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Journal

Journal of Cardiothoracic and Vascular Anesthesia, 28(2)

ISSN

1053-0770

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Publication Date

2014-04-01

DOI

10.1053/j.jvca.2013.06.022

Peer reviewed

Perioperative Dexmedetomidine Improves Mortality in Patients Undergoing Coronary Artery Bypass Surgery

Fuhai Ji, MD,*§ Zhongmin Li PhD,† Nilas Young, MD,‡ Peter Moore, MD, PhD,§ and Hong Liu, MD§

Objective: This study retrospectively investigated the effect of dexmedetomidine on outcomes of patients undergoing coronary artery bypass graft (CABG) surgery.

Design: Retrospective investigation.

Setting: Patients from a single tertiary medical center.

Participants: A total of 724 patients undergoing CABG surgery met the inclusion criteria and were categorized into 2 groups: 345 in the dexmedetomidine group (DEX) and 379 in the nondexmedetomidine group (Non-DEX).

Interventions: Perioperative dexmedetomidine was used as an intravenous infusion (0.24 to 0.6 µg/kg/hour) initiated after cardiopulmonary bypass and continued for less than 24 hours postoperatively in the intensive care unit.

Measurements and Main Results: Major outcome measures of this study were in-hospital, 30-day and 1-year all-cause mortality, delirium and major adverse cardiocerebral events. Perioperative dexmedetomidine infusion was associated with significant reductions in in-hospital, 30-day, and 1-year mortalities, compared with the patients who did not received dexmedetomidine. In-hospital, 30-day, and 1-year mortalities were 1.5% and 4.0% (adjusted odds ratio [OR], 0.332; 95% CI, 0.155 to 0.708; p = 0.0044), 2.0% and 4.5% (adjusted OR, 0.487; 95% CI, 0.253 to 0.985; p = 0.0305), and 3.2% and 6.9% (adjusted OR 0.421; 95% CI, 0.247 to 0.718, p = 0.0015), respectively. Perioperative dexmedetomidine infusion was associated with a reduced risk of delirium from 7.9% to 4.6% (adjusted OR, 0.431; 95% CI, 0.265-0.701; p = 0.0007).

Conclusion: Dexmedetomidine infusion during CABG surgery was more likely to achieve improved in-hospital, 30-day, and 1-year survival rates, and a significantly lower incidence of delirium.

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KEY WORDS: coronary artery bypass graft, dexmedetomidine, outcomes, delirium, mortality

CORONARY ARTERY DISEASE (CAD) continues to be the leading cause of morbidity and mortality in the United States. Although epidemiologic evidence suggests that there has been a reduction in death attributable to coronary heart disease in recent years, it still has considerably high morbidity and mortality rates.[1] The 30-day mortality was about 1.2% in the on-pump coronary artery bypass graft (CABG) surgery, and in elderly patients (>65 years), mortality was 8.1% at 1 year.[1,2] The major complications include postoperative delirium, infection, acute renal failure (ARF), and major adverse cardiocerebral events that include permanent or transient stroke, coma, perioperative myocardial infarction (MI), heart block, and cardiac arrest.[3] Although there are many contributing factors to these adverse events, surgical stress is one of the most important factors in the pathogenesis of these complications. Surgical stimuli cause increased plasma levels of epinephrine and norepinephrine and result in myocardial oxygen supply/demand imbalance and myocardial ischemia, especially in patients with a compromised coronary blood flow.[4,5]

Dexmedetomidine is a highly selective, shorter-acting intravenous alpha-2 agonist with a tenfold greater alpha-2-to-alpha-1-receptor selectivity than clonidine.[6] Intraoperative intravenous infusion of dexmedetomidine to patients undergoing CABG and vascular surgery decreased intraoperative sympathetic tone-attenuated hyperdynamic response and improved patient perioperative hemodynamics.[7,8] Laboratory studies have found that dexmedetomidine has a more profound protection against ischemia/reperfusion (I/R) and other forms of injuries in the heart, brain, kidneys, liver, and lungs.[9–12] Moreover, dexmedetomidine has been shown to have anti-inflammatory and anti-delirium properties.[13,14] This group's previous study found that perioperative dexmedetomidine use could reduce mortality in patients undergoing cardiac surgery, but there were no significant effects on the incidence of acute cardiac events.[15] However, studies have reported that other alpha-2 agonists (mivazerol and clonidine) significantly reduced the incidence of cardiac events in noncardiac patients with coronary artery disease.[16,17] Therefore, the specific aim of this study was to investigate the effect of dexmedetomidine on outcomes that include mortality and the postoperative complications of patients who underwent CABG surgery only as a subgroup analysis.

