

# Impact of Dexmedetomidine on Hemodynamics, Plasma Catecholamine Levels, and Delirium Incidence Among Intubated Patients in the ICU--A Randomized Controlled Trial

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**Objective:** To investigate the impact of various sedative medications on hemodynamics and plasma levels of epinephrine (E) and norepinephrine (NE) in mechanically ventilated patients postoperatively in the intensive care unit (ICU).

**Methods:** Ninety-seven patients admitted to the ICU undergoing postoperative mechanical ventilation with tracheal intubation and continuous analgesic sedation following general anesthesia were randomly assigned to either the observation group (dexmedetomidine) ( $n = 49$ ) or the control group (propofol) ( $n = 48$ ) in this randomized controlled trial. Upon transfer to the ICU, vital signs (heart rate [HR], respiratory rate [RR], mean arterial pressure [MAP]) were recorded prior to the initiation of the sedation treatment (T0), at one-hour post sedation (T1) and two hours following tracheal extubation (T2), plasma levels of epinephrine (E) and norepinephrine (NE) were measured at these time points. The incidence of delirium was recorded in both groups.

**Results:** MAP between the two groups at both T0 and T1 At T2 plasma NE and HR were found to be lower in the observation group compared to the control group ( $P < 0.001$ ). Among the patients receiving antihypertensive medication in the ICU, NE levels were significantly lower in the observation group compared to the control group ( $P = 0.019$ ) Among the patients not receiving antihypertensive medication, both NE ( $P < 0.001$ ) and MAP ( $P = 0.001$ ) levels were lower in the observation group compared to the control group. The incidence of delirium in the observation group (dexmedetomidine) was not significantly different from that in the control group (propofol).

**Conclusion:** With dexmedetomidine sedation, blood pressure fluctuated less, plasma catecholamine levels were lower, and sympathetic inhibition was stronger in patients before and after extubation. However, it did not significantly reduce the incidence of postoperative delirium.

**Keywords:** delirium, intensive care unit, hemodynamics, plasma norepinephrine, delirium

## Background

Sedation plays a crucial role in alleviating agitation and anxiety among patients in the ICU,<sup>1</sup> with the primary objective of promoting patient cooperation with treatment and facilitating calm expression of their needs, particularly for analgesia.<sup>2</sup> Current clinical guidelines advocate for the use of sedative medications such as propofol, benzodiazepines (most commonly midazolam and lorazepam),<sup>3</sup> and dexmedetomidine, which mitigates sympathetic stress. Studies have demonstrated that maintaining patients under mild sedation can contribute to improved clinical outcomes, including reduced duration of mechanical ventilation and ICU treatment. Therefore, it is recommended to aim for mild sedation whenever feasible for patients in the ICU.<sup>3</sup>

Dexmedetomidine is a highly selective  $\alpha_2$  adrenergic receptor agonist, primarily targeting the  $\alpha_2$  receptors within the locus coeruleus. This action leads to significant inhibition of sympathetic excitation within the central nervous system resulting in sedative and anti-sympathetic effects.<sup>4-6</sup> A notable characteristic of its pharmacology is its ability to promote

a natural sleep pattern allowing patients to be easily awakened from sedation, thereby achieving sedation while maintaining a relatively awake state without inducing significant respiratory depression.<sup>7,8</sup> Moreover, dexmedetomidine exhibits analgesic properties and can significantly reduce the requirement for opioids.<sup>9</sup> Extensive clinical evidence supports the safety and efficacy of dexmedetomidine across various clinical practices. Additionally, emerging research highlights its protective effects on organs subjected to ischemic and hypoxic injuries, including cardioprotection, neuroprotection, and nephroprotection.<sup>10</sup>

As a peripheral adrenergic  $\alpha_2$  receptor agonist, dexmedetomidine significantly modulates sympathetic nerve activity by competitively binding to peripheral norepinephrine (NE) receptors. Additionally, its high affinity for locus coeruleus cells in the nervous system enables it to reduce the synthesis of norepinephrine by these cells, thereby attenuating the effects of norepinephrine, a major catecholamine, through both source and receptor binding pathways. This mechanism allows dexmedetomidine to achieve its therapeutic effect in suppressing the sympathetic storm.

While previous studies have suggested that dexmedetomidine may elevate the risk of hypotension and bradycardia,<sup>11,12</sup> relatively few studies have examined its specific effects on hemodynamics and plasma catecholamine levels. Delirium in ICU patients is a common acute alteration in mental status characterized by symptoms such as confusion, disorientation, cognitive impairment, emotional disturbances, and abnormal behaviors. Glumac<sup>13</sup> showed that the pathogenesis of postoperative delirium (POD) is still poorly understood and that POD is considered a strong predictor of postoperative cognitive decline (POCD) development, which usually occurs within the first 3 postoperative days. However, POCD occurs at the end of the first week and has no effect on consciousness, and its duration may be significantly prolonged. This study also compared the effects of different sedatives on the incidence of postoperative delirium in surgical patients. Hence, the purpose of this study is to compare the effects of dexmedetomidine and propofol on hemodynamics, plasma catecholamine levels, and the incidence of postoperative delirium.

