Dexmedetomidine use and Mortality in Mechanically-Ventilated Patients with Severe Burns: A Cohort Study Using a National Inpatient Database in Japan

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Abstract

Background: Dexmedetomidine is an alpha 2-adrenergic receptor agonist. Apart from its sedative effects, dexmedetomidine has the potential to reduce mortality through its anti-inflammatory effect. However, the impact of dexmedetomidine on in-hospital outcomes of patients with severe burns remains unclear. Therefore, we aimed to elucidate the association between dexmedetomidine and mortality in mechanically-ventilated patients with severe burns, using a Japanese nationwide database of in-hospital patients.

Methods: We included adults with severe burns (burn index ≥ 10) who were registered in the Japanese Diagnosis Procedure Combination national inpatient database from 2010 to 2018, started mechanical ventilation within 3 days of admission, and received any sedative drug (dexmedetomidine, midazolam, or propofol). One-to-one propensity score matching was performed between patients who received dexmedetomidine on the day of mechanical ventilation initiation (dexmedetomidine group) and those who did not receive dexmedetomidine (control group). The primary outcome was all-cause 30-day in-hospital mortality. Secondary outcomes were length of hospital stay and duration of mechanical ventilation in all patients and survivors.

Results: Eligible patients (n = 1,888) were classified into the dexmedetomidine group (n = 371) or the control group (n = 1,517). After one-to-one propensity score matching, we compared 329 patients from each of the two groups. No significant difference was observed in 30-day mortality between patients in the dexmedetomidine and control groups (22.8% vs. 22.5%, respectively; odds ratio, 1.02; 95% confidence interval, 0.71-1.46). Moreover, there were no significant differences between patients in the dexmedetomidine and control groups in terms of the length of hospital stay or the duration of mechanical ventilation.

Conclusions: We found no significant association between dexmedetomidine use and in-hospital outcomes (mortality, length of hospital stay, and length of mechanical ventilation) in mechanically-ventilated patients with severe burns. Dexmedetomidine use may not improve the above-mentioned outcomes; therefore, its selection should be based on the patient's general condition and the target level of sedation.

Background

Burns constitute a major cause of trauma. Although the mortality from burns is improving in developed countries, it remains high, at about 20%, in patients with a total burn surface area of at least 20% [1–3]

Dexmedetomidine is an alpha 2-adrenergic receptor agonist that inhibits the release of endogenous noradrenalin. It is primarily used as a sedative for controlling critically ill patients into a good quality, light sedative state compared to midazolam and propofol [4]. Compared to benzodiazepines, dexmedetomidine has a more considerable effect in delirium risk reduction [5]. A few reports have examined the effects of dexmedetomidine on sedation and delirium in patients with burns [6–8].

In addition to its sedative effects, several studies have reported better outcomes with dexmedetomidine among critically ill patients compared to those of other sedative agents [9]. A systematic review of 1624 patients showed that the use of dexmedetomidine was associated with a reduction in the length of intensive care unit (ICU) stay and with mechanical ventilation use [9]. However, the impact of dexmedetomidine on short-term outcomes in patients with severe burns remains unclear[4, 10].

Dexmedetomidine is also expected to improve burn outcomes due to its anti-inflammatory effects [10, 11]. However, to our knowledge, no studies have examined a possible association between dexmedetomidine and mortality in patients with severe burns. Therefore, we aimed to investigate a possible association between dexmedetomidine use and

mortality in mechanically-ventilated patients with severe burn, using a Japanese nationwide database of in-hospital patients.

Methods

Data source

We used the Japanese Diagnosis Procedure Combination database, which has been used for clinical studies on various topics, including burns [13–17]. The database contains discharge abstracts and administrative billing data from more than 1,000 voluntary participating hospitals in Japan. Until 2010, annual data were collected over a six-month period, from July 1 to December 31. Since 2011, data have been collected on a year-round basis. Larger hospitals were more likely to contribute their data to the database, with all 82 hospitals being academic; more than 90% of tertiary emergency hospitals were in the database, and ≅90% (90/100) of institutions were board-certified by the Japanese Society for Burn Injuries to impart training to burn specialists [13].

The dataset includes hospital identification number, hospital academic status, patient demographic characteristics, admission and discharge dates, main and comorbid diagnoses at admission, in-hospital complications (which were coded according to the International Classification of Diseases [ICD-10]), discharge status, procedure or operation dates and codes (in Japanese), and prescribed medications. Physicians attended to patient records to establish diagnoses at discharge. In order to optimise the accuracy of the recorded diagnosis, the attending physician was obligated to record the diagnosis with reference to the medical record.

Moreover, the database includes burn indices, which are calculated using both burn surface area and thickness: burn index = full thickness of total burn surface area + 1/2 partial thickness of total burn surface area [13, 18]. Previous reports suggested that the burn index was a good predictor of patient mortality [13, 19].

