Cardiac complications associated with goal-directed therapy in high-risk surgical patients: a meta-analysis

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Editor’s key points
- This meta-analysis tested whether or not goal-directed therapy (GDT) in high-risk surgical patients is associated with increased cardiac complications.
- Twenty-two randomized controlled trials met the criteria for inclusion.
- There was no increased incidence of pulmonary oedema, myocardial ischaemia, or both with GDT.
- Importantly, carefully conducted GDT led to decreased cardiac complications in high-risk patients.

Summary. Patients with limited cardiopulmonary reserve are at risk of mortality and morbidity after major surgery. Augmentation of oxygen delivery index (DO2I) with i.v. fluids and inotropes (goal-directed therapy, GDT) has been shown to reduce postoperative mortality and morbidity in high-risk patients. Concerns regarding cardiac complications associated with fluid challenges and inotropes may prevent clinicians from performing GDT in patients who need it most. We hypothesized that GDT is not associated with an increased risk of cardiac complications in high-risk, non-cardiac surgical patients. We performed a systematic search of Medline, Embase, and CENTRAL databases for randomized controlled trials (RCTs) of GDT in high-risk surgical patients. Studies including cardiac surgery, trauma, and paediatric surgery were excluded. We reviewed the rates of all cardiac complications, arrhythmias, myocardial ischaemia, and acute pulmonary oedema. Meta-analyses were performed using RevMan software. Data are presented as odds ratios (ORs), [95% confidence intervals (CIs)], and P-values. Twenty-two RCTs including 2129 patients reported cardiac complications. GDT was associated with a reduction in total cardiovascular (CVS) complications [OR=0.54, (0.38–0.76), P=0.0005] and arrhythmias [OR=0.54, (0.35–0.85), P=0.007]. GDT was not associated with an increase in acute pulmonary oedema [OR=0.69, (0.43–1.10), P=0.12] or myocardial ischaemia [OR=0.70, (0.38–1.28), P=0.25]. Subgroup analysis revealed the benefit is most pronounced in patients receiving fluid and inotrope therapy to achieve a supranormal DO2I, with the use of minimally invasive cardiac output monitors. Treatment of high-risk surgical patients GDT is not associated with an increased risk of cardiac complications; GDT with fluids and inotropes to optimize DO2I during early GDT reduces postoperative CVS complications.

Keywords: cardiovascular complications; goal-directed; haemodynamic monitoring; high-risk surgery; perioperative

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Recent data suggest that major surgery is associated with a significant mortality risk. An even higher number of patients develop postoperative complications. The associated health and financial impact associated with postoperative complications is important, as these patients are at greater risk of long-term morbidity and mortality. Identifying patients who are at greatest risk of perioperative complications enable appropriate preventive measures to be taken. A limited cardiopulmonary reserve is a major risk factor for perioperative morbidity and mortality; as such, patients are less likely to meet the increased oxygen demand incurred during major surgery. Perioperative goal-directed therapy (GDT) utilizes flow-based haemodynamic monitoring and therapeutic interventions as a means to augment the patients’ global oxygen delivery to achieve a predetermined haemodynamic endpoint. This is with the aim of ensuring that those with poor perioperative cardiovascular (CVS) performance achieve the DO2I seen in survivors without postoperative complications. When carried out early, in the right patient cohort, and with a clearly defined protocol, GDT has been shown to reduce postoperative mortality and morbidity.