## Participants and Methods

### Participants of the Study

This study was conducted as a single-center, prospective, randomized controlled trial with ethical clearance granted (ethical approval number: 2021-KY-0037-01/02). Data were collected from patients admitted to the ICU of Peking University International Hospital between April 1, 2022, and November 30, 2023, who required continuous sedation and analgesia following endotracheal intubation-assisted mechanical ventilation. All enrolled patients met the predefined criteria and were assigned to the observation group (dexmedetomidine group) or the control group (propofol group) using a random-number method.

Inclusion criteria: (1) Patients aged between 18 and 80 years; (2) Patients who underwent non-neurosurgical procedures. Exclusion criteria: (1) Patients who are pregnant; (2) Patients who have central nervous system diseases; (3) Patients with acute hepatitis or severe liver disease (class C in Child-Pugh); (4) Patients with basal bradycardia (heart rate less than 55 beats/min), third-degree atrioventricular block, or individuals with implanted cardiac pacemakers; (5) Patients requiring intravenous administration of vasoactive medications such as epinephrine (E) and NE; (6) Patients with a history of adrenal tumors or adrenal surgery; (7) Patients diagnosed with dementia according to the diagnostic criteria of Mini-Mental State Examination (MMSE).

### Research Methods

Patients who were transferred to the ICU with tracheal intubation following general anesthesia received continuous intravenous analgesia with remifentanyl hydrochloride immediately upon admission to the ward. All enrolled patients exhibited a Critical care Pain Observation Tool (CPOT) score of 0. Sedation initiation occurred when patients achieved a Richmond Agitation-Sedation Scale (RASS) score of 0 post-admission. Patients in the observation group received continuous infusion of dexmedetomidine at a rate of 0.20 to 0.63  $\mu\text{g}/\text{kg}/\text{h}$ , while those in the control group received continuous infusion of medium and long-chain fatty acid propofol at a rate of 0.33 to 3.33  $\text{mg}/\text{kg}/\text{h}$ . Since, all the patients underwent postoperative general anesthesia procedures, none received a loading dose of sedative medication. The analgesic effect was assessed following sedation with RASS scores in both groups reaching  $-1$  to  $-2$  points.

Following admission to the ward, as a result of tracheal intubation, patients may experience elevated blood pressure, pain, and other adverse stimuli. In cases where analgesic treatment was followed by treatment with or without sedation, if the blood pressure of the patient was elevated (systolic blood pressure  $\geq 150$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg), continuous infusion of nicardipine hydrochloride injection was administered to maintain blood pressure within normotensive levels or restore it to previous levels. Whenever a patient required a blood pressure-raising medication, such as NE injection or dopamine injection due to hypotension, they were withdrawn from the study.

Sedative medications were discontinued one hour prior to extubation to assess consciousness and autonomous respiration. Following confirmation of adequate autonomous respiration, the endotracheal tube was removed and alternative oxygen therapy methods were initiated. Continuous intravenous analgesic administration was maintained from admission to discharge with a CPOT score of 0.

## Observation Indexes

(1) General information: This includes demographic details such as age, gender, and medical history including hypertension, coronary heart disease, diabetes mellitus, chronic lung disease, and tumors. Additionally, Acute Physiology and Chronic Health Evaluation II (APACHE II) score and laboratory tests including liver function, renal function, coagulation function, and markers of myocardial injury were recorded.

(2) Primary observation index: The primary focus is on the variance in plasma E and NE levels subsequent to the administration of different sedative medications.

(3) Secondary observation indexes: Vital signs encompass heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP). Furthermore, the incidence of delirium in the ICU post-extubation is assessed using the Confusion Assessment Method Intensive Care Unit (CAM-ICU) delirium scale.

## Data Analysis

Statistical analysis was conducted using SPSS version 29.0 software. The Kolmogorov–Smirnov test was utilized to assess the adherence of measurement data to normal distribution. For intergroup comparisons, normally distributed data are expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) and analyzed using independent samples *t*-test. Non-normally distributed data are presented as median (interquartile range) and analyzed utilizing the Mann–Whitney *U*-test. Group comparisons for categorical data are performed utilizing the chi-squared ( $\chi^2$ ) test, with Fisher's exact test employed when any cell had a frequency of less than 5. A *P*-value  $< 0.05$  was considered as a statistically significant difference.

## Results

### General Condition

Before the administration of sedative medications, the baseline characteristics of the two patient groups were compared. There were no statistically significant differences observed between the two groups for the following parameters: demographic characteristics such as gender, age, presence of chronic underlying diseases, and body mass index (BMI); surgery-related factors including intraoperative dosage of sedative drugs and duration from the cessation of anesthesia to initiation of sedation in the ICU; admission APACHE-II scores; results of pre-sedation blood tests including liver function, renal function, coagulation function, and cardiac indexes; the number of antihypertensive medications administered during ICU sedation (Table 1).

