

## The anesthesiologist role in risk reduction and outcome improvement in cardiac surgery

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The patient with coronary artery disease (CAD) undergoing coronary artery surgery (CABG) presents a special challenge to the anesthesiologist. The combination of increased surgical stress response with limited coronary reserve exposes the patient to a special vulnerable situation during the perioperative period. Typically, the patients with CAD are older with higher rate of comorbidities and thus more sensitive for the development of hemodynamic instability and organ dysfunction. The current trend of more aggressive intra-coronary cardiologic interventions in sicker patients creates a requirement for the development of more comprehensive approach to the perioperative management of these patients.

Cardiac anesthesia is a challenging specialty dealing with patients with severe heart disease in whom the margin for surgical and anesthetic complications and adverse outcome is narrow. The history of cardiac anesthesia started back in the early twenties with the first surgical attempts of mitral valvulotomy. It is difficult to imagine the challenges the anesthesiologist had faced at that time struggling to keep the patient alive while the surgeon is pushing a dilating device through the tip of the left ventricle and occluding blood flow through the mitral valve with his finger. Today, the continual search for defining new standards of patient care is of particular relevance for the cardiovascular anesthesiologists. Developing new monitoring modalities and new anesthetic strategies are creating the processes that make it possible to survive complex operations and may change patient outcome.

It still remains unclear whether specific anesthetic technique offer any benefit in terms of improved patient outcome. Sometime it is the anesthetic strategy, such as systematic preoperative evaluation, intraoperative patient monitoring, medical control of heart rate, control of the systemic inflammatory response, prevention of blood prothrombotic state, preservation of normothermia, and continuation of strict pa-

tient monitoring in the postoperative period that are the important factors responsible for improved patient outcome.

**Current trends in cardiac anesthesia education:** In recent years we have witnessed dramatic changes in patient management with extensive involvement of the anesthesiologist in clinical decision making in the cardiac surgical patient. Advancement in monitoring technology and pharmacological management and support promoted new layers of education for the anesthesiologist -in - training. An important aspect of education is implementing patient safety practices in the daily routine. Patient safety practice is defined as a process whose application reduces the probability of adverse events resulting from medical action or procedure. Not all interventions, no matter how commonsense or physiologically sound they are, will stand the scrutiny of evidence - based medicine and fulfill standards of safety and effectiveness. Thus, particularly in the face of limited resources we have to prioritize treatment strategies which promote quality improvement and patient safety. We have to promote practice methods which emphasize prevention of adverse events and not only, although important, prevention of errors.

By using the «Timeout» procedure not only to verify basic patient information and planned procedure, but also to express concerns and suggest a contingency plan in case of expected complication, the anesthesiologist may enhance patient safety. Among the methods which promote safety is the use of transesophageal echocardiography (TEE). Its use introduced new dimension for elaborated evaluation of cardiac chambers and valves, hemodynamic assessment of ventricular function and guidance of instrumentation insertion during percutaneous approach for minimally - invasive direct -vision CABG procedures. All those are of particular importance in reducing medical errors, promoting quality improvement and patient satisfaction.

Integral part of the progress in education in cardiac anesthesia is the involvement of the anesthesiologist - in - training in clinical research. Whatever we achieve in basic research is only applicable after testing in human. Such task becomes more difficult every day with more strict regulations, but we should insist on performing hypothesis - driven original research in addition to multi - center and industry - supported studies. Only the original research will promote in - depth involvement and specific interest of our residents and fellows in cardiovascular medicine.

The physiological perturbations in the CABG perioperative period are related to the increased effect of the stress response on the coronary circulation during surgery and anesthesia. Activation of peripheral and central neural responses has major impact on the coronary circulation, which promote peripheral release of local inflammatory mediators and central activation of the hypothalamic - pituitary - adrenal axis. Cardiovascular morbidity is therefore related to the sustained burst in the body's inflammatory response and immune function. The continuation of the stress response in these CAD patients into the postoperative period, and the surgical pain, both promote coronary and peripheral vasoconstriction, increased afterload, and hypercoagulability and thus, increased risk for myocardial ischemia. As the average patient presenting for cardiac surgery is sicker today than ever, and the fact that he is more dependent on his chronic medical therapy, including new generation of anti - thrombotic therapy, emphasizes our need for a broader insight in the pharmacological management of the cardiac patient during the perioperative period. Specifically, I will present new information on the importance of continuing the patient's medical therapy throughout surgery and the role of pharmacological myocardial protection when the classical cardioplegic arrest of the heart is not applicable.

