Acta Anaesth. Bel., 2022, 73 | Suppl. 1: *135-139*

Master thesis | Original study

The effect of perioperative use of dexmedetomidine on time to extubation and ICU stay after coronary artery bypass graft surgery: a single-center retrospective cohort study

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Abstract

Background: **Dexmedetomidine plays an important role in postoperative respiratory weaning after cardiac surgery due to its sedative and analgesic properties without causing respiratory depression.**
Objectives: **To evaluate if dexmedetomidine could shorten postoperative ventilation time, ICU stay (primary outcomes) and total hospital stay (secondary outcome).**
Methods: **All patients who underwent elective CABG surgery**
between January 1st 2019 and March 3rd 2021 in AZ Sint-Jan, Bruges, Belgium were included in this retrospective single-center study. 175 of them received dexmedetomidine perioperative, opposed to 248 patients who did not.
Results: **When looking at the postoperative length of ICU stay, no significant difference could be detected between the dexmedetomidine and non-dexmedetomidine group (median of 2 days, CI95% [2 - 3] vs 2 days CI95% [2-3] respectively; p= 0,5462). No difference in postoperative hospital stay could be detected between the dexmedetomidine and non-dexmedetomidine group either (median of 7 days, CI95% [7 - 8] vs 7 days, CI95% [7 - 7] respectively; p=0,4731). Time to extubation was significantly lower in the group with perioperative dexmedetomidine administration in comparison to those who did not receive dexmedetomidine during surgery (mean of 375 minutes; CI95% [332 - 418] vs 487 minutes; CI95% [420 - 555] respectively; p=0,0059).**
Conclusion: **Dexmedetomidine can play an important role in postoperative respiratory weaning after elective CABG surgery by reducing the postoperative mechanical ventilation time. No effect on ICU stay and total length of hospital stay could be detected.**

Keywords (MeSH): **dexmedetomidine, coronary artery bypass, weaning, Intensive Care Units.**

Introduction

Fast-track protocols after cardiac surgery have been used for some time now and have been proven to shorten the time of postoperative mechanical ventilation and ICU stay, reducing healthcare-associated costs with risks of mortality and major postoperative complications similar to those of conventional care[1,2].

Dexmedetomidine plays an important role in postoperative respiratory weaning due to its sedative and analgesic properties without causing respiratory depression. After initiation of dexmedetomidine, other sedatives and/or analgesics that cause respiratory depression (such as opiates) can often be reduced or discontinued which could in turn facilitate the respiratory weaning process.

Besides the beneficial effect of dexmedetomidine on postoperative respiratory weaning, it has some other useful effects. Postoperative infusion of dexmedetomidine may reduce myocardial

Approval granted by the ethics committee of AZ Sint-Jan Bruges, Ruddershove 10, 8000 Bruges, Belgium. Internal reference number: 2867. Date of approval: 21st of May 2021. Chairman: Vanopdenbosch L., MD PhD.

reperfusion injury after cardiopulmonary bypass and a positive effect on postoperative delirium has been demonstrated by multiple meta-analyses when being compared to a propofol sedation[3-7].
Furthermore, dexmedetomidine is a promising drug to reduce the incidence of acute kidney injury after cardiac surgery[8,9].
Known side effects of dexmedetomidine are bradycardia and hypotension. This is more common when a loading dose is administered or when high infusion rates (>0.7 µg/kg/h) are maintained[10].

The use of dexmedetomidine in AZ Sint-Jan, Bruges during cardiac surgery was introduced in 2018 with primary intent to reduce the dosage of opiates used during and after cardiac surgery.
This study was designed to evaluate if the addition of dexmedetomidine during cardiac surgery could shorten postoperative ventilation time, ICU stay (primary outcomes) and total hospital stay (secondary outcome).

Methods

Approval to perform this retrospective non-interventional cohort study was granted by the ethics committee of AZ Sint-Jan Bruges on 21st of May 2021 by chairman Vanopdenbosch Ludo, MD PhD. Internal reference number for this study is 2867. All patient data was anonymized after collection.

All patients who underwent elective cardiac surgery in AZ Sint-Jan, Bruges, Belgium between January 1st 2019 and March 3rd 2021 were identified in the hospital records database. This came down to a number of 586 patients in total. All patients who had concomitant surgery (e.g. valve repair, electrical isolation of the pulmonary veins, carotid endarterectomy, closure of a patent foramen ovale, …) were excluded from this study. This was applicable for 155 patients.

After data extraction for these 433 patients, another 10 patients had to be excluded for missing essential data (see Figure 1).

In 175 of the remaining 423 patients, a dexmedetomidine infusion was found to be started after induction of anaesthesia.