### Changes in Vital Signs and Plasma E and NE Levels

Blood samples were obtained at T0, T1, and T2 [Prior to the initiation of the sedation treatment (T0), at one-hour post sedation (T1), and two hours following tracheal extubation (T2)] to assess the plasma E and NE levels in both patient groups and comparisons were made accordingly. At T0, there was no significant disparity in the levels between the observation and the control groups, indicating baseline equivalence between the two groups. Similarly, at T1, the levels in the observation group did not differ significantly from those in the control group. However, at T2, the plasma NE level

**Table 1** General Information

	Observation group (n = 49)	Control group (n = 48)	P-value
Gender			
Male (%)	24(49.0)	26(54.2)	0.609
Age (years)	64.94±8.40	63.44±9.35	0.407
Chronic underlying diseases			
Hypertension (%)	26(53.1)	23(47.9)	0.612
Coronary heart disease (%)	11(22.4)	10(20.8)	0.847
Diabetes (%)	15(30.6)	14(29.2)	0.876
Tumor (%)	37(75.5)	43(89.5)	0.068
Number of people receiving antihypertensive drugs in ICU (%)	12(24.5)	11(22.9)	0.885
Intraoperative dosage of dexmedetomidine (µg)	120(76–166)	98(74–127)	0.086
Intraoperative dosage of propofol (mg)	1050(590–1660)	892(725–1187.5)	0.542
The time from the end of anesthesia to the start of sedation in the ICU (min)	80(57–105.5)	72.5(54.25–95)	0.341
APACHE-II score at admission to the ICU (points)	6.90±5.60	16.33±6.169	0.638
BMI (kg/m <sup>2</sup> )	24.07±3.48	23.30±3.08	0.251
Liver function			
ALT (U/L)	18(10–55)	14(9.25–44)	0.355
AST (U/L)	26(17–68.5)	24(17.25–64)	0.681
ALB (g/L)	32.20±4.67	32.93±5.42	0.963
TB (µmol/L)	17.5(8.55–31.5)	13.15(8.25–43.15)	0.963
Kidney function			
BUN (mmol/L)	5.45(4.09–8.01)	5.11(4.05–7.42)	0.409
Cr (mmol/L)	67(56.5–92)	66(54–81.75)	0.168
Coagulation function			
PT (s)	12(11.28–12.95)	12.3(11.4–13.68)	0.224
APTT (s)	28.7(26.7–30.15)	29.5(27.1–31.9)	0.144
FIB (g/L)	299(251–357.67)	294.5(247–360.5)	0.740
D-dimer (mg/L)	1015.65±320.68	1379.04±357.84	0.061
Heart indicators			
TNT (µg/L)	12.13(8.69–18.32)	8.79(7.45–13.71)	0.066
NT-proBNP (pg/mL)	184.5(88.33–459.3)	152.8(66.95–297.85)	0.674

in the observation group was  $952.90 \pm 338.02$  pmol/L, which was significantly lower than that in the control group at ( $1420.90 \pm 468.26$  pmol/L) ( $P < 0.001$ ), while there was no substantial difference observed in plasma E levels (Table 2).

The vital signs including heart rate, blood pressure, and respiratory rate were compared between the patients at T0, T2, and T3, respectively. At both T0 and T1, there were no significant differences observed in hemodynamic indices including HR, SBP, DBP, RR, and MAP between the two groups. However, at T2, a notable difference in HR between the two groups was evident ( $P < 0.05$ ), with the HR value in the observation group being lower than that in the control group. Conversely, there were no significant differences in RR, SBP, DBP, and MAP between the two groups at T2 (Table 2).

## Difference in the Incidence of Delirium

The incidence of delirium was compared from the time of tracheal intubation removal to ICU discharge in both groups, each consisting of two cases; however, there were no significant differences between them (Table 3).

## Subgroup Analysis

The observation group exhibited significantly lower HRs and plasma NE levels compared to the control group at T2. However, there were no significant differences observed in blood pressure and RR between the two groups. Among the

**Table 2** Changes in Vital Signs and Plasma E and NE Levels of the Two Groups of Patients at Different Time Points

	Observation group (n = 49)	Control group (n = 48)	P-value
HR (times/minute)			
T0	85.49±9.51	84.60±5.50	0.577
T1	80.55±5.29	79.29±5.88	0.270
T2	82.35±5.05	85.15±6.24	0.017
RR (times/minute)			
T0	14(12–17)	14(12–17)	0.876
T1	14(13–16)	14(12–15)	0.131
T2	17(15–20)	18(15–20.75)	0.825
SBP(mmHg)			
T0	144.73±30.85	141.19±23.99	0.529
T1	130.29±6.66	130.96±6.78	0.623
T2	133.55±14.20	131.75±12.85	0.514
DBP(mmHg)			
T0	72.16±7.15	72.23±5.80	0.960
T1	66.61±7.09	65.77±4.01	0.475
T2	66.82±4.19	67.48±5.36	0.498
MAP(mmHg)			
T0	92.29±8.32	97.27±5.50	0.992
T1	87.00±5.61	85.46±7.13	0.361
T2	88.10±9.79	91.96±11.59	0.080
E (pmol/L)			
T0	212.12±85.68	200.00±83.60	0.482
T1	231.12±98.44	201.28±54.48	0.069
T2	216.49±75.92	224.18±68.14	0.601
NE (pmol/L)			
T0	777.32±352.51	664.76±273.54	0.083
T1	792.72±324.35	724.54±299.50	0.285
T2	952.90±338.02	1402.90±468.26	<0.001