Despite this, postoperative GDT is not carried out widely. This may relate to lack of resources or doubts about its benefits. Many of the studies performed include limited patient numbers, are single-centre studies; some are considered outdated, with high mortality rates not representative of current clinical practice. Many studies to date have used the pulmonary artery catheter (PAC), the use of which has been largely superseded by less invasive CO monitoring methods because of concerns regarding the safety of the PAC. A recent meta-analysis has demonstrated that although studies before 2000 demonstrate a benefit in terms of mortality and morbidity, studies conducted after 2000 demonstrate a significant reduction in complication rates, despite a smaller effect on mortality. This may, in part, be related to better patient selection and refined surgical and anaesthetic techniques. In addition, the reduction in complication rates is irrespective of the type of haemodynamic monitor used.
The risk–benefit balance of GDT in high-risk surgical patients has been debated.9 There may be risk associated with the use of fluid boluses and inotropes in patients with a known limited cardiopulmonary reserve who have arterial pressure and heart rate within the ‘normal physiological range’. Treatment-related cardiopulmonary complications (total CVS complications, arrhythmias, acute pulmonary oedema, and acute myocardial ischaemia) have not been assessed previously. We hypothesized that goal-directed use of fluid and inotrope guided by haemodynamic monitoring in GDT is not associated with an increase in cardiopulmonary complications among high-risk surgical patients undergoing non-cardiac surgery.

Methods

Eligibility criteria

We only included randomized controlled trials (RCTs) reporting any of the following CVS outcomes: total CVS complications, arrhythmias, acute pulmonary oedema, and acute myocardial ischaemia. The analysis was limited to studies containing an adult general surgical population. GDT was defined as the use of haemodynamic monitoring and therapies aimed at manipulating haemodynamics during the perioperative period to achieve a predetermined flow-related endpoint(s). GDT must have been started pre-emptively in the perioperative period (24 h before, intraoperative, or immediately after surgery) and applied after a clear protocol. The protocol must contain predetermined step-by-step instructions for the clinicians based on data obtained from a haemodynamic monitor or surrogates (e.g. lactate, oxygen extraction ratio), and direct therapy to achieve predefined goals. Therapies included fluid administration alone or fluids and inotropes together. Studies not fulfilling these criteria, studies in cardiac surgery, and studies that did not titrate inotropes aimed at specific goals (‘fixed dose’ studies) were excluded from the analysis.

Information sources

Suitable studies were identified by conducting a systematic literature search of MEDLINE (via Ovid), EMBASE (via Ovid), and the Cochrane Controlled Clinical trials register (CENTRAL, Issue 4 of 2012). Only articles in the English language were considered. Date restrictions were not applied to the CENTRAL and MEDLINE searches. EMBASE was restricted to the years 2009–2012.10 The last search update was in April 2012.

Search strategy

The following search terms were entered in the electronic databases: goal-directed therapy, optimization, haemodynamic, goal oriented, goal targeted, cardiac output, cardiac index, oxygen delivery, oxygen consumption, cardiac volume, stroke volume, fluid therapy, fluid loading, fluid administration, optimization, supranormal, lactate, and extraction ratio. Search terms were entered into the electronic databases using search strategy methods validated by the Cochrane collaboration (see Appendix for search strategies used).11 In addition to searching electronic databases, previous review articles on the subject were hand-searched for further references.

Quality of included studies

The Jadad criteria were used for assessing methodological quality of included studies.12 These criteria include methods of analyses used for random assignment, blinding, and flow of patients in clinical trials. The range of possible scores is 0 (lowest quality) to 5 (highest quality). Studies were not excluded based on Jadad scores.

Analysis of outcomes

Titles and abstracts were independently screened by three investigators to identify relevant studies. Pertinent full-text articles were then retrieved and analysed for eligibility against the previously outlined inclusion criteria. Information from selected studies was extracted using a standardized data collection form. Two investigators (N.A. and C.C.) independently collected data using a standardized data collection form and discrepancies were resolved by a third author (M.C.).

CVS morbidity, expressed as the number of patients suffering from overall CVS complications, was the primary outcome of our study. Secondary outcomes were defined as subsets of CVS complications; arrhythmias, acute myocardial ischaemia, and acute pulmonary oedema. Within these subgroups, studies were also analysed according to the type of monitor used, type of interventions, and therapeutic goals. 'Supranormal' DO2I is used to describe the therapeutic goal of a DO2I > 600 ml min⁻¹ m⁻².

