UC Davis

UC Davis Previously Published Works

Title

The Effect of Dexmedetomidine on Outcomes of Cardiac Surgery in Elderly Patients

Permalink

https://escholarship.org/uc/item/015237zd

Journal

Journal of Cardiothoracic and Vascular Anesthesia, 30(6)

ISSN

1053-0770

Authors

Cheng, Hao
Li, Zhongmin
Young, Nilas
et al.

Publication Date

2016-12-01

DOI

10.1053/j.jvca.2016.02.026

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

The Effect of Dexmedetomidine on Outcomes of Cardiac Surgery in Elderly Patients

Hao Cheng, MD,*† Zhongmin Li, PhD,‡ Nilas Young, MD,§ Douglas Boyd, MD,§ Zane Atkins, MD,§ Fuhai Ji, MD,* and Hong Liu, MD†

Objective: **The goal of this retrospective study was to investigate the effects of perioperative use of dexmedetomidine (Dex) on outcomes for older patients undergoing cardiac surgery.**

Design: **Retrospective investigation.**

Setting: **Patients from a single tertiary medical center.**

Participants: **A total of 505 patients (≥65 years old) who underwent coronary artery bypass graft (CABG) or valve surgery. CABG and/or valve surgery plus other procedures were divided into 2 groups: 283 received intravenous Dex infusion (Dex group) and 222 did not (Non-Dex group).**

Interventions: **Perioperative Dex intravenous infusion (0.24 to 0.6 μg/kg/h) initiated after cardiopulmonary bypass and continued for <24 hours postoperatively in the ICU.**

Measurements and Main Results: **Data were risk adjusted, propensity score weighted, and multivariate logistic regression was used. The primary outcome was mortality. Secondary outcomes included postoperative stroke, coma, myocardial infarction, heart block, cardiac arrest, delirium, renal failure, and sepsis. Perioperative Dex infusion significantly decreased in-hospital mortality (0.90% *v* 2.83%; adjusted odds ratio (OR), 0.099; 95% confidence interval (CI), 0.030-0.324; p = 0.004) and operative mortality (1.35% *v* 3.18%; adjusted OR, 0.251; 95% CI, 0.077-0.813; p = 0.021). Perioperative Dex treatment also reduced the risk of stroke (0.90% *v* 1.77%; adjusted OR, 0.15; 95% CI, 0.038-0.590; p = 0.007), and delirium (7.21% *v* 10.95%; adjusted OR, 0.35; 95% CI, 0.212-0.578; p < 0.0001).**

Conclusions: **Results from this study (ClinicalTrials.gov identifier: NCT01683448) suggested perioperative use of dexmedetomidine was associated with decreases in in-hospital and operative mortality in elderly patients following cardiac surgery. It also reduced incidences of postoperative stroke and delirium in elderly patients.**

© ***2016 Elsevier Inc. All rights reserved.***

KEY WORDS: dexmedetomidine, elderly cardiac surgery, outcome operative mortality, hospital mortality

INTRODUCTION

Cardiovascular disease is the most common cause of death in the elderly population. With the advancement of technology, cardiac surgery is feasible in elderly patients with acceptable risks. Currently, more than 67% of patients presenting for cardiac surgery are older than 65 years and have increased comorbidities.[1] Cardiovascular, pulmonary, and renal diseases are more common and contribute to greater perioperative complications, and this may influence perioperative outcomes in patients with advanced age.[2] Elderly high-risk patients usually require prolonged intensive care unit (ICU) stays and are at an increased risk for mortality and morbidity.[3-5] It is well known that surgical stress and cardiopulmonary bypass (CPB) can increase plasma levels of norepinephrine and epinephrine. Dexmedetomidine (Dex) is a highly selective α_2-adrenergic agonist that strongly modulates the activity of the sympathetic nervous system by binding to the α_2-receptors present in both the central and peripheral nervous systems and inhibiting the release of norepinephrine, thus modulating sympathetic activity.[6,7] Because of this, Dex has been used extensively in the ICU as a sedative and during surgery as an adjuvant anesthetic to attenuate perioperative hemodynamic abnormalities. Multiple studies have demonstrated that Dex has a protective effect on the heart, brain, and kidneys.[8-11] It was associated with decreased mortality, time to extubation, and hospital length of stay (LOS) in cardiac surgical patients.[12-15] The authors previously have published a study describing the effects of Dex on outcomes of patients undergoing cardiac surgery.[12] In that study, Dex reduced in-hospital, 30-day, and 1-year mortality and decreased the incidences of postoperative complications and delirium. Portions of these data also were used in the study published in the *Journal of Cardiothoracic and Vascular Anesthesia,* which found that Dex infusion during coronary artery bypass graft (CABG) surgery was more likely to achieve improved in-hospital, 30- day, and 1-year survival rates, and a significantly lower incidence of delirium.[15] The authors now report the results of another study using the same database. The aim of this subanalysis was to investigate the effects of perioperative use of Dex on outcomes for older patients undergoing cardiac surgery.

