Comparing The Impact On The Prognosis of Acute Myocardial Infarction Critical Patients of Using Midazolam, Propofol, and Dexmedetomidine for Sedation

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Research Article

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Abstract

Background: There are less studies focusing on the sedative therapy of acute myocardial infarction (AMI) critical patients. This study aim to compare the impact on the prognosis of AMI critical patients of using midazolam, propofol and dexmedetomidine.

Methods: We collected clinical data from the Medical Information Mart for Intensive Care III (MIMIC III) database. Data on 427 AMI patients with sedatives using were recruited from in Coronary Heart Disease Intensive Care unit (CCU) .

Results: There were 143 patients in midazolam using, 272 in propofol using and 28 in dexmedetomidine using. The rate of 28-days mortality was 23.9% in overall patients. Through logistic regression analysis, midazolam using was significant association with increased 28-days mortality when compared with non-midazolam using group (propofol or dexmedetomidine using). In the subgroup analysis of age, gender, body mass index (BMI), white blood cell (WBC), beta-block, and revascularization, the association between midazolam using and increased 28-days mortality remained significantly. Through propensity score matching, 140 patients using midazolam groups and 192 using non-midazolam on the sedation were successfully matched, the midazolam using group presented with higher rate of CCU mortality, hospital mortality and 28-days mortality, longer of mechanical ventilation time and CCU duration.

Conclusion: Propofol or dexmedetomidine is prefer to be used in AMI critical patients for sedative therapy.

Background

AMI critical patients' primary concerns in CCU are respiratory and hemodynamic supports, and usually treated with many invasive therapies, which may cause discomfort and anxiety. Sedative therapy is assumed to reduce discomfort from care interventions, increase tolerance of mechanical ventilation, prevent accidental removal of instrumentation, and reduce metabolic demands during cardiovascular and respiratory instability[1]. Midazolam, propofol, and dexmedetomidine are widely used sedatives in clinical practice. Midazolam, a ganna-aninobutyric acid agonist, is a traditional sedative for critically ill patients and a short duration of effect. Dexmedetomidine is an alpha-2 adrenoreceptor agonist with a unique mechanism of action. Based on experimental myocardial infarction rats, midazolam was demonstrated with increased ventricular arrhythmias and death and infarct size following reperfusion[2], and dexmedetomidine with increased the cardiac infarct size[3], and propofol with myocardial protective effect by reducing release of inflammatory factors[3]. An small sample clinical study has demonstrated that sedation with dexmedetomidine and propofol may cause hypotension or bradycardia[5].

However, there are none clinical study focusing on the effect of different sedatives on AMI critical patients. The aim of our study is to compare the impact on the prognosis among midazolam, propofol and dexmedetomidine in AMI critical patients for sedative therapy.

Methods

MIMIC III Database

Clinical information of patients in our study were collected from MIMIC III database, which was illustrated by the Massachusetts institute of technology and had over 40000 patients admitted between 2001 and 2012. Patients in the database were fully anonymized. One author(X J) gained access involves MIMIC III database (certification number 9195641) and extracted the data.

Inclusion criteria & exclusion criteria

Acute myocardial infarction patients with treatment records indicating sedatives using after CCU admission were initially screened. Sedatives included midazolam, propofol, and dexmedetomidine, and using time more than 12 hours. Patients who were < 18 years or > 90 years old were excluded. For patients who had more than once CCU inpatient record, only the first CCU inpatients record was collected.

Data extraction and missing data management

Data on the patients' characteristics, past medical history, vital sign, biochemistry, sedatives and other treatments were recruited from the database. Variables with missing data are very common in the database of MIMIC III. Serum tropoin and RASS score, with more than 30% missing, were removed from this analysis. For continuous variables with less than 5% missing, we used imputation method with linear regression.

Outcomes

The primary outcome was defined as 28-days mortality. The secondary outcomes included CCU mortality, hospital mortality, length of mechanical ventilation duration and CCU stay.