Statistical analysis

The meta-analysis was performed using review manager (‘Revman’) for MAC (Version 5.1, Cochrane collaboration, Oxford, UK). Dichotomous data outcomes were analysed using a Mantel–Haenszel random-effects model and results presented as an odds ratio (OR) with 95% confidence intervals (CIs). Statistical difference between the groups was considered to be present if the pooled 95% CI did not include 1 for the respective OR. All P-values were two-tailed and considered statistically significant if <0.05. I² methodology was used to assess statistical heterogeneity. Inconsistency and heterogeneity were considered significant when an I² value of >50% was present.13

Results

Included trials

A total of 12 398 study titles were obtained after searching electronic databases (Fig. 1). Titles and abstracts were screened and 307 references were identified as relevant to perioperative GDT. Further screening of titles and abstracts against our inclusion criteria resulted in 85 references retrieved for full-text analysis. Thirteen studies were excluded after detailed full-text evaluation, as they were not RCTs.14–26 The remaining RCTs were analysed against inclusion criteria and the following studies were excluded: studies focusing on fluid
management strategies, that is, liberal vs restrictive,\textsuperscript{27–36} and use of ‘fixed dose’ inotropic agents not titrated to a predetermined goal.\textsuperscript{37–41} Specific populations were excluded to minimize heterogeneity, including cardiac surgery,\textsuperscript{42–47} trauma,\textsuperscript{48–57} paediatric surgery,\textsuperscript{58} and critically ill medical populations.\textsuperscript{59–67} A study not using protocols to direct application of GDT was also excluded.\textsuperscript{68} A total of 30 studies were identified as being suitable for the meta-analysis.\textsuperscript{69–98} However, eight of these studies did not provide specific details on the number of patients with CVS complications.\textsuperscript{76–77, 81–83, 87, 91, 92, 94} A total of 22 studies including 2129 patients were included in the meta-analysis (Table 1).\textsuperscript{69–75, 78–80, 82, 84–86, 88–90, 93, 95–98}

**Description of studies**

These 22 studies included a total of 2129 patients; 1104 in the GDT arm and 1025 in the control treatment arm. Fifteen studies reported rates of arrhythmias, 16 studies reported rates of acute myocardial ischaemia, and 15 studies reported rates of acute pulmonary oedema. The studies reporting arrhythmias, acute myocardial ischaemia, and acute pulmonary oedema included 1393, 1508, and 1468 patients, respectively. There were similar numbers of patients in the GDT and control arms. Eleven studies initiated GDT at the start of surgery, while the other studies initiated GDT before or immediately after surgery. The quality of the trials was analysed using the Jadad score. The median Jadad score was 3 (Fig. 2).