METHODS

Study Design

After obtaining local Institutional Review Board approval, all patients (≥65 years old) who underwent cardiac surgery with CPB at the UC Davis Medical Center from January 1, 2006 to December 31, 2011 were entered into the study. This study was a single-center, retrospective cohort study involving 561 consecutive patients. Patients in this study met the

*From the Departments of *Anesthesiology, First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China, †Anesthesiology and Pain Medicine, University of California Davis Health System, Sacramento, CA, ‡Internal Medicine, University of California Davis Health System, Sacramento, CA; and §Surgery, University of California Davis Health System, Sacramento, CA.*

Funding: *This work was supported by the Department of Anesthesiology and Pain Medicine, the Department of Surgery, and the Department of Internal Medicine of University of California Davis Health System and NIH grant UL1 TR000002 of the University of California Davis Health System. This work also was supported by grants from the National Natural Science Foundation of China NO 81471835 and NO 81471889.*

Address reprint requests to Hong Liu, MD, Department of Anesthesiology and Pain Medicine, University of California Davis Health System, 4150 V Street, Suite 1200, Sacramento, CA 95817. E-mail: hualiu@ucdavis.edu

© *2016 Elsevier Inc. All rights reserved.*

1053-0770/2601-0001$36.00/0
http://dx.doi.org/10.1053/j.jvca.2016.02.026

ARTICLE IN PRESS

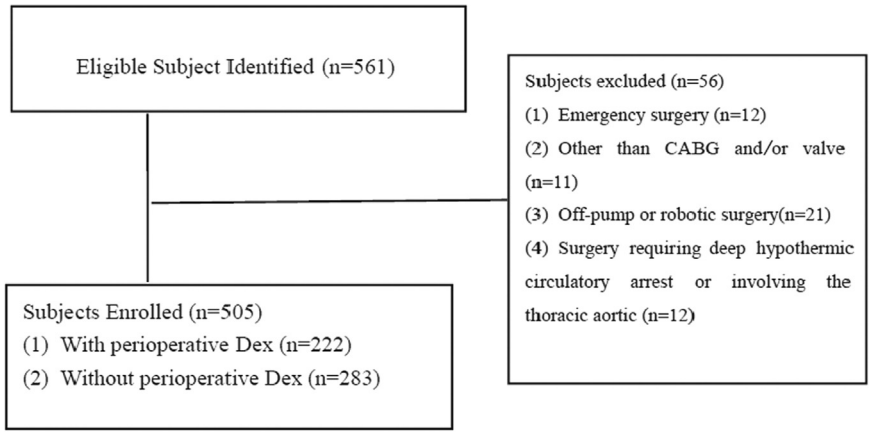


Fig 1. Study population recruitment summary. Abbreviations: Dex, dexmedetomidine; CABG, coronary artery bypass graft.

following criteria: CABG or valve surgery, or CABG or valve surgery combined with other procedures (Maze operation). Patients excluded from this study were those undergoing emergency surgery, off-pump or robotic surgery, surgery demanding deep hypothermic circulatory arrest, or surgery involving the thoracic aorta (Fig 1). A total of 505 patients met the inclusion criteria and were divided into 2 groups: those who used Dex (Dex group; n = 283, 56.04%) and those who did not use Dex (Non-Dex group; n = 222, 43.96%) in surgery (Fig 1).

Data Collection

The patient data were collected and organized following the template of the Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database and the hospital medical records, which included demographics, patient past medical and surgical histories, preoperative risk factors, preoperative medications, intraoperative data, postoperative stroke, coma, myocardial infarction (MI), heart block, cardiac arrest, acute renal failure, dialysis required, and in-hospital, operative, and 1-year all-cause mortality. Data were collected independently as part of the STS database on each patient during the course of the hospitalization. After routine monitoring, general anesthesia was induced with midazolam, lidocaine, propofol or etomidate, fentanyl, and rocuronium, maintained with sevoflurane. Ventilation with 50% oxygen in air was controlled to an end-tidal CO_2 of 35 to 45 mmHg by adjustment of tidal volume and respiratory rate. Arterial catheter, pulmonary artery catheter, and transesophageal echocardiography were used as hemodynamic and cardiac function monitoring after anesthesia induction. Perioperative Dex administration was defined as an intravenous infusion (0.24 to 0.6 μg/kg/h) initiated after CBP and continued for <24 hours postoperatively in the ICU. The infusion rate of Dex was adjusted according to the patients' hemodynamic changes in response to stimulation.

Major and Secondary Outcomes

Major outcomes of this study were in-hospital, operative, and 1-year mortality. Secondary outcomes included postoperative permanent or transient stroke, coma, MI, heart block, cardiac arrest, renal failure or new dialysis requirement, delirium, postoperative length of mechanical ventilation, length of ICU stay, LOS, and 30-day readmission. On the basis of the STS criteria, the following definitions were used. Permanent stroke was defined as a postoperative stroke (any confirmed neurologic deficit of abrupt onset caused by a disturbance in blood supply to the brain) that did not resolve within 24 hours. Transient ischemic attack was defined as a loss of neurologic function that was abrupt in onset but with complete return of function within 24 hours. The definition of coma was a new postoperative coma that persisted for at least 24 hours secondary to anoxic/ischemic or metabolic encephalopathy, thromboembolic event, or cerebral bleed. Cardiac arrest included one of the following: (a) ventricular fibrillation; (b) rapid ventricular tachycardia with hemodynamic instability; (c) asystole; (d) implantable cardioverter-defibrillator shocks. Heart block was defined as a new-onset block requiring the implantation of a permanent pacemaker of any type before discharge. The STS definition of postoperative renal failure was used to determine postoperative acute kidney injury (AKI). This definition included the highest Cr level recorded in the postoperative course that was $\geq$ 3-fold baseline Cr or Cr ≥ 4 with an acute increase of ≥ 0.5mg/dl or new requirement for postoperative dialysis. Finally, sepsis was defined as a systemic inflammatory response syndrome when at least two of the following criteria were present: hypothermia or hyperthermia (>38.5 or $<36.0^{\circ}$C), tachycardia or bradycardia, tachypnea, leukocytosis or leukopenia, or thrombocytopenia. Delirium was defined as illusions, confusion, and cerebral excitement during hospital stay and having a comparatively short course. Any complication included all postoperative events occurring during the hospitalization, including the entire postoperative period up to discharge, even if >30 days.