METHODS

This study was a single-center, retrospective, cohort study involving 1,080 consecutive patients who underwent cardiac surgery at a university medical center from January 1, 2006 to December 31, 2011. The study was reviewed and approved by the Institutional Review Board. The inclusion criteria were patients who underwent CABG surgery only. The patients excluded from this study were those who underwent valvular surgery, combined CABG with other procedures, surgery involving the aorta, or any cardiac surgeries other than CABG surgery. Patients with emergency surgery and surgeries requiring deep hypothermic circulatory arrest, off-pump, robotic surgery, and

redo CABG surgery also were excluded from this study (Fig 1). A total of 724 patients (mean age 66 years old) met the inclusion criteria. Patients were divided into 2 groups: Patients using dexmedetomidine (DEX group, n = 345, 47.65%) or not using dexmedetomidine (Non-DEX group, n = 379, 52.35%) during the perioperative period (Fig 1).

The patient data were collected and organized to follow the template of the Society of Thoracic Surgeons (STS) National Database, and patient hospital medical records, including demographic characteristics, patient medical history, preoperative risk factors, preoperative medications, intraoperative data, postoperative stroke, coma, MI, heart block and cardiac arrest, ARF, sepsis, delirium, and in-hospital, 30-day, and 1-year all-cause mortality. Independent investigators prospectively collected the data on each patient during the course of hospitalization for CABG surgery. General anesthesia was induced with midazolam, propofol or etomidate, fentanyl, lidocaine, and rocuronium. Anesthesia was maintained with oxygen and sevoflurane. Ventilation was controlled to an end-tidal CO_2 of 30 mmHg to 40 mmHg by adjusting tidal volume and/or respiratory rate. A right radial arterial catheter was placed for continuous blood pressure monitoring. A pulmonary artery catheter was placed via the right/left internal jugular vein. Transesophargeal echocardiography(TEE) was used in all cases for assessing cardiac function during surgery. Dexmedetomidine use was given as intravenous infusion of this medication at a dose of 0.24 to –0.6 μg/kg/hour after cardiopulmonary bypass (CPB) and continued for less than 24 hours postoperatively in the intensive care unit (ICU).

Major outcomes of this study were in-hospital, 30-day, and 1-year all-cause mortality, MI, postoperative ARF/dialysis requirement, stroke, coma, delirium, heart block, and cardiac arrest. Other outcomes were 30-day readmission, postoperative length of ICU stay, and postoperative length of hospital stay (LOS). Based on the STS criteria, permanent stroke is defined as a postoperative stroke of any confirmed neurologic deficit of abrupt onset caused by a disturbance in cerebral blood supply that did not resolve within 24 hours. Delirium indicates whether the patient experienced delirium tremens in the postoperative period marked by illusions, confusion, cerebral excitement, and having a comparatively short course. MI is documented by the following criteria (<24 hours postoperatively): The creatine phosphokinase-MB (CK-MB) must be greater than or equal to 5 times the upper limit of normal, with or without new Q-waves present in 2 or more contiguous electrocardiograph (ECG) leads, no symptoms required; or as documented by at least one of the following criteria (>24 hours postoperatively): (1) evolutionary ST- segment elevations, (2) development of new Q-waves in 2 or more contiguous ECG leads, (3) new or presumably new left bundle-branch block pattern on the ECG, and (4) the CK-MB must be greater than or equal to 3 times the upper limit of normal; heart block as a new heart block requiring the implantation of a permanent pacemaker of any type prior to discharge; postoperative renal failure as acute or worsening renal failure resulting in one or more of the following: Increase in serum creatinine >2.0 mg/dL and 2 times the most recent preoperative creatinine level over baseline or new requirement for dialysis postoperatively. Patients diagnosed as septic required positive blood cultures in the postoperative period. Any complication included postoperative events occurring during the hospitalization for surgery. This included the entire postoperative period up to discharge, even if over 30 days. The remaining definitions are available at http://www.sts.org/documents/pdf/trainingmanuals/adult2.73/V-c-AdultCVDataSpecifications2.73.pdf (accessed June 30, 2012).

Continuous and categoric variables were reported as mean ± SD or percentages, and compared with the t tests or χ^2 test (two-tailed), respectively. Univariate and multivariate logistic regressions were performed to assess associations of demographic, therapeutic, and clinical outcome variables. To mitigate selection bias in dexmedetomidine infusion, the authors computed the propensity score; that is, the conditional probability of each patient receiving dexmedetomidine with a multivariate logistic regression model that included patient demographic and clinical risk factors (Table 1, Supplemental Figure 1).

