EDITORIAL

Goal-directed Therapy: Does It Work in Postcardiac Surgery Patients, Unlike in Sepsis?

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Although postoperative mortality remains low following cardiac surgery (about 1–5%, depending on the complexity of the surgical procedure and preoperative comorbidities), complications remain moderately high and are associated with prolonged postoperative care.[1] Cardiac surgery is associated with complications, such as infection, respiratory failure, and acute kidney injury (AKI). Renal replacement therapy (RRT) is needed in 1% of patients which increases mortality and a few patients may even require long-term RRT.[2] Perioperative hemodynamic optimization may therefore improve the outcome in cardiac surgery patients, whereas inadequate oxygen delivery could lead to complications including organ dysfunction, prolonged ICU stay, or mortality.[3]

Optimizing hemodynamic parameters in critically ill patients including patients with septic shock and in those undergoing major surgery has been an elusive goal.[4,5] Goal-directed therapy (GDT) is the term used to describe the use of various hemodynamic parameters including heart rate, blood pressure, cardiac output, or similar parameters to guide intravenous fluid and vasopressor and inotropic therapy in these patients.[3] In 1988, Shoemaker et al. published their seminal paper in which they showed in an RCT in perioperative patients that targeted supra-normalization of cardiac output in the perioperative period was associated with reduced mortality.[6] They described the concept of oxygen debt and its relevance for the postsurgical period and the development of complications. Subsequent studies did not confirm the benefit of targeted supra-normalization of hemodynamics. Goal-directed therapy came back into focus after the publication of Rivers' study where patients with septic shock were randomized to a complex set of interventions that were guided by central venous oxygen saturation (ScvO2) which was used as a measure of tissue hypoperfusion, and increased oxygen extraction by underperfused tissues could result in low ScvO2 values below 70% indicating the need for further enhancing oxygen delivery.[7] The interventions in this study included fluid administration and vasopressors as first-line interventions to achieve central venous pressure and mean arterial pressure targets, followed by the addition of inotropic drugs and packed RBC (pRBC) transfusions to raise the hematocrit >30% in order to increase the oxygen delivery if ScvO2 remained <70%.[7] The authors found a statistically significant reduction in 28-day mortality in the GDT group.[7] This study shifted the focus from therapeutic goals based on the "upstream" variables, like arterial pressure and cardiac output that focused on the oxygen delivery, to the "downstream" indicators like ScvO2 and lactate, as an estimate of the mismatch between tissue oxygen demand and oxygen delivery.

In the years that followed, this concept was extrapolated to perioperative care and perioperative GDT was extensively studied. Even though the cardiothoracic surgical patients do not behave like septic patients, the use of cardio-pulmonary bypass (CPB) does cause a complex systemic inflammatory response, along with coagulation disorders and multi-organ dysfunction.[8] Aya et al. found that more than a hundred studies were published till 2013 on perioperative GDT.[1] These studies attempted goal-directed manipulation of cardiac preload, afterload, and contractility to achieve a balance between systemic oxygen demand and delivery. Several important meta-analyses and systematic reviews have been published on this subject.[1,8,9] The primary outcome studied was mortality and secondary outcomes were morbidity and length of hospital stay in patients undergoing open heart and also off-pump cardiac surgery.[10] Patients randomized to goal-directed hemodynamic therapy had less morbidity and significantly shorter hospital stay compared to those in the control group, mortality did not differ.[1,8–11] In a more recent study,[9] the GDT strategy reduced the incidence of infection (12.9% vs 29.7%; $p = 0.022$) and low cardiac output syndrome (6.5% vs 26.6%; $p = 0.002$). There was no significant difference between groups in 30-day mortality rates (4.8% vs 9.4%, respectively; $p = 0.492$), stroke (0% vs 7.8%; $p = 0.058$), acute respiratory distress syndrome (0% vs 0%), myocardial ischemia (8.1% vs 6.2%; $p = 0.742$), reoperation (4.8% vs 1.6%; $p = 0.361$), or AKI requiring dialysis or hemofiltration (3.2% vs 0%; $p = 0.240$).[9]

However, perioperative GDT has not been widely practiced in cardiac surgery patients because of the heterogeneity in the protocols and end points in various studies, which in fact reflect the wide variation in perioperative monitoring practiced in different ICUs. Pulmonary artery catheter (PAC) has been the gold standard in intraoperative and postoperative management of hemodynamics in cardiac surgery patients. Most of the recent studies have used esophageal Doppler to measure CO, and GDT cannot be continued after extubation.[8–11] Less invasive techniques of volume responsiveness, particularly those which rely on pulse contour and pulse pressure variation, have been used along with ScvO2 or lactate levels as indicators of adequacy of tissue perfusion.[10,11] Modern monitors have been used in recent trials with flow-related

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upstream variable-based goals that measure SV, CO, cardiac index (CI), systemic vascular resistance (SVR), global diastolic index (GDI), extravascular lung water (EVLW), and global end-diastolic volume (GEDV).[8] However, many of these modalities fall victim to inaccuracy in a setting like arrhythmias (atrial fibrillation occurs in 15–40%), extreme bradycardia, spontaneous breathing or mechanical ventilation with low tidal volumes, and the presence of intra-aortic balloon pump, all of which are common postcardiac surgery. Nevertheless, unlike in septic shock where RCTs have shown that the GDT has no advantage over conventional treatment, multiple meta-analyses of RCTs have confirmed the beneficial role of perioperative GDT in reducing morbidity and shortening hospital stay in postcardiac surgery patients.