Statistical Methods

Continuous variables were assessed as mean ± standard deviation and compared by use of the *t*-test; categorical variables were reported as percentages and compared by use of the χ^2 test (2-tailed). Univariate and multivariate logistic regressions were performed to evaluate the associations of demographic, therapeutic, and clinical outcome variables. To decrease selection bias in patients who received Dex administration, the authors computed the propensity score, that is, the

ARTICLE IN PRESS

conditional probability of each patient receiving Dex, with a multivariable logistic regression model that included patient demographic and clinical risk factors (Table 1).

The multivariate model analysis used to assess any complication included Dex use, age, gender, status of the procedure, smoking, chronic lung disease, cerebrovascular disease, peripheral vascular disease, family history of coronary artery disease (CAD), dyslipidemia, hypertension, MI, congestive heart failure, surgery type, and perfusion time. The multivariate model assessing delirium included Dex use, age, gender, body mass index (BMI), cerebrovascular disease, family history of CAD, dyslipidemia, ejection fraction, and surgery type. The multivariate model used to assess stroke included Dex use and surgery types. The multivariate model used to assess in-hospital mortality included Dex use and surgery types. The multivariate model used to assess operative mortality included Dex use and status of the procedure (urgent *v* elective). The multivariate model used to assess 1-year mortality included Dex use, age, status of the procedure, chronic lung disease, diabetes, MI, renal failure, last creatinine level, dyslipidemia, intra-aortic balloon pump (IABP), and perfusion time.

Table 1. Demographic and Clinical Characteristics.

Characteristics	Dex (N = 222)	Non-Dex (N = 283)	p value
Age, year	73.6 (6.1)	73.5 (6.2)	0.798
Female sex, n (%)	71 (32.0)	87 (30.7)	0.766
BMI, mean (SD)	28.3 (5.7)	29.7 (7.3)	0.020
Non-white race, n (%)	57 (25.7)	64 (22.6)	0.424
Past medical history, n (%)			
Smoking	24 (10.8)	43 (15.2)	0.150
Chronic lung disease	36 (16.2)	50 (17.7)	0.667
Cerebrovascular disease	48 (21.6)	84 (29.7)	0.041
Peripheral vascular disease	48 (21.6)	43 (15.2)	0.062
Family history of CAD	41 (18.5)	69(24.4)	0.110
Diabetes mellitus	70 (31.5)	90 (31.8)	0.948
Hypertension	176 (79.3)	224 (79.2)	0.972
Dyslipidemia	147 (66.2)	155 (54.8)	0.009
History of renal failure	10 (4.5)	2 (0.7)	0.005
Preoperative myocardial infarction	67 (30.2)	102 (36.0)	0.166
CHF	85 (38.3)	19 (6.7)	<0.0001
EF %	52.8 (12.6)	51.0 (13.2)	0.119
Preoperative last creatinine level	1.18 (0.66)	1.11 (0.53)	0.159
Preoperative medication, n (%)			
ACEI	106 (47.8)	154 (54.4)	0.137
β-blockers	147 (66.2)	183 (64.7)	0.716
ADP Inhibitor	16 (7.2)	24 (8.5)	0.599
Nitrates	7 (3.2)	9 (3.2)	0.986
Anticoagulants	43 (19.4)	75 (26.5)	0.060
Coumadin	20 (9.0)	30 (10.6)	0.552
Inotropes	1 (0.5)	2 (0.7)	0.710
Steroids	5 (2.3)	12 (4.2)	0.219
Aspirin	179 (80.6)	225 (79.5)	0.754
Lipid lowering	148 (66.7)	160 (56.5)	0.021
Glycoprotein IIb/IIIa inhibitor	7 (3.2)	16 (5.7)	0.181
Propensity score	0.611 (0.256)	0.305 (0.197)	<0.0001

NOTE. Values are n (%) for categorical variables and mean ± SD for continuous variables.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ADP, adenosine diphosphate; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; Dex, dexmedetomidine; EF, ejection fraction; SD, standard deviation.

To achieve model parsimony and stability, the backward selection procedure was applied, with a dropout criterion of $p > 0.1$. The candidate risk factors were selected on the basis of the literature reviews, clinical possibility, and variables collected in the database. The candidate independent variables included age, sex, race, status of the procedure, BMI, creatinine level, smoking, chronic lung disease, cerebrovascular disease (CVD), peripheral vascular disease (PVD), family history of CAD, diabetes mellitus, hypertension, hypercholesterolemia, dyslipidemia, renal failure, MI, congestive heart failure, IABP, β-blockers, nitrates, angiotensin-converting enzyme inhibitors (ACEI), adenosine diphosphate (ADP) inhibitors, glycoprotein IIb/IIIa inhibitors, coumadin, inotropes, aspirin, lipid-lowering drugs, surgery type, ejection fraction, perfusion time, cross-clamp time, and year of surgery. The parsimonious multivariable propensity model for Dex infusion included emergency status of patients, preoperative CVD, preoperative PVD, preoperative dyslipidemia, preoperative congestive heart failure, surgery type, and year of surgery (Fig 2). Then the authors created a propensity-weighted logistic regression model for 1-year mortality, The C statistic was reported as a measure of predictive power. The authors compared the propensity-weighted and risk-adjusted 1-year mortality between the cohort with Dex use and with no Dex use. The results are reported as percentages and odds ratios (OR) with corresponding 95% confidence intervals (CI). A parsimonious Cox proportional hazards model was created to estimate the effect of Dex for 1-year survival. All reported p values were 2-tailed, and values of $p < 0.05$ were considered to be statistically significant. All statistical analyses were performed with SAS version 9.3 for Windows (SAS Institute, Cary, NC).