To achieve model parsimony and stability, the backward selection procedure was applied with the dropout criterion p > 0.05. The candidate risk factors were selected on the basis of the literature reviews, clinical plausibility, and variables collected in the database. The candidate independent variables included demographic and clinical risk factors (Table 1). The parsimonious multivariate propensity final model for dexmedetomidine use included status of procedure, preoperative diabetes, preoperative congestive heart failure (CHF), number of vessels bypassed, and year of surgery (Fig 2). The risk-adjusted odds ratios for all outcomes were calculated with the use of a stepwise logistic regression model with patient risk factors as independent control variables and dexmedetomidine use included in the model as the independent study variable of interest. A propensity-weighted logistic regression model was used for 1-year mortality in which an inverse (estimated) propensity score as weights for patients with dexmedetomidine and the inverse of 1 minus the propensity score for patients without dexmedetomidine and added dexmedetomidine as an
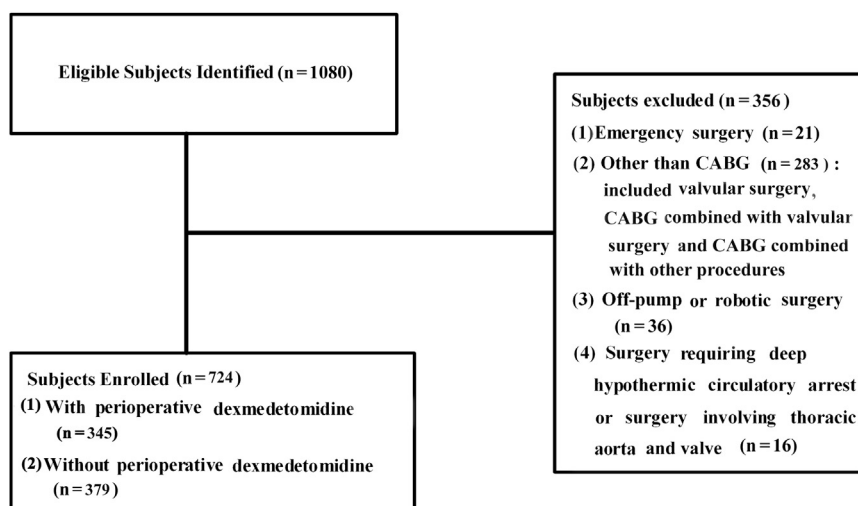

Fig 1. Recruiting of study samples.

Table 1. Demographic and Clinical Characteristics

Characteristics	Dexmedetomidine		p Value
	Yes (n = 345)	No (n = 379)	
Age	62.9 ± 11.8	64.1 ± 11.4	0.1694
Sex (F)	92 (26.7)	108 (28.5)	0.5827
Race (White)	118 (34.2)	118 (31.1)	0.3794
BMI	29.4 ± 6.1	29.8 ± 7.0	0.4665
Hemoglobin (g/dL)	14.9 ± 2.8	15.1 ± 3.1	0.5322
Past medical history			
Smoking	185 (53. 6)	208 (54.9)	0.7345
Current Smoking	70 (20.3)	77 (20.3)	0.9929
Chronic lung disease	48 (13.9)	57 (15.0)	0.6380
Cerebrovascular Disease	57 (16.5)	69 (18.2)	0.8701
Peripheral Vascular Disease	45 (13.0)	51 (13.5)	0.8701
Family History CAD	65 (18.8)	103 (27.2)	0.0080
Diabetes	129 (37.4)	113 (29.8)	0.031
Hypertension	271 (78.6)	289 (76.3)	0.4611
Hypercholesterolemia	241 (69.9)	304 (80.2)	0.0013
Dyslipidemia	233 (67.5)	158 (41.7)	<0.0001
History of Renal Failure	17 (4.9)	8 (2.1)	0.0383
Dialysis	12 (3.5)	7 (1.9)	0.1706
Pre-op Last Creatinine Level	1.23 ± 1.1	1.14 ± 0.68	0.1982
Pre-op MI	121 (35.1)	167 (44.1)	0.0136
CHF	104 (30.1)	27 (7.1)	<0.0001
EF %	49.7 ± 13.3	51.9 ± 13.0	0.0219
Preoperative Medication			
ACEi	165 (47.8)	220 (58.1)	0.0059
Beta-blockers	242 (70.10)	255 (67.30)	0.4073
ADP Inhibitors	19 (5.5)	45 (11.9)	0.0026
Nitrates	11 (3.2)	13 (3. 4)	0.8561
Antiplatelets	6 (1.7)	4 (1.1)	0.4314
Anticoagulants	65 (18.8)	92 (24.3)	0.0024
Coumadin	26 (7.5)	26 (6.9)	0.7251
Inotropes	2 (0.6)	4 (1.1)	0.4810
Aspirin	270 (78.3)	305 (80.7)	0.4093
Lipid-Lowering Medications	138 (40.0)	252 (66.5)	<0.0001
GPIIb/IIIa Inhibitors	8 (2.3)	24 (6.3)	0.0087
Propensity score	0.38 (0.22)	0.63 (0.22)	P<0.0001

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

Abbreviations: BMI, body mass index; CAD, coronary artery disease; Pre-op MI, preoperative myocardial infarction (MI); CHF, congestive heart failure; EF, ejection fraction; ACEi, angiotensin-converting enzyme inhibitors; ADP, adenosine diphosphate; GPIIb/IIIa inhibitors, glycoprotein IIb/IIIa inhibitors.

