NONINVASIVE/MINIMALLY INVASIVE HEMODYNAMIC MONITORING

SUMMARY
Noninvasive or minimally invasive hemodynamic monitoring technologies are widely used to guide volume resuscitation. The results of clinical trials investigating the use of such technologies are conflicting. Controversy surrounds the optimal clinical setting in which to effectively utilize these monitors, but there is promising data that postoperative complications may be reduced with a goal-directed approach to fluid management.

RECOMMENDATIONS

- **Level 1**
  - None
- **Level 2**
  - Intraoperative stroke volume variation (SVV) monitoring of low- to moderate-risk surgical patients is associated with earlier return of bowel function.
  - Intraoperative SVV or pulse pressure variation (PPV) monitoring of high-risk surgical patients lowers complication rates including infection.
  - Changes in plethysmographic variability index (PVI) can predict improvement in cardiac index after volume loading in mechanically ventilated patients.
- **Level 3**
  - PPV may be useful for directed fluid management when positive end-expiratory pressure (PEEP) levels exceed 10 cm H₂O
  - Noninvasive or minimally invasive hemodynamic monitors do not predict the amount of fluid needed for adequate resuscitation

INTRODUCTION
Central to effective shock resuscitation is optimization of oxygen delivery. Cardiac index (CI), a product of stroke volume and heart rate [\(CI = \text{stroke volume} \times \text{heart rate} / \text{body surface area}\)], remains a critical component to focus upon and optimize during patient resuscitation. Instrumentation to monitor CI is helpful to discern what interventions are necessary to improve tissue perfusion. Fluid administration remains the most common intervention to improve oxygen delivery as it improves stroke volume and overall systemic perfusion by increasing preload via the Starling curve (1).

Goal-directed fluid therapy during resuscitation, for the purpose of strategic intravascular volume replacement, has evolved significantly. For years, pulmonary artery catheterization (PAC) remained the key modality to guide patients’ resuscitation. In the past decade, noninvasive or minimally invasive hemodynamic monitors have been extensively studied in their ability to provide efficacious goal-directed hemodynamic therapy to patients with cardiovascular compromise. This guideline focuses on three such strategies: stroke volume variation (SVV), pulse pressure variation (PPV), and plethysmographic variability index (PVI).

EVIDENCE DEFINITIONS
- **Class I**: Prospective randomized controlled trial.
- **Class II**: Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III**: Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment**: A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS
- **Level 1**: Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2**: Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3**: Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.
LITERATURE REVIEW

**Stroke volume variation (SVV)**

A prospective randomized study in 2010 sought to identify possible benefits of intraoperative fluid optimization for 215 high-risk patients undergoing abdominal surgery (2). High-risk status was assigned if at least one criterion from procedure-related and patient-related risk factors was present. Two groups were provided fluids based on routine intraoperative care and SVV. Routine care was defined by the administration of fluid or vasoactive medications based on heart rate, urine output, and central venous pressure (CVP). In the investigation group, intervention with fluid or vasoactive medication was provided when the SVV measurement rose by more than 10% over a period of five minutes. Intraoperatively, the SVV group received more colloid during surgery (1425 ml vs. 1000 ml) and had fewer hypotensive episodes (2 vs. 3.5). SVV patients were observed to have lower lactate levels immediately following surgery (1.78 mmol/L vs. 2.25 mmol/L). Moreover, lactate levels remained significantly higher in the control group up to 8 hours postoperatively. Fewer patients experienced complications in the SVV group (18 patients vs. 35 patients) and the overall number of complications was reduced in the SVV group (34 vs. 77). There was no reported difference in ICU length of stay or overall mortality. Thus the authors concluded that the use of intraoperative goal-directed intervention based on SVV >10% resulted in decreased serum lactate at the conclusion of surgery and improved hemodynamics during surgery. SVV guided therapy also resulted in fewer complications.