RESULTS

Baseline and Intraoperative Parameters

The demographic and clinical data are presented in Table 1. There were no significant differences between the two groups with respect to age, sex, race, medical history (smoking, chronic lung disease, PVD, family history of CAD, diabetes mellitus, hypertension, MI, ejection fraction, or last creatinine level) and preoperative medical therapy (ACEI, β-blockers, ADP inhibitors, nitrates, coumadin, inotropes, glycoprotein IIb/IIIa inhibitor, or aspirin). However, the patients in the Dex group presented with a greater incidence of renal failure (4.5% *v* 0.7%, $p = 0.005$), congestive heart failure (38.3% *v* 6.7%; $p < 0.0001$), dyslipidemia (66.2% *v* 54.8%; $p = 0.009$), and the use of lipid-lowering medications (66.7% *v* 56.5%; $p < 0.0001$). The patients in the Dex group presented with a lower BMI (28.3% *v* 29.7%; $p = 0.02$), less urgent surgery (45.5% *v* 58%, $p = 0.005$), and lower incidence of CVD (21.6% *v* 29.7%, $p = 0.041$).

Procedural Characteristics

In terms of surgery types, CABG only (45.5% *v* 53.4%, $p < 0.0001$) was less frequent and valve/valve + other (21.6%

ARTICLE IN PRESS

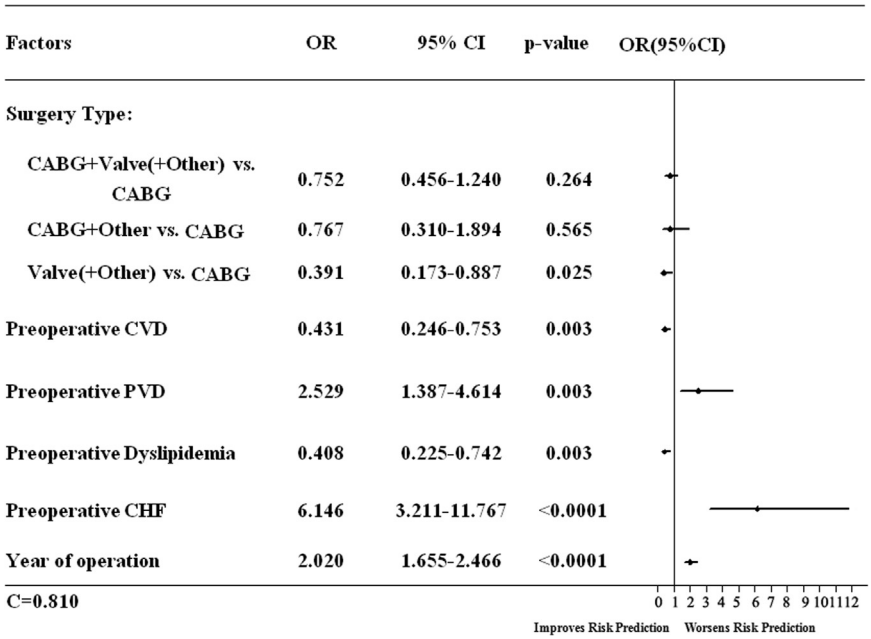


Fig 2. The Parsimonious multivariable propensity model for dexmedetomidine use. Abbreviations: CABG, coronary artery bypass graft; CVD, cerebrovascular disease; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; EF, ejection fraction; OR, odds ratio.

v 6.7%, $p < 0.0001$) were more frequent in the Dex group. CBP time (181.7 ± 61.2 *v* 203.7 ± 79.4 minutes; $p = 0.001$) and aortic cross-clamp time (129.2 ± 50.8 *v* 141.9 ± 58.9 minutes; $p = 0.009$) were significantly shorter and the incidence of perioperative IABP use (5% *v* 13.1%; $p = 0.002$) was significantly lower in the Dex group (Table 2).

Postoperative Complications and Mortality

Univariate analysis demonstrated that 11 out of the total of 505 patients (2.18%) died in the hospital, 12 patients (2.37%) died during surgery, and 39 patients (7.72%) died within 1 year. In-hospital, operative, and 1-year mortality were 0.9%, 1.35%, and 7.21%, respectively, in the Dex group and were 2.83%, 3.18%, and 8.13% in the Non-Dex group. Total length of ICU stay (142.5 ± 191.5 *v* 106.2 ± 132.8 hours, $p = 0.017$) was longer in the Dex group. Between the two groups, no differences were seen in the incidence of postoperative complications: MI, coma, heart block, cardiac arrest, delirium, renal failure, sepsis, ventilation time, or LOS, readmission within 30 days, in-hospital, operative, and 1-year mortality (Fig 3).

Table 2. Procedural Characteristics.