The other 248 patients did not receive any dexmedetomidine perioperative (see Figure 2). Whether or not dexmedetomidine was added to the standard anesthesia protocol (see below), was related to the anesthesiologist who performed the anesthesia. In total, nine different anesthesiologists performed the anesthesia for all included patients. Five of them never used dexmedetomidine, while the other four always used it. Thus, the use of dexmedetomidine was not affected by the surgeon, patient co-morbidity or any other patient-related factors.

For induction and maintenance of anesthesia, a standard protocol was followed: a combination of etomidate (0.1-0.2 mg/kg), midazolam (1-5 mg), sufentanil (50-100 mcg) and cisatracurium (0.1-0.2 mg/kg) was administered in bolus for all patients after which endotracheal intubation was performed.

For maintenance of anesthesia: propofol and remifentanil were initiated in continuous infusion after induction of anesthesia. The additional infusion of dexmedetomidine (if used) was started after placement of the central venous catheter at an infusion rate of 0.5 to 0.7 µg/kg/h and was continued throughout the whole operation until extubation on the ICU. No patients received a loading dose of dexmedetomidine.

Dosage of perioperative propofol sedation was titrated using Bispectral Index (BIS) monitoring.

Continuous infusion of cisatracurium at a rate of 0.15 mg/kg/h was used in all patients. This infusion was stopped after cessation of the cardiopulmonary bypass. Infusions of propofol and remifentanil were continued postoperative until the start of respiratory weaning on the ICU.

All surgeries were performed with the use of a cardiopulmonary bypass, surgical access was through median full sternotomy for all patients.

For respiratory weaning in the ICU, a fast-track protocol was maintained. Respiratory weaning from the ventilator was started after arrival on the ICU

Fig. 1 — Data collection.

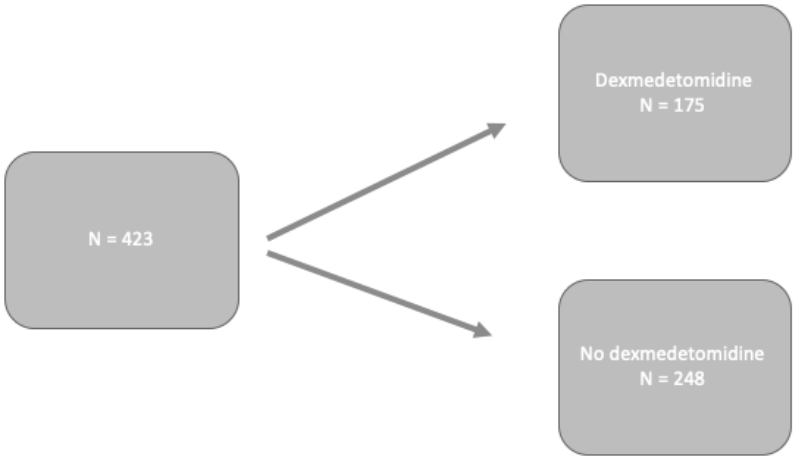

Fig. 2 — Overview of cohort size.

if patient temperature was above 36°C, no signs of significant postoperative bleeding or hemodynamic instability could be detected and adequate oxygenation was achieved. Propofol sedation was decreased and remifentanil discontinued. Dexmedetomidine (if used) was continued until extubation of the patient.

An intravenous loading dose of 5 mg piritramide in combination with an intramuscular dose of 5 to 10 mg of piritramide was administered, depending on the patient's weight, age and sex.

Following demographic data were collected for every included patient: age, gender and Body Mass Index (BMI).

ICU stay was measured in whole days, the date of surgery was counted as day zero (D0).

Postoperative hospital stay was measured in whole days and counting started from the operation date until discharge from hospital, this consequently included the whole ICU stay.

Time to extubation was measured in minutes and counting started from arrival on the ICU until the endotracheal tube was removed, which was registered by the ICU nurse.

Statistical analysis was performed using JMP pro 15.

Depending on the calculation of equal or unequal variances, a two-sample t-test or a Welch's-test was used respectively.

Confidence intervals of 95% (CI95%) and an alpha level of 0.05 were used for all statistical tests. All p-values represent two-tailed tests.

Results

The demographics of the two groups were homogeneous: no significant differences in age, gender or BMI could be detected (see Table I).

When looking at the postoperative length of ICU stay, no significant difference could be detected between the dexmedetomidine and non-dexmedetomidine group (median of 2 days, CI95% [2 - 3] vs 3 days CI95% [2 - 3] respectively; p= 0,5462) (see Table II).

No difference in postoperative hospital stay could be detected between the dexmedetomidine and non-dexmedetomidine group either (median of 7 days, CI95% [7 - 8] vs 7 days, CI95% [7 - 7] respectively; p=0,4731) (see Table II).

