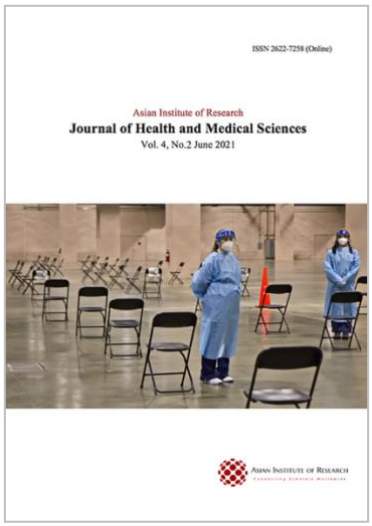

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Dexmedetomidine as a Heart Rate Control for Off-Pump Coronary Artery Bypass Surgery

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Abstract
Introduction: The traditional surgical approach is performed under cardiac arrest with cardiopulmonary bypass (CPB), which has the potential to result in myocardial injuries. In 1990s, when researchers developed efficient mechanical stabilizer devices, Off-pump coronary artery bypass (OPCAB) gained more widespread interest, as it's associated with many significant benefits. Avoidance of tachycardia is a goal for anesthetic management during OPCAB surgery. A short-acting Beta-blocker is needed for lowering excessive increases in heart rate. However, in some hospitals these drugs were not available. Case: A 53-yr-old, 73 kg man with a three-vessel coronary arterial disease with left main disease was scheduled for elective OPCAB surgery. Patient has a medical history of heart attack and hypertension. Preoperative echocardiography shows reduced LV systolic function, diastolic dysfunction grade I, with LVEF 47%. Throughout the hour after induction, HR increased in a constant manner to a persistent of 85-90 bpm despite additional fentanyl given. We didn't have any intravenous beta blocker drug and therefore we started dexmedetomidine. HR decreased to 55-60 bpm and remained at that value throughout the surgical procedure. Patient extubated in OR and transferred to ICU. After 6 days, he was discharged from the hospital without any complications. Conclusion: Perioperative administration of Dexmedetomidine is an effective adjuvant to general anaesthesia, attenuates the stress response to intubation, provides minimal heart rate variations, enabling smooth extubation, also provides adequate sedation in the post-operative period.

Keywords: Anesthesia Management, OPCAB, Dexmedetomidine

Introduction

Coronary artery bypass grafting (CABG) is an effective method of treating coronary artery stenosis. The traditional surgical approach is performed under cardiac arrest with cardiopulmonary bypass (CPB), which has the potential to result in myocardial injuries. The inherent risks of CPB and aortic cross-clamping continued to be a major factor in CABG morbidity and mortality. Avoiding CPB altogether seemed to offer a solution. It was not until the middle to late 1990s, when surgical researchers developed efficient mechanical stabilizer devices that minimized motion around the anastomotic site, Off-pump coronary artery bypass (OPCAB) gained more widespread interest. OPCAB was related to significant decreases in AF, quantities of patients transfused, respiratory infections, need for inotropes, duration of ventilation, ICU LOS, and hospital LOS. The pace and tempo of OPCAB surgery differ significantly from that of conventional CABG. Surgical manipulations involve a

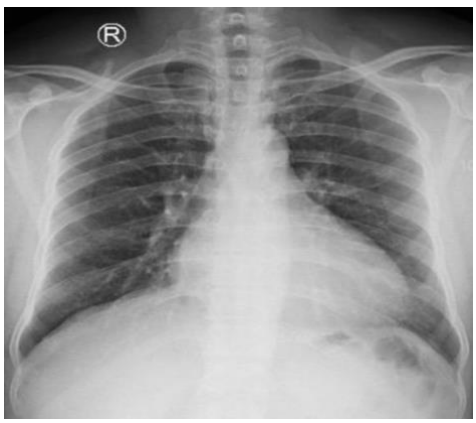
variety of geometric distortions of the cardiac anatomy, with resulting hemodynamic impacts. Communication between all members of the surgical team and anticipation of these changes are vitally important to minimize resulting adverse hemodynamic effects on the heart and different organs (Kaplan, 2018).

Increasing myocardial oxygen supply and reducing demand/ consumption can improve myocardial oxygen balance. Oxygen consumption is accomplished by lowering the heart rate and contractility, and can be accomplished through pharmacological agents such as beta-blockers and calcium antagonists. Avoidance of tachycardia is a commonly described goal for anesthetic management during coronary artery bypass graft OPCAB surgery. A short-acting Beta-blocker is needed for lowering excessive increases in heart rate (Chassot *et al.*, 2004).