independent factor to the model. All model fit analysis was evaluated with the Hosmer-Lemeshow goodness-of-fit statistic. The C statistic was reported as a measure of predictive power. Based on the propensity of dexmedetomidine use, the authors classified all patients into quintiles, where quintile 1 contained patients with the lowest propensity scores and quintile 5 contained patients with the highest propensity scores. Then, with a general linear model, the authors compared the propensity-weighted and risk-adjusted 1-year mortality between the cohort of dexmedetomidine used and the cohort of no dexmedetomidine used for each propensity-matched quintile. Results are reported as percentages and odds ratios (OR) and with 95% confidence intervals (CI). The model was calibrated among deciles of observed and expected risks for 1-year mortality (Hosmer-Lemeshow χ^2: 12.018, c = 0.781, p = 0.1504), dexmedetomidine use (Hosmer-Lemeshow χ^2: 15.2236; c = 0.785, p = 0.0549).

Furthermore, the authors performed survival analysis and presented Kaplan-Meier curves for patients in DEX group versus patients in Non-

DEX group. A parsimonious Cox proportional hazards model was created to evaluate the effect of dexmedetomidine for 1-year survival. All reported p values were two-sided, and p values <0.05 were considered to be statistically significant. Statistical analysis was performed with SAS version 9.3 for Windows (SAS Inc., Cary, NC).

RESULTS

Demographic and clinical data of the patients who did and did not receive perioperative dexmedetomidine therapy are presented in Table 1. Patients in the DEX group presented more often with a history of CHF, low ejection fraction, ARF, dyslipidemia, and diabetes. Patients in the DEX group also presented with more preoperative use of beta-blockers and lipid-lowering medications. However, patients in the Non-DEX group presented more often with a history of family history CAD, hypercholesterolemia, and preoperative MI. Patients in the Non-DEX group also presented more with preoperative use of angiotensin-converting enzyme inhibitors (ACEi), adenosine diphosphate (ADP) inhibitors, anticoagulants, and glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors.

Procedural characteristics, including the number of vessels bypassed, and intra-aortic balloon pump use were similar in both groups. In contrast, perfusion time (185.5 ± 777 v 197.7 ± 82.2, p = 0.0106) and aortic cross-clamp time (129.3 ± 63.6 v143.0 ± 60.9, p = 0.003) were significantly longer in the Non-DEX group (Table 2).

By univariate analysis, perioperative infusion of dexmedetomidine was associated with significantly reduced in-hospital and 1-year mortalities, but not 30-day mortality. In-hospital mortality was 1.5% in the DEX group versus 4.0% in the Non-DEX group (OR, 0.357; 95% CI, 0.128 to 0.993; p = 0.0398). One-year mortality was 3.2% in the DEX group versus 6.9% in the Non-DEX group (OR, 0.447; 95% CI, 0.218 to 0.919; p = 0.0251) (Fig 3). The perioperative use of dexmedetomidine was associated with a significantly reduced incidence of any complication (44.1% v 52.20%, OR, 0.720; 95% CI, 0.537 to 0.965; p = 0.0278) (Fig 3).

For propensity and multivariate analysis, the risk-adjusted results for all outcomes are summarized in Figure 3. The observed reduction in in-hospital (adjusted OR, 0.332; 95% CI, 0.155 to 0.708; p = 0.0044) and 1-year (adjusted OR, 0.421; 95% CI, 0.247 to 0.718; p = 0.0015) mortalities in patients receiving perioperative dexmedetomidine continued to be significantly after propensity adjustment. Thirty-day mortality (adjusted OR, 0.487; 95% CI, 0.253 to 0.985; p = 0.0305) was reduced significantly in patients receiving perioperative dexmedetomidine after adjustment. The adjusted rates of delirium (adjusted OR, 0.431; 95% CI, 0.265 to 0.701; p = 0.0007) were also statistically significant between the DEX and Non-DEX groups. However, there were no statistical differences in the incidence of any complication between groups after adjusting for differences between groups, although the OR point estimates favor perioperative dexmedetomidine use (Fig 3).