Characteristics	Dex (n=222)	Non-Dex (n=283)	p value
Perfusion time, min	181.7 (61.2)	203.7 (79.4)	0.001
Cross-clamp time, min	129.2 (50.8)	141.9 (58.9)	0.009
IABP used, n (%)	11 (5.0)	37 (13.1)	0.002
Surgery type, n (%)			
CABG only	101 (45.5)	151 (53.4)	<0.0001
CABG+valve+(other)	61 (27.5)	93 (32.9)	0.192
CABG+other	12 (5.4)	20 (7.1)	0.447
Valve+(valve+other)	48 (21.6)	19 (6.7)	<0.0001

NOTE. Values are n (%) for categorical variables and mean ± SD for continuous variables.

Abbreviations: CABG, coronary artery bypass graft; Dex, dexmedetomidine; IABP. intra-aortic balloon pump; SD, standard deviation.

Results of the multivariate analysis are summarized in Figure 3. The observed reduction in-hospital (adjusted OR, 0.099; 95% CI, 0.030-0.324; $p = 0.004$), operative (adjusted OR, 0.251; 95% CI, 0.077-0.813; $p = 0.021$) mortality in patients receiving Dex persisted after propensity adjustment. Postoperative delirium (adjusted OR, 0.350; 95% CI, 0.212-0.578; $p < 0.0001$) and stroke (adjusted OR, 0.15; 95% CI, 0.038-0.590; $p = 0.007$) also were decreased significantly in the Dex group. There were no statistical differences in the incidence of any complication (adjusted OR, 0.799; 95% CI, 0.606-1.055; $p = 0.113$), cardiac arrest (adjusted OR, 1.213; 95% CI, 0.280-5.261; $p = 0.796$), postoperative renal failure (adjusted OR, 1.356; 95% CI, 0.681-2.698; $p = 0.386$), or sepsis (adjusted OR, 2.509; 95% CI, 0.533-11.808; $p = 0.244$) between the groups after adjustment (Fig 3). Postoperative ventilation times (33.9 *v* 53.1 hours, $p = 0.046$) were shorter and total ICU times (153.4 *v* 103.0 hours, $p < 0.0001$) were longer after adjustment in the Dex group.

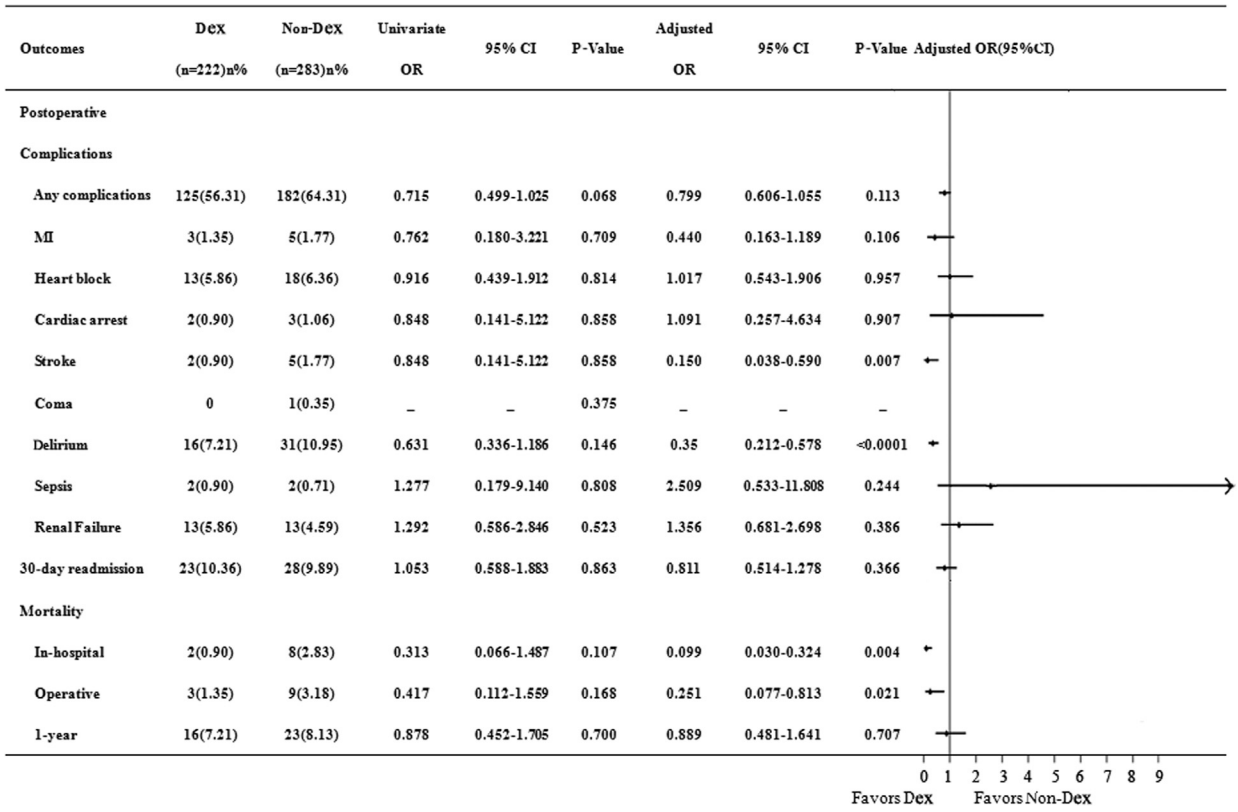
One-Year Mortality

After risk adjustment, a Cox proportional hazards model analysis revealed that older age, urgent surgery, preoperative last creatinine level, and perfusion time significantly increased the 1-year mortality; Dex was no longer a contributing factor for the 1-year survival rate (Fig 4).