Statistical analysis

Data analyses were performed using StataMP software version 16. Numeric variables were summarized as the mean (standard deviation). Categorical variables were reported as counts (percentage). The student's test, ^{2} test, Wilcoxon rank-sum test was used, as appropriate. Univariate and multivariate logistic regression were to explore significantly factors for 28-days mortality. The log-rank test was used to assess differences in 28-days mortality between groups divided by midazolam, propofol, and dexmedetomidine. Subgroup analysis was utilized with ^{2} test to detect any interaction between midazolam and 28-days mortality, and stratification was performed according to age (<60, >=60), gender(male, female), BMI(<24, >=24), WBC(<=10, >10), beta-block (Yes, No), and revascularization (Yes, No). Propensity score matching (PSM) could decrease the influence of confounding factors. The propensity score was allocated based on the probability of a patient who receive midazolam therapy and estimated with using a multivariable logistic regression model. The nearest neighbor matching algorithm was applied using a caliper width of 0.02. There were variables selected to establish the propensity score: age, male, hypertension, creatinine (Scr), myocardial infarction (NSTEMI, AWSTEMI, NAWSTEMI), beta-blocker, stain, vasopressor, and revascularization. Graph of the p score were used to examine the PSM

degree. Finally, 140 patients from midazolam groups and 192 from non-midazolam groups were selected and used to further analyses. Two-sided P values less than 0.05 were considered statistically significant.

Results

Baseline clinical characteristics

Information about 427 AMI patients with sedative therapy were recruited. As many as 143 patients in the midazolam using, 272 patients in propofol using and 28 patients in the dexmedetomidine using. The overall 28-days mortality rate was 23.9%, and mechanical ventilation using was 93.4%. The comparisons of characteristics stratified by 28-days mortality are show in Table 1. There were no significant differences among the groups regarding sex, BMI, diabetes, PLT, using of clopidogrel and mechanical ventilation. Compared with 28-days survival, patients with 28-days mortality had older age, higher rate of hypertension and midazolam using and lower rate of using aspirin, betablocker, and revasucularization therapy(all $p < 0.01$).

Table 1
Comparisons of the clinical characteristics between groups stratified by 28-days mortality

Variables	N = 427	28-days		P value
		Mortality	Survival	
		N = 102	N = 325	
Mortality	102(23.9)	-	-	-
MI	121(28.3)	32(31.4)	89(27.4)	0.179
NSTEMI	126(29.5)	35(34.3)	91(28.0)	0.020
AWSTEMI	180(42.1)	35(34.3)	145(44.6)	0.274
NAWSTEMI	66.9 ± 12.3	69.4 ± 13.3	66.2 ± 11.9	0.871
Age, years	304(71.8)	69(67.6)	238(73.2)	0.001
Male, n(%)	28.0 ± 5.5	28.1 ± 5.9	27.9 ± 5.4	0.222
BMI, kg/m^2	55(12.9)	23(22.5)	32(9.8)	0.059
Past medical history	138(32.3)	38(37.2)	100(30.8)	0.681
Hypertension, n(%)	49(11.5)	17(16.7)	32(9.8)	0.485
Diabetes, n(%)	77(1.6)	17(16.7)	60(18.5)	0.019
CHF, n(%)	70(1.6)	19(18.6)	51(15.7)	0.007
COPD, n(%)	86.7 ± 14.5	89.6 ± 17.8	85.7 ± 13.2	0.000
Peripheral, n(%)	77.2 ± 8.1	75.3 ± 9.8	77.8 ± 7.4	0.128
Heart rate, bpm	97.5 ± 2.2	96.7 ± 3.3	97.8 ± 1.6	0.000
MBP, mmHg	0(−2,0)	−0.5(−3,0)	0(−1,0)	0.753
SpO2, %	14.1 ± 7.1	16.8 ± 8.7	13.3 ± 6.4	0.788
*RASS score	220.7 ± 99.0	223.4 ± 101.5	219.8 ± 98.3	0.008
Biochemistry	10.8 ± 2.0	10.7 ± 1.9	10.8 ± 2.1	0.000
WBC, K/uL	1.1 ± 2.5	1.7 ± 4.8	0.9 ± 0.7	0.000
PLT, K/uL	181.8 ± 105.1	229.9 ± 122.7	166.6 ± 94.2	0.995
	1.3 ± 1.2	1.7 ± 1.2	1.2 ± 1.2	0.000
	4.3 ± 0.7	4.3 ± 0.7	4.3 ± 0.7	0.000
	7.9 ± 1.5	7.6 ± 1.3	7.9 ± 1.5	0.154
	323(79.6)	55(53.9)	268(82.5)	0.000
	142(33.3)	28(29.4)	114(35.1)	0.000

Abbreviation: MI, myocardial infarction; NSTEMI, non-ST segment elevated myocardial infarction; AWSTEMI, anterior wall ST segment elevated myocardial infarction; NAWSTEMI, non-anterior wall ST segment elevated myocardial infarction; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MBP, mean arterial pressure; WBC, white blood cell; PLT, platelet; HGB, hemoglobin; TB, total bilirubin; Glu, glucose; Scr creatinine; *, 141 patients with RASS scores records, include 40 patients in mortality group and 101 in survival group; & 289 patients with serum tropoin record, include 201 patients in mortality group and 88 in survival group; #, include percutaneous coronary intervention and coronary artery bridge graft.