Study Participants

We included patients aged 15 years or older, with emergency hospitalisation for burns (based on ICD-10 codes T20-T30) between July 2010 and March 2018, who started mechanical ventilation within 3 days of admission, and were administered at least one of the following sedative agents: dexmedetomidine, midazolam, or propofol [4, 16, 20]. In addition, we restricted the study participants to patients with severe burns, defined as burn index ≥ 10 [3, 14, 15]. We excluded patients with missing records of burn index, and those who died on the day of mechanical ventilation initiation to avoid immortal time bias.

Exposure

The exposure of interest was the use of dexmedetomidine. The dexmedetomidine group was made of patients who were administered dexmedetomidine on the day of mechanical ventilation initiation, whereas the control group was made of patients who were administered either propofol or midazolam on the day of mechanical ventilation initiation. A small number of patients receiving both dexmedetomidine and propofol or midazolam were included in the dexmedetomidine group since our interest was the effect of dexmedetomidine.

Outcomes

The primary outcome was all-cause 30-day in-hospital mortality. Secondary outcomes included length of hospital stay and duration of mechanical ventilation in all patients and survivors.

Covariates

We considered the following characteristics as potential confounding factors: age; sex; body mass index; Charlson comorbidity index; burn index; the presence of inhalation injury and head/neck burns; Japan Coma Scale score at admission; hospital characteristics, including academic/non-academic status, the presence or absence of certification by the Japanese Society for Burn Injuries, and hospital volume; ICU admission; transportation from another hospital; and mechanical ventilation initiation day (i.e., day 0, 1, 2, or 3). Furthermore, we considered the following treatment regimens on the day of mechanical ventilation initiation: the use of other sedatives (propofol and midazolam), opioids, vasoactive agents (dopamine, dobutamine, adrenaline, noradrenaline, and vasopressin), albumin, intravenous antibiotics, transfusion (red blood cells, platelets, and fresh frozen plasma), continuous renal replacement therapy, enteral tube feeding, and surgery.

The body mass index, calculated using the formula: body mass index = mass (in kg)/height squared (in m^2), was categorized into four groups: <18.5, 18.5 to < 25, 25 to < 30, and ≥ 30 kg/m^2 [21]. The Charlson comorbidity index reflects the underlying disease or condition [22], and is defined based on ICD-10 codes recorded in the database [23]. In this study, Charlson comorbidity index was categorised into three groups as follows: low, 0; medium, 1; and high, ≥ 2. The Japan Coma Scale score is used to assess the level of consciousness, and correlates with the Glasgow Coma Scale score. Neurologic dysfunction scored at 100 points on the Japan Coma Scale is equivalent to scores of 6–9 on the Glasgow Coma Scale [24]. We categorised the Japan Coma Scale scores into four groups: 0, alert; 1–3, delirium; 10–30, somnolence; and 100–300, coma. Hospital volume was defined as the number of patients with severe burns admitted per year during the study period and was categorised into low, medium, and high hospital volume. Hospital types were categorised based on the accreditation status issued by the Japanese Society for Burn Injuries.

Statistical analysis

We evaluated baseline characteristics and crude 30-day in-hospital mortality in the dexmedetomidine and control groups. Continuous and ordinal variables were expressed as medians and interquartile ranges. Categorical variables were presented as numbers and percentages. Comparisons were performed using the t-test for continuous variables and chi-squared test for categorical variables.

We conducted a one-to-one propensity score matched analysis to determine the conditional probability or the likelihood of administering dexmedetomidine using measured pre-treatment factors. The propensity score was estimated using a multivariable logistic regression model that adjusted for the aforementioned covariates (i.e., patient characteristics including age, squared terms of age, sex, comorbidities, degree of burn, consciousness; hospital characteristics and treatment regimen on the day of mechanical ventilation initiation). Each patient in the dexmedetomidine group was matched to a patient in the control group using nearest-neighbour matching, a calliper width equal to 0.2 of the standard deviation of the propensity score, and without replacement. The C-statistic was calculated to evaluate the discriminative ability of the propensity score estimation. We used the standardized difference to measure covariate balance, whereby an absolute standardized difference > 10% represented meaningful imbalance [25].

In the propensity score-matched patients, we performed logistic regression analyses fitted with generalised estimating equations and paired t-tests to examine the association between dexmedetomidine use and 30-day mortality, as well as

the length of hospital stay and the duration of mechanical ventilation in all eligible patients and survivors (to account for competing risk of death) [25].

We also conducted several sensitivity analyses. In the first sensitivity analysis, we used the inverse probability of treatment weighting (IPTW) method. First, we estimated the propensity score of receiving dexmedetomidine using the aforementioned covariates. Thereafter, we calculated the inverse probability of treatment. Finally, we estimated the effect of dexmedetomidine use on 30-day in-hospital mortality using a generalised linear model with a logit link function for a binomial outcome weighted by IPTW [26, 27]. In the second sensitivity analysis, the outcome definition was changed to all cause in-hospital mortality.