DISCUSSION

This was a subanalysis using the data the authors used before[12] to investigate the effect of Dex on outcomes for the elderly cardiac surgery population. The current study found that perioperative Dex use significantly reduced in-hospital and

ARTICLE IN PRESS



Outcomes	Dex (n=222)n%	Non-Dex (n=283)n%	Univariate OR	95% CI	P-Value	Adjusted OR	95% CI	P-Value	Adjusted OR(95%CI)
Postoperative Complications									
Any complications	125(56.31)	182(64.31)	0.715	0.499-1.025	0.068	0.799	0.606-1.055	0.113	
MI	3(1.35)	5(1.77)	0.762	0.180-3.221	0.709	0.440	0.163-1.189	0.106	
Heart block	13(5.86)	18(6.36)	0.916	0.439-1.912	0.814	1.017	0.543-1.906	0.957	
Cardiac arrest	2(0.90)	3(1.06)	0.848	0.141-5.122	0.858	1.091	0.257-4.634	0.907	
Stroke	2(0.90)	5(1.77)	0.848	0.141-5.122	0.858	0.150	0.038-0.590	0.007	
Coma	0	1(0.35)	_	_	0.375	_	_	_	
Delirium	16(7.21)	31(10.95)	0.631	0.336-1.186	0.146	0.35	0.212-0.578	<0.0001	
Sepsis	2(0.90)	2(0.71)	1.277	0.179-9.140	0.808	2.509	0.533-11.808	0.244	
Renal Failure	13(5.86)	13(4.59)	1.292	0.586-2.846	0.523	1.356	0.681-2.698	0.386	
30-day readmission	23(10.36)	28(9.89)	1.053	0.588-1.883	0.863	0.811	0.514-1.278	0.366	
Mortality									
In-hospital	2(0.90)	8(2.83)	0.313	0.066-1.487	0.107	0.099	0.030-0.324	0.004	
Operative	3(1.35)	9(3.18)	0.417	0.112-1.559	0.168	0.251	0.077-0.813	0.021	
1-year	16(7.21)	23(8.13)	0.878	0.452-1.705	0.700	0.889	0.481-1.641	0.707	

Fig 3. The effects of dexmedetomidine on postoperative complications and mortality in patients undergoing cardiac surgery. NOTE. Values are numbers (percent) for categorical variables. Abbreviations: CI, confidence interval; Dex, dexmedetomidine; MI, myocardial infarction; OR, odds ratio.

operative mortality and was associated with improved early survival rates in elderly patients undergoing cardiac surgery. The authors' results further suggested that perioperative intravenous Dex was associated with a reduced incidence of postoperative stroke and delirium after cardiac surgery.

Perioperative Dex infusion may affect the mortality rates in elderly cardiac surgical patients. Age has been suggested as an independent risk factor for cardiac surgery outcomes.[12] Frilling and colleagues[16] found that in-hospital mortality in geriatric patients undergoing aortic valve replacement (AVR) was 2.56% in isolated valve replacement and 3.38% in patients who had additional bypass surgery. The authors' results revealed the in-hospital mortality (2.83%) and operative mortality (3.18%) in the Non-Dex group was similar to the previous reports (2%-4.4%).[12,16-18] However, in-hospital (0.9%) and operative mortality (1.35%) were significantly lower in patients who received Dex. The 1-year total mortality was 7.72%; that was similar to the other published study.[19] Barreto-Filho and colleagues found that 30-day and 1-year mortality were 3.5% and 9.9% in isolated AVR versus 5.1% and 12.3% in AVR with concomitant CABG, respectively.[19] The authors of this study found that although in-hospital and operative mortality rates were lower in the Dex group, there were no statistical differences in 1-year mortality (7.21% *v* 8.13%, $p = 0.878$) between the two groups. Dex was no longer a contributing factor in the Cox proportional hazards analysis as to the 1-year survival rate, which differed from the other study.[12,15] Thus, perioperative Dex use may be associated with an improved short-term survival rate but did not improve the 1-year survival rate in older cardiac surgical patients.

Stroke is a devastating complication following cardiac surgery and it has been reported that the prevalence of stroke was 1.6 to 5.25% among patients undergoing different cardiac surgeries.[3,20-22] Dex, a highly selective α_2-adrenoceptor agonist, provides sedation, sympatholysis, and analgesia without respiratory depression.[23] In the current study, Dex use decreased the incidence of postoperative stroke after risk adjustment. The exact cause of stroke after surgery is understood poorly. A preclinical study showed significant neurologic improvement in Dex-treated animals following stroke.[24] The neuroprotective effect of Dex was suggested to be mediated by activation of the α_{2A}-adrenergic receptor subtype that modulates neurotransmitter release in the central and peripheral sympathetic nervous systems.[9] Microembolization produced during CPB, O_2 supply/demand imbalance, and the systemic inflammatory response may be contributing factors.[9,25] Chi and colleagues suggested Dex could improve microregional O_2 supply/consumption balance and may have contributed to the decreased size of cortical infarction in the early stage of reperfusion in an animal study.[25]

Postoperative delirium is common among older patients undergoing cardiac surgery.[26,27] The incidence of postoperative delirium was reported to range from 30% to 55% in elderly patients undergoing cardiac surgery.[26,28-32] The authors of this study also