Variables	N = 427	28-days Mortality N = 102	Survival N = 325	P value
	257(83.6)	58(56.9)	299(92.0)	0.000
	287(67.2)	41(40.2)	246(75.7)	0.752
	335(78.5)	94(92.2)	241(74.2)	0.000
HGB, g/dl	399(93.4)	96(94.1)	303(93.2)	0.000
TB, mg/dl	299(70.0)	47(46.1)	252(77.5)	0.000
Glu, mg/dl	272(63.7)	45(44.1)	227(69.8)	0.032
Scr, mg/dl	143(33.5)	56(54.9)	87(26.8)	
Potassium, mEq/L	28(6.5)	2(2.0)	26(8.0)	
&Serum tropoin, ng/ml				
Treatments				
Aspirin, n(%)				
Clopidogrel, n(%)				
Betablock, n(%)				
Stain, n(%)				
Vasopressor, n(%)				
Mechanical ventilation, n(%)				
#Revascularization, n(%)				
Propofol, n(%)				
Midazolam, n(%)				
Dexmedetomidine, n(%)				

Abbreviation: MI, myocardial infarction; NSTEMI, non-ST segment elevated myocardial infarction; AWSTEMI, anterior wall ST segment elevated myocardial infarction; NAWSTEMI, non-anterior wall ST segment elevated myocardial infarction; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MBP, mean arterial pressure; WBC, white blood cell; PLT, platelet; HGB, hemoglobin; TB, total bilirubin; Glu, glucose; Scr creatinine; *, 141 patients with RASS scores records, include 40 patients in mortality group and 101 in survival group; & 289 patients with serum tropoin record, include 201 patients in mortality group and 88 in survival group; #, include percutaneous coronary intervention and coronary artery bridge graft.

Worse Prognosis In Midazolam Using Groups

Through logistic regression analysis, we founded that only midazolam using was significant association with 28-days mortality among three sedatives(Table 2). The Kaplan-Meier curves revealed that a increased 28-days mortality was significantly associated with midazolam using (Fig. 1). In Table 3, when

compared with non-midazolam using, the rate of CCU and hospital mortality were significantly higher, and the time of mechanical ventilation duration and CCU stay were significantly longer in midazolam using. Subgroup analysis was performed according to the age, gender, BMI, WBC, beta-block, and revascularization (Fig. 2). The HR of midazolam use was significant in the age subgroups(< 60 years old: HR 3.44, 95%CI 1.71–6.94; >=60 years old: RR 2.14, 95%CI 1.46–3.13), gender subgroups(male: RR 2.58, 95%CI 1.71–3.88; female: RR 2.07, 95%CI 1.16–3.68), BMI subgroups(< 24: RR 2.15, 95%CI 1.16–3.98; >=24: RR 2.54, 95%CI 1.71–3.78), WBC subgroups(< = 10: HR 3.12, 95%CI 1.50–6.52; >10: RR 2.13, 95%CI 1.47–3.10), beta-block subgroups(Yes: RR 2.43, 95%CI 1.53–3.87; No: RR 1.53, 95%CI 1.05–2.22), and revascularization subgroups(Yes: RR 3.91, 95%CI 2.31–6.59; No: RR 2.17, 95%CI 1.61–2.91), and there were none significant interaction was observed.

Table 2
Using logistic regression to analysis Crude odds ratio and adjusted odds ratio of 28-days mortality

Variables	Crude odds ratio 95%CI	*p* value	Adjusted odds ratio 95%CI	*p* value
Midazolam	3.33(2.10,5.28)	0.000	2.20(1.29,3.77)	0.004
Dexmedetomidine	0.23(0.05,0.98)	0.048	0.34(0.07,1.66)	0.182
Propofol	0.34(0.22,0.54)	0.000	0.95(0.50,1.83)	0.889
MI	0.93(0.52, 1.68)	0.824	0.21(0.11,0.39)	0.000
Age	1.02(1.00,1.04)	0.021	0.36(0.21,0.63)	0.000
Hypertension	2.66(1.48,4.81)	0.001	0.34(0.20,0.58)	0.000
Heart rate	1.02(1.01,1.03)	0.020		
MBP	0.96(0.93,0.98)	0.007		
SpO2	0.81(0.73,0.90)	0.000		
WBC	1.07(1.03,1.10)	0.000		
TB	1.18(0.95,1.46)	0.129		
Glu	1.00(1.00,1.01)	0.000		
Scr	1.32(1.10,1.57)	0.002		
RASS score	1.04(0.71, 1.53)	0.842		
cTNI	1.12(1.07, 1.17)	0.000		
Aspirin	0.25(0.15,0.40)	0.000		
Betablock	0.11(0.07,0.20)	0.000		
Stain	0.22(0.13,0.35)	0.000		
Revascularization	0.25(0.15,0.40)	0.000		