In the third sensitivity analysis, we judged the exposure status (the use or non-use of dexmedetomidine) on the day of or the day following mechanical ventilation initiation. For this analysis, we excluded patients who died on the day of or day following mechanical ventilation initiation to avoid immortal time bias.

All tests of significance were two-tailed, and $p < .05$ was considered significant. Variables were analysed using Stata version 15 (Stata-Corp, College Station, TX, USA).

Results

We included 1,888 eligible patients, including 371 and 1,517 patients in the dexmedetomidine and control groups, respectively (Fig. 1). Patients in both groups had similar ages and sexes; however, those in the dexmedetomidine group had a lower burn index, and were more likely to receive catecholamines (dopamine, adrenalin, and noradrenalin) than those in the control group (Table 1, left columns). The crude 30-day mortality was 24.3% (90/371) in the dexmedetomidine group and 28.0% (425/1517) in the control group.

Table 1
Characteristics of the patients before and after propensity score matching

	Crude			propensity score matched		
	Dexmedetomidine (N = 371)	Control (N = 1517)	Standardized difference (%)	Dexmedetomidine (N = 329)	Control (N = 329)	Standardized difference (%)
Sex(male), n (%)	226 (60.9)	953 (62.8)	-1.5	204 (62)	211 (64.1)	-4.4
Age (year), median (IQR)	67 (51–79)	64 (48–77)	16.3	67 (51–79)	66 (49–78)	10.7
Burn index	22.5 (15.0–36.0)	27.0 (17.5–42.5)	-28.7	21.0 (15.0-35.5)	22.0 (16.0-34.5)	-2.3
Inhalation injury, n (%)	140 (37.7)	556 (36.7)	4.0	125 (38)	134 (40.7)	-5.6
Facial burn, n(%)	103 (27.8)	349 (23)	15.3	98 (29.8)	106 (32.2)	-5.3
Body mass index, n (%)			0.0			0.0
18.5–25	198 (53.4)	801 (52.8)	0.5	198 (60.2)	194 (59)	2.5
< 18,5	32 (8.6)	172 (11.3)	-10.0	32 (9.7)	36 (10.9)	-4.0
25–30	70 (18.9)	261 (17.2)	4.3	70 (21.3)	74 (22.5)	-2.9
30<	29 (7.8)	102 (6.7)	4.3	29 (8.8)	25 (7.6)	4.4
Charlson Comorbidity Index, n (%)			0.0			0.0
0	332 (89.5)	1398 (92.2)	-7.1	296 (90)	300 (91.2)	-4.2
1	7 (1.9)	33 (2.2)	-4.8	5 (1.5)	5 (1.5)	0.0
≥ 2	32 (8.6)	86 (5.7)	10.4	28 (8.5)	24 (7.3)	4.5
Japan Coma Scale,n (%)			0.0			0.0

IQR interquartile range, Burn index = full thickness of total burn-surface area + 1/2 partial thickness of total burn-surface area. Body mass index was categorized into four groups: <18.5, 18.5 to < 25, 25 to < 30 and ≥ 30. The Charlson Comorbidity Index was categorized into the three groups in the current study as follows: low, 0; medium, 1; and high, > 2. The Japan Coma Scale score was categorized into four groups: 0, alert; 1–3,delirium; 10–30, somnolence; and 100–300, coma. Hospital volume was defined as the number of patients with severe burn (burn index > 10) admitted within the study period, categorized into tertiles (e.g., low, medium and high).

	Crude			propensity score matched		
clear	161 (43.4)	558 (36.8)	10.9	142 (43.2)	140 (42.6)	1.2
delirium	93 (25.1)	380 (25)	2.1	85 (25.8)	95 (28.9)	-6.8
somnolence	41 (11.1)	166 (10.9)	-1.7	35 (10.6)	35 (10.6)	0.0
coma	76 (20.5)	413 (27.2)	-13.7	67 (20.4)	59 (17.9)	6.2
Interhospital transfer, n (%)	100 (27)	348 (22.9)	7.0	87 (26.4)	87 (26.4)	0.0
ICU admission, n (%)	275 (74.1)	1119 (73.8)	-0.2	243 (73.9)	246 (74.8)	-2.1
Hospital volume, n (%)			0.0			0.0
Low	103 (27.8)	370 (24.4)	11.4	88 (26.7)	83 (25.2)	3.5
Middle	154 (41.5)	490 (32.3)	15.4	132 (40.1)	140 (42.6)	-4.9
High	114 (30.7)	657 (43.3)	-25.4	109 (33.1)	106 (32.2)	1.9
Academic hospital, n (%)	180 (48.5)	724 (47.7)	2.4	164 (49.8)	168 (51.1)	-2.4
Burn society certified hospital, n (%)	172 (46.4)	690 (45.5)	2.2	154 (46.8)	155 (47.1)	0.6
Initial day of mechanical ventilation			0.0			0.0
1	280 (75.5)	1240 (81.7)	-17.1	246 (74.8)	248 (75.4)	-1.4
2	59 (15.9)	208 (13.7)	7.4	53 (16.1)	52 (15.8)	0.8
3	32 (8.6)	69 (4.5)	17.4	30 (9.1)	29 (8.8)	1.1

