Intraoperative Fluid Management (IOFM) technologies and patient outcome: a meta-analysis.

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A substantial body of evidence exists to support the use of intraoperative fluid management (IOFM), which, has resulted in the process forming one of the core components of Enhanced Recovery programmes. The aims of this meta-analysis were to review the evidence for IOFM using a SV optimisation (SVO) algorithm, and determine whether the outcomes were comparable across technologies. Overall, IOFM resulted in significant reductions in the incidence of postoperative complications; however, the effect was not consistent across technologies. Studies using the oesophageal Doppler (ODM) for IOFM demonstrated a reduction in the incidence of postoperative complications (OR: 0.446; P<0.001), whereas studies using SVO-guided IOFM with an arterial pressure based device (PPWA) did not (OR: 0.706; P=0.080). Similarly, data from ODM-guided IOFM demonstrated a 1.1-day reduction in length of hospital stay (P=0.008), an outcome not observed with PPWA technologies (-0.4 days (P=0.140). The results of this analysis indicate differences in the efficacy of the technologies used for IOFM.

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A variety of technologies are used during surgery for Intraoperative Fluid Management (IOFM), each utilising a different method (with differing accuracy and precision) for measuring or deriving blood flow.

In March 2011, NICE recommended that the CardioQ-ODM “should be considered for use in patients undergoing major or high-risk surgery or other surgical patients in whom a clinician would consider using invasive cardiovascular monitoring” [1]. Subsequently, the NHS Innovation, Health, and Wealth report identified ODM as one of six high-impact innovations that should be implemented as standard care [2]. The recent NHS England Standard Contract Technical Guidance for 2014/15 mandates that, by March 2015, all hospitals should "demonstrate to commissioners that trajectories for the Intraoperative Fluid Management (IOFM) technologies are in place which are consistent with NTAC (now the Heath Technology Adoption Programme)".

The purpose of this meta-analysis was to include the most recent studies and bring up to date the evidence for IOFM as guided by a 10% Stroke Volume Optimisation (SVO) algorithm. Cedar conducted an independent assessment of IOFM technologies in December 2013, however a meta-analysis was not included in their report [3]. The 10% SVO algorithm was used in the clinical trials of ODM and was the basis of the NICE recommendation.

There are two main algorithms used to guide fluid administration in the intraoperative environment: SVO, and the minimisation of the respiratory variation of Stroke Volume or Pulse Pressure, known as Stroke Volume Variation (SVV) or Pulse Pressure Variation (PPV). SVO involves the administration of small (200-250 mL) boluses of fluid, and the corresponding change in SV measured. A change >/< 10% indicates the patient is haemodynamically responsive/non-responsive. This method was designed based on the precision (repeatability) of the oesophageal Doppler (ODM). Alternatively, the minimisation of SVV/PPV involves the administration of fluid until the parameters are <10-15%.

However, recent evidence questions the safety of the valid use of SVV/PPV for IOFM [4]. One of the requirements for reliable SVV/PPV measurement is a tidal volume >8 mL/kg. A French multi-centre study found a 60% reduction in postoperative complications, and two-day reduction in length of hospital stay when a protective ventilation strategy (tidal volume = 6 mL/kg) was used over a non-protective ventilation strategy (tidal volume = 10 mL/kg) in patients undergoing abdominal surgery.

The aim of this meta-analysis was to review the clinical outcome evidence for IOFM, as guided by SVO, on a technology-specific basis. The report includes published/peer-reviewed RCTs and audit studies where device efficacy was evaluated by comparing technology-guided IOFM with a control group (typically standard care). Study data on two outcome measures (incidence of postoperative complications, and length of hospital stay (LOS)) were compared.

The main technologies used for IOFM are:

- Oesophageal Doppler (ODM),
- Pulse Pressure Waveform Analysis (PPWA) – collective term for all technologies that derive flow from the arterial pressure waveform, including:
  - Edwards Vigileo/FloTrac
  - LiDCOplus and LiDCOrapid
  - PICCO and PulsioFlex
- Bioimpedance/NICOM Bioreactance.
In total, 25 studies were identified based on the aforementioned criteria. A list of these studies is detailed below.

Table 1: IOFM studies included in meta-analysis

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Technology</th>
<th>Study Type</th>
<th>IOFM Algorithm</th>
<th>Report Postoperative Complications?</th>
<th>Report LOS?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venn, 2002 [8]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Gan, 2002 [9]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Wakeling, 2005 [10]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Challand, 2011 [12]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Brandstrup, 2012 [14]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>El Sharkawy, 2013 [16]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>McKenny, 2013 [17]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Zakhaleva, 2013 [18]</td>
<td>ODM</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Kuper, 2011 [19]</td>
<td>ODM</td>
<td>Audit</td>
<td>SVO</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Figus, 2011 [20]</td>
<td>ODM</td>
<td>Audit</td>
<td>SVO</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Feldheiser, 2012 [21]</td>
<td>ODM</td>
<td>Audit</td>
<td>SVO</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Chattopadhyay, 2013 [22]</td>
<td>ODM</td>
<td>Audit</td>
<td>SVO</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Mannova, 2013 [23]</td>
<td>ODM</td>
<td>Audit</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Cecconli, 2011 [25]</td>
<td>FloTrac (PPWA)</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Bartha, 2012 [26]</td>
<td>LiDCOplus (PPWA)</td>
<td>RCT</td>
<td>SVO^</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Bisgaard, 2013-a [27]</td>
<td>LiDCOplus (PPWA)</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Bisgaard, 2013-b [28]</td>
<td>LiDCOplus (PPWA)</td>
<td>RCT</td>
<td>SVO</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Pearse, 2014 [29] *</td>
<td>LiDCOrapid (PPWA)</td>
<td>RCT</td>
<td>SVO^</td>
<td>Y§</td>
<td>Y</td>
</tr>
</tbody>
</table>