Abbreviation as in Table 1

Table 3
Comparison of outcomes in acute myocardial farction patients between using midazolam or non-midazolam for sedative therapy

Variables	Midazolam N = 143	Non-midazolam N = 284	P value
Mechanical ventilation time, hours	101.6 ± 9.9	43.1 ± 4.4	0.000
CCU time, days	9.9 ± 0.9	5.6 ± 0.4	0.000
CCU mortality, n(%)	43(30.1)	36(12.7)	0.000
Hospital mortality,n(%)	47(32.9)	39(13.7)	0.000
28-days mortality, n(%)	56(39.2)	46(16.2)	0.000
Abbreviation: CCU, Coronary Heart Disease Intensive Care unit			

PSM

Using PSM, 140 patients from midazolam groups and 192 from non-midazolam groups matched from each group were generated(Table 4). In order to assess the quality, we compared the standardized difference of the means and the ratio of the variances between pairs, and drawed the propensity scores(Fig. 3). None significant difference was founded between the two matched groups concerning all nine covariates. After PSM, we found that the rate of CCU mortality, hospital mortality, 28-days mortality and the length of CCU stay, mechanical ventilation were all significantly higher or longer in the modazolam using.

Table 4
Comparison of the covariates after propensity score matching

Variables	Midazolam n = 140	Non-midazolam n = 192	*p* value
Age, years	67.0 ± 1.0	66.6 ± 0.9	0.761
Male, n(%)	96(68.5)	134(69.7)	0.182
Hypertension, n(%)	24(17.1)	25(13.0)	0.296
Scr, mg/dl	1.5 ± 0.1	1.3 ± 0.1	0.209
MI	41(29.3)	49(25.5)	0.578
NSTEMI, n(%)	39(27.9)	63(32.8)	0.209
AWSTEMI, n(%)	60(42.9)	80(41.7)	0.109
NAWSTEMI, n(%)	109(77.9)	160(83.3)	0.566
Beta-blocker, n(%)	79(56.4)	125(65.1)	0.107
Stain, n(%)	113(80.7)	150(78.1)	0.000
Vasopressor, n(%)	82(58.6)	129(67.2)	0.000
Revascularization, n(%)	103.2 ± 10.1	49.5 ± 6.0	0.013
Clinicals outcomes	10.1 ± 0.9	6.1 ± 0.5	0.007
Mechanical ventilation time, hours	41(29.3)	34(17.7)	0.001
CCU time, days	45(32.1)	37(19.3)	
CCU mortality, n(%)	54(38.6)	43(22.4)	
Hospital mortality,n(%)			
28-days mortality, n(%)			
Abbreviation as in Table1 and Table3			

Discussion

In this study, we evaluated the rate of CCU mortality, hospital mortality, 28-days mortality, and the longer of mechanical ventilation duration, CCU stay in AMI patients with sedatives therapy. Among 427 patients, the overall 28-days mortality rate was 23.9%, and mechanical ventilation using was 93.4%. Our study revealed that compared with propofol and dexmedetomidine using, midazolam using for sedative therapy in AMI patients was significantly associated with longer mechanical ventilation duration and CCU stay, higher rate of CCU mortality, hospital mortality and 28-days mortality. There was robust of result in the PSM analysis after adjustment for age, male, hypertension, Scr, MI, beta-blocker, stain, vasopressor, and

revascularization. Our finding are suggestive of a disadvantageous role for midazolam in sedative therapy of AMI patients, which has not been reported in past study.