**Table 3** The Incidence of Delirium Post-Extubation in the Two Groups of Patients in the ICU

	Delirium		Total	Delirium Incidence (%)
	Yes	No		
Observation group	2	47	49	4.08
Control group	2	46	48	4.17
Total	4	93	97	4.12

patients, 12 in the observation group and 11 in the control group had elevated blood pressure (SBP  $\geq$  150 mmHg and/or DBP  $\geq$  90 mmHg for more than 10 min was considered as elevated blood pressure), which was managed through continuous infusion of nicardipine hydrochloride injection during sedation until after extubation. To further investigate whether the lack of significant difference in blood pressure between the two groups was associated with the utilization of nicardipine hydrochloride injection, the patients were grouped based on the administration of antihypertensive medications and compared.

Prior to conducting subgroup analysis, the RASS scores of both groups were compared to assess whether there were significant differences, aiming to exclude the possibility of variation in HR and blood pressure attributed to differences in

sedation depth. The RASS scoring data exhibited non-normal distribution and were subjected to the Mann–Whitney *U*-test for comparison. The analysis revealed no significant statistical difference between the groups.

### Antihypertensive Drug Group

Initially, the baseline characteristics of patients in the two groups were compared, including demographic characteristics (such as gender, age, presence of chronic underlying disease status, and BMI), surgery-related indicators (intraoperative dose of sedative medication and time from the end of anesthesia to the start of sedation in the ICU), APACHE-II scores upon admission to ICU, and results of pre-sedation blood tests (comprising liver function, renal function, coagulation function, and cardiac indices). No significant differences were observed (Table 4). Additionally, the RASS scores of the two patient groups were compared with no significant statistical difference.

Next, the duration of administration and total dose of nicardipine hydrochloride injection in the two groups of patients were compared. The Kolmogorov–Smirnov test revealed that the duration of administration of nicardipine hydrochloride injection conformed to normal distribution, whereas the total dose did not. The total dose of nicardipine hydrochloride injection was transformed using natural logarithm and re-tested for normal distribution. No statistically significant difference was found in either the duration of administration of nicardipine hydrochloride injection or the natural logarithm of the total dose used between the two groups of patients (Table 5).

Furthermore, the vital signs including HR, blood pressure, and RR were compared at the three time points of T0, T1, and T2, respectively. No statistically significant difference was observed for any of the vital signs (Table 6).

**Table 4** General Information of Patients Receiving Antihypertensive Drugs

	Observation group (n = 12)	Control Group (n = 11)	P-value	PI value
Gender				
Male (%)	4(33.3)	5(45.5)	0.522	
Age (years)	67.75±6.05	65.82±9.99	0.577	
Chronic underlying diseases				
Hypertension (%)	5(41.7)	7(63.6)	0.292	
Coronary heart disease (%)	3(25.0)	3(27.3)		1.000
Diabetes (%)	3(25.0)	4(36.4)		0.667
Tumor (%)	7(58.3)	10(90.9)	0.076	
Intraoperative dosage of dexmedetomidine (µg)	97(72.9–126.9)	60(21.6–100)	0.151	
Intraoperative dosage of propofol (mg)	654(442.5–1083.75)	860(324–1060)	0.786	
The time from the end of anesthesia to the start of sedation in the ICU (min)	85(54.8–146.5)	95(70–143)	0.487	
APACHE-II score at admission to the ICU (points)	18.00±7.00	19.73±5.66	0.525	
BMI (kg/m <sup>2</sup> )	25.09±3.29	22.93±3.75	0.158	
Liver function				
ALT (U/L)	15.50(9.25–48.25)	14(11–94)	0.928	
AST (U/L)	18.50(16.25–47.0)	24(18–121)	0.566	
ALB (g/L)	33.60(28.78–38.08)	36.70(30.5–38.9)	0.525	
TB (µmol/L)	11.55(6.53–17.98)	12.10(7.80–22.80)	0.608	
Kidney function				
BUN (mmol/L)	6.83±3.64	8.41±5.33	0.410	
Cr (mmol/L)	67.00(58.00–92.50)	81(69–148)	0.316	
Coagulation function				
PT (s)	11.75±0.97	11.80±1.23	0.915	
APTT (s)	28.75(27.68–29.50)	29.6(25.2–33.5)	0.379	
FIB (g/L)	298.50 (253.75–346.00)	316(292–364)	0.288	
D-dimer (mg/L)	745.00 (552.50–2806.50)	352(240–1186)	0.211	
Heart indicators				
TNT (µg/L)	14.03(8.33–21.16)	11.10(8.16–23.73)	0.974	
NT-proBNP (pg/mL)	299.70(79.60–655.90)	162.65(105.48–3285.47)	0.863	

