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Early Goal-Directed Therapy Following Cardiac Surgery

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Early goal-directed therapy (EGDT) is a therapeutic strategy based on haemodynamic monitoring and pre-defined goals. The roots of this approach come from observational studies in non-cardiac surgery that showed that poor post-operative outcomes and higher mortality were associated with decreased oxygen delivery in the perioperative period (Clowes et al. 1960; Shoemaker 1972).

Following those studies several strategies have been tested in clinical trials attempting to manipulate the cardiovascular performance in order to achieve haemodynamic goals associated with reduction of complications and survival outcome (Wilson et al. 1999; Shoemaker et al. 1988; Boyd et al. 1993; Lobo et al. 2000; Gan et al. 2002; Kern et al. 2002; Wakeling et al. 2005; Pearse et al. 2005; Noblett et al. 2006; Donati et al. 2007; Giglio et al. 2009; Mayer et al. 2010; Dalfino et al. 2011).

Rationale

The mechanism of this therapy is likely to be attributed to the improvement of oxygen delivery (Mythen et al. 1993; Mokart et al. 2002). A constant supply of oxygen is required for the mitochondria to maintain aerobic metabolism. In health the cardiovascular system delivers the oxygen supply (DO2), and adapts to changes in metabolic demand to prevent cytopathic hypoxia (Navarrete et al. 2013). Once mitochondrial damage takes place, the insult becomes permanent (Hollenberg and Cunnion 1994), and correction of oxygen delivery is futile. The cellular oxygen demand following major surgery increases as a consequence of several factors, such as stress response to surgery, pain, shivering and anxiety among others (Routsi et al. 1993). Many cardiac surgical procedures involve cardiopulmonary bypass, which is associated with vasospasm, impaired platelet function and inflammatory response. This can result in impaired microcirculation and subsequent organ dysfunction (Silvestry 2012). The EGDT aims to prevent organ dysfunction by correcting the imbalance between oxygen consumption and oxygen delivery.

Evidence in Cardiac Surgery

Although postoperative mortality remains low following cardiac surgery (about 1-5%, dependent on surgical procedure and preoperative comorbidities), complications remain moderately high, and are associated with prolonged postoperative care (Ghotkar et al. 2006), longer intensive care unit (ICU) stays and worse long-term survival (Pivatto et al. 2010; Gaudino et al. 2007). Patients with complications use a greater amount of resources (Scott et al. 2005), and therefore these patients are associated with higher healthcare costs.

Few studies have investigated the role of GDT in cardiac surgery (Polonen et al. 2000; Mythen and Webb 1995; McKendry et al. 2004; Kapoor et al. 2008; Smetkin et al. 2009). Unfortunately, the evidence is limited by the fact that these studies are on small sample sizes from single centres, and with single blinding.

In a recent meta-analysis of EGDT in cardiac surgery (Aya et al. 2013), no improvement in mortality with GDT was found. However, EGDT can reduce the risk of postoperative complications and length of stay. The mortality in the control group was already low in these studies; in fact there were two studies with zero mortality, so that in order to observe a real difference in mortality larger studies with sufficient statistical power are required.

Outcomes Measures in EGDT

Choosing outcome measures for studies in a population with low mortality rates can be problematic. Complications associated with cardiac surgery remain an important issue, which is widely reported within the literature. Combining complications for outcome measures and designing a study based on composite end points will have multiple confounding factors, and may dilute the impact of the intervention, but selecting an appropriate primary outcome is challenging.

Postoperative complications go together with an increased length of stay and more costly care (Speir et al. 2009). It is not therefore a surprise that a lower incidence of postoperative morbidity is often accompanied by shorter length of hospital stay. However, length of stay is heavily influenced by clinical decisions on discharge readiness, social factors and patients' perception of relative independence. These outcome measures may remain too crude, and more objective measurements should be adopted.

A study investigating the effects of EGDT on gut perfusion was conducted, which was shown to be of benefit and was associated with improved outcome (Mythen and Webb 1995). Gastric tonometry has been described as the haemodynamic monitor of choice, as the gut is particularly sensitive to episodes of ischaemia (Heard 2003). However, it is not widely used within the ICU, and its effectiveness at assessing blood flow by translation of pH has been criticised (Uusaro et al. 1995). Other markers of end organ perfusion may be considered when choosing an appropriate outcome measure.