A smaller study performed across multiple centers was completed in 2013 (3). Again, the study utilized SVV intraoperatively in high-risk surgical patients. This study was intentionally small in order to document the feasibility of carrying out a much larger study with a similar protocol across multiple centers. The objective of the study was to determine the proportion of patients developing postoperative complications in a control group and a group using SVV. Outcomes documented and compared were sequential organ failure assessment (SOFA) score, therapeutic intervention scoring system (TISS) scores, ICU discharge criteria being met, ICU length of stay, and 28 day mortality. In the control group, a standardized approach was utilized but not explicitly defined. In the investigation group, intervention with 200 ml of colloid was administered if SVV rose above 10%. Intraoperatively, the SVV group received more colloid (1589 ml vs. 927 ml). Meanwhile, the control group received more red blood cells (319 ml vs 685 ml). Postoperatively, the SVV group had a significantly reduced rate of infection (0 infections vs. 7 infections). The maximum SOFA score and the cumulative TISS score were lower in the SVV group but not statistically significant. The number of ventilator days was lower in the SVV group (2.4 days vs 4.8 days) but not statistically significant.

In 2012, a similarly designed study observed the outcomes when SVV guided therapy was compared to routine care in low to moderate risk patients undergoing abdominal surgery (4). This study used an SVV of >12% as a threshold for intervention in the investigation group. Intervention in the control group was guided by routine cardiovascular monitoring based on heart rate, blood pressure, and urine output. Colloid and crystalloid were again used for intervention in both groups. The primary outcome was documentation of return of gastrointestinal function. Both groups had SVV data available, but in the control group the anesthesiologist was blinded to the data. No significant differences were discovered in intraoperative fluid balance, change in hemoglobin concentration, urine output, surgery time, or opioid administration. However, length of stay was shorter (5.0 days vs. 7.5 days), return of bowel function was faster (3.0 days vs. 4.0 days), soft diet initiation was sooner (4.0 days vs. 5.0 days). Based on these results, the authors conclude that the benefit of goal-directed hemodynamic therapy using SVV may not be limited to only high risk surgical patients.

In 2015, authors from a large single center utilized SVV as goal-directed therapy (GDT) and compared results to standardized care during liver resection (5). The authors described the two basic phases of liver resection fluid management. The first phase consists of strict fluid restriction and active interventions to lower the central blood pressure prior to liver transection. The first phase did not vary between the two groups. The second phase, the resuscitative phase, occurs post-transection and was the focus of this study. Primary outcome was 30 day morbidity. The study included 69 patients in the GDT arm and 66 patients in the control arm. Demographics were similar between groups. The only significant difference
that was reported in this study was the amount of fluids given intraoperatively (2.0 liters in the GDT group and 2.9 liters in the standard group). Overall morbidity did not reach significance. In fact, the study was ended early based on futility. The authors did however conclude safety of the technique of GDT for liver resections. They call for a study coupling intraoperative GDT with postoperative GDT for liver resections. Limitations of this study include wide variability in surgeon resuscitation in the very early postoperative period (i.e. in the PACU) such as interventions to improve hypotension, low platelets, or deranged PT/INR.

**Pulse Pressure Variation (PPV)**

In 2013, a multicenter randomized prospective study was conducted with a hypothesis that goal-directed therapy in the form of optimizing PPV, cardiac index trending, and mean arterial pressure would result in reduced complications, reduced length of stay and quicker return of bowel function. The study was conducted intraoperatively in patients undergoing major abdominal surgery (6). The study consisted of 160 patients total with 79 patients in the study group and 81 patients in the control group. The study group algorithm consisted of two phases: an initial assessment and ongoing intraoperative treatment. Intervention was based on keeping a PPV <10%, keeping the CI >2.5 L/min/m² and keeping the MAP >65 mmHg. Fluids, inotropes, and vasopressors were administered respectively. Intervention in the control group was based on the discretion of the anesthesiologist according to routine intraoperative monitoring. The total number of complications was lower in the study group (52 vs. 72; p=0.038). Infectious complications, in particular, were lower in the study group (13 vs. 26; p=0.023). No significant differences were noted for return of bowel movement, or length of hospital stay.