Patients who received dexmedetomidine in all 5 quintiles were significantly lower with respect to 1-year mortality compared with the patients in the Non-DEX group (Table 3).
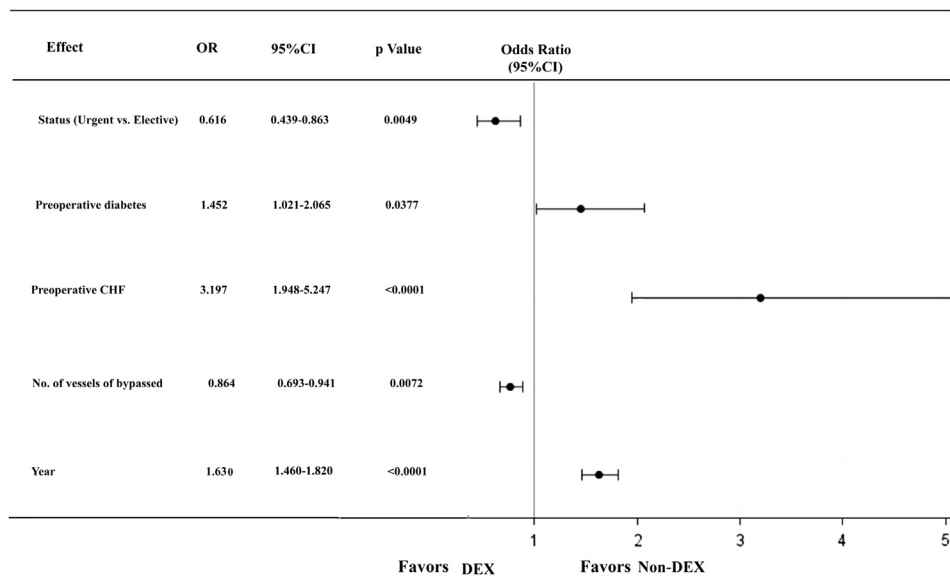
Fig 2. Parsimonious multivariate propensity model for dexmedetomidine use. Abbreviations: OR, odds ratio; CI, confidence interval; CHF, congestive heart failure; DEX, dexmedetomidine.

Survival probability was calculated using Kaplan-Meier methods and compared with the use of a log-rank test (χ^2 = 5.6312, p = 0.0176). For 1 year, there were significant differences in survival between the DEX and Non-DEX groups (propensity adjusted: 97.28% v 92.23%, OR 0.421, 95% CI 0.247 to 0.718, p = 0.00115) (Fig 4).

After risk adjustment, a Cox proportional hazard model analysis revealed that older patients (age >65 years), urgent surgery, preoperative last creatinine level, number of vessels bypassed, and perfusion time significantly increased the 1-year mortality, whereas perioperative dexmedetomidine infusion significantly reduced the risk of death during the first year (hazard ratio, 50.4%; 95% CI, 0.247 to 0.818; p = 0.0025) compared with those in the Non-DEX group at any time within 1 year after CABG surgery (Fig 5).

DISCUSSION

This study is the first to demonstrate that dexmedetomidine administered during CABG surgery improved in-hospital, 30-day, and 1-year survivals. The results also suggest that perioperative dexmedetomidine use reduced postoperative incidence of delirium.

CAD continues to be the leading cause of morbidity and mortality in the United States. CABG is a main treatment procedure but comes with a considerably high morbidity and mortality.[1] Approximately 500,000 CABG surgeries are performed annually in the United States.[18] The most common postoperative complications include permanent or transient stroke, coma, perioperative MI, heart block and cardiac arrest, ARF, central nerve system dysfunction, and infections. The pathogenesis of these complications is multifactorial and involves surgical stress, systemic inflammatory response syndrome (SIRS), and I/R injury in patients undergoing on-pump CABG.

Cardiocerebral complications often are presented immediately after cardiac surgery, including stroke (1.4%-4.6%),

cardiac arrest (0.7%-2.9%), and MI (3.1%-9.1%).[3,19-21] Although this study found that the risk of postoperative cardiocerebral events, including MI, heart block, cardiac arrest, stroke, and coma appeared to not significantly decrease during perioperative use of dexmedetomidine after CABG surgery, the OR values of these events are all in favor of perioperative use of dexmedetomidine. Studies have demonstrated the effectiveness of dexmedetomidine as a stress suppressing, anti-inflammatory, and anti-I/R injury agent in the prevention and treatment of cardiovascular events.[6,7] Intraoperative intravenous infusion of

Table 2. Procedural Characteristics

Characteristics	Dexmedetomidine		
	Yes (n = 345)	No (n = 379)	p Value
Perfusion Time (min)	182.5 ± 77.7	197.7 ± 82.2	0.0106
IABP used, no. (%)	28 (8. 1)	43 (11.4)	0.1447
Cross-clamp time (min)	129.3 ± 63.6	143.0 ± 60.9	0.0030
No. of vessels bypassed	3.92 ± 1.16	4.01 ± 1.08	0.337
No. of vessels bypassed (>4)	233 (67.5)	264 (69.7)	0.539
Surgery, no			
2006	32 (9.28)	81 (21.37)	0.0112
2007	52 (15.07)	68 (17.94)	0.0793
2008	63 (18.26)	55 (14.51)	0.1027
2009	52 (15.07)	69 (18.21)	0.07351
2010	69 (20.0)	63 (16.62)	0.2141
2011	77 (22.32)	43 (11.35)	0.03265
Surgeon, no/no. (%)			
#1	270/343 (78.7)		
#2	129/154 (83.7)		
#3	203/247 (82.2)		
#4	122/144 (84.7)		

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

Abbreviations: IABP, intra-aortic balloon pump; no/no. number of enrolled patients/total numbers of cardiac surgeries performed by one specific surgeon.