AMI critical patients' primary concerns are hemodynamic and respiratory suppports. Most patients in our study received therapy of mechanical ventilation (93.4%) and vasopressor (78.5%) therapy. We speculated that causes of relative lower rate of using aspirin (75.6%), clopidogrel (33.3%), and revascularization (77%) in this study were due to poor physical condition of patients with less chance to perform surgery and huge risk of bleeding. Sedative therapy is necessary to increase tolerance, reduce discomfort, prevent accidental removal of instrumentation in AMI patients. In this study there were 143 patients in the midazolam using, 272 patients in propofol using and 28 patients in the dexmedetomidine using. Although propofol was reported to have vasorelaxant effect to influence myocardial perfusion and coronary flow reserve[6], propofol maybe result in aggressive blood pressure reduce in AMI patients due to impaired left ventricular function in AMI patients. However, both propofol and dexmedetomidine using in AMI patients for sedative therapy did not show significant associated with 28-days mortality in this study. The sample size of dexmedetomidine using was relatively small in our study, and need more deeply study in future. But a randomised placebo-controlled trial in past paper have showed that dexmedetomidine did not decrease postoperative atrial fibrillation in patients recovering from cardiac surgery[7].

Midazolam was showed closely associated with increased rate of 28-days mortality, and had obviously higher rate of 28-days mortality when compared with propofol or dexmedetomidine using. This phenomenon could be attributed to the following factors. Midazolam has many serious cardiorespiratory events and possible paradoxical reactions. Some cardiovascular side effects are premature ventricular contractions, vasovagal episodes, bradycardia, tachycardia, nodal rhythm, as well as variations in blood pressure and pulse rate[8]. Midazolam using could introduce coronary artery spasm[9].

Not only midazolam's worse on mortality was confirmed in our study, but also increase length of mechanical ventilation, CCU and hospital stay when compared with propofol and dexmedetomidine. A meta-analysis demonstrated that dexmedetomidine could reduced the length of ICU stay[10]. A few records of RASS scores were presented in our study, which might attribute to the arousable and light sedation. But with a longer time sedation, midazolam was founded to be similar to propofol and dexmedetomidine[11], and in deep sedation midazolam significantly increased the time at target sedation[12]. Long stay in the CCU adds to the burden of health care costs.

PSM is a powerful method to distinguish unbalanced groups. In this study, we chose age, male, hypertension, Scr, MI, beta-blocker, stain, vasopressor, and revascularization as confounding factors. And we found that compared with propofol & dexmedetomidine, midazolam using in AMI patients was still significant associated with increased rate of CCU mortality, hospital mortality, 28-days mortality, and the length of mechanical ventilation, CCU stay.

Several limitations should be reported in this study. First, potential bias remain exist as other unrecorded factors (such as the sedative and ventilation weaning protocol, pre-treatment drugs and door-to-balloon

time, the incomplete records of RASS scores and serum tropoin) were not available in MIMIC III database. Secondly, due to the cohort design, only the association instead of causal relationship can be inferred from this study. Third, the sample size of dexmedetomidine using was relatively small, further studies are needed to explore the association between dexmedetomidine and propofol, midazolam and dexmedetomidine.

Conclusion

The authors concluded that compared with propofol and dexmedetomidine, midazolam using for sedative therapy of AMI patients was significant associated with higher rate of CCU mortality, hospital mortality, 28-days mortality, and longer of mechanical ventilation duration, CCU stay. Propofol or dexmedetomidine is prefer to be used in AMI critical patients for sedative therapy.

Abbreviations

AMI, acute myocardial infarction (AMI); MIMIC III, Medical Information Mart for Intensive Care III; CCU, Coronary Heart Disease Intensive Care unit; BMI, body mass index; WBC, white blood cell; PLT, platelet; HGB, hemoglobin; TB, total bilirubin; Glu, glucose; Scr, creatinine; NSTEMI, non-ST segment elevated myocardial infarction; AWSTEMI, anterior wall ST segment elevated myocardial infarction; NAWSTEMI, non-anterior wall ST segment elevated myocardial infarction; CHF, congestive heart failure;COPD, chronic obstructive pulmonary disease; MBP, mean arterial pressure;

Declarations

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Availability of data and materials

All data are freely available with reasonable requirements from authors.

Authors' contributions

Xiaowei Jiang were responsible for designing the study, analysing and interpreting the data, and revising the manuscript prior to submission. Min Yan were involved in the drafting and revising the manuscript prior to submission.

Ethics approval and consent to participate

This study was performed in accordance with the principals of the Declaration of Helsinki. MIMIC III database used in the present study is publicly available database and was approved by the Institutional Review Boards (IRB) of the Massachusetts Institute of Technology (Cambridge, MA). All protected health information were fully anonymized for researcher, and a waiver of the requirement for informed consent was included in the IRB approval of Massachusetts Institute of Technology (Cambridge, MA). Therefore, the ethical approval statement and the need for informed consent were waived for this manuscript.