**Continuation of patient's medical therapy:** A number of studies have assessed the effects of therapeutic agents aimed at reducing perioperative cardiovascular morbidity and mortality. Intensive postoperative analgesia and sedation<sup>(1,2)</sup>, continuation of beta blockade (BB)<sup>(3,4)</sup>, alpha - 2 agonists<sup>(5)</sup> when BB are contraindicated, and statins<sup>(6)</sup>, have demonstrated reduction in the incidence or severity of operative myocardial ischemia. Nevertheless, despite significant improvement in both surgical and medical management, a significant number of patients still experience perioperative morbidity adversely affecting quality of life, prolonging hospitalization, and increasing resource utilization.

BB therapy has been demonstrated to reduce the risk of death in patients with myocardial infarctions following CABG<sup>(7,8)</sup>. The risk of withdrawal of BB in the perioperative period has been also clearly demonstrated<sup>(9)</sup>. In patient undergoing CABG surgery the use of perioperative BB has

been clearly and repeated demonstrated to reduce the risk of postoperative atrial fibrillation<sup>(8,10)</sup>.

The EPI - 2 Multicenter study which was conducted by the Multicenter Study of Perioperative Ischemia (McSPI) on 4,302 patients undergoing CABG using cardiopulmonary bypass demonstrated the importance of continuation of medical therapy in these patients. Withdrawal of beta - blockers, calcium channel blockers, or nitrate therapy was strongly associated with an increased incidence of cardiac, renal, and central nervous system morbidity and even mortality. Forty - two percent (42%) of patients were withdrawn from beta - blocker therapy post operatively with an increase in the incidence of myocardial ischemia, CHF, MI, mental status changes, and renal failure<sup>(9)</sup>.

Earlier studies on perioperative use of angiotensin - converting enzyme inhibitors (ACEI) in cardiac surgery have suggested marked vasoplegia following induction of anesthesia and in the setting of CPB necessitating greater vasopressor and fluid resuscitation. As a result, withdrawal of ACEI therapy before cardiac surgery became a common practice. Subsequent studies addressing such hemodynamic and other relevant clinical effects have since challenged this view<sup>(11)</sup>. Of interest, in our cohort of EPI - 2 patients on continuous ACEI therapy<sup>(12)</sup>, these patients did have higher requirement for inotropic and vasopressor support after CPB; however, there was no appreciable differences in hemodynamic, or any effect on patient outcome. On the contrary, treatment with ACEI before and after coronary surgery was associated with significant reduction of cardiovascular and overall composite events; de novo addition of ACEI therapy postoperatively lowered overall composite outcomes by a third; and, notably, withdrawal of ACEI treatment after surgery was associated with doubling odds of cerebral, cardiac and renal ischemic events.

**Cardiac risk evaluation by natriuretic peptides measurement:** The presence of CHF carries a particular high postoperative risk in patients with hip fractures. An accurate early estimate of severity of disease should enable us to offer a perioperative therapeutic strategy to reduce the incidence of adverse outcome. Blood levels for N - terminal pro - brain natriuretic peptide (NTproBNP) predict perioperative cardiovascular complications and thus provide a quantitative measure of heart failure severity in the preoperative period of patients scheduled for heart surgery. The novel approach in these patients should be that NT - proBNP may be used to direct the medical team to provide intensive preoperative preparation, as well as guidance for postoperative management.

Recent works showed a close correlation between preoperative high levels of NT - proBNP and post

cardiac surgery outcome<sup>(13)</sup>. Those studies showed the high predictive value of BNP for length of ICU stay and 28 - day mortality. It seems that BNP may be used for overall perioper-

ative risk stratification; however its yield in guiding perioperative management has not been proven yet. In a preliminary study we performed on hip fracture elderly patients urgently referred to surgery, we observed that preoperative BNP levels correlated to their Lee risk index status, but not to the NYHA class. Postoperative complications were accompanied by elevated postoperative BNP levels. We concluded that the use of pre - and postoperative BNP concentrations to guide intensive therapy may reduce the incidence of adverse outcomes especially those due to cardiac problems.

**Pharmacological myocardial protection:** CABG surgery performed without the use of CPB (OPCAB) is an established alternative technique of myocardial revascularization. In the absence of cardioplegic arrest of the heart, particularly in those undergoing multiple graft repairs, the compression and elevation of the heart results in severe global ischemia, added to the regional ischemia in the watershed zone of the vessel under repair and is often accompanied by severe hemodynamic instability. Upon completion of the anastomoses and reinstitution of blood flow, the stunned myocardium is exposed to reperfusion injury, the severity of the clinical symptoms of which is dependent on the extent and duration of occlusion and severity of the pre - existing coronary disease. This myocardial ischemia and injury mandates the development of myocardial protection methods for use during OPCAB operations.