SVO, Stroke Volume Optimisation. Note: Data from one identified study were excluded from analysis because of difficulties discerning the effect of the technology vs. the effect of study fluid (study had two treatment groups) [30] * Perioperative protocol (treatment group received intervention from beginning of surgery until 6 h postoperatively); ^ In addition to dobutamine/dopexamine for DO2 target; § Composite of 30-day mortality and moderate or major postoperative complications.
There was large variance in the method of reporting postoperative complications within the studies. Data on the ‘number of patients with complications’ was favoured, with ‘total number of complications’ extracted if the former were not available.

No published/peer-reviewed studies were identified using the PiCCO, PulsioFlex, or NICOM technologies for IOFM, and therefore these technologies could not be included in the analysis.

Data are reported as ‘odds ratios (OR)’ for postoperative complications, and ‘difference in means’ for length of hospital stay. An OR is a measure of an association between exposure to the treatment and outcome. An OR < 1 indicates exposure to IOFM was associated with a lower risk of postoperative complication. All analyses were conducted using Comprehensive Meta-Analysis software (Biostat Inc., USA).

**Results: postoperative complications**

Analysis of all studies revealed a significant effect of IOFM in reducing complications following surgery (odds ratio (OR): 0.557; P<0.001). The OR fell to 0.446 (P<0.001) when only data from ODM studies were included (Figure 1), and rose to 0.706 (P=0.080) with PPWA technologies only. Overall patients who received SVO-guided IOFM with the ODM are ~55% less likely to develop a postoperative complication than those patients who received routine fluid management.

**Figure 1:** Meta-analysis of studies assessing the efficacy of SV optimisation-guided IOFM with different technologies on postoperative complications.
Results: length of hospital stay (LOS)
Grouped analysis revealed a trend towards a reduction in LOS with SVO-guided IOFM (-0.6 days; P=0.008). However, by-technology analysis revealed differences between the technologies.

Use of ODM for IOFM reduced LOS by 1.1 days on average (P=0.008; Figure 2), whereas studies utilising SV optimisation for IOFM with PPWA technologies failed to demonstrate significant reductions in LOS (-0.4 days; P=0.140).

Figure 2: Meta-analysis of studies assessing the efficacy of SV optimisation-guided IOFM with different technologies on length of hospital stay.
Conclusions
Although grouped data revealed that SV optimisation-guided IOFM results in significant reductions in the incidence of postoperative complications and length of hospital stay, there are differences in the efficacy of the commercially available technologies. This analysis reveals that the ODM is the only IOFM technology in which studies demonstrate significant reductions in both postoperative complications and length of hospital stay.

Numerous studies have reported differences between the IOFM technologies, especially in their response to typical surgical interventions such as fluid and vasoactive drug administration [31-33], and may provide explanation as to the differing efficacy of the technologies.

Schlöglhofer et al. [34] conducted a meta-analysis comparing five PPWA systems and their agreement with thermodilution CO. They concluded, “Despite continued efforts to introduce improved products to the market, the main outcome of our analysis is that a clear recommendation cannot be given for any single system that can accurately monitor hemodynamically unstable patients. This limitation also applies to reliable intraoperative monitoring during surgery accompanied by hemodynamic instability. The informative value of pulse contour-based CO monitoring during hemodynamically stable conditions should be questioned, since CO data provided by these monitors parallel the arterial pressure as long as the compliance and resistance remain unaffected”.

Hadian et al. [35] also compared technologies and concluded “if clinical trials of resuscitation based on CO values show efficacy when using one of these devices, it is not clear whether performing the identical trial with another CO monitoring device will also show similar benefit. Thus, until the agreement among minimally invasive CO measuring devices improves, each device needs to have its own clinical efficacy validated.”

The SVO algorithm demonstrated superior efficacy when used with ODM technology. This algorithm was designed for use with the ODM technology based on its precision, being such that the user can be 99% confident that a measured change in SV of ≥10% is indicative of a real change in flow and not measurement error [36]. Other technologies with poorer precision appear to be less effective when using the SVO algorithm for IOFM. Alternative methodologies using suppression of respiratory swing have limitations in patient application, with <10% of surgical patients meeting the requirements for valid use of SVV/PPV [37].

The ODM is the only technology recommended for SVO-guided IOFM [1], a recommendation supported by the findings of this meta-analysis.
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References