Competing interests

None

References

1. Sydow M, Neumann P: **Sedation for the critically ill**. *Intensive Care Med* 1999, **25**(6):634–636.
2. Ter Horst EN, Krijnen P, Flecknell P, Meyer KW, Kramer K, van der Laan AM, Piek JJ, Niessen H: **Sufentanil-medetomidine anaesthesia compared with fentanyl/fluanisone-midazolam is associated with fewer ventricular arrhythmias and death during experimental myocardial infarction in rats and limits infarct size following reperfusion**. *Lab Anim* 2018, **52**(3):271–279.
3. Mimuro S, Katoh T, Suzuki A, Yu S, Adachi YU, Uraoka M, Sano H, Sato S: **Deterioration of myocardial injury due to dexmedetomidine administration after myocardial ischaemia**. *RESUSCITATION* 2010, **81**(12):1714–1717.
4. Zhang WY, Zhang QL, Xu MJ: **Effects of propofol on myocardial ischemia reperfusion injury through inhibiting the JAK/STAT pathway**. *Eur Rev Med Pharmacol Sci* 2019, **23**(14):6339–6345.
5. Chang YF, Chao A, Shih PY, Hsu YC, Lee CT, Tien YW, Yeh YC, Chen LW: **Comparison of dexmedetomidine versus propofol on hemodynamics in surgical critically ill patients**. *J SURG RES* 2018, **228**:194–200.
6. Rasmussen T, Follin B, Kastrup J, Christensen TE, Hammelev KP, Kjaer A, Hasbak P: **Myocardial perfusion of infarcted and normal myocardium in propofol-anesthetized minipigs using (82)Rubidium PET**. *J NUCL CARDIOL* 2016, **23**(3):599–603.
7. Turan A, Duncan A, Leung S, Karimi N, Fang J, Mao G, Hargrave J, Gillinov M, Trombetta C, Ayad S *et al*: **Dexmedetomidine for reduction of atrial fibrillation and delirium after cardiac surgery (DECADE): a randomised placebo-controlled trial**. *LANCET* 2020, **396**(10245):177–185.
8. Mancuso CE, Tanzi MG, Gabay M: **Paradoxical reactions to benzodiazepines: literature review and treatment options**. *PHARMACOTHERAPY* 2004, **24**(9):1177–1185.
9. Ates AH, Kul S: **Acute coronary syndrome due to midazolam use: Kounis syndrome during a transurethral prostatectomy**. *Turk Kardiyol Dern Ars* 2015, **43**(6):558–561.
10. Liu X, Hong H, Zhang H, Xu Z, Liu J, Qiu L: **Treatment Strategies for Primary Tumors of the Heart in Children: A 10-Year Experience**. *ANN THORAC SURG* 2015, **100**(5):1744–1749.

11. Jakob SM, Ruokonen E, Grounds RM, Sarapohja T, Garratt C, Pocock SJ, Bratty JR, Takala J: **Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials**. *JAMA* 2012, **307**(11):1151–1160.
12. Ruokonen E, Parviainen I, Jakob SM, Nunes S, Kaukonen M, Shepherd ST, Sarapohja T, Bratty JR, Takala J: **Dexmedetomidine versus propofol/midazolam for long-term sedation during mechanical ventilation**. *Intensive Care Med* 2009, **35**(2):282–290.