IQR interquartile range, Burn index = full thickness of total burn-surface area + 1/2 partial thickness of total burn-surface area. Body mass index was categorized into four groups: <18.5, 18.5 to < 25, 25 to < 30 and ≥ 30. The Charlson Comorbidity Index was categorized into the three groups in the current study as follows: low, 0; medium, 1; and high, > 2. The Japan Coma Scale score was categorized into four groups: 0, alert; 1–3,delirium; 10–30, somnolence; and 100–300, coma. Hospital volume was defined as the number of patients with severe burn (burn index > 10) admitted within the study period, categorized into tertiles (e.g., low, medium and high).

	Crude			propensity score matched		
Propofol, n (%)	226 (60.9)	904 (59.6)	-1.7	193 (58.7)	202 (61.4)	-5.6
Midazolam, n (%)	166 (44.7)	1027 (67.7)	-44.8	150 (45.6)	162 (49.2)	-7.3
Opioid, n (%)	318 (85.7)	1209 (79.7)	12.2	279 (84.8)	280 (85.1)	-0.8
Antibiotics, n (%)	232 (62.5)	804 (53)	18.9	206 (62.6)	201 (61.1)	3.1
Dopamine, n (%)	77 (20.8)	192 (12.7)	23.2	68 (20.7)	68 (20.7)	0.0
Dobutamine, n (%)	19 (5.1)	67 (4.4)	4.0	16 (4.9)	17 (5.2)	-1.4
Adrenalin, n (%)	40 (10.8)	75(4.9)	22.9	37 (11.2)	29 (8.8)	8.1
Noradrenalin, n (%)	130 (35)	229 (15.1)	41.5	107 (32.5)	102 (31)	3.3
Vasopressin, n (%)	5 (1.3)	18 (1.2)	-2.8	3 (0.9)	5 (1.5)	-5.5
Albumin, n (%)	167 (45)	604 (39.8)	7.1	143 (43.5)	145 (44.1)	-1.2
Blood transfusion, n (%)	38 (10.2)	131 (8.6)	5.1	34 (10.3)	33 (10)	1.0
continuous renal replacement therapy, n (%)	14 (3.8)	67 (4.4)	-6.2	10 (3)	19 (5.8)	-13.0
Enteral nutrition, n (%)	95 (25.6)	297 (19.6)	12.6	85 (25.8)	82 (24.9)	2.1
Skin graft surgery or debridement, n (%)	38 (10.2)	105 (6.9)	12.4	35 (10.6)	37 (11.2)	-1.9

IQR interquartile range, Burn index = full thickness of total burn-surface area + 1/2 partial thickness of total burn-surface area. Body mass index was categorized into four groups: <18.5, 18.5 to < 25, 25 to < 30 and ≥ 30. The Charlson Comorbidity Index was categorized into the three groups in the current study as follows: low, 0; medium, 1; and high, > 2. The Japan Coma Scale score was categorized into four groups: 0, alert; 1–3,delirium; 10–30, somnolence; and 100–300, coma. Hospital volume was defined as the number of patients with severe burn (burn index > 10) admitted within the study period, categorized into tertiles (e.g., low, medium and high).

We matched 329 pairs according to the propensity score of receiving dexmedetomidine. The C-statistic was 0.737. The covariates in the matched cohort were well balanced (Table 1, right columns). After propensity score matching, the 30-day mortality was 22.8% (75/329) in the dexmedetomidine group and 22.5% (74/329) in the control group ($p = 0.93$).

In the logistic regression analysis fitted with generalised estimating equations, dexmedetomidine administration was not associated with 30-day mortality (odds ratio, 1.02; 95% confidence interval, 0.71–1.46) (Fig. 2). As for secondary outcomes, there were no differences in the length of hospital stay in all patients (dexmedetomidine 52 days vs. control 49 days, $p = 0.86$) and survivors (dexmedetomidine 73 days vs. control 78 days, $p = 0.19$), akin to the duration of mechanical ventilation in all patients (dexmedetomidine 16 days vs. control 16 days, $p = 0.27$) and survivors (dexmedetomidine 17 days vs. control 18 days, p = 0.18) (Table 2).