**Overall CVS complications**

One of the studies did not report any CVS complications in either the control or the intervention group.\textsuperscript{74} Among the 2129 patients, 275 (12.9%) patients suffered CVS complications (Table 2). Among patients with complications, 23% had arrhythmias, 11% had acute myocardial ischaemia, and 19% had acute pulmonary oedema.
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Jadad score</th>
<th>Type of surgery</th>
<th>No. of patients in the GDT group</th>
<th>No. of patients in the control group</th>
<th>Type of monitor in the GDT group</th>
<th>Intervention type</th>
<th>Goals in the GDT group</th>
<th>Goals in the control group</th>
<th>CVS complications, GDT (%)</th>
<th>CVS complications, control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bender and colleagues</td>
<td>1997</td>
<td>1</td>
<td>Elective vascular/aortic surgery</td>
<td>51</td>
<td>53</td>
<td>PAC</td>
<td>Fluid and inotropes</td>
<td>CI ≥ 2.8; PAWP 8–14; SVR &lt; 1100; SVV &lt; 10%; CI ≥ 2.5</td>
<td>Standard care MAP &gt; 65; HR &lt; 100; CVP 8–12</td>
<td>4 (7.8)</td>
<td>6 (11.3)</td>
</tr>
<tr>
<td>Benes and colleagues</td>
<td>2010</td>
<td>3</td>
<td>Elective abdominal surgery</td>
<td>60</td>
<td>60</td>
<td>Flotrac</td>
<td>Fluid and inotropes</td>
<td>CI ≥ 2.8; PAWP 8–14; SVR &lt; 1100</td>
<td>Standard care</td>
<td>6 (10.0)</td>
<td>12 (20.0)</td>
</tr>
<tr>
<td>Berlauk and colleagues</td>
<td>1991</td>
<td>2</td>
<td>Peripheral vascular surgery</td>
<td>68</td>
<td>21</td>
<td>PAC</td>
<td>Fluid and inotropes</td>
<td>CI ≥ 3.0; PWP 10–18; SVR &lt; 1450; DO2I &gt; 600</td>
<td>Standard care</td>
<td>5 (7.4)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>Bonazzi and colleagues</td>
<td>2002</td>
<td>2</td>
<td>Elective vascular surgery</td>
<td>50</td>
<td>50</td>
<td>PAC</td>
<td>Fluid and inotropes</td>
<td>CI ≥ 2.8; PAWP 8–14; SVR &lt; 1100</td>
<td>Standard care</td>
<td>2 (4.0)</td>
<td>4 (8.0)</td>
</tr>
<tr>
<td>Boyd and colleagues</td>
<td>1993</td>
<td>1</td>
<td>Abdominal/vascular surgery</td>
<td>53</td>
<td>54</td>
<td>PAC</td>
<td>Fluid and inotropes</td>
<td>MAP 80–110; PAWP 12–14; S P02 &gt; 94%; Hb &gt; 12%</td>
<td>MAP 80–12; PAWP 12–14; S P02 &gt; 94%; UO &gt; 0.5 ml kg h2; DO2I &gt; 600</td>
<td>5 (9.4)</td>
<td>14 (25.9)</td>
</tr>
<tr>
<td>Buettner and colleagues</td>
<td>2008</td>
<td>2</td>
<td>Major abdominal or gynaecological</td>
<td>40</td>
<td>40</td>
<td>PICCO</td>
<td>Fluids</td>
<td>SV change; DO2I &gt; 600</td>
<td>Standard care</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Cecconi and colleagues</td>
<td>2011</td>
<td>4</td>
<td>Hip THR</td>
<td>20</td>
<td>20</td>
<td>Flotrac</td>
<td>Fluid and inotropes</td>
<td>CI ≥ 2.8; PAWP 8–14; SVR &lt; 1100</td>
<td>Standard care</td>
<td>0 (0.0)</td>
<td>6 (30.0)</td>
</tr>
<tr>
<td>Donati and colleagues</td>
<td>2007</td>
<td>3</td>
<td>Elective major abdominal/aortic</td>
<td>68</td>
<td>67</td>
<td>CVC</td>
<td>Fluids</td>
<td>O2 ER &lt; 27%; MAP 80–100; UO &gt; 0.7; CVP 8–12; Hb &gt; 10</td>
<td>MAP 80–100; PAWP 12–14; S P02 &gt; 94%; UO &gt; 0.5 ml kg h-1</td>
<td>1 (1.5)</td>
<td>5 (7.5)</td>
</tr>
<tr>
<td>Forget and colleagues</td>
<td>2010</td>
<td>2</td>
<td>Major intra-abdominal surgery</td>
<td>41</td>
<td>41</td>
<td>Masimo pulsoximeter</td>
<td>Fluids</td>
<td>PVI &lt; 13%</td>
<td>Standard care</td>
<td>4 (9.8)</td>
<td>8 (19.5)</td>
</tr>
<tr>
<td>Gan and colleagues</td>
<td>2002</td>
<td>5</td>
<td>Elective general, urological, gynaecological</td>
<td>50</td>
<td>50</td>
<td>OD</td>
<td>Fluids</td>
<td>FTC &gt; 0.35; SV change</td>
<td>Increase HR &gt; 20% baseline; sAP &lt; 90 or CVP &lt; 20% baseline</td>
<td>1 (2.0)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td>Jhanji and colleagues</td>
<td>2010</td>
<td>3</td>
<td>Major surgery</td>
<td>45</td>
<td>45</td>
<td>LiDCO</td>
<td>Fluids</td>
<td>DOI &gt; 600</td>
<td>Standard care</td>
<td>0 (0.0)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Lobo and colleagues</td>
<td>2000</td>
<td>3</td>
<td>Major surgery</td>
<td>19</td>
<td>18</td>
<td>PAC</td>
<td>Fluid and inotropes</td>
<td>DOI &gt; 600</td>
<td>Standard care</td>
<td>3 (17.6)</td>
<td>8 (50.0)</td>
</tr>
<tr>
<td>Lopes and colleagues</td>
<td>2007</td>
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<td>Major surgery</td>
<td>17</td>
<td>16</td>
<td>IBPplus; Dixtal</td>
<td>Fluids</td>
<td>DOI &gt; 600</td>
<td>Standard care</td>
<td>3 (17.6)</td>
<td>8 (50.0)</td>
</tr>
<tr>
<td>Mayer and colleagues</td>
<td>2010</td>
<td>2</td>
<td>Major GI surgery</td>
<td>30</td>
<td>30</td>
<td>Flotrac</td>
<td>Fluid and inotropes</td>
<td>CI ≥ 2.5; SVV &lt; 12%; CVP 8–12; MAP 60–100; CI ≥ 2.5</td>
<td>Standard care MAP &gt; 65; HR &lt; 100; CVP 8–12</td>
<td>2 (6.7)</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>Pearse and colleagues</td>
<td>2005</td>
<td>3</td>
<td>Major surgery</td>
<td>62</td>
<td>60</td>
<td>LiDCO</td>
<td>Fluid and inotropes</td>
<td>DOI &gt; 600</td>
<td>Standard care</td>
<td>8 (12.9)</td>
<td>16 (26.7)</td>
</tr>
</tbody>
</table>