Figures

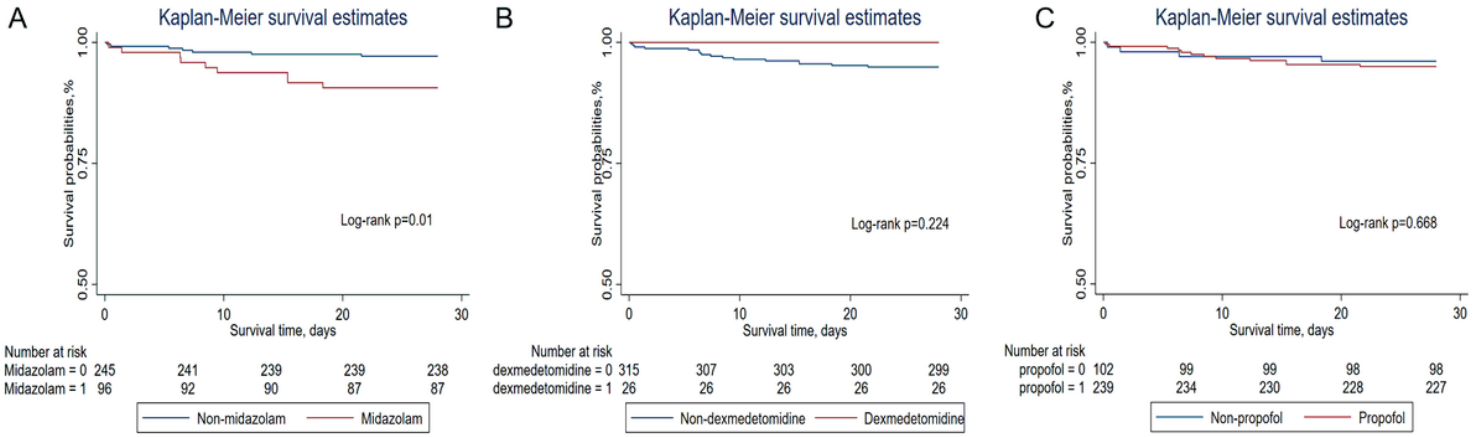

Figure 1

Kaplan-Meier method estimated 28-days mortality in patients with myocardial infarction stratified by midazolam(A), dexmedetomidine(B) or propofol(C).

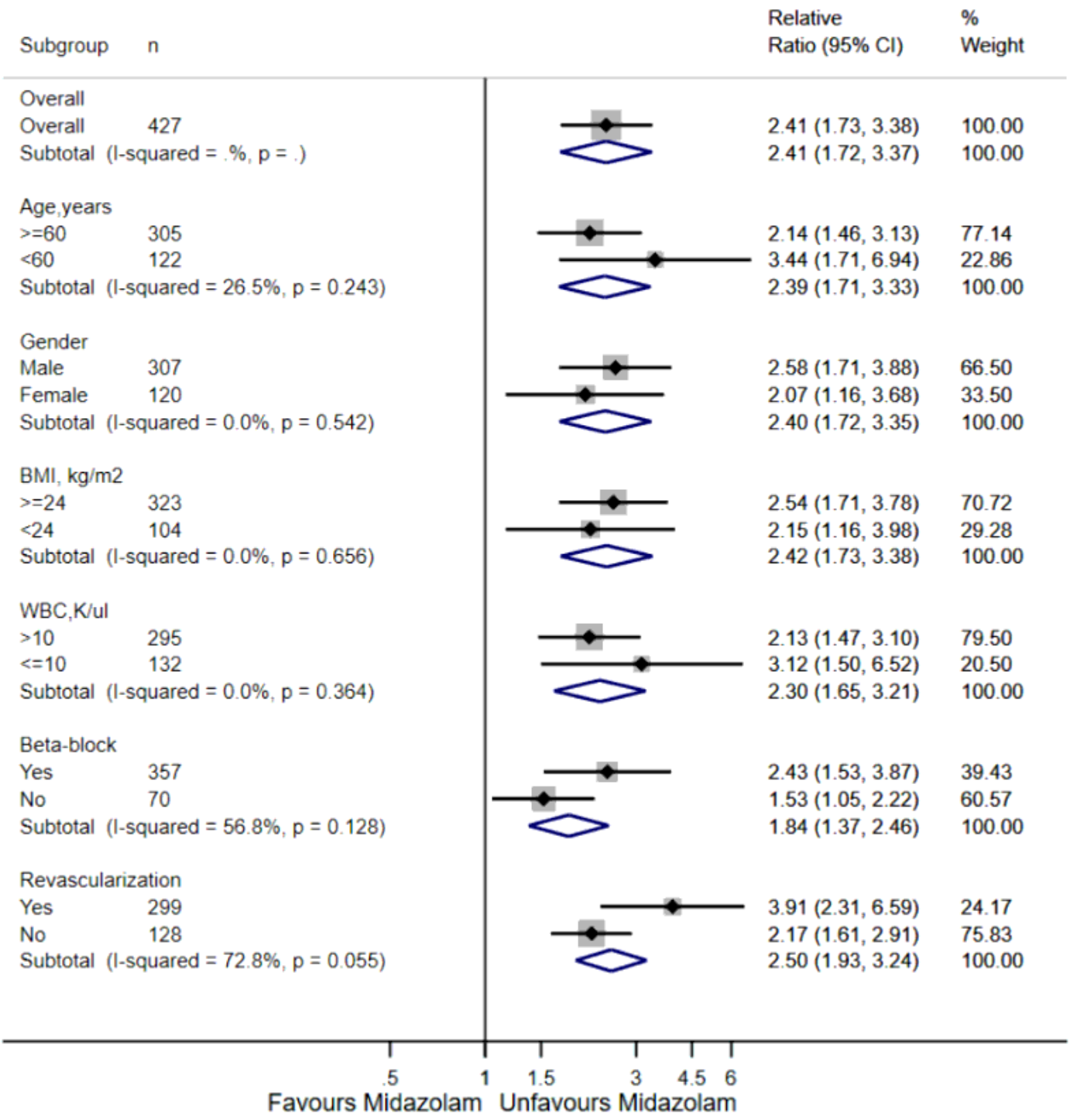

Figure 2

Subgroup analysis of the association between 28-days mortality and midazolam using