In 2007, PPV was studied during high-risk surgery in a single center prospective randomized control trial (7). The primary endpoint was length of postoperative hospitalization. Colloid bolus was administered to the study group if the PPV rose above 10%. Intervention in the control group was based on anesthesiologist discretion. 33 patients were randomized, with 16 in the control group and 17 in the study group. The study produced a number of significant results. Intraoperatively, far more fluids were administered to the study group (4.6 L vs 1.6 L). No colloid was given the control group. Postoperatively, the mean arterial blood pressure was significantly higher in the study group (80 mmHg vs 66 mmHg). 24 hours postoperatively, the study group had fewer patients requiring vasoactive support (2 vs 8) and lower arterial lactates (0.7 mmol/L vs. 1.9 mmol/L). Clinically, the study group saw a fewer number of patients experience complications and a few number of total complications. Ventilator days, ICU days, and hospital days were all lower in the study group. This study was a pilot study with a low number of patients and the authors, while making conclusions of improved outcomes with the use of intraoperative PPV, call for larger studies to be completed.

Michard et al. in 1999 completed a study regarding the deleterious cardiovascular effects of PEEP (8). The study was born out of the observation that patients are more likely to die a death from multisystem organ failure rather than from hypoxemia. The 1999 study concluded that the PPV may be useful in predicting and assessing the hemodynamic effects of PEEP and fluid loading. They observed predictable decreases in cardiac index and increases in pulse pressure variation over respiratory cycles with PEEP delivery greater than 10 cm H2O. Additionally, they were able to see reversible changes in the CI and the PPV after a fluid load. This study led to many further investigations as to how PPV could be used to provide goal directed fluid therapy during ventilation strategies.

The OPTIMISE trial is one of the largest prospective randomized multicenter investigations to date investigating the potentially beneficial effects of minimally invasive cardiac output-guided therapy (9). The study took place in the operating room and in the PACU. PPV, SVV, and systolic pressure variation (SPV) data were all available via the proprietary monitoring device used in the study. The study included 734 patients spanning two years duration across multiple hospitals in the UK. 368 patients were randomized to the study group and 366 patients were randomized to the control group. In contrast to some of the other smaller studies, this large study noted similar volumes of intravenous fluids were administered during surgery between the arms of the study. The primary outcomes included a 30-day moderate or major complication and mortality. Secondary outcomes included morbidity on day 7, infection, critical-care free days, all-cause mortality at 30 days, all-cause mortality at 180 days, and length.

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of hospital stay. This large study failed to find any significant benefit in the used of cardiac output-guided hemodynamic therapy in terms of the primary outcomes of the study (RR, 0.84 [95% CI, 0.71-1.01; absolute risk reduction, 6.8% [95% CI, -0.3%-13.9%]; P=0.07). None of the secondary outcomes proved statistically significant.

Following the OPTIMISE trial, the authors performed a literature search and performed a meta-analysis which included their data (9). They were able to capture 38 trials with 6595 patients. They observed less frequent complications (31.5% vs. 41.6%; RR, 0.77 [95% CI, 0.71-0.83]) in the groups that were treated according to goal-directed hemodynamic therapy. Specifically, the intervention lowered the rate of infections (21.8% vs. 25.4%). According to the authors, the majority of the trials included in the review were small single center trials with low power and a high risk of bias based on their design.

In 2015, a study was published questioning the routine use of PPV and SVV to predict fluid responsiveness. The study was an observational sub-study of the OPTIMISE trial (10). Patients had undergone major gastrointestinal surgery. SVV and PPV measurements were made throughout the administration of three 250 ml intraoperative colloid boluses. The same protocol was repeated postoperatively. The endpoint was documentation of predictive value of the monitoring modality to predict fluid responsiveness. Based on this observational study, the authors concluded that predictive accuracy of SVV and PPV for fluid responsiveness did not meet statistical significance and recommendations endorsing the routine use of the monitors could not be made.

In 2011, Takala et al. published findings from a multicenter randomized controlled trial conducted at three university hospitals in Europe (11). 388 hemodynamically unstable patients were randomized to receive hemodynamic guided therapy or standard resuscitation. The study began within a patients’ first six hours of arrival to the ICU. The technology employed calculated SVV and CI. The endpoint of the study was documentation of the proportion of patients who achieved hemodynamic stability within 24 hours. The study failed to produce any statistically significant differences from the control group in the amount of fluid administered, vasoactive medications administered, time to hemodynamic stability, length of ICU care, and mortality.