Table 2
Study outcomes before and after propensity score matching

	Crude			Propensity score matched		
	Dexmedetomidine (N = 371)	Control (N = 1517)	*p*-value	Dexmedetomidine (N = 329)	Control (N = 329)	*p*-value
Length of stay (overall) day, median (IQR)	52 (19–96)	49(13–95)	0.86	54 (20–101)	61 (13–95)	0.98
Length of stay (survivors) day, median (IQR)	73 (42–115)	78 (45–122)	0.19	74 (46–116)	78 (45–122)	0.90
Duration of mechanical ventilation (overall) day, median (IQR)	16 (6–36)	16 (6–38)	0.27	16 (7–36)	16 (7–35)	0.69
Duration of mechanical ventilation (survivors) day, median (IQR)	17 (7–36)	18 (8–40)	0.18	17 (7–36)	15 (8–34)	0.65
30-day mortality, n (%)	90 (24.3)	425 (28.0)	0.15	75 (22.8)	73 (22.2)	0.93
in-hospital mortality, n (%)	132 (35.6)	621 (40.9)	0.06	115 (35)	112 (34)	0.87

IQR Interquartile range

The sensitivity analyses showed similar results with those of our main analysis (Fig. 2). In the first sensitivity analysis, the IPTW method resulted in an adjusted odds ratio of 0.98 (95% confidence interval 0.69–1.39) for 30-day mortality. In the second sensitivity analysis, the odds ratio (and 95% confidence interval) of setting the outcome as the in-hospital mortality was 1.03 (0.75–1.40). In the third sensitivity analysis, the odds ratio (and 95% confidence interval) of judging the exposure status on the day of or day following mechanical ventilation initiation was 0.99 (0.70–1.38) (Fig. 2).

Discussion

Using a Japanese national in-hospital database, we examined the association between dexmedetomidine administration and in-hospital outcomes in mechanically-ventilated patients with severe burns. We found no significant differences between patients in the dexmedetomidine and control groups in terms of mortality, length of hospital stay, and duration of mechanical ventilation. Several sensitivity analyses led to the same conclusions.

A systematic review showed that dexmedetomidine administration was associated with a reduced duration of mechanical ventilation and hospital stay in ICU patients [9]. However, this result may not be applicable to patients with

burns because previous studies often excluded patients with burns, and the systematic review did not specifically examine the effect of dexmedetomidine in patients with burns [4, 10].

Recently, several studies have examined the use of dexmedetomidine in patients with sepsis [20, 28–30]. A meta-analysis of observational studies and a secondary analysis of randomized control trials have shown significant differences in duration of ventilator-free days and short-term mortality [28, 29]. An observational study also found a reduction in mortality and ventilation duration with dexmedetomidine use [20]. Nonetheless, randomized control trials have not shown prognosis improvements with dexmedetomidine use [30]. Therefore, the effect of dexmedetomidine on mortality remains inconclusive, even in sepsis.

We expected that dexmedetomidine could improve severe burn outcomes through sedation amelioration, delirium risk reduction [4, 31] and anti-inflammatory effects that are organo-protective [11, 12, 32–35]. However, in the current study, we did not find any benefit of dexmedetomidine in patients with severe burns for several possible reasons. First, burns are very heterogeneous. Mortality could be influenced by a variety of patient (burn severity and location) and hospital factors (the availability of specialists and equipment for severe burn management). In such situations, dexmedetomidine may play a relatively small role in saving patients' lives. Second, in Japan, the average hospital length of stay in an acute care hospital tends to be longer [36]. This may be driven by factors such as wound complexity and general management conditions, especially for burns. Social factors, rather than medical conditions, may play a role in the longer hospital length of stay [37], which may explain why there was no difference in the lengths of hospital stay. Third, the duration of mechanical ventilation may be influenced not only by systemic conditions but also by localised burn conditions (e.g., inhalation injury or facial injury) and surgery timing. These factors cannot be modified by dexmedetomidine.

Limitation

This study has several limitations. First, this was a retrospective cohort study, and therefore unmeasured or residual confounding factors could have masked the potential association between use dexmedetomidine use and in-hospital outcomes. Although we believe that we could adjust for important confounding factors (e.g., the combination of burn index and age, which have been reported to be valid outcome predictors in patients with burns [13]), there may be some outcome-predicting factors such as vital signs and blood test results. Second, if the effect of dexmedetomidine was small, we might not have been able to detect it with our sample size. Furthermore, subgroup analysis was not performed because of the small sample size. Thus, it remains a possibility that a small group of patients might benefit from dexmedetomidine. Finally, only in-hospital mortality was assessed in the present study. Post-discharge data were not available because the follow-up ended on the date of discharge. However, the overall mean length of hospital stay in the current study was approximately 50 days, and we believe the drug's impact on acute illness could be assessed within this timeframe.

Conclusion

Using a nationwide inpatient database in Japan, we did not find an association between dexmedetomidine and improved in-hospital outcomes (mortality, length of hospital stay, and length of mechanical ventilation) in mechanically-ventilated patients with severe burns. Thus, dexmedetomidine use may not be justified for the purpose of improving the aforementioned outcomes, and the choice of sedatives should depend on the patient's general condition and sedation target level. Further studies are warranted to elucidate the merits and demerits of dexmedetomidine in patients with severe burns.

Abbreviations

ICU
intensive care unit
ICD-10
International Classification of Diseases
IPTW
inverse probability of treatment weighting

Declarations

Ethics approval and consent to participate

Patient identifiers were removed from this database. Informed consent was waived because patient data were anonymous, and the study was approved by the Institutional Review Board of the University of Tokyo.