In this issue of the journal, Patel et al. have published their results of a comparatively large study in 478 Indian patients, 251 patients treated by conventional therapy and 227 patients with GDT. They used a protocol very similar to that in Rivers' study.[7] The authors found no difference in mortality, but a significant reduction in complications especially in AKI.[12] However, it is not clear whether this was a randomized study and also the details of vasopressors and inotropes used in the study and the thresholds for adding a second drug are lacking. A notable difference was the use of larger volumes of fluids in the GDT group.[12]

Of all the interventions in a GDT protocol, the optimization of fluids seems to be the most crucial aspect of GDT.[3,13] The importance of fluid management has been discussed beautifully in an editorial by Fergerson and Manecke.[3] Most cardiac surgeons and cardiac anesthesiologist are extremely conservation with fluids due to concerns related to left ventricular dysfunction in most of the postcardiac surgery patients. Fergerson and Manecke[3] write "there are, however, several limitations to a 'blind' fluid restriction approach, even in patients with poor cardiac function." While conventional fluid therapy is guided by cardiac output, ejection fraction, pulmonary artery wedge pressure, and echocardiography, the GDT protocol that incorporates incorporates volume and cardiac output related parameters along with oxygen delivery goals and downstream parameters of adequacy of tissue perfusion seems to improve the outcomes by reducing the complications. Fergerson and Manecke term GDT as "goal-directed fluid restriction" in contrast to the traditional "blind fluid restriction."[3]

In May 2019, the enhanced recovery after surgery (ERAS) guidelines for perioperative care in cardiac surgery were released.[13] These guidelines strongly recommend goal-directed fluid therapy [strength of recommendation = I (strong); level of evidence = BR (moderate quality evidence from 1 or more RCT or meta-analysis of moderate-quality RCTs)].[13] The guidelines recommend that goal-directed fluid therapy using a standardized algorithm for all patients with quantified goals includes blood pressure, CI, systemic venous oxygen saturation, urine output along with oxygen consumption, oxygen debt, and lactate levels should be used to reduce complication rates and length of stay in cardiac surgery patients.[13]

Lastly, we urge readers to note that the ERAS guideline refers to this as "goal-directed fluid therapy;" it does not discuss the use of interventions like pRBC transfusions to maintain hematocrit >30% in order to enhance tissue oxygen delivery and normalize ScvO2, which has been a component of several GDT protocols.

References

1. Aya HD, Cecconi M, Hamilton M, Rhodes A. Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis. Br J Anaesth 2013;110(4):510–517. DOI: 10.1093/bja/aet020.
2. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol 2006;1(1):19–32. DOI: 10.2215/CJN.00240605.
3. Fergerson BD, Manecke Jr GR. Goal-directed therapy in cardiac surgery: are we there yet? J Cardiothorac Vasc Anesth 2013;27(6): 1075–1078. DOI: 10.1053/j.jvca.2013.08.004.
4. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med 2017;43(3):304–377. DOI: 10.1007/s00134-017-4683-6.
5. Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, et al. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. JAMA 2014;311(21):2181–2190. DOI: 10.1001/jama.2014.5305.
6. Shoemaker WC, Appel PL, Kram HB, Waxman K, Lee TS. Prospective trial of supranormal values of survivors as therapeutic goals in high-risk surgical patients. Chest 1988;94(6):1176–1186. DOI: 10.1378/chest.94.6.1176.
7. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345(19):1368–1377. DOI: 10.1056/NEJMoa010307.
8. Arulkumaran N, Corredor C, Hamilton MA, Ball J, Grounds RM, Rhodes A, et al. Cardiac complications associated with goal-directed therapy in high-risk surgical patients: a meta-analysis. Br J Anaesth 2014;112(4):648–659. DOI: 10.1093/bja/aet466.
9. Osawa EA, Rhodes A, Landoni G, Galas FRBG, Fukushima JT, Park CHL, et al. Effect of perioperative goal-directed hemodynamic resuscitation therapy on outcomes following cardiac surgery: a randomized clinical trial and systematic review. Crit Care Med 2016;44(4):724–733. DOI: 10.1097/CCM.0000000000001479.
10. O'Neal JB, Shaw AD. Goal-directed therapy in the operating room: is there any benefit? Curr Opin Anaesthesiol 2016;29(1):80–84. DOI: 10.1097/ACO.0000000000000273.
11. Goldthwaite Z, Firstenberg MS, Botsch A. Hemodynamic early goal-directed therapy: explaining the fine print. Int J Crit Illn Inj Sci 2019;9(2):54–56. DOI: 10.4103/IJCIIS.IJCIIS_38_19.
12. Patel H, Parikh N, Shah R, Patel R, Thosani R, Shah P, et al. Effect of goal-directed hemodynamic therapy in postcardiac surgery patients. Indian J Crit Care Med 2020;24(5):321–326.
13. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Seenu Reddy V, Arora RC, et al. Guidelines for perioperative care in cardiac surgery: enhanced recovery after surgery society recommendations. JAMA Surg 2019;154(8):755–766. DOI: 10.1001/jamasurg.2019.1153.