Time to extubation was significantly lower in the group with perioperative dexmedetomidine administration in comparison to those who did not receive dexmedetomidine during surgery (mean of 375 minutes; CI95% [332 - 418] vs 487 minutes; CI95% [420 - 555] respectively; p=0,0059) (see Table II).

In both groups, two patients died within 30 days after surgery (1,14% for the dexmedetomidine group and 0,81% for the group without dexmedetomidine).

Discussion

Dexmedetomidine can facilitate extubation in the ICU in patients who had proven difficult to wean due

Table I. — Demographics of the study population.

	Dexmedetomidine	No dexmedetomidine
Number of patients (n)	175	248
Mean age (years) [CI95%]	71,2 [69,9 - 72,5]	70,2 [69,0 - 71,4]
Male/female (%)	81,1/18,9	83,9/16,1
Mean BMI (kg/m2) [CI95%]	27,55 [26,97 - 28,13]	28,57 [28,05 - 29,09]

Table II. — Overview of study results.

	Dexmedetomidine	No dexmedetomidine	P-value
Median ICU stay (days) [CI95%]	2 [2 - 3]	2 [2 - 3]	0,5462
Median postoperative hospital stay (days) [CI95%]	7 [7 - 8]	7 [7 - 7]	0,4731
Mean postoperative ventilation time (minutes) [CI95%]	375 [332 - 418]	487 [420 - 555]	0,0059

to agitation. However, its significance for reducing the time of postoperative mechanical ventilation after cardiac surgery remains controversial.

Only few randomized controlled trials (RCT's) treat dexmedetomidine as an additional sedative agent and compare them to a control group who receive normal saline. In contrast, a lot of studies compare dexmedetomidine with a midazolam, morphine, remifentanil, propofol sedation or a combination of these drugs.

Many RCT's focus on postoperative delirium as a primary outcome while mechanical ventilation time, duration of ICU stay and total hospital stay are secondary outcomes.

One RCT comparing dexmedetomidine as an additional sedative perioperatively to a placebo control group, found no effect on extubation time after cardiac surgery[11].In this study however, a loading dose of dexmedetomidine was used, only patients undergoing cardiac valve surgery were included and sample size was relatively small (sixty patients in total).

In a more recent RCT with a bigger sample size (thee hundred and eight patients), dexmedetomidine or normal saline infusion was started after chest closure and continued for ten hours postoperative in the ICU[12].No significant effect on duration of mechanical ventilation, ICU stay or total length of hospital stay could be detected.

Another RCT with a sample size of two hundred eighty-five patients in total, compared dexmedetomidine with a placebo control group[13]. This study did show a significantly shorter duration of postoperative mechanical ventilation after cardiac surgery. Also, the fraction of patients who were extubated in the first 24 hours postoperative was much higher in the dexmedetomidine group versus the placebo control group (95% vs 85% respectively). No difference in postoperative hospital stay and total length of hospital stay could be detected in this study either.

It is worth mentioning that the type of cardiac surgery performed is also an important factor. One meta-analysis of four RCT's compared dexmedetomidine to a propofol sedation after cardiac surgery[5]. Subgroup analysis showed that faster extubation was only achieved in the patients who received CABG surgery but no significant statistical difference in the duration of mechanical ventilation could be detected in the patients who received valve or mixed cardiac surgery. This could be explained by the fact that patients undergoing valve or mixed cardiac surgery are generally less fit and have more postoperative complications when compared to patients undergoing CABG surgery, thus slowing or delaying the respiratory weaning process[14-16].

This study has some major limitations. No data on patient comorbidity (e.g. left ventricular ejection fraction, diabetes, previous surgery, …) was collected, leaving no possibility to detect any possible confounders that may have influenced the study results.

No data on the continuation of the dexmedetomidine infusion after extubation of the patient was collected, this could have potentially influenced the duration of ICU and total length of hospital stay. Also, no data on dosages of peri-en postoperative sedation with propofol and/or remifentanil was collected.

Furthermore, because of the study design (retrospective cohort study) the grade of evidence remains low when compared to a prospective trial.

Conclusion

This retrospective study showed that the perioperative use of dexmedetomidine can reduce the mechanical ventilation time after elective CABG surgery. Complications associated with mechanical ventilation may possibly be reduced and this could be beneficial to the overall outcome of the patients. This strengthens the belief that dexmedetomidine is a valuable drug in fast-track protocols after cardiac surgery.

No effect on ICU stay and total length of hospital stay could be detected.

More RCT's or meta-analyses comparing dexmedetomidine to a placebo control group after cardiac surgery are required to assess the effect on

postoperative mechanical ventilation time, ICU stay, total hospital stay and outcome factors after cardiac surgery.

Acknowledgements and conflicts of interest: No conflicts of interest to be declared.

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doi.org/10.56126/73.S1.26