**Notes:** I: Comparisons between groups were made using Fisher's exact test.

**Table 5** Usage of Nicardipine Hydrochloride Injection

	Observation group (n = 12)	Control group (n = 11)	P-value
Duration of medication (h)	11.40±4.97	9.77±7.65	0.549
Total dose of Ln	3.00±0.95	2.79±1.19	0.664

**Table 6** Changes in Vital Signs and Plasma E and NE Levels of Two Groups of Patients Receiving Antihypertensive Drugs at Different Time Points

	Observation group (n = 12)	Control group (n = 11)	P-value
HR (times/minute)			
T0	84.17±7.88	84.36±5.68	0.946
T1	77.92±6.76	77.91±5.52	0.998
T2	81.83±4.95	84.64±5.54	0.274
RR (times/minute)			
T0	14(13–14.75)	16(10–17)	0.651
T1	16(15–16)	15(15–16)	0.379
T2	18(16.25–20.5)	19(17–22)	0.190
SBP(mmHg)			
T0	157.83±19.76	165.09±19.73	0.389
T1	129.00±7.06	132.09±6.35	0.284
T2	135.67±15.65	126.91±17.47	0.219
DBP(mmHg)			
T0	72.67±7.86	73.09±5.63	0.884
T1	68.08±5.90	65.27±4.54	0.218
T2	67.92±3.85	69.18±6.32	0.564
MAP(mmHg)			
T0	86.41±6.19	85.73±8.20	0.538
T1	87.00±5.61	85.46±7.13	0.821
T2	94.00±9.84	90.81±14.74	0.554
E (pmol/L)			
T0	162.31±61.68	168.21±91.02	0.856
T1	245.84±93.05	202.32±45.54	0.175
T2	216.52±72.13	228.13±48.02	0.657
NE (pmol/L)			
T0	785.27±168.94	653.97±199.96	0.175
T1	891.85±324.35	911.66±196.54	0.833
T2	1124.73±238.11	1493.51±437.39	0.019

Finally, blood samples were collected at T0, T1, and T2 to determine the plasma E and NE levels of the two groups of patients using antihypertensive drugs, which were then compared at the three time points. At T0, there was no significant difference in plasma E and NE levels between the observation group and the control group, indicating baseline equivalence between the groups. Similarly, at T1, there was still no statistically significant difference in the two indicators. However, at T2, the plasma NE level of the observation group was significantly lower than that of the control group (1124.73 ± 238.11 pmol/L compared to 1493.51 ± 437.39 pmol/L, respectively; ( $P < 0.001$ )), while there was no significant difference in the plasma E level between the two groups (Table 6).

### Two Groups Without Antihypertensive Drugs

Initially, the baseline conditions of patients in the two groups were compared, including demographic characteristics (such as gender, age, chronic underlying disease status, and BMI), surgery-related parameters (intraoperative dosage of

sedative medication and time elapsed from the end of anesthesia to the initiation of sedation in the ICU), APACHE-II scores upon admission to the ICU, and results of pre-sedation blood tests including liver function, renal function, coagulation function, and cardiac indices. No statistically significant differences were observed between the groups in any of their parameters (Table 7). Additionally, the RASS scores of the two patient groups were compared with no significant statistical difference in sedation depth between the groups.

Next, the vital signs (including HR, blood pressure, and RR) of the patients were compared at three time points: T0, T1, and T2, respectively. At T0 and T1, there were no statistically significant differences in HR, RR, SBP, DBP and MAP. However, at T2, statistically significant differences were observed in HR and MAP ( $P < 0.05$ ), while no significant differences were found in RR, SBP, DBP (Table 8).

Additionally, blood samples were collected at T0, T1, and T2 to determine the plasma E and NE levels in the two groups of patients who did not use antihypertensive drugs and were then compared at three time points. There was no statistically significant difference in the levels of plasma E and NE at T0, indicating that the two groups were well matched at baseline. Similarly, at T1, there was still no statistically significant difference observed. However, at T2, the plasma NE level in the observation group ( $924.94 \pm 381.63$  pmol/L) was significantly lower than that of the control group ( $1399.31 \pm 480.66$  pmol/L) ( $P < 0.001$ ), while there was no statistically significant difference in the plasma E level between the two groups (Table 8).