**Pleth Variability Index (PVI)**

Forget et al. conducted a single center randomized control trial in 2008 (12). The study hypothesized that PVI would lower intraoperative fluid administration and lower perioperative arterial lactate levels. 82 patients were randomized to PVI-directed fluid management (250 ml colloid bolus) versus standard care (fluid challenge based on MAP and CVP). The study group had significantly lower volumes of infusions and the lactate levels were significantly lower. These findings were true both immediately postoperatively and 48 hours postoperatively. No significant differences regarding complications, mortality, or length of stay was discovered.

A study in 2007 observed PVI in twenty-five (25) patients undergoing coronary bypass grafting (13). After induction, patient baseline hemodynamics were recorded and then a 500 ml bolus of 6% hetastarch was administered over 10 minutes. Hemodynamics were then recorded 3 minutes following the infusion. All patients within this protocol received a pulmonary artery catheter and CI was recorded. The pulse oximetric plethysmographic (POP) tracings were recorded and the delta POP was calculated throughout the respiratory cycle. Additionally, PPV was recorded through the respiratory cycle. Correlation between PPV and deltaPOP throughout the respiratory cycle is important based on the past reports that PPV is able to accurately predict fluid responsiveness when measured throughout the respiratory cycle. The authors report a 0.90 correlation coefficient and the correlation held true before and after volume expansion. The authors reported a significant reduction in deltaPOP before and after volume expansion (11.1 to 6.2; P<0.01) and an overall increase in CI (2.0 to 2.3; P<0.001). They also reported their ability to predict “fluid responders” and “fluid nonresponders”. Baseline deltaPOP prior to expansion in responders was 16.7%. Meanwhile, baseline deltaPOP prior to expansion in nonresponders was 5.8%. When analyzed by receiver operator characteristic (ROC) curves, the authors found that a threshold deltaPOP of 13% was able to predict with 93% sensitivity and 90% specificity whether a patient could be classified a fluid responder vs a fluid nonresponder. The authors do advise caution in extrapolating these
results to a wider variety of clinical settings. Based on these data, the authors conclude that deltaPOP may accurately predict the response to volume expansion and may be able to quantify the effects hemodynamically while patients are in the operating room on a mechanical ventilator. Moreover, they see more potential in the ability of the pleth to aid in resuscitation outside its current uses.

The year prior, Natalini et al. published data also attempting to predict fluid responders and nonresponders (14). The purpose of their study was to compare the indices of direct arterial blood pressure measurements throughout the respiratory cycle to indices of the plethysmogram obtained from the pulse oximeter. They proceeded by then using these values to correlate change in the CI following a fluid bolus. 32 volume expansions were performed in 22 hypotensive patients who were all mechanically ventilated. Hemodynamic data was recorded before and after volume expansion. Any patient who did increase their cardiac index by 15% was classified as a nonresponder to expansion. Nonresponding patients showed a lower baseline plethysmographic pulse variation at baseline (12% in nonresponders vs. 21% in responders; p=0.034). Similar to the study presented above, the area under the ROC curve for arterial and plethysmographic pulse variations was able to predict fluid responsiveness (0.74 vs 0.72; p=0.90) and fluid recalcitrance (0.80 vs 0.87; p=0.40). The authors concluded that dynamic indices of respiratory-induced variations in plethysmographic waveforms were as reliable as variations in arterial blood pressure. Moreover, the former modality is noninvasive.

Conclusion
The disparity in study findings among the various trials described above may be explained by differences in mechanical ventilation strategy in each study. Many of the initial studies suggesting a benefit of SVV, PPV, and PVI were performed in patients receiving general anesthesia and therefore on controlled mechanical ventilation. All three parameters are well-known to vary during the respiratory cycle and spontaneous respiratory efforts on the part of the patient introduce variability into the accuracy of these measurements. Studies that allowed spontaneous breathing (such as in an ICU-setting) could therefore be expected to see greater measurement variability than studies in patients under general anesthesia. Further studies will be necessary to identify the clinical situations and patient populations in which SVV, PPV, and PVI are most effective in predicting fluid responsiveness.

REFERENCES

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