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from the Ministry of Health, Labour, and Welfare; however, these data were used under license for the current study, and therefore are not publicly available.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YE, MI, AT, KM, TA, and TK designed and conceived this study, performed statistical analysis, and edited the initial manuscript draft. TK, RI, HY, YI, and NT provided professional suggestions on the conduct of the study and interpretation of study results. KU contributed to data collection and management. All authors approved the final manuscript.

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Figures

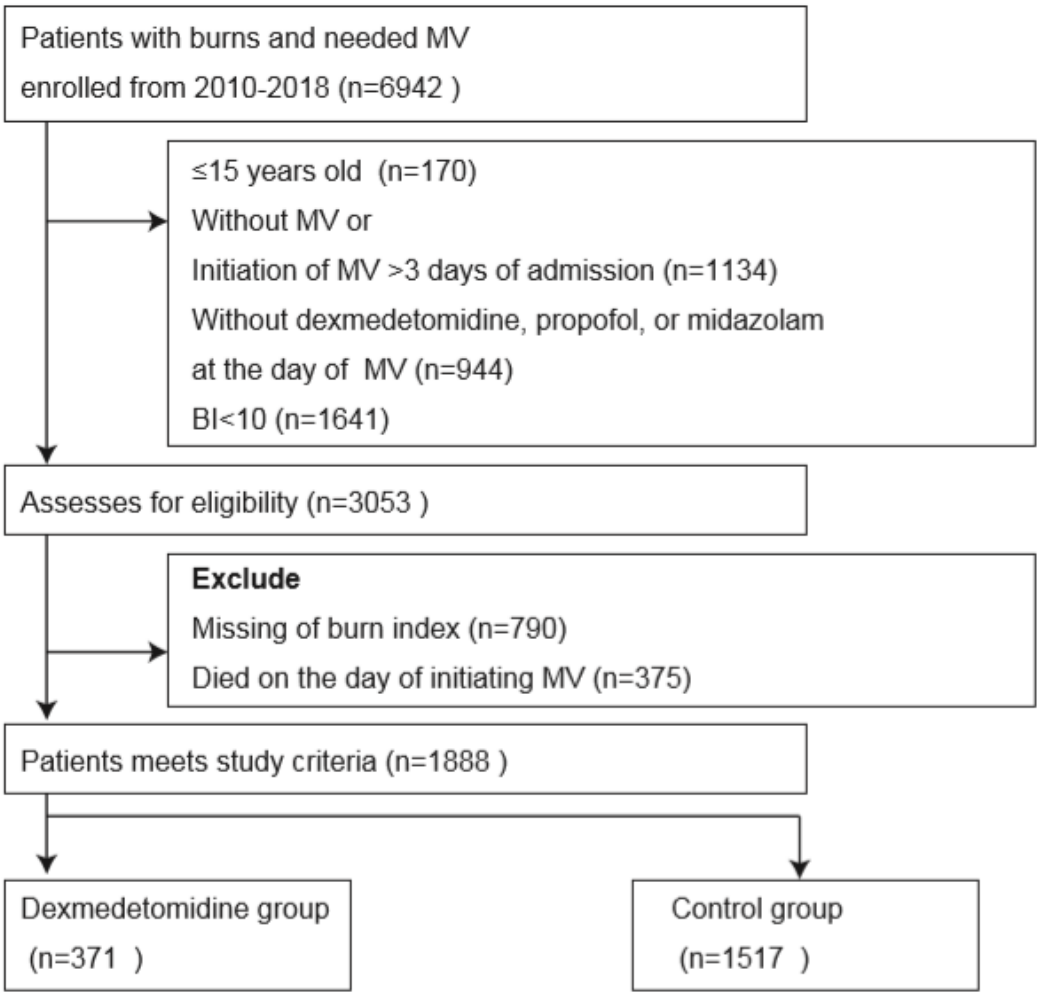
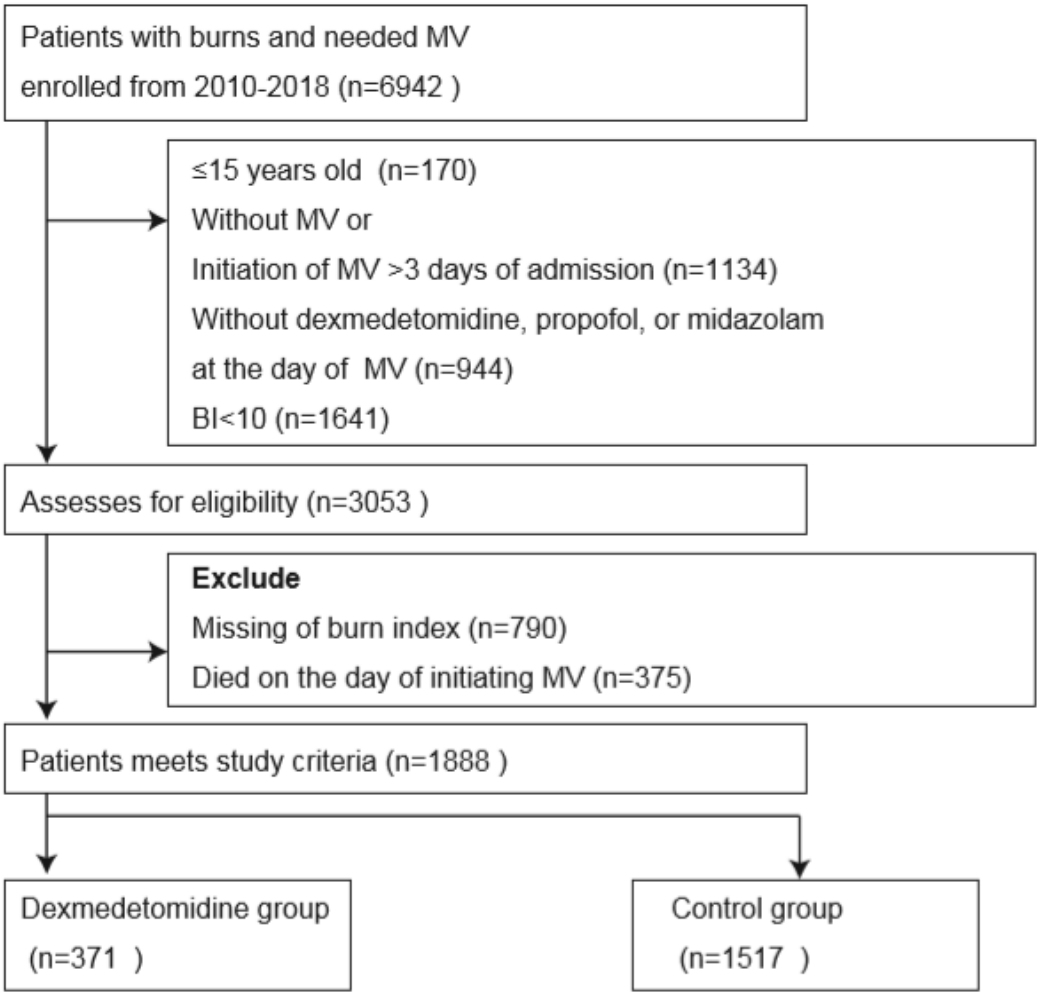