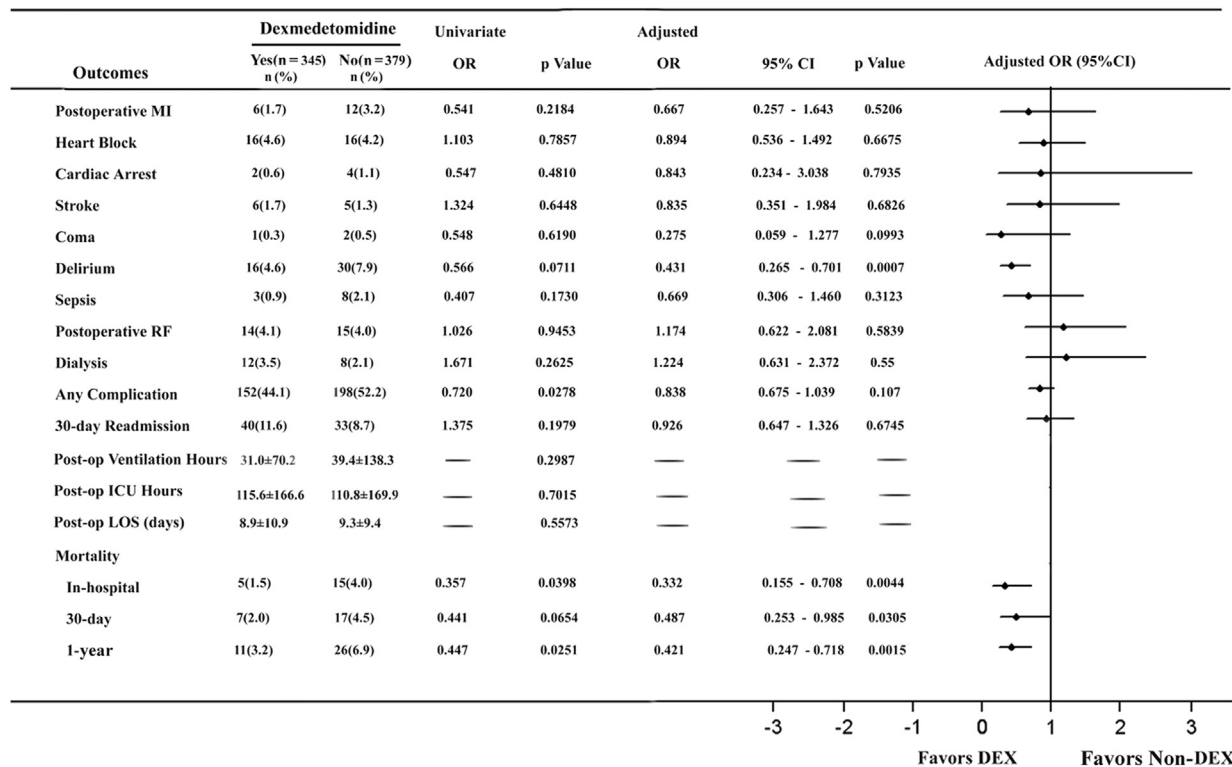| Outcomes	Dexmedetomidine		Univariate		Adjusted				
	Yes(n = 345) n (%)	No(n = 379) n (%)	OR	p Value	OR	95% CI	p Value	Adjusted OR (95%CI)	
Postoperative MI	6(1.7)	12(3.2)	0.541	0.2184	0.667	0.257 - 1.643	0.5206		
Heart Block	16(4.6)	16(4.2)	1.103	0.7857	0.894	0.536 - 1.492	0.6675		
Cardiac Arrest	2(0.6)	4(1.1)	0.547	0.4810	0.843	0.234 - 3.038	0.7935		
Stroke	6(1.7)	5(1.3)	1.324	0.6448	0.835	0.351 - 1.984	0.6826		
Coma	1(0.3)	2(0.5)	0.548	0.6190	0.275	0.059 - 1.277	0.0993		
Delirium	16(4.6)	30(7.9)	0.566	0.0711	0.431	0.265 - 0.701	0.0007		
Sepsis	3(0.9)	8(2.1)	0.407	0.1730	0.669	0.306 - 1.460	0.3123		
Postoperative RF	14(4.1)	15(4.0)	1.026	0.9453	1.174	0.622 - 2.081	0.5839		
Dialysis	12(3.5)	8(2.1)	1.671	0.2625	1.224	0.631 - 2.372	0.55		
Any Complication	152(44.1)	198(52.2)	0.720	0.0278	0.838	0.675 - 1.039	0.107		
30-day Readmission	40(11.6)	33(8.7)	1.375	0.1979	0.926	0.647 - 1.326	0.6745		
Post-op Ventilation Hours	31.0±70.2	39.4±138.3	—	0.2987	—	—	—		
Post-op ICU Hours	115.6±166.6	110.8±169.9	—	0.7015	—	—	—		
Post-op LOS (days)	8.9±10.9	9.3±9.4	—	0.5573	—	—	—		
Mortality									
In-hospital	5(1.5)	15(4.0)	0.357	0.0398	0.332	0.155 - 0.708	0.0044		
30-day	7(2.0)	17(4.5)	0.441	0.0654	0.487	0.253 - 0.985	0.0305		
1-year	11(3.2)	26(6.9)	0.447	0.0251	0.421	0.247 - 0.718	0.0015		