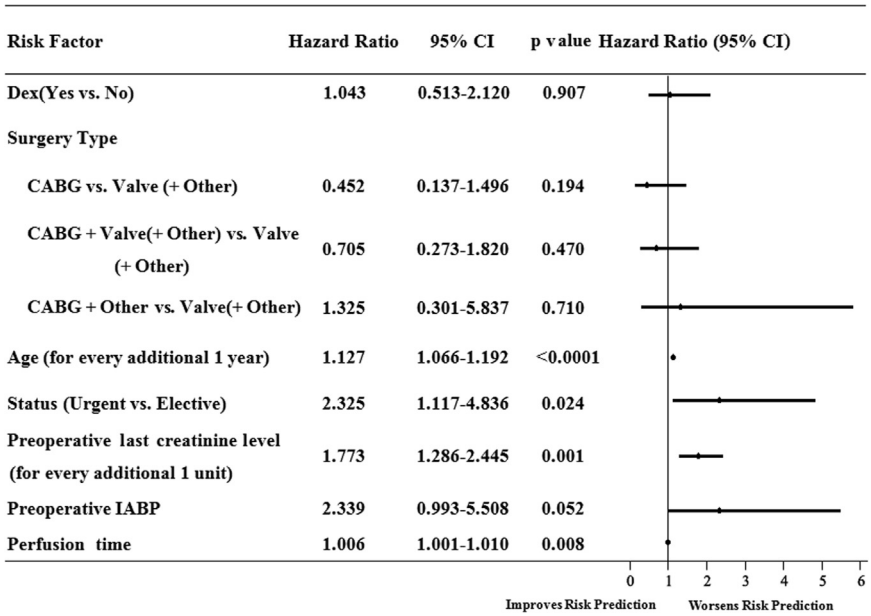


Fig 4. The Cox proportional hazards model for 1-year mortality after cardiac surgery in elderly patients. Abbreviations: CABG, coronary artery bypass graft; IABP, Intra-aortic balloon pump; CI, confidence interval.

found that those who received Dex had a significantly lower incidence of delirium after cardiac surgery. At the same time, the authors observed the prevalence of delirium in the present study was lower than most reported results.[26,28-31] The reason may have been that the authors included only patients with hyperactive delirium in this database; many patients with hypoactive delirium were therefore likely to be undetected. A study had shown that hypoactive delirium was the most common motor subtype in geriatric patients.[32] Pandharipande and colleagues found hyperactive delirium in no more than 1% of surgical ICU patients, whereas the majority of patients had hypoactive (64%) delirium in the postoperative period.[33] On the other hand, delirium assessment is somewhat subjective and may be susceptible to observational bias. A study showed that Dex could provide neurocognitive protection in an animal model.[34] In a retrospective cohort study, use of Dex was associated with a decrease in postoperative AKI,[11] particularly in patients with normal preoperative kidney function or mild chronic kidney disease.[10] However, the authors' data failed to show the relationship between the use of Dex and the reduction of AKI in the aged population.

In a randomized trial, Dex-treated patients spent less time on the ventilator.[35] A meta-analysis confirmed the results.[14] The mean postoperative time to extubation and length of hospital stay were shorter in the Dex group when compared with the propofol group, and Dex-based sedation resulted in achievement of early extubation more frequently than propofol-based sedation.[13] In this study, while durational mechanical ventilation was shorter in the Dex-treated patients, the ICU length of stay was longer; it was different from the other studies,[12,13,35] However the length of hospital stay did not differ between the two groups. The reason for the discrepancy in the results was unclear. Further studies to confirm this result are needed.

There were several limitations of this study. This was a single-center, observational cohort study. Multivariate regression in combination with propensity score adjustments were applied to this study population to reduce the bias; however, the potential confounding bias associated with a nonrandomized study remains. The sample size of this study was relatively small. Further prospective, multicenter, randomized, and controlled studies with a larger sample size are required to confirm the effects in this study.

CONCLUSIONS

The retrospective analysis demonstrated that elderly cardiac surgical patients who received Dex after CPB surgery had better in-hospital and operative survival rates. Perioperative use of Dex also was associated with significant decreases in the incidences of postoperative stroke and delirium. A prospective, randomized, multicenter study focused on the use of dexmedetomidine in elderly cardiac surgery patients is indicated to confirm these findings.

REFERENCES

1. Shehabi Y, Grant P, Wolfenden H, et al: Prevalence of delirium with dexmedetomidine compared with morphine based therapy after cardiac surgery: A randomized controlled trial (Dexmedetomidine Compared to Morphine-DEXCOM Study). Anesthesiology 111:1075-1084, 2009

2. Oresanya LB, Lyons WL, Finlayson E: Preoperative assessment of the older patient: A narrative review. J Am Med Assoc 311:2110-2120, 2014

3. Fruitman DS, MacDougall CE, Ross DB: Cardiac surgery in octogenarians: Can elderly patients benefit? Quality of life after cardiac surgery. Ann Thorac Surg 68:2129-2135, 1999

4. Sündermann S, Dademasch A, Praetorius J, et al: Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. Eur J Cardiothorac Surg 39:33-37, 2011

ARTICLE IN PRESS

5. Lee DH, Buth KJ, Martin BJ, et al: Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation 121:973-978, 2010

6. Gertler R, Brown HC, Mitchell DH, et al: Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent) 14: 13-21, 2001

7. Jalonen J, Hynynen M, Kuitunen A, et al: Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. Anesthesiology 86:331-345, 1997

8. Biccard BM, Goga S, de Beurs J: Dexmedetomidine and cardiac protection for non-cardiac surgery: A meta-analysis of randomised controlled trials. Anaesthesia 63:4-14, 2008