However, in some hospitals, intravenous beta blocker drugs were not available as for the situation at the author's hospital. Several alternative steps are taken to lower the pulse, one of them is utilizing Dexmedetomidine. Dexmedetomidine with the central 2 agonist effect decreases the central sympathetic drive and hence decreases the stress response to *intubation*. By minimizing the variability in the heart rate it provides a suitable condition for grafting in off pump coronary artery bypass grafting surgeries. Dexmedetomidine with its sedation and analgesic property when continued post-operatively provides adequate sedation also reduces the hemodynamic stress response during extubation. Lack of respiratory depression, arousal sedation and hemodynamic stability makes Dexmedetomidine a better choice to attenuate the pressor response to extubation with an added advantage of preventing emergence delirium (Chassot *et al.*, 2004).

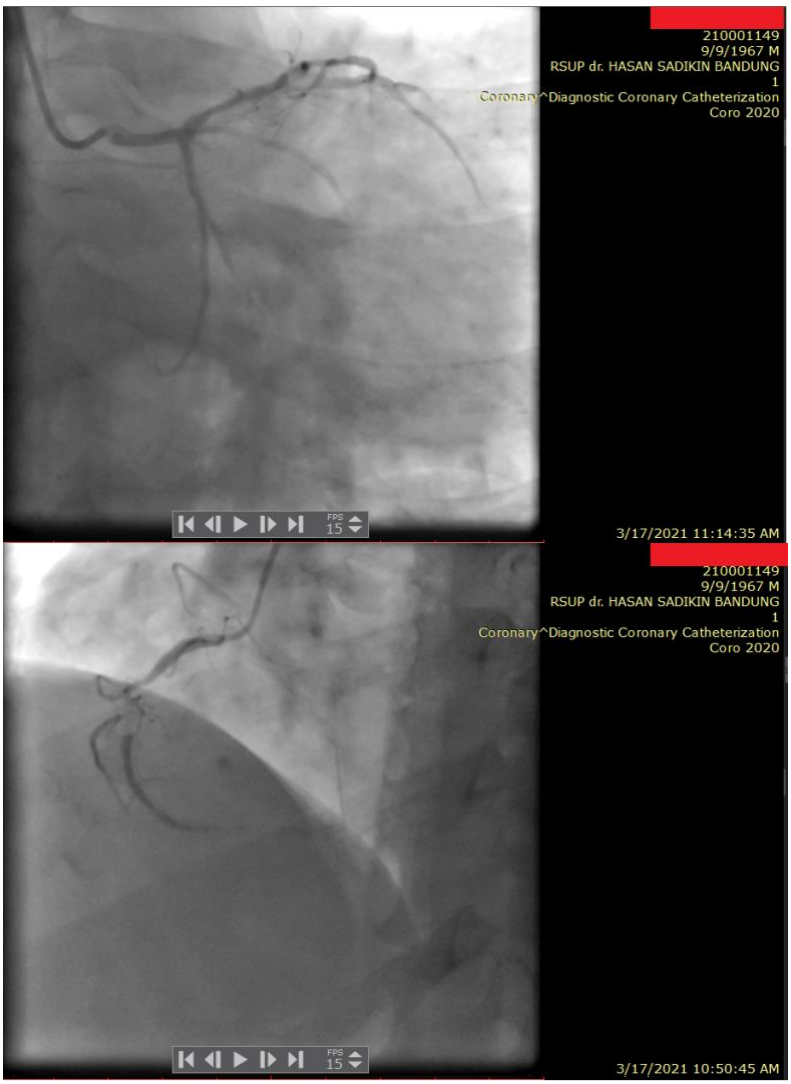
Case Report

A 53-yr-old, 73 kg man with a three vessel coronary arterial disease with left main disease was scheduled for elective Off-pump coronary revascularization (OPCAB). Patients with complaints of chest pain and shortness of breath especially during strenuous activities. Patient has a medical history of heart attack and hypertension. The patient had no history of diabetes, or obesity and was taking Glyceryl trinitrate 2x 2.5 mg, Bisoprolol 1x5 mg, Simvastatin 1x40mg, Acetylsalicylic Acid 80 mg. Patient was a smoker and his preoperative respiratory function tests result was mild restrictive and cardiomegaly was found on the X-rays (fig 1). Arterial blood gas analysis was normal. In the preoperative review of echocardiography we given result: dilated LA, concentric LVH, reduced LV systolic function with RMWA, diastolic dysfunction grade I, normal valves, low probability of PH, normal RV contractility with LVEF 47%.



Picture 1: Patient Chest Xray

After placement of a radial artery catheter and a pulmonary artery catheter, we installed standard monitoring and preoxygenated with 100% oxygen. Preinduction hemodynamic variables were all within normal range: BP was 150/70 mm Hg, HR was 75 bpm (sinus rhythm), and pulmonary artery pressure was 22/10 mm Hg. The preinduction arterial blood gas analysis showed pH 7.35, Po2 102 mm Hg, Pco2 38,6 mm Hg, HCO3 21,6 Base excess -3 mmol/L, Hemoglobin 14,6, Hematocrit 40,6%, Na 137 mmol/L, K 4.1 mmol/L, and glucose 111 mg/dL.