**Table 7** General Information of Patients Not Receiving Antihypertensive Drugs

	Observation group (n = 37)	Control group (n = 37)	P-value
Gender			
Male (%)	20(54.1)	21(56.8)	0.815
Age (years)	64.03±8.91	62.73±9.17	0.539
Chronic underlying diseases			
Hypertension (%)	21(56.8)	16(43.2)	0.245
Coronary heart disease (%)	8(21.6)	7(18.9)	0.772
Diabetes (%)	12(32.4)	10(27.0)	0.611
Tumor (%)	30(81.1)	33(89.2)	0.327
Intraoperative dosage of dexmedetomidine (µg)	120(75.8–166.0)	106.8(84–136.8)	0.489
Intraoperative dosage of propofol (mg)	1060(537.5–1660)	900(750–1335)	0.791
The time from the end of anesthesia to the start of sedation in the ICU (min)	80(55–105.5)	60(51.5–85.5)	0.132
APACHE-II score at admission to the ICU (points)	6.59±4.50	15.76±4.97	0.450
BMI (kg/m <sup>2</sup> )	23.64±3.46	23.41±2.91	0.755
Liver function			
ALT (U/L)	34.84±14.05	36.89±15.22	0.548
AST (U/L)	53.0(31.5–60.0)	49(31.5–60.5)	0.978
ALB (g/L)	31.96(28.30–34.67)	34.61(28.49–37.14)	0.263
TB (µmol/L)	18.59(13.95–26.62)	14.78(12.10–25.30)	0.452
Kidney function			
BUN (mmol/L)	10.85(9.93–11.81)	10.39(9.33–11.85)	0.284
Cr (mmol/L)	76(69.50–81.00)	77(65.5–83.5)	0.991
Coagulation function			
PT (s)	12.17±0.63	12.63±1.23	0.051
APTT (s)	28.10(27.42–29.54)	28.91(27.16–31.36)	0.162
FIB (g/L)	298.57(277.10–346.50)	317.14(277.36–347.19)	0.910
D-dimer (mg/L)	1157.57±327.56	1262.00±302.57	0.159
Heart indicators			
TNT (µg/L)	15.03(12.70–18.06)	16.58(12.14–17.95)	0.685
NT-proBNP (pg/mL)	315.16±127.14	315.66±44.92	0.982



**Table 8** Changes in Vital Signs and Plasma E and NE Levels in the Two Groups of Patients Not Receiving Antihypertensive Drugs at Different Time Points

	Observation group (n = 37)	Control group (n = 37)	P-value
HR (times/minute)			
T0	85.81±10.15	84.68±5.52	0.552
T1	79.73±5.35	79.70±6.00	0.984
T2	82.41±5.24	85.30±6.49	0.038
RR (times/minute)			
T0	14(13–15)	14(13–16)	0.891
T1	16(15–17)	15(15–18)	0.987
T2	19(17.5–21)	20(18–22)	0.132
SBP(mmHg)			
T0	145.38±33.25	138.22±21.47	0.275
T1	130.68±6.53	130.62±6.95	0.973
T2	133.30±14.05	133.19±11.02	0.971
DBP(mmHg)			
T0	71.86±7.07	71.97±5.90	0.943
T1	66.54±6.79	65.92±3.90	0.631
T2	66.43±4.27	66.97±5.02	0.619
MAP(mmHg)			
T0	97.41±8.77	97.89±5.57	0.777
T1	87.30±5.32	85.38±10.73	0.333
T2	86.24±9.12	92.30±10.70	0.011
E (pmol/L)			
T0	227.73±85.41	209.44±80.14	0.345
T1	229.51±107.63	199.49±55.28	0.136
T2	212.22±78.30	223.00±73.59	0.544
NE (pmol/L)			
T0	761.88±380.05	686.89±277.31	0.336
T1	788.79±316.79	739.18±284.76	0.481
T2	924.94±381.63	1399.31±480.66	<0.001

## Discussion

The main findings of this study indicate that compared to propofol, dexmedetomidine effectively lowers plasma norepinephrine levels, reduces post-extubation tachycardia, and moderately decreases blood pressure. These effects collectively help alleviate stress responses in patients undergoing endotracheal intubation-assisted mechanical ventilation in the Intensive Care Unit (ICU). These results suggest that dexmedetomidine, as a sedative agent, holds significant clinical implications in ICU patients, particularly in managing hemodynamic stability and reducing postoperative stress in patients.

Mechanical ventilation is a crucial therapeutic intervention for patients in the ICU, serving to alleviate the work of breathing, reduce oxygen consumption, and elevate the blood oxygen levels by regulating ventilation. This effectively boosts oxygen delivery to vital organs and enhances the overall oxygen supply balance in the body. However, aside from the discomfort caused by mechanical ventilation itself, ICU patients with severe respiratory conditions often undergo procedures like sputum suction, repositioning, and invasive interventions exacerbating their discomfort. Hence, effective analgesia and sedation are vital for ICU patients, particularly those undergoing endotracheal intubation. Clinical evidence has demonstrated the significant benefits of sedative medications such as dexmedetomidine, propofol, and midazolam in improving outcomes for ICU patients.<sup>13,14</sup> With a clearer understanding of the pharmacological mechanism of dexmedetomidine, its use in the ICU has become more prevalent. However, there is limited research on its effects on plasma catecholamine levels and the incidence of delirium. Thus, in this study, we aimed to investigate the impact of

dexmedetomidine on plasma catecholamine levels and the incidence of delirium in patients undergoing tracheal intubation-assisted mechanical ventilation by comparing it with the control group.