The most commonly reported and investigated complication following cardiac surgery is acute kidney injury (AKI). AKI occurs in around 30% (Rosner and Okusa 2006) of the cardiac surgery population, and is associated with increased short-term and longterm mortality.

Though AKI has many confounding factors in cardiac surgery, the pathogenesis of postoperative renal dysfunction includes hypoperfusion that remains undetected when relying on basic haemodynamic monitoring such as heart rate, blood pressure and central venous pressure.

Goals

The use of cardiac output monitoring and flow-related goals is the basis of EGDT strategy. In a subgroup analysis, Hamilton et al. (2011) demonstrated that those studies that used flow-related goals were able to reduce mortality after non-cardiac surgery. This approach could help in preventing organ hypoperfusion (Pearse et al. 2005) and particularly acute kidney injury (2014). A meta-analysis by Brienza et al. (2009) confirmed this notion in the non-cardiac surgical population.

Practicalities of Implementation

Implementing EGDT in the cardiac surgery population is simple, as therapy should start on arrival in the intensive care unit. Intraoperative use of EGDT is complex, as the use of cardiopulmonary bypass makes the fluid status of the patient difficult to assess.

Intensive care units provide the ideal setting for patients recovering from cardiac surgery for several reasons:

1. Each patient has additional nursing staff;

2. ICUs are familiar with the use of minimally invasive cardiac output devices;

3. Continuous monitoring allows the implementation of an EGDT protocol and adaptation to the patient's needs.

Intensive care nurses are familiar with such equipment, and most cardiac output monitoring technologies are able to assess stroke volume changes, and provide the ability to implement the simplest component of EGDT (Thomson et al. 2014).

The ease in application of an EGDT protocol was demonstrated in several studies in both non-cardiac and cardiac surgery populations (Pearse et al. 2005; McKendry et al. 2004; Thomson et al. 2014), which were all implemented by nursing staff.

A safe and effective protocol should include safety triggers for nursing colleagues to escalate potential harm to the medical staff. In the cardiac surgery population this might include central venous pressure (CVP) monitoring to be used as a safety mechanism. A sharp rise of 5mmHg in CVP or more during a fluid challenge should prompt the nursing staff to cease fluid administration (Cecconi et al. 2011; Cecconi et al. 2013). This allows medical staff to exclude right ventricular dysfunction and/or cardiac tamponade, which are common concerns applicable to cardiac surgery patients in the immediate postoperative period.

Cost-Effectiveness

Despite extensive evidence that supports the effectiveness of EGDT in improving outcomes, its implementation is still not clearly accepted. The main concern comes from the additional costs that a routine protocol of EGDT may imply for the health system. A recent cost-effectiveness study (Ebm et al. 2014) enlightens this reasonable concern: goal-directed therapy decreased costs by £2,631.77 per patient and by £2,134.86 per hospital survivor. The authors conclude that the additional costs can be offset by savings due to reduced costs resulting from a reduction in complication rates and hospital length of stay.

Cardiac surgery is associated with complications, such as infection, respiratory failure and acute kidney injury (AKI). AKI requiring renal replacement therapy (RRT) occurs in 1% of patients (Rosner and Okusa 2006), which increases mortality and postoperative complications such as infection, is associated with an increased duration of stay, and may go on to require further longterm RRT. Renal replacement therapy and prolonged ventilation are both available only within the ICU. Not only are there associated costs, but there is an impact on bed availability, and this can lead to cancellations of elective surgery. EGDT has demonstrated reductions in ICU stay, as optimising haemodynamics ensures patients' readiness for discharge is achieved on average four hours earlier (Thomson et al. 2014).

Conclusion

Early goal-directed therapy following cardiac surgery can be achieved using a stratified approach to fluid administration. Preventing hypervolaemia, maintaining flow and sustaining organ perfusion can improve patients' outcome, reduce cost and length of stay.

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