICU stays and shorter MV duration in the CO_2-gap group.[29] It is necessary to confirm these findings in a larger RCT.

Exhaled CO_2 with capnography

While we have an inverse correlation between CO_2-gap and CO, there is a direct correlation between changes in exhaled CO_2 ($EtCO_2$) and CO, as long as we have a condition of constant minute Ventilation and CO_2 production (VCO_2). This condition is feasible in sedated patients, with constant tidal volume and short periods of time of observation in which metabolism is constant. $EtCO_2$ measured by mainstream CO_2 sensors during Passive Leg Raising (PLR) tests are able to track changes in CO in ICU patients.[26] Other authors reported PLR-induced increases in CO and $EtCO_2$ strongly correlated ($R2 = 0.79$; $p < 0.0001$), besides increases ≥ 5% in $EtCO_2$ during the test being predictive of fluid responsiveness with 90.5% (95% CI 69.9–98.8%) Sensitivity/Specificity in surgical patients.[30] Thus, it could provide a noninvasive and easily available method at the bedside for predicting fluid responsiveness in paralyzed patients on mechanical ventilation. Fluid responsiveness tests should preferably be performed with an automated bed. Nonetheless, $EtCO_2$ variation was correlated with changes in CO even when induced by a simplified PLR maneuver with a dedicated ICU bed.[31] One recent meta-analysis confirmed that $EtCO_2$ variation performed moderately in predicting fluid responsiveness during the PLR test in patients with mechanical ventilation.[32]

Limits of safety for fluid administration: central venous and intra-abdominal pressures

Another important point is when we should stop giving fluids or start deresuscitation. Assuming the limitations of CVP to evaluate fluid responsiveness, extremes values of CVP can be used to stratify patients of lower or higher risk of harm if receiving further fluid loading.[33] In addition, a high CVP is a major factor compromising organ perfusion. Systemic Perfusion Pressure (SPP) is dependent on the difference between MAP and CVP (SPP = MAP - CVP) and mishandling these parameters is associated with organ congestion and dysfunction, particularly acute kidney injury.[34,35]

There is an association between Intra-Abdominal Pressure (IAP) and fluid balance, fluid loading or fluid removal.[36] IAP monitoring with a Foley manometer in the bladder is a very simple, reliable, and cost-effective clinical tool for patients at risk of Intra-Abdominal Hypertension (IAH). IAH is frequently associated with positive fluid balance and organ dysfunction after complex operations.[37]

Conclusion

Indices and pressure parameters were depicted in Table 1. Of course, most of these proposals come as suggestions based on current literature and our own bias and should be tested in larger RCTs. Furthermore, bedside ultrasound/echocardiography is a promising tool for hemodynamic monitoring in low resource settings, including assessment of cardiovascular function, differentiation between causes of shock, prediction of fluid responsiveness, and extravascular lung water, but it still demands initial investment and training.[38] Nonetheless in the absence of cardiac output monitors, these parameters may be a readily available and less expensive. In fact, hemodynamic optimization therapy based on CO measurements is cost-effective and would increase efficiency and decrease the burden on the public health system.[39] Expert consensus recommends discussions with national/hospital decision-makers about cost-effectiveness, as the extra cost due to hemodynamic monitoring when implementing a perioperative GDT strategy is counterbalanced by the reduction in postoperative complications and hospital length of stay in high-risk surgeries.

The main limitation of our review is the fact that it was not a systematic review. Non-systematic reviews are influenced by authors' own opinions and practices and may not consider other technologies such as noninvasive ones. Nevertheless, costs associated with noninvasive tools are in general impeditive for low-resources settings.

Authors' contributions

All authors made contributions to the conception, design of the work; or the acquisition, analysis; drafted the work or revised it critically for important intellectual content; approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of interest

The authors declare no conflicts of interest.

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Table 1 Tools for hemodynamic optimization and adequate management in the operating room and ICU.

Parameters	Goals
Mean arterial pressure (MAP) [15]	Within 10% resting values
	> 65 mmHg
Central venous pressure (CVP) [33, 38]	> 8 mmHg
O_2/CO_2-derived parameters	
Central venous oxygen saturation ($ScvO_2$)	> 70–75%
Oxygen Extraction Rate (O_2ER) [23]	< 27%
Venoarterial carbon dioxide gradient (CO_2-gap)	< 5 mmHg
Serum lactate (ICU)	10% decline/hour
Fluid responsiveness (consider giving fluids if no harm)	
Pulse Pressure Variation (PPV) [19,20]	> 13%
Pulse Pressure Variation (PPV $TV_{6\text{-}8}$)* [21]	> 3.5%
SvO_2 increase after fluid bolus [22]	> 2%
Δ E_TCO_2 (exhaled CO_2) increase after fluid bolus [31,32]	> 5%
Attention /consider stop giving fluids	
Intra-Abdominal Pressure (IAP) [36]	> 11 mmHg
Lung ultrasound	B lines

Figure 1 Pressure, oxygen, and carbon dioxide derived indices. MAP, Mean Arterial Pressure; PPV, Pulse Pressure Variation; SaO_2, Arterial Oxygen Saturation; $PaCO_2$, Arterial Blood Partial Pressure of Carbon Dioxide; CVP, Central Venous Pressure; $ScvO_2$, Central Venous Oxygen Saturation; $PvCO_2$, Venous Blood Partial Pressure of Carbon Dioxide; IAP, Intra-Abdominal Pressure; SPP, Systemic Perfusion Pressure; O_2ER, Oxygen Extraction Rate; CO_2-gap, Veno-Arterial Carbon Dioxide Gradient, APP, Abdominal Perfusion Pressure.

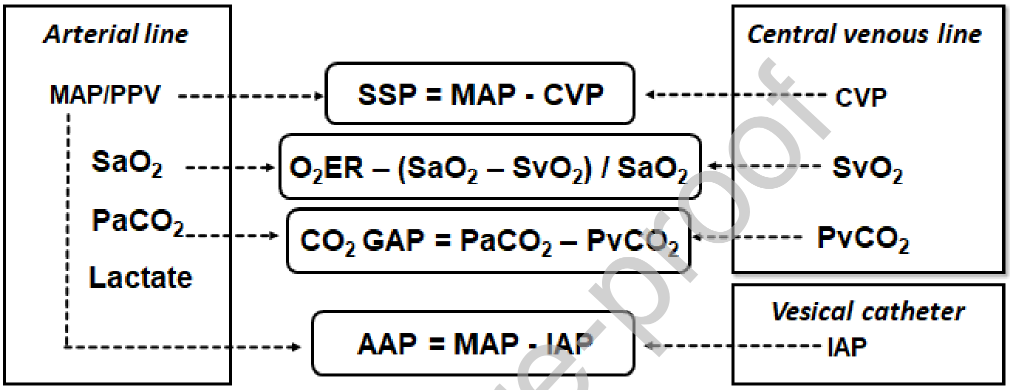

Figure 2 Assessment of volume responsiveness. HR/RR, Heart rate/Respiratory Rate; TV, Tidal Volume; IBW, Ideal Body Weight.