

## Commentary

# Optimal management of the high risk surgical patient: beta stimulation or beta blockade?

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See related research by Pearse *et al.* in this issue [<http://ccforum.com/content/9/6/R687> and <http://ccforum.com/content/9/6/R694>]

## Abstract

Several groups of investigators have shown that peri-operative goal directed therapy (GDT) may reduce mortality in high-risk surgical patients. GDT usually requires the use of beta-adrenergic agents, however, and these may also carry the risk of cardiac ischemia, especially in patients with ischemic diseases. In this commentary, we will discuss the apparent contradiction between studies showing beneficial effects of GDT in high-risk surgical patients and studies showing the benefit of beta-blockade in high-risk surgery. One of the key differences between both types of studies is that GDT is applied in patients with high risk of post-operative death, excluding patients with cardiac ischemic disease, while studies reporting beneficial effects of beta-blockade have investigated patients with high risk of cardiac ischemia but moderate risk of death related to the surgical procedure itself. It is likely that beta-blockade should be proposed in patients with moderate risk of death, whereas GDT using fluids and inotropic agents should be applied in patients with high risk of peri-operative death. Monitoring central venous oxygen saturation may be useful to individualize therapy, but further studies are required to validate this option.

The peri-operative care of high-risk surgical patients remains a challenge. Despite improvement in surgical and anesthesiological procedures, the mortality of high-risk surgical procedures remains above 10%. In these patients, peri- and post-operative alterations in oxygen transport are closely related to the development of organ failure and death [1,2]. This led to the concept that increasing deliberately oxygen delivery (DO<sub>2</sub>) may prevent the development of organ failure. Several studies have reported that peri-operative hemodynamic optimization (goal directed therapy (GDT)) guided by the pulmonary artery catheter may decrease morbidity and mortality [3-7]. GDT is usually based on generous fluid administration and, if needed, beta-adrenergic agents, including dobutamine [3,6] and dopexamine [4,5]. Several

questions remain unanswered, however, and limit the wide application of GDT in patients submitted to high-risk surgery.

## Can GDT be initiated only after admission in the intensive care unit?

One major limitation of GDT is that it was usually initiated in the operating room or even sometimes before the intervention. This is usually difficult to apply, either because of bed shortage or because the assessment of peri-operative risk of death is sometimes difficult before the surgical intervention. Some surgical interventions may indeed be much easier than predicted, and the patients would then have been submitted to useless or even deleterious GDT, while other interventions are sometimes unexpectedly complicated and GDT is not provided to these patients. In this issue of *Critical Care*, Pearse *et al.* [8] elegantly avoided these problems. They investigated the effects of GDT applied only when the patient is admitted to the intensive care unit (ICU), when peri-operative risk of death may be more easily determined. They used fluids and dopexamine to increase DO<sub>2</sub> (to a target of 600 mL/min.m<sup>2</sup>) for 8 h. The DO<sub>2</sub> target was achieved in 80% of the GDT group and in 45% of the control group. Fewer patients developed complications in the GDT group than in the control group (this was the primary outcome of the study), leading to a shortened hospital stay. Mortality (at 28 days) was similar in both groups and lower than the mortality predicted by the P-POSSUM score (actual 9.7% versus predicted 18.5% in GDT and actual 11.7% versus predicted 13.7% in control group). Thus, Pearse *et al.* [8] nicely demonstrated that GDT can be successfully initiated after ICU admission.

## Should GDT be individualized?

GDT therapy is based on the principle that DO<sub>2</sub> should be deliberately increased in order to prevent tissue hypoxia.

However, DO<sub>2</sub> is probably unnecessarily increased in some patients in whom a lower DO<sub>2</sub> value may also be adequate. Mixed venous and central venous (ScvO<sub>2</sub>) oxygen saturations reflect the balance between oxygen requirements and DO<sub>2</sub>, and may thus be used to assess the adequacy of DO<sub>2</sub>. Pearse *et al.* [9] also measured ScvO<sub>2</sub> in most of the patients investigated in their study assessing the efficacy of GDT [8]. They reported that ScvO<sub>2</sub> fluctuated over the 8 h period, independently of changes in DO<sub>2</sub> [9]. Patients with lower ScvO<sub>2</sub> values had more post-operative complications. The ScvO<sub>2</sub> cut-off value of 64.4% can be used to discriminate patients with complicated and with uncomplicated post-operative course. Future studies are required to investigate whether post-operative optimization should be guided by ScvO<sub>2</sub> or based on predefined DO<sub>2</sub> values.

### Are beta-blocking agents indicated in some patients?

These data suggesting that GDT should be implemented in high risk surgical patients should be balanced by some data suggesting that beta-blocker agents may be beneficial in these patients [10,11]. Lindenauer and colleagues [11] recently suggested that patient safety may be enhanced by increasing the use of beta-blockers in high-risk patients submitted to major non-cardiac surgery. This was a retrospective non-interventional study. Beta-blocking agents were used in 18% of 700,000 patients who had no contraindication for beta-blockade, and the outcome of these patients receiving beta-blockade was compared to the other patients, using a propensity score to match patients for confounding factors. In that study, beta-blockade was associated with a reduced risk of in-hospital death only in the subgroup of patients with Revised Cardiac Risk Index (RCRI) scores of 3 or more. This study deserves several comments. First, the subgroup with a RCRI score of 3 or more was very small, representing only 1.9% of the propensity matched cohort. Given the very limited number of available patients in this category (6,264 patients), it is very likely that matching groups was incomplete so that confounding factors may participate in differences in outcome. On the contrary, evidence that beta-blockade therapy increased the risk of death in patients with RCRI scores below 2 is much more robust, as this analysis included the vast majority of the patients (80% of the cohort). Second, RCRI assess specifically the cardiac risk of the patient, not the mortality related to the surgical procedure. Accordingly, mortality was 6% to 7% in the patients with RCRI scores of 3 and more. A high-risk surgical procedure was performed in a minority of the patients, and the effects of beta-blockade were neutral in these patients.

### How to reconcile these apparently opposed results?

In an attempt to reconcile both views, one could propose that patients with a high risk of peri-operative cardiovascular events (high RCRI scores) should be dissociated from

patients with high risk of peri-operative death. In the first group, beta-blockade should be proposed, whereas in the second one, GDT using fluids and inotropic agents should be applied. Patients combining high cardiac risk and high peri-operative risk of death have not been studied, it may appear logical to provide GDT, but limiting as much as possible the use of beta-stimulation in these patients.

Maybe ScvO<sub>2</sub> should be used to guide therapy in place of DO<sub>2</sub>. This may appear attractive, as it may be justified to further attempt to increase DO<sub>2</sub> when ScvO<sub>2</sub> is low while it may be justified to avoid the use of beta-adrenergic agents when ScvO<sub>2</sub> is high enough. This should be tested in further studies.

### Competing interests

The author(s) declare that they have no competing interests.

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