Fig 3.   Effects of dexmedetomidine on postoperative complications and mortality in patients undergoing CABG surgery. Values are numbers (%) for categoric variables and mean ± SD for continuous variables. Abbreviations: OR, odds ratio; CI, confidence interval; MI, myocardial infarction; RF, renal failure; Post-op, postoperative; ICU, intensive care unit; LOS, length of stay; DEX, dexmedetomidine.

dexmedetomidine in patients undergoing CABG surgery decreased plasma norepinephrine (NE) concentration, and reduced intraoperative and postoperative episodes of hypertension and tachycardia.[6] In an animal study, dexmedetomidine reduced serum catecholamine, heart rate, and contractility, increased coronary blood flow, and decreased myocardial oxygen consumption.[22]

Delirium is a common complication and increases morbidity and mortality in older ICU patients with a prevalence of 20%-50% after cardiac surgery.[23–25] The prevalence of delirium in this study was only 6.25% after CABG surgery, because the authors only analyzed patients with hyperactive delirium. However, the major type of delirium is emotional (hypoactive) delirium instead of hyperactive delirium. Peterson et al recently reported that the incidence of hyperactive delirium was only 1.6% in medical ICU patients, whereas most had either a mixed (54.9%) or hypoactive (43.5%) delirium.[26] Dexmedetomidine has been reported to reduce the incidence of delirium and its duration in septic and cardiac patients.[27,28] It also has been reported being used to treat ICU-associated delirious agitation.[29] This study also confirmed that the incidence of delirium was significantly lower in the patients who received dexmedetomidine. Although the causes of delirium remain hypothetical, the abnormalities in neurotransmission, inflammation, and anesthetic agents are among the leading causes of this brain dysfunction.[30–32]

This study demonstrated the in-hospital, 30-day, and 1-year mortalities were significantly lower in patients who

received dexmedetomidine. It reduced the risk of death by 49.6% during the first year. In a Cox proportional hazard model for 1-year mortality, age, urgent surgery, preoperative creatinine level, number of vessels bypassed, and perfusion time appeared to adversely affect 1-year mortality. The mechanism of the reduction of mortalities is likely associated with sympatholytic, anti-inflammatory, and anti-delirium effects. Therefore, the authors believe the reduction of mortality represented the overall effects of dexmedetomidine.

This investigation had some limitations. In a retrospective study, although multivariate regression in combination with

Table 3. Predicted 1-Year Mortality by Quintile of Propensity Score

	Number		Propensity score			Mortality		
Quintile	DEX	Non-DEX	DEX	Non-DEX	p Value	DEX	Non-DEX	p Value
1	17	127	0.180	0.158	0.7964	0.0266	0.08051	0.0022
2	46	98	0.305	0.300	0.999	0.0357	0.0798	0.0005
3	63	83	0.453	0.449	1	0.0305	0.0711	0.0007
4	104	41	0.632	0.629	1	0.0234	0.0703	0.0003
5	115	30	0.837	0.832	1	0.0250	0.0673	0.0092