Figure 1

Outline of patient selection MV: mechanical ventilation



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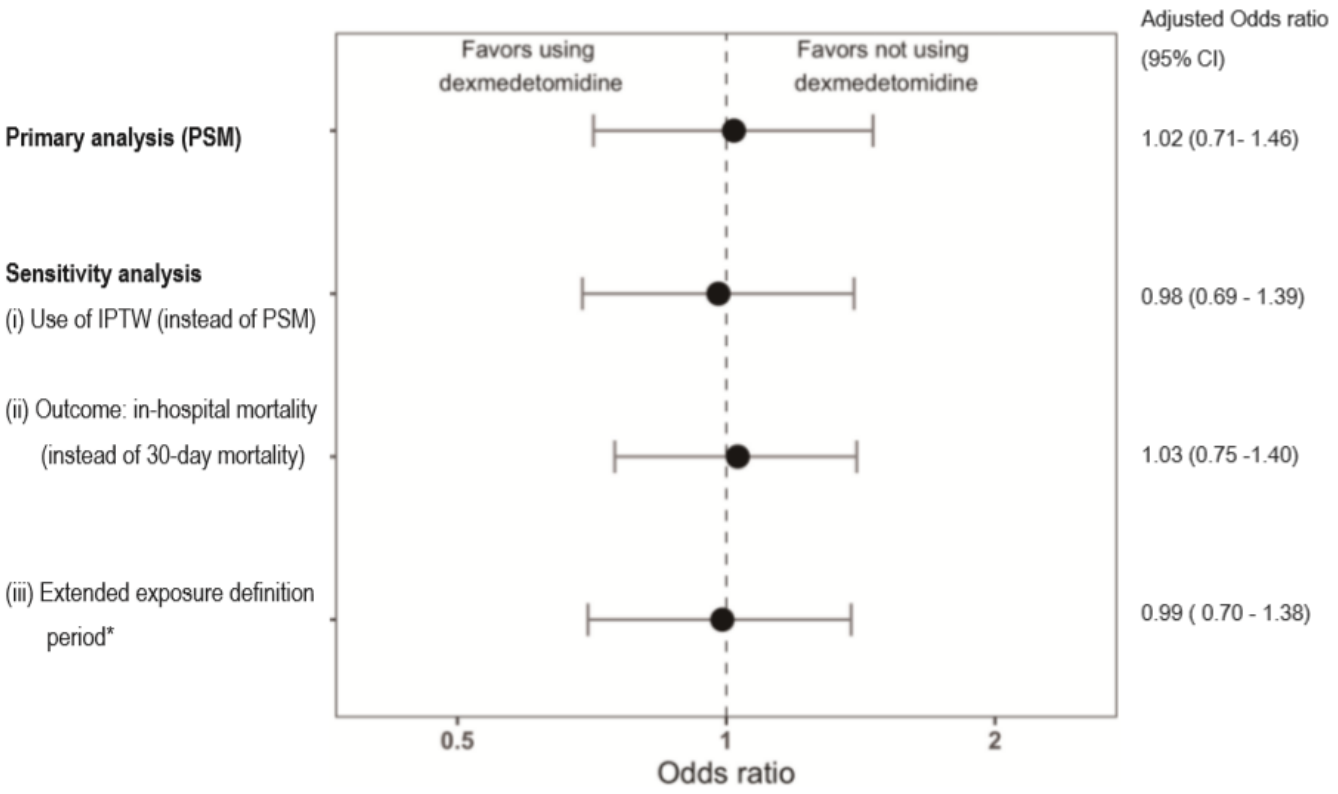
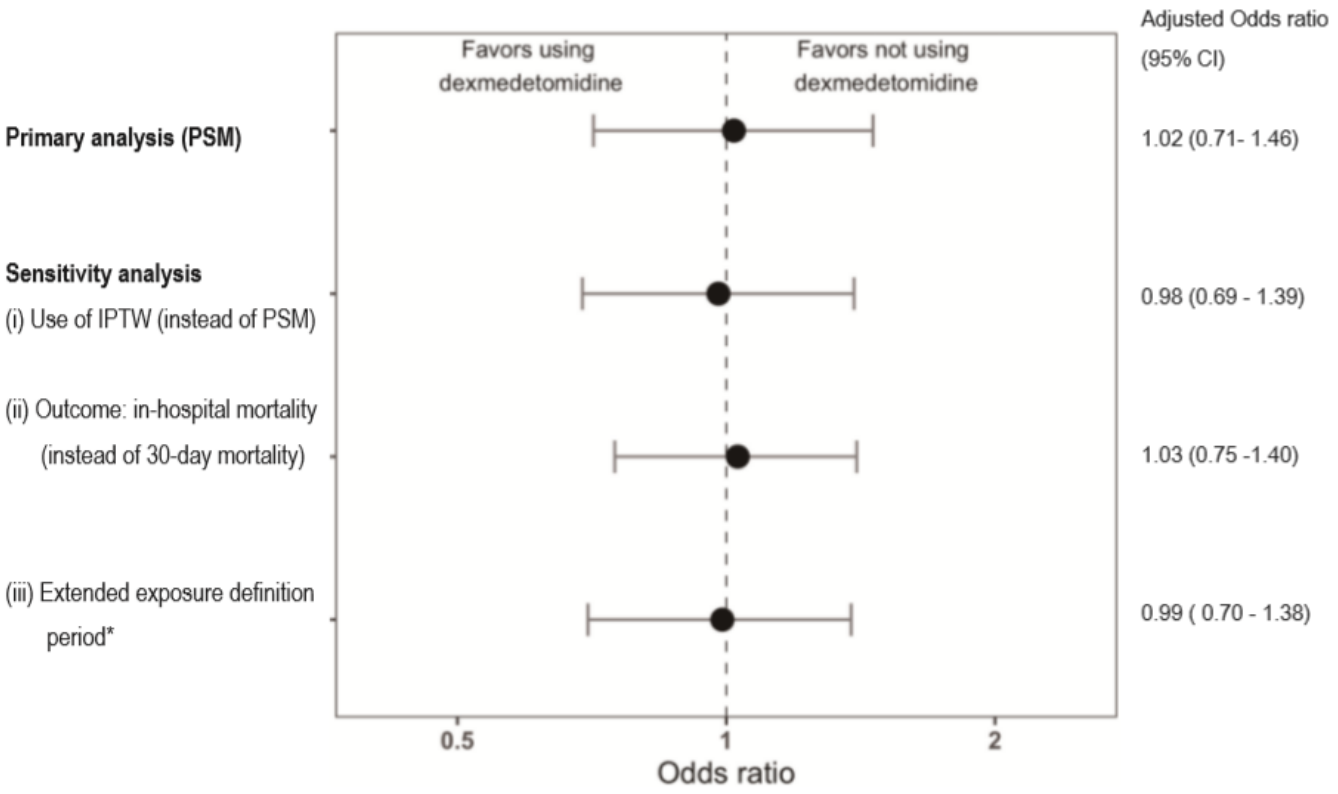


Figure 2

Thirty-day hospital mortality in patients in the dexmedetomidine and control groups and the result of sensitivity analysis PSM: propensity score matching, IPTW: inversed probability treatment weighting * We classified the exposure status (the use or non-use of dexmedetomidine) on the day of or day following mechanical ventilation initiation



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