Picture 2: Coronary angiograph

Anesthesia was induced with Midazolam 7 mg, Fentanyl 400 mcg, Propofol 20mg and Rocuronium 70 mg. During the minutes after the induction and intubation, the BP decreased to 125/70 mm Hg; all other variables remained unchanged. Anesthesia was maintained with Sevoflurane 2-3vol% with end-tidal concentrations of 32-36 mmHg. An additional dose of 50 mcg fentanyl was given before incision. Patient's lung was ventilated with a volume controlled mode with 50% oxygen.

Throughout the hour after incision, while the surgeon was dissecting the internal mammary artery and starting the graft anastomosis, the HR increased in a constant manner to a persistent of 85-90 bpm despite additional fentanyl given. BP increased simultaneously to 140/65 mm Hg. Central venous pressure, pulmonary artery pressure remained unchanged. No additional drugs had been administered. Furthermore, throughout the entire operation the pulse oximeter read saturations of 100%, the end-tidal CO2 concentrations ranged from 32 to 36 mm Hg, and the patient was not febrile.

In the rapidly changing setting of OPCAB surgery, we didn't have any intravenous beta blocker drug and therefore we started dexmedetomidine, which is usually administered for ICU transfer and ventilator weaning. The initial loading dose, which is usually started after chest closure, was initiated. Dexmedetomidine infusion was started at a rate of 0.3 mcg/kg/hour. Within 15 min, the HR decreased to 55-60 bpm and remained at that value throughout the remainder of the surgical procedure. BP decreased within 30 min to 105/55 mm Hg and remained in that range until ooperation is over. Patient extubated in OR and transferred to ICU with stable hemodynamic. Dexmedetomidine infusion 0,2 mcg/kg/hour was continued in the ICU, and HR remained at 70–75 bpm over 24 h. After 6 days, he was discharged from the hospital without any complications.

OPCAB

The inherent risks of CPB and aortic cross-clamping kept on being a main consideration in CABG morbidity and mortality. Avoiding CPB altogether appeared to offer a solution. It was not until the middle to late 1990s, when surgical researchers created efficient mechanical stabilizer devices that minimized movement around the anastomotic site, that OPCAB surgery gained more widespread interest OPCAB was associated with significant decreases in AF (odds ratio [OR] = 0.58), quantities of patients transfused (OR = 0.43), respiratory infections (OR = 0.41), need for inotropes (OR = 0.48), duration of ventilation (weighted mean difference [WMD] of 3.4 hours), ICU LOS (WMD of 0.3 day), and hospital LOS (WMD of 1.0 days). Changes in neurocognitive dysfunction were not different in the immediate postoperative period; they were altogether significantly improved at 2 to 6 months (OR = 0.57), yet there were no differences seen at 12 months (Kaplan, 2018).

A working group of the AHA Council on Cardiovascular Surgery and Anesthesia concluded that OPCAB presumably was related with less bleeding, less renal dysfunction, less short term neurocognitive dysfunction (especially in patients with calcified aortas), and shorter hospital LOS. However, they likewise saw that it is more technically demanding, has a greater learning curve, and might be related with lower rates of long-term graft patency. Perhaps related to the greater technical demands, surgeons appear to place fewer grafts compared with on-pump CABG, and incomplete revascularization may influence long-term result. Puskas and colleagues reviewed 12,812 patients with CABG (1997–2006) and compared in-hospital major adverse events and long-term survival after OPCAB versus on-pump CABG. Long-term (10-year follow-up) results did not differ significantly between on-pump and off-pump patients. OPCAB was associated with significant reductions in short-term outcomes such as operative mortality, stroke, and major adverse cardiac events. Further information examination showed that short-term outcome (i.e., operative mortality rate) did not differ between the two groups for patients at low risk (i.e., The Society of Thoracic Surgeons [STS] predicted risk of death), whereas lower mortality rates were found for OPCAB surgery in high-risk patients (Kaplan, 2018).

Perioperative medication

In patients experiencing from coronary artery disease (CAD), perioperative utilization of b-blocking agents has been shown to be the most effective preventive measure. Possible advantage has been obtained with a2-agonists such as clonidine. Preoperative therapy of patients scheduled for coronary revascularization is maintained and included in the premedication. During the operation, a short-acting selective b1-blocker like esmolol, given as repeated bolus or continuous infusion, is effective in lowering excessive heart rate. However, it might seriously reduce LV function, as measured by a 42% decrease in mean arterial pressure and a 35% drop in cardiac output, resulting in a decrease in SvO2 from 81 to 65%. This LV depression leads to an increase in the pulmonary arterial pressure (PAP), whereas right intraventricular pressure might already be elevated because of right outflow tract compression or sudden mitral regurgitation (Chassot *et al.*, 2004).