9. Ma D, Hossain M, Rajakumaraswamy N, et al: Dexmedetomidine produces its neuroprotective effect via the a2A-adrenoceptor subtype. Eur J Pharmacol 502:87-97, 2004

10. Ji F, Li Z, Young JN, et al: Post-bypass dexmedetomidine use and postoperative acute kidney injury in patients undergoing cardiac surgery with cardiopulmonary bypass. PLoS One 8:e77446, 2013

11. Balkanay OO, Goksedef D, Omeroglu SN, et al: The dose-related effects of Dexmedetomidine on renal functions and serum neutrophil gelatinase-associated lipocalin values after coronary artery bypass grafting: A randomized, triple-blind, placebo-controlled study. Interact Cardiovasc Thorac Surg 20:209-214, 2015

12. Ji F, Li Z, Nguyen H, et al: Perioperative dexmedetomidine improves outcomes of cardiac surgery. Circulation 127: 1576-1584, 2013

13. Curtis JA, Hollinger MK, Jain HB: Propofol-based versus dexmedetomidine-based sedation in cardiac surgery patients. J Cardiothorac Vasc Anesth 27:1289-1294, 2013

14. Lin YY, He B, Chen J, et al: Can dexmedetomidine be a safe and efficacious sedative agent in post-cardiac surgery patients? A meta-analysis. Crit Care 16:R169, 2012

15. Ji F, Li Z, Young N, et al: Perioperative dexmedetomidine improves mortality in patients undergoing coronary artery bypass surgery. J Cardiothorac Vasc Anesth 28:267-273, 2014

16. Frilling B, von Renteln-Kruse W, Riess FC: Evaluation of operative risk in elderly patients undergoing aortic valve replacement: The predictive value of operative risk scores. Cardiology 116:213-218, 2010

17. Ferguson TB Jr, Coombs LP, Peterson ED: Society of Thoracic Surgeons National Adult Cardiac Surgery Database. Preoperative beta-blocker use and mortality and morbidity following CABG surgery in North America. J Am Med Assoc 287:2221-2227, 2002

18. Bridgewater B: Almanac 2012-adult cardiac surgery: The national society journals presents elected research that has driven recent advances in clinical cardiology. Heart 98:1412-1417, 2012

19. Barreto-Filho JA, Wang Y, Dodson JA, et al: Trends in aortic valve replacement for elderly patients in the United States, 1999-2011. J Am Med Assoc 310:2078-2085, 2013

20. Tarakji KG, Sabik JF 3rd, Bhudia SK, et al: Temporal onset, risk factors, and outcomes associated with stroke after coronary artery bypass grafting. J Am Med Assoc 305:381-390, 2011

21. Whitlock R, Healey JS, Connolly SJ, et al: Predictors of early and late stroke following cardiac surgery. Can Med Assoc J 186: 905-911, 2014

22. Almassi GH, Sommers T, Moritz TE, et al: Stroke in cardiac surgical patients: Determinants and outcome. Ann Thorac Surg 68: 391-397, 1999

23. Hoy SM, Keating GM: Dexmedetomidine: A review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. Drugs 71:1481-1501, 2011

24. Sato K, Kimura T, Nishikawa T, et al: Neuroprotective effects of a combination of dexmedetomidine and hypothermia after incomplete cerebral ischemia in rats. Acta Anaesthesiol Scand 54:377-382, 2010

25. Chi OZ, Grayson J, Barsoum S, et al: Effects of dexmedetomidine on microregional O2 balance during reperfusion after focal cerebral ischemia. J Stroke Cerebrovasc Dis 24:163-170, 2015

26. Smulter N, Lingehall HC, Gustafson Y, et al: Delirium after cardiac surgery: Incidence and risk factors. Interact Cardiovasc Thorac Surg 17:790-796, 2013

27. Koster S, Hensens AG, Schuurmans MJ, et al: Risk factors of delirium after cardiac surgery: A systematic review. Eur J Cardiovasc Nurs 10:197-204, 2011

28. Burkhart CS, Dell-Kuster S, Gamberini M, et al: Modifiable and nonmodifiable risk factors for postoperative delirium after cardiac surgery with cardiopulmonary bypass. J Cardiothorac Vasc Anesth 24: 555-559, 2010

29. Rudolph JL, Inouye SK, Jones RN, et al: Delirium: An independent predictor of functional decline after cardiac surgery. J Am Geriatr Soc 58:643-649, 2010

30. Bakker RC, Osse RJ, Tulen JH, et al: Preoperative and operative predictors of delirium after cardiac surgery in elderly patients. Eur J Cardiothorac Surg 41:544-549, 2012

31. Rudolph JL, Jones RN, Levkoff SE, et al: Derivation and validation of a preoperative prediction rule for delirium after cardiac surgery. Circulation 119:229-236, 2009

32. Robinson TN, Raeburn CD, Tran ZV, et al: Motor subtypes of postoperative delirium in older adults. Arch Surg 146:295-300, 2011

33. Pandharipande P, Cotton BA, Shintani A, et al: Motoric subtypes of delirium in mechanically ventilated surgical and trauma intensive care unit patients. Intensive Care Med 33:1726-1731, 2007

34. Sanders RD, Xu J, Shu Y, et al: Dexmedetomidine attenuates isoflurane-induced neurocogitive impairment in neonatal rats. Anesthesiology 110:1077-1085, 2009

35. Riker RR, Shehabi Y, Bokesch PM, et al: Dexmedetomidine vs midazolam for sedation of critically ill patients. J Am Med Assoc 301: 489-499, 2009