Propensity score reflected mean propensity score; mortality reflected mean predicted 1-year mortality. Quintile 1 contains patients with lowest propensity scores, and quintile 5 contains patients with the highest propensity scores. DEX, dexmedetomidine.
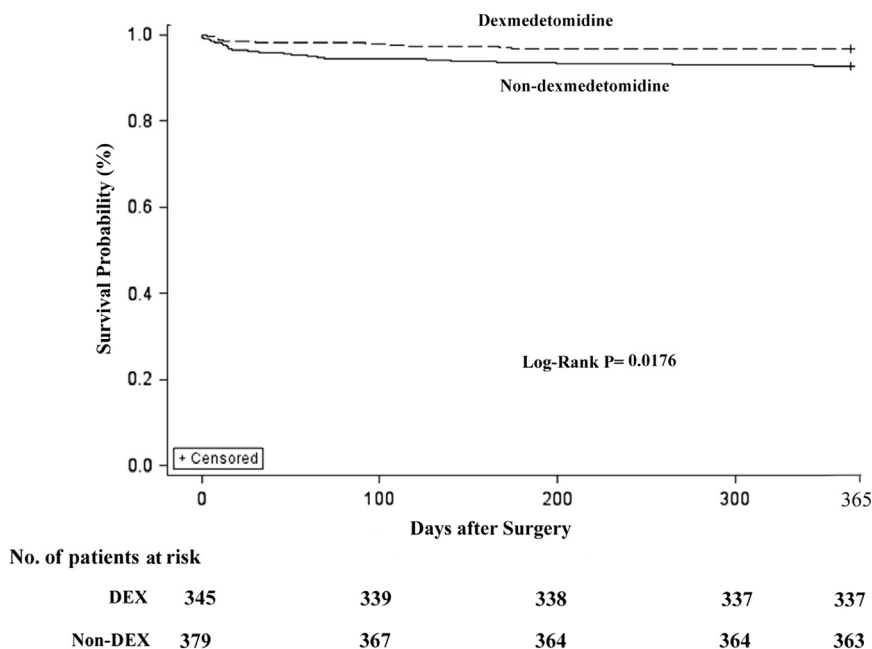
Fig 4. Survival estimates after CABG surgery between 2 groups. Survival probability was calculated with the use of Kaplan-Meier methods and compared with the use of a log-rank test (log-Rank test, $\chi^2 = 5.6312$, p = 0.0176). DEX group, using dexmedetomidine after weaning off bypass; Non-DEX, not using dexmedetomidine after weaning off bypass.

the propensity score adjustment was applied to reduce evident biases, the potential confounding variables following a nonrandomized study may not have been removed completely. The timing of dexmedetomidine use in this study was after CPB and lasted up to 24 hours postoperatively, which is different from another report, which showed dexmedetomidine administration had a protection against I/R injury only before ischemia.[33] However, the peak intraoperative plasma concentrations of norepinephrine and epinephrine occurred after CPB.[34]

CONCLUSIONS

This study was the first to demonstrate that on-pump CABG surgery patients who received the intravenous dexmedetomidine infusion during surgery were more likely to have better in-hospital, 30-day, and 1-year survival rates after surgery. Perioperative use of dexmedetomidine also is associated with a significantly lower incidence of postoperative delirium. However, a well-designed, prospective, multicenter randomized study is needed to focus on the use of dexmedetomidine in CABG surgery patients to confirm these findings.
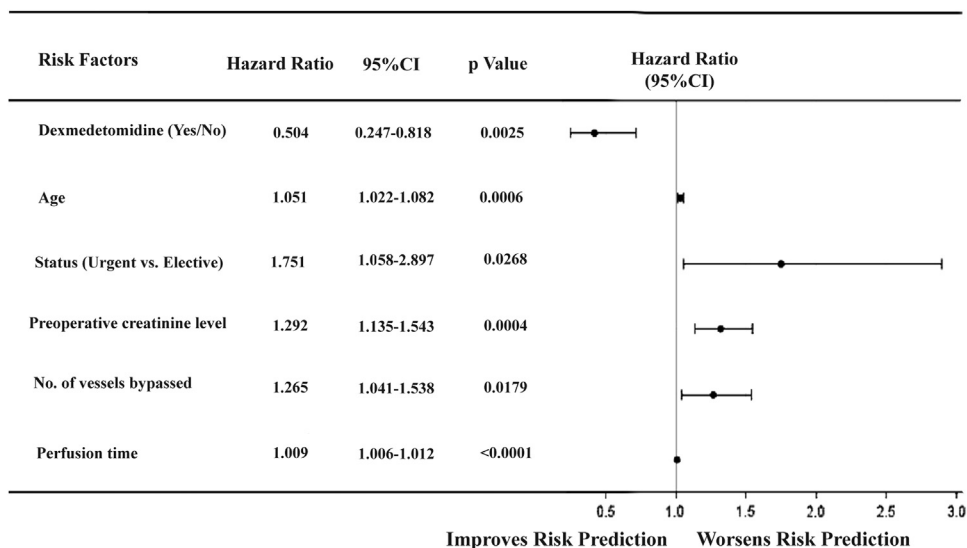

Risk Factors	Hazard Ratio	95%CI	p Value
Dexmedetomidine (Yes/No)	0.504	0.247-0.818	0.0025
Age	1.051	1.022-1.082	0.0006
Status (Urgent vs. Elective)	1.751	1.058-2.897	0.0268
Preoperative creatinine level	1.292	1.135-1.543	0.0004
No. of vessels bypassed	1.265	1.041-1.538	0.0179
Perfusion time	1.009	1.006-1.012	<0.0001

Fig 5. Cox proportional hazard model for 1-year mortality following cardiac surgery. Values are numbers (%) for categoric variables and mean ± SD for continuous variables. CI, confidence interval.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version at 10.1053/j.jvca.2013.06.022.

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