A calcium antagonist such as diltiazem may have some theoretical advantages over b-blockers in the intraoperative period. It has been shown that, for the same decrease in heart rate, diltiazem lowers PAP, **though** esmolol tends to increase it. In addition to reducing AV conduction and heart rate as b-blockers do, calcium antagonists offer the advantage of inducing vasodilation in arterial conduits. Moreover, as an increase in intracellular free calcium is one of the primary causes of reperfusion injury and post ischemic myocardial dysfunction, calcium antagonists might prevent some post-ischaemic lesions. Some centers administer a continuous infusion of diltiazem (0.1 mg kg±1 h±1) from incision to chest closure. However, there is no objective evidence that calcium antagonists may improve outcome in OPCAB surgery.[2] Magnesium ions, up to 20 mmol in the form of chloride or sulphate, act similarly on myocardial cells; the only side effect is a slight arterial vasodilation. Moreover, its use during cardiac surgery tends to decrease the incidence of atrial tachycardia. Some centers recommend the use of MgCl2 or MgSO4 before pericardial opening (Chassot *et al.*, 2004).

In spite of the fact that progressions in cardiac surgery have remarkably reduced the incidences of mortality and serious complications, effective medication is needed to benefit patients going through cardiac surgery. Several studies have revealed that dexmedetomidine may have beneficial effects on clinical outcomes in patients with

cardiac surgery (Wang *et al.*, 2018). Dexmedetomidine, a potent a2 agonist decreases the sympathoadrenal activity leading to stability in heart rate and blood pressure. Its central CNS stimulation of parasympathetic outflow and inhibition of sympathetic outflow from locus coeruleus in the brainstem plays a prominent role in sedation and anxiolysis (V., S.R. and Adoni, 2018).

Dexmedetomidine treatment results in a sympathetic blockade, as it influences the α2-receptors in the central nervous system, restrains the release of the central sympathetic neurotransmitter (predominantly norepinephrine), reduces the peripheral sympathetic nervous tension and simultaneously excites the vagus nerve to reduce the heart rate (Ren *et al.*, 2013). When the heart rate decreases, the post-surgical cardiac oxygen demand also decreases, thus facilitating the maintenance of the myocardial oxygen supply and demand balance. In this manner, these effects not only protect the ischemic myocardium prior to grafting, , yet in addition decrease the post-surgical incidence of myocardial injury (Ren *et al.*, 2013).

Strong supportive evidence is found by pooling data from qualified RCTs, the utilization of dexmedetomidine led to significantly beneficial effects on systolic arterial pressure, mean arterial blood pressure, pulmonary artery mean pressure, and heart rate. A Meta analysis in 2018 also observed that administration of dexmedetomidine was related with a significant reduction in the duration of ICU stay and surgery, occurrence of postoperative delirium and the incidence of tachycardia (Wang *et al.*, 2018).

Dexmedetomidine is suggested to have sedative, anxiolytic, and analgesic abilities in patients undergoing cardiac surgery . In 2018 study, suggested that patients that were treated with dexmedetomidine had a lower heart rate, along with lower mean arterial blood pressure, systolic arterial pressure, pulmonary artery mean pressure, and reduced ICU stay than those in the control group (any treatment without dexmedetomidine). The occurrences of tachycardia, hypotension, and delirium decreased in the dexmedetomidine group, when compared to the control (any treatment without dexmedetomidine) group, demonstrating that patients who were treated with dexmedetomidine had lower risks of getting these events. Regarding bradycardia, the rate of this event was increased by about 3.4 times than those that did not ultilize dexmedetomidine. This suggested that the heart rates of patients using dexmedetomidine should be carefully monitored. Other unfavorable occasions including renal failure, stroke, pulmonary edema, and mortality were also compared, and the results did not suggest that there were any significant differences between dexmedetomidine and other medications or placebo, proving the safety of dexmedetomidine. Their findings also suggest that dexmedetomidine may not increase the incidence of hemodynamic complication (Wang *et al.*, 2018). Other investigation in 2018 concluded dexmedetomidine enabling smooth extubation with significant reduction in cough, breath holding and laryngospasm. Dexmedetomidine also provide adequate sedation in the post-operative period without causing respiratory depression (V., S.R. and Adoni, 2018).

Conclusion

Perioperative administration of Dexmedetomidine is an effective adjuvant to general anaesthesia, attenuates the stress response to intubation, provides minimal heart rate variations in hemodynamic parameters in OPCAB intraoperatively and enabling smooth extubation, also provides adequate sedation in the post-operative period.

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