Continued
Patients who were treated with GDT had a significant reduction in the total number of perioperative CVS events compared with those in the control arm [OR 0.54, (0.38–0.76), P = 0.0005]. Subgroup analyses revealed that fluid and inotrope therapy [OR 0.55, (0.34–0.89), P = 0.01] was associated with a reduction in CVS events: the OR for fluids alone was 0.57, (0.31–1.04), P = 0.07. Only a supranormal oxygen delivery goal was associated with a reduction in CVS complications [OR 0.50, (0.31–0.79), P = 0.002]. GDT using the minimally invasive cardiac output monitors, targeting either normal or supranormal physiological goals, was associated with a significant reduction in the CVS events [OR 0.47, (0.31–0.73), P = 0.0008], whereas GDT using the PAC was not associated with any benefit or harm [OR 0.70, (0.38–1.29), P = 0.25]. Minimally invasive cardiac output monitors include the oesophageal Doppler monitor, and arterial pressure waveform analysis monitors.

**Specific CVS complications**

Fifteen studies including 1393 patients reported the rates of arrhythmias. A total of 7.2% patients were reported to have had perioperative arrhythmias. GDT was associated with a significant reduction in arrhythmias compared with patients treated in the control arm [OR 0.54, (0.35–0.85), P = 0.007]. The reduction in perioperative arrhythmias was associated with the use of fluids and inotropes [OR 0.58, (0.35–0.96), P = 0.03], a supranormal oxygen delivery goal [OR 0.55, (0.32–0.94), P = 0.03], and the use of minimally invasive cardiac output monitoring devices [OR 45, (0.24–0.83), P = 0.01] in the GDT-treated group.

Fifteen studies including 1468 patients reported the rates of acute pulmonary oedema. A total of 5.6% of patients were reported to have had perioperative acute pulmonary oedema. The use of minimally invasive cardiac output monitors in GDT-treated patients was associated with a trend in the reduction in the rate of acute pulmonary oedema [OR 0.45, (0.18–1.11), P = 0.08]. There was no increased risk of acute pulmonary oedema among any subgroup of patients in the GDT group.

Sixteen studies including 1508 patients reported the rates of acute myocardial ischaemia. A total of 3.2% of patients were reported to have had perioperative acute myocardial ischaemia. There was no increase in the incidence of acute myocardial ischaemia among patients in the GDT group.