Dexmedetomidine is classified as a highly selective  $\alpha_2$ -adrenoceptor agonist.<sup>15</sup> The  $\alpha_2$ -adrenergic receptor plays a crucial role in various physiological functions and is widely distributed throughout the body, contributing to a complex pharmacological profile.<sup>10,16</sup> Different subtypes of  $\alpha_2$  receptors mediate distinct pharmacological effects of dexmedetomidine. For instance, activation of  $\alpha_2a$  receptors promotes sedation, hypnosis, analgesia, antisympathetic effects, neuroprotection, and inhibition of insulin secretion.<sup>5</sup> Moreover, stimulation of  $\alpha_2b$  receptors leads to vasoconstriction in peripheral arteries.<sup>10</sup> Notably, the activation of  $\alpha_2c$  receptors is believed to be associated with the regulation of adrenaline secretion from the adrenal medulla. Additionally, all three  $\alpha_2$  receptor subtypes may influence the inhibition of NE release.<sup>10</sup> Consequently, the administration of dexmedetomidine may exert a significant impact on blood pressure and plasma catecholamine levels in ICU patients.

In this study, no statistically significant difference in catecholamine levels between the two groups was observed one hour after administration. However, at the two hour mark after extubation, the NE level in the observation group was notably lower than that in the control group ( $952.90 \pm 338.02$  pmol/L vs  $1402.90 \pm 468.26$  pmol/L,  $P < 0.001$ ), aligning with the findings from previous studies.<sup>10</sup> This suggests that dexmedetomidine might suppress NE release through the activation of  $\alpha$ -receptors, thereby reducing its plasma concentration. Although, the E level in the observation group also decreased two-hour post-extubation compared to baseline, the difference was not statistically significant, and it did not deviate significantly from the level in the control group. The lack of difference could potentially be attributed to the relatively short experimental duration during which the effect of dexmedetomidine may not have induced significant changes in epinephrine levels.

Furthermore, dexmedetomidine is known to commonly induce hypotension and bradycardia as its side effects alongside its impact on peripheral arterial constriction potentially influencing blood pressure regulation.<sup>17,18</sup> Thus, in this study, we closely monitored and recorded the blood pressure, HR, and RR of ICU patients with tracheal intubation receiving either dexmedetomidine or propofol. Results indicated that the HR of the patients in the observation group was lower than that of the control group two-hour post-extubation ( $82.35 \pm 5.05$  beats/min vs  $85.15 \pm 6.24$ ,  $P = 0.017 < 0.05$ ). Upon ICU admission, varying numbers of patients in both groups were administered antihypertensive drugs to manage blood pressure, with no statistically significant differences in these numbers. Subsequent subgroup analysis demonstrated that patients on and off antihypertensive medications in the observation group exhibited lower plasma NE levels two-hour post-extubation compared to their counterparts in the control group. Analysis of vital signs revealed no significant differences in HR, RR, and MAP between the two groups among patients receiving antihypertensive drugs. In the observation group, patients who did not receive antihypertensive medication exhibited lower HR, MAP, and plasma NE levels compared to the control group two-hour post-extubation. Furthermore, the trend observed in these three indicators was consistent. This suggests that the observed HR difference at two-hour post-extubation may be attributed to the use of antihypertensive medications during treatment, indicating that differences in blood pressure may be more pronounced in the absence of antihypertensive drugs use.

Moreover, prior research suggests that dexmedetomidine could reduce the incidence of postoperative delirium in patients by affecting the plasma melatonin levels.<sup>19,20</sup> However, in the present study, the incidence of delirium in the observation group did not significantly differ from that in the control group.

However, certain limitations in this study should be noted. Firstly, the sample size was relatively small, necessitating further expansion to enhance generalizability. Secondly, the study duration was brief, and observations were limited to blood pressure, HR, RR, plasma catecholamine levels, and delirium incidence was recorded one hour after medication and two-hour post-extubation. Complete monitoring of observational parameters throughout the entire ICU stay is warranted for future investigation. Finally, different surgical and anesthesia techniques have different risks for the development of POD, and the fact that surgeons did not screen patients for dementia (eg, with MMSE) before surgery is also a limitation of this study when comparing the incidence of POD.

## Conclusion

This study demonstrated that dexmedetomidine in comparison to propofol effectively decreased plasma norepinephrine levels, attenuated post-extubation tachycardia, and modestly lowered blood pressure in patients undergoing tracheal

intubation-assisted mechanical ventilation in the ICU. These effects collectively contribute to stress reduction in these patients.

