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Goal-directed therapy to maintain haemostasis

C. Oscier, MBBS, FRCA, EDIC, MSc, Registrar in Anaesthesia *, M. Cecconi, MD, FRCA, FICM, PhD, Consultant in Intensive Care Medicine and Anaesthesia

Department of Anaesthesia and Intensive Care Medicine, St George's Hospital, London, SW170QT, UK

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Perioperative goal-directed therapy typically involves the use of haemodynamic targets to optimise oxygen delivery. Common goals include stroke volume, cardiac output and arterial blood pressure, although future protocols may also incorporate an assessment of vascular tone and the microcirculation. This article reviews the current evidence for goal-directed therapy and discusses future directions.

Introduction

Approximately 4% of patients die in hospital following major surgery [1]. The mortality rate increases for emergency surgery, and it has been estimated to be around 12% for those deemed preoperatively to be 'high risk' [2,3]. Although the causes of post-operative morbidity and mortality are multifactorial, it is likely that an inability to compensate for the increased metabolic demand seen with major surgery contributes significantly [4].

Following the introduction to clinical practice of the pulmonary artery (PA) flotation catheter in the early 1970s [5], Shoemaker and others observed higher post-operative indices for oxygen delivery in survivors than in non-survivors of major surgery, as well as reduced oxygen debt [4,6,7]. They saw the ability to maintain oxygen supply in the face of increased perioperative demand as a key determinant of good post-operative outcome, and they demonstrated improved survival when the higher indices of oxygen delivery found in survivors were used as targets [8,9].

Although these early findings were challenged by later studies [10,11], a number of meta-analyses have suggested there may be a role for goal-directed therapy (GDT), the use of fluids and/or inotropes to target haemodynamic goals to improve oxygen delivery, in certain groups of patients [12–14].

* Corresponding author.
E-mail address: chrisoscier@gmail.com (C. Oscier).

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Three major studies published since 2014 have, however, failed to show benefits above the usual care [14–16], and a re-evaluation – of both the techniques used and the goals that are targeted – is necessary to demonstrate benefit against a background of continuously improving perioperative care.

The physiological rationale for goal-directed therapy

By the late 1980s, several studies had demonstrated that survivors of critical illness were able to sustain greater oxygen delivery than non-survivors; furthermore, measurements of global oxygen delivery were able to predict outcome [6,7,9]. Indices of oxygen delivery in survivors were above normal resting values, leading Shoemaker and co-workers to hypothesise that improvements in post-operative morbidity and mortality would be seen if these 'supranormal' values were used as targets for high-risk patients undergoing major non-cardiac surgery.

Initial findings were positive; typical goals were a cardiac output of >4.5 l min m^2, oxygen delivery of >600 ml min m^2 and oxygen consumption of >170 ml min m^2 (defined from median values of patients surviving critical surgical illnesses) [9]. A PA catheter-based protocol using a combination of fluids and vasoactive drugs was shown to significantly reduce mortality in high-risk non-cardiac surgical patients [9], and it was later demonstrated that reducing the post-operative oxygen debt (the difference between post-operative oxygen consumption and the estimated post-operative oxygen requirement based on baseline preoperative values) using a PA catheter-guided protocol similarly reduced organ failure and death [4].

The evidence for current goal-directed haemodynamic protocols

The enthusiasm for targeting supranormal values was tempered by two large randomised controlled trials (RCTs); PA catheters were first shown to be associated with increased mortality in the intensive care setting [17]; subsequently, in an RCT of nearly 2000 patients [10], a PA catheter-guided protocol targeting supranormal values was shown to have no benefit beyond usual care in elderly high-risk surgical patients. A Cochrane review in 2006 (recently updated in 2013 [18]) further concluded that the available evidence did not support the routine use of PA catheters in general surgical patients. A number of authors argued that the use of PA catheters in general surgical and general intensive care patients was subject to potentially inaccurate data, iatrogenic risk, lack of knowledge on the part of treating clinicians, overtreatment (for example, with vasoactive drugs) and the generation of data that were not clinically useful [19].

With the declining use of PA catheters, and without access to the haemodynamic data previously available, the focus began to shift away from targeting supranormal values, and researchers started to investigate the merit of optimisation or maximisation of an individual patient's cardiac output. Numerous protocols were developed for use in the perioperative period, usually involving fluid boluses titrated to increases in stroke volume, and/or the use of an inotrope to achieve a predefined cardiac output. Less invasive monitoring methods were introduced, such as the use of oesophageal Doppler ultrasonography and pulse contour analysis. The aim was, as with the targeting of supranormal values of oxygen delivery, to increase the available oxygen supply to the tissues and organs to compensate for the increased metabolism seen both during major surgery and in the days after.

The last decade has seen considerable research in both the intensive care and the surgical settings. In 2011, Hamilton et al. [12] performed a meta-analysis of the use of perioperative goal-directed therapy in moderate- and high-risk patients. The authors included 29 RCTs performed after 1985, with a variety of therapeutic protocols and strategies. A significant benefit for pre-emptive intervention was seen, with a reduction in mortality shown in studies using a PA catheter, studies using supranormal targets and studies using cardiac index or oxygen delivery as targets. A number of issues were highlighted in the discussion: most significantly, the quality of research was generally poor; most studies were single centre with small sample size; and there was large heterogeneity with regard to the monitoring, protocols and interventions. In addition, no mortality benefit was seen for low-risk patients, and no distinction could be made between therapeutic interventions, whereas the morbidity of the control group was found to decrease over time,