Among the methods proposed to preserve myocardial function, is the phenomenon of myocardial ischemic preconditioning (IPC); protection of the heart provided by initiating intrinsic adaptation mechanisms. Endogenous adenosine production is believed to play a role in the protection afforded by IPC, with activation of the protein kinase C (PKC) pathway and intracellular signal transduction mechanisms. Those lead to activation of inhibitory processes mediated by the sarcolemmal and mitochondrial ATP - dependent potassium channels (KATP), which promote ATP conservation and prevention of excessive intracellular accumulation of calcium ions<sup>(14)</sup>. We have shown<sup>(15)</sup> that coronary occlusion during OPCAB surgery, results in increased production of ischemia - related metabolic products. Application of methods such as IPC or volatile anesthesia appears to attenuate the metabolic deficit, free radical production and physiological changes.

During CPB - supported CABG surgery, pharmacological compounds such as the modern volatile anesthetics<sup>(16)</sup> have shown some degree of myocardial protective properties during surgery, which were attributed to their PC properties. However, the optimal timing of administration, the dosage and the best agent, have not been determined yet, and the overall impact on patient outcome still needs to be validated in a large scale prospective study.

## REFERENCES

1. Mangano DT, Siliciano D, Hollenberg M, et al. Postoperative myocardial ischemia. Therapeutic trials using intensive analgesia following surgery. The Study of Perioperative Ischemia Research Group. *Anesthesiology* 1992;76:342-53.
2. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. *Br J Anaesth* 2001;87:684-90.
3. Wallace A, Layug B, Tateo I, et al, for the McSPI Research Group: Prophylactic atenolol reduces postoperative myocardial ischemia. *Anesthesiology* 1998;88:7-17.
4. Chen J, Radford MJ, Wang Y, et al. Are beta - blockers effective in elderly patients who undergo coronary revascularization after acute myocardial infarction? *Arch Intern Med* 2000;160:947-52.
5. Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology* 2004;101:284-93.
6. Collard CD, Body SC, Shernan SK, et al. Preoperative statin therapy is associated with reduced cardiac mortality after coronary artery bypass graft surgery. *J Thorac Cardiovasc Surg* 2006;132:392-400.
7. Ferguson Jr TB, Coombs LP, Peterson ED. Preoperative beta - blocker use and mortality and morbidity following CABG surgery in North America. *JAMA* 2002;287:2221-7.
8. Coleman CI, Perkerson KA, Gillespie EL, et al. Impact of prophylactic postoperative betablockade on post - cardiothoracic surgery length of stay and atrial fibrillation. *Ann Pharmacother* 2004;38:2012-6.
9. Wallace AW, Fontes M, Drenger B, Wang S. McSPI Research Group: The Effect of anti - ischemic agents on morbidity and mortality after coronary artery bypass surgery. *Anesthesiology* 2003;99:A255.
10. Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. *JAMA* 2004;291:1720-9.
11. Ryckwaert F, Colson P, Ribstein J, et al. Haemodynamic and renal effects of intravenous enalaprilat during coronary artery bypass graft surgery in patients with ischaemic heart dysfunction. *Br J Anaesth* 2001;86:169-75.
12. Drenger B, Gozal Y, Fontes M, Mangano D. McSPI Research Group: The association between ACE inhibitors pattern of use and patient outcome after coronary artery bypass surgery. *Anesthesiology* A1737, 2006.
13. Cuthbertson BH, Croal BL, Rae D, et al. N - terminal pro - B - type natriuretic peptide levels and early outcome after cardiac surgery: a prospective cohort study. *Br J Anaesth*. 2009;103:647-53.
14. Zaugg M, Lucchinetti E, Uecker M, et al. Anaesthetics and cardiac preconditioning. Part I. Signalling and cytoprotective mechanisms. *Br J Anaesth* 2003;91:551-65.
15. Drenger B, Gilon D, Chevion M, et al. Myocardial metabolism altered by ischemic preconditioning and enflurane anesthesia in off - pump coronary surgery. *J Cardiothor Vasc Anesth* 2008;22:369-76.
16. De Hert SG, Turani F, Mathur S, Stowe DF. Cardioprotection with volatile anesthetics: mechanisms and clinical implications. *Anesth Analg* 2005;100:1584-93.