**Discussion**

Early GDT in high-risk surgical patients has been shown to reduce mortality and overall complication rates. We performed this meta-analysis to test the hypothesis that high-risk patients undergoing major non-cardiac surgery are not at an increased risk of treatment-related cardiac complications. We have demonstrated that administration of fluid challenges and inotropes guided by haemodynamic monitoring is not associated with an increased rate of CVS events in this cohort of patients. Early GDT was associated with a reduction in the total number of CVS events, particularly arrhythmias. We could not find any evidence of increased CVS complications.
associated with GDT in subgroup analyses. The greatest association of a reduction in morbidity was in patients who were treated to achieve supranormal oxygen delivery targets, the use of fluids and inotropes, and minimally invasive cardiac output monitors. We found an absolute difference of 4.4% in CVS complications between the GDT-treated patients and the control group patients.

Patients who received inotropes in addition to fluids would have been more likely to achieve supranormal oxygen delivery targets. We found a significantly lower incidence of arrhythmias associated with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. Reduced systemic inflammation due to improved microvascular perfusion or an association with these factors. 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Table 2  Cardiovascular complications. *P < 0.05

<table>
<thead>
<tr>
<th>Total CVS events</th>
<th>No. of studies</th>
<th>No. of patients in the GDT group</th>
<th>CVS in the GDT group (%)</th>
<th>No. of patients in the control group</th>
<th>CVS in the control group (%)</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>22</td>
<td>1104</td>
<td>117 (10.6)</td>
<td>1025</td>
<td>158 (15.4)</td>
<td>0.54</td>
<td>0.38–0.76</td>
<td>0.0005*</td>
</tr>
<tr>
<td>Fluid/inotropes</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Fluid</td>
<td>9</td>
<td>479</td>
<td>31 (6.4)</td>
<td>453</td>
<td>47 (10.3)</td>
<td>0.57</td>
<td>0.31–1.04</td>
<td>0.07</td>
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<tr>
<td>Fluid + inotrope</td>
<td>13</td>
<td>625</td>
<td>89 (14.2)</td>
<td>572</td>
<td>111 (19.4)</td>
<td>0.55</td>
<td>0.34–0.89</td>
<td>0.01*</td>
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<tr>
<td>Goal</td>
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<tr>
<td>Supranormal</td>
<td>12</td>
<td>593</td>
<td>83 (13.9)</td>
<td>532</td>
<td>107 (20.1)</td>
<td>0.50</td>
<td>0.31–0.79</td>
<td>0.002*</td>
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<td>Normal</td>
<td>10</td>
<td>511</td>
<td>37 (6.6)</td>
<td>493</td>
<td>51 (10.3)</td>
<td>0.61</td>
<td>0.35–1.06</td>
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<td></td>
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<tr>
<td>PAC</td>
<td>9</td>
<td>453</td>
<td>73 (16.1)</td>
<td>402</td>
<td>70 (17.4)</td>
<td>0.70</td>
<td>0.38–1.29</td>
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<tr>
<td>Other</td>
<td>13</td>
<td>651</td>
<td>47 (7.2)</td>
<td>623</td>
<td>88 (14.1)</td>
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<tr>
<td>Total</td>
<td>15</td>
<td>752</td>
<td>41 (5.4)</td>
<td>641</td>
<td>60 (9.3)</td>
<td>0.54</td>
<td>0.35–0.85</td>
<td>0.007*</td>
</tr>
<tr>
<td>Fluid/inotropes</td>
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<tr>
<td>Fluid</td>
<td>4</td>
<td>208</td>
<td>8 (3.8)</td>
<td>183</td>
<td>16 (8.7)</td>
<td>0.38</td>
<td>0.11–1.26</td>
<td>0.11</td>
</tr>
<tr>
<td>Fluid + inotrope</td>
<td>11</td>
<td>544</td>
<td>33 (6.0)</td>
<td>458</td>
<td>44 (9.6)</td>
<td>0.58</td>
<td>0.35–0.96</td>
<td>0.03*</td>
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<td>Goal</td>
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<tr>
<td>Supranormal</td>
<td>9</td>
<td>452</td>
<td>29 (6.4)</td>
<td>358</td>
<td>39 (10.8)</td>
<td>0.55</td>
<td>0.32–0.94</td>
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<tr>
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<td>6</td>
<td>300</td>
<td>12 (4.0)</td>
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<td>21 (7.4)</td>
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<tr>
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<tr>
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<td>0 (0.0)</td>
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<tr>
<td>Fluid + inotrope</td>
<td>12</td>
<td>605</td>
<td>39 (6.4)</td>
<td>552</td>
<td>41 (7.4)</td>
<td>0.72</td>
<td>0.44–1.18</td>
<td>0.19</td>
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<tr>
<td>Supranormal</td>
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<td>37 (6.4)</td>
<td>512</td>
<td>40 (7.8)</td>
<td>0.68</td>
<td>0.42–1.13</td>
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<tr>
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<td>4 (2.1)</td>
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<tr>
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<td></td>
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<tr>
<td>PAC</td>
<td>9</td>
<td>453</td>
<td>33 (7.2)</td>
<td>402</td>
<td>29 (7.2)</td>
<td>0.81</td>
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<td>453</td>
<td>33 (7.2)</td>
<td>402</td>
<td>29 (7.2)</td>
<td>0.81</td>
<td>0.66–1.41</td>
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</table>