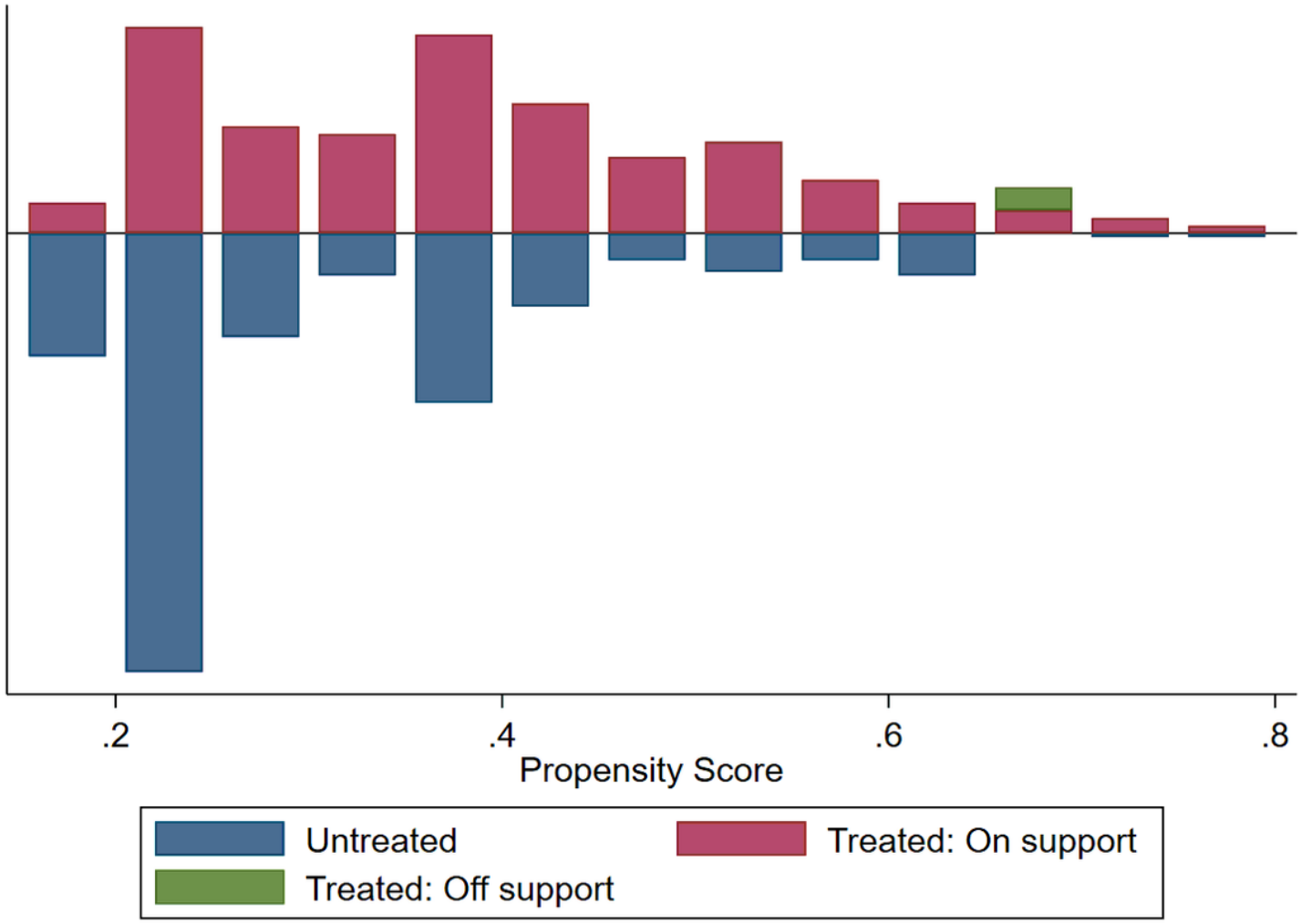

Figure 3

Matching graph of the propensity score before and after propensity score matching