## Abbreviations

ICU, Intensive Care Unit; E, Epinephrine; NE, Norepinephrine; HR, heart rate; RR, respiratory rate; MAP, mean arterial pressure; CPOT, Critical care Pain Observation Tool; RASS, Richmond Agitation-Sedation Scale; APACHE II, Acute Physiology and Chronic Health Evaluation II; SBP, systolic pressure; DBP, diastolic pressure; MMSE Mini-Mental State Examination; POD, postoperative delirium; POCD, postoperative cognitive decline; CAM-ICU, Confusion Assessment Method Intensive Care Unit; BMI, Body Mass Index; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; ALB, Albumin; TB, Total Bilirubin; BUN, Blood Urea Nitrogen; Cr, Creatinine; PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; FIB, Fibrinogen; D-dimer, D-dipolymer; TNT, Troponin T; NT-proBNP, N-Terminal Pro-Brain Natriuretic Peptide.

## Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Ethics Approval and Consent to Participate

I confirm that I have read the Editorial Policy pages. This study was conducted with approval from the Ethics Committee of Peking University International Hospital. Approval number is 2021-KY-0037-01/02. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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## Disclosure

The authors declare that they have no competing interests.

## References

1. Altshuler J, Spoelhof B. Pain, agitation, delirium, and neuromuscular blockade: a review of basic pharmacology, assessment, and monitoring. *Crit Care Nurs Q*. 2013;36(4):356–369. doi:10.1097/CNQ.0b013e3182a10dbf
2. Mantz J, Jossierand J, Hamada S. Dexmedetomidine: new insights. *Eur J Anaesthesiol*. 2011;28(1):3–6. doi:10.1097/EJA.0b013e32833e266d
3. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41(1):263–306. doi:10.1097/CCM.0b013e3182783b72
4. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. *Curr Opin Crit Care*. 2001;7(4):221–226. doi:10.1097/00075198-200108000-00002
5. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. *Curr Opin Anaesthesiol*. 2005;18(4):412–418. doi:10.1097/01.aco.0000174958.05383.d5
6. Haselman MA. Dexmedetomidine: a useful adjunct to consider in some high-risk situations. *AANA J*. 2008;76(5):335–339.
7. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. *Anesth Analg*. 2000;90(3):699–705. doi:10.1097/00000539-200003000-00035
8. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. *Br J Anaesth*. 2001;87(5):684–690. doi:10.1093/bja/87.5.684
9. Ramsay MA, Saha D, Hebel RF. Tracheal resection in the morbidly obese patient: the role of dexmedetomidine. *J Clin Anesth*. 2006;18(6):452–454. doi:10.1016/j.jclinane.2006.02.004
10. Panzer O, Moitra V, Sladen RN. Pharmacology of sedative-analgesic agents: dexmedetomidine, remifentanyl, ketamine, volatile anesthetics, and the role of peripheral Mu antagonists. *Anesthesiol Clin*. 2011;29(4):587–vii. doi:10.1016/j.anclin.2011.09.002
11. Gorowara S, Ganguly NK, Mahajan RC, Goyal J, Walia BN. Role of calcium and calmodulin in Giardia lamblia-induced diarrhoea in mice. *J Diarrhoeal Dis Res*. 1991;9(2):111–117.
12. Jakob SM, Ruokonen E, Grounds RM, et al. Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. *JAMA*. 2012;307(11):1151–1160. doi:10.1001/jama.2012.304

13. Glumac S, Kardum G, Karanovic N. Postoperative cognitive decline after cardiac surgery: a narrative review of current knowledge in 2019. *Med Sci Monit.* 2019;25:3262–3270. doi:10.12659/MSM.914435
14. Batra A, Verma R, Bhatia VK, Chandra G, Bhushan S. Dexmedetomidine as an anesthetic adjuvant in intracranial surgery. *Anesth Essays Res.* 2017;11(2):309–313. doi:10.4103/0259-1162.194555
15. Carollo DS, Nossaman BD, Ramadhani U. Dexmedetomidine: a review of clinical applications. *Curr Opin Anaesthesiol.* 2008;21(4):457–461. doi:10.1097/ACO.0b013e328305e3ef
16. Belleville JP, Ward DS, Bloor BC, Maze M. Effects of intravenous dexmedetomidine in humans. I. Sedation, ventilation, and metabolic rate. *Anesthesiology.* 1992;77(6):1125–1133. doi:10.1097/00000542-199212000-00013
17. Chrysostomou C, Schmitt CG. Dexmedetomidine: sedation, analgesia and beyond. *Expert Opin Drug Metab Toxicol.* 2008;4(5):619–627. doi:10.1517/17425255.4.5.619
18. Elvan EG, Oç B, Uzun S, Karabulut E, Coşkun F, Aypar U. Dexmedetomidine and postoperative shivering in patients undergoing elective abdominal hysterectomy. *Eur J Anaesthesiol.* 2008;25(5):357–364. doi:10.1017/S0265021507003110
19. Mo Y, Zimmermann AE. Role of dexmedetomidine for the prevention and treatment of delirium in intensive care unit patients. *Ann Pharmacother.* 2013;47(6):869–876. doi:10.1345/aph.1AR708
20. Sharma A, Malhotra S, Grover S, Jindal SK. Incidence, prevalence, risk factor and outcome of delirium in intensive care unit: a study from India. *Gen Hosp Psychiatry.* 2012;34(6):639–646. doi:10.1016/j.genhosppsych.2012.06.009

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