*BJA Arulkumaran et al.*
monitoring devices and others. However, it was not the aim of this article.

Perioperative GDT is beneficial in high-risk surgical patients despite the various targets and monitors used. Markers of organ perfusion and circulation that can be directly measured are used as surrogates of tissue perfusion. GDT uses this practical approach of optimizing circulatory volume, flow, and perfusion (with fluids and inotropes) to prevent tissue hypoperfusion in the high-risk surgical patient.

We have analysed data extracted from studies, rather than data of individual patients. As some of the studies included were carried out several years ago, obtaining data on individual patients has not been possible. We also recognize that many studies were conducted in single centres with limited patient numbers, and not all studies conducted were of a high-quality design. This is reflected by the median Jadad score of 3. However, the results remain consistent across many subgroups of patients, supporting our hypothesis.

A recent Cochrane review on perioperative GDT found no differences in the rates of arrhythmia, myocardial infarction, congestive cardiac failure, or pulmonary oedema between patients treated with perioperative GDT and control group patients. This review included 31 studies with 5292 participants; the results are ‘dominated by a single large RCT’ with a weighting of more than 60% of the overall population. This particular RCT was excluded from our analysis as we excluded all studies without a clearly defined GDT protocol. This is consistent with recent meta-analysis demonstrating that perioperative GDT is associated with a significant reduction in postoperative complications when carried out using a treatment algorithm or protocol.

Heterogeneity in the year of study, patient characteristics, type and urgency of surgery, and healthcare facilities among the different studies are likely to account for the difference in CVS events. Although differences in patient characteristics are not modifiable, optimal management of the high-risk surgical patient during the perioperative phase may improve overall outcomes.

The reductions in immediate postoperative complications translate to overall benefits in healthcare costs, despite a requirement for an increase in healthcare resources to offer early GDT. Any perceived increase in resource allocation results in a lower patient mortality, morbidity, and therefore a financial benefit. Furthermore, a reduction in immediate postoperative complications has far-reaching effects, with a potential beneficial effect on long-term survival.

Early GDT using administration of fluid challenges and inotropes guided by haemodynamic monitoring does not result in an increased rate of cardiac events in this cohort of patients with limited cardiopulmonary reserve. GDT in high-risk surgery is beneficial in reducing CVS events. This holds true irrespective of the choice of the monitored physiological parameter or haemodynamic monitor in use. It is unclear if the use of a haemodynamic monitor alone or the combination of an algorithm and a haemodynamic monitor confers the benefit. The benefit is most pronounced in patients receiving fluid and inotrope therapy to achieve a supranormal
oxygen delivery target, with the use of minimally invasive cardiac output monitors.

Authors’ contributions

N.A. and C.C.: design of study, literature search, statistics, and writing manuscript. M.C., M.A.H., J.B., R.M.G., and A.R.: design of study, editing manuscript, and statistics.

Declaration of interest


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