**ABSTRACT**

**Background:** Differences in short-term cognitive function between mechanically ventilated patients treated with multicomponent interventions and those receiving routine nursing care have not been established because of the lack of follow-up in previous studies.

**Purpose:** This study was designed to evaluate the effects of the pain, agitation, and delirium (PAD) care bundle on delirium occurrence and clinical outcomes, specifically in terms of short-term cognitive function, in mechanically ventilated patients.

**Methods:** Data on 243 patients with mechanical ventilation were analyzed from January 2017 to February 2019. The eligible patients were divided randomly into two groups. The control group (n = 120) received usual care, whereas the intervention group (n = 123) received the PAD bundle, including pain monitoring and management, light sedation and daily awakening, early mobility, sleep promotion, and delirium monitoring. The incidence and duration of delirium, ventilator time, and intensive care unit (ICU) length of stay were compared between the two groups. Upon discharge from the ICU and at 3 and 6 months after discharge, cognitive function was assessed using the Montreal Cognitive Assessment scale and compared between the two groups.

**Results:** The incidence of delirium was reduced significantly in the intervention group, and significant decreases in the duration of delirium, ventilator time, and ICU length of stay were found. Cognitive impairment in the intervention group was significantly lower at the 3-month follow-up assessment.

**Conclusions/Implications for Practice:** The PAD bundle was shown to be associated with a lower incidence of delirium and improved clinical outcomes. Short-term cognitive impairment occurred in fewer patients who were managed with the PAD bundle after ICU discharge. Our findings indicate that the PAD bundle has the potential to improve clinical outcomes. The administrative staff of ICUs should use strategies, such as interdisciplinary teamwork, to facilitate the buy-in and implementation of interventions.

**Key Words:** delirium, cognition, patient care bundles, mechanical ventilation, intensive care units.

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**Introduction**

Delirium in patients in intensive care units (ICUs) is a common medical problem. ICU delirium is a syndrome characterized by the acute onset of cerebral dysfunction with a change or fluctuation in baseline mental status, inattention, and disorganized thinking or altered level of consciousness (American Psychiatric Association, 2013). Given their critical status, which may include immobility, metabolic disorder, or being under the influence of medications, critically ill patients in the ICU, especially patients with mechanical ventilation, are at a high risk of developing delirium. The incidence of delirium in patients with mechanical ventilation has been reported to be 60% or higher (Li et al., 2018; Nguyen et al., 2020). Studies have shown that ICU delirium is an independent predictor in ICU patients of poor clinical prognoses such as prolonged mechanical ventilation, prolonged length of stay (LOS) in the ICU and the hospital, higher healthcare costs, and increased mortality (Marra et al., 2017; Senel et al., 2017). In addition, delirium has been found to be an independent predictor of cognitive impairment and has been associated with poor functional and cognitive recovery after a critical illness (Bulic et al., 2015).

**Background**

In the past decade, clinical practice directed at the assessment, prevention, and management of ICU delirium has been explored. A study (Colombo et al., 2012) on the use of a re-orientation strategy and acoustic, visual, and environmental stimulations showed that this intervention approach successfully lowered the occurrence of delirium. Kamdar et al. (2013) reported a significant reduction in the incidence and duration of delirium in critically ill patients who underwent...
a series of interventions aimed at improving sleep quality. Álvarez et al. (2017) conducted a randomized controlled trial with 140 patients in the ICU and reported a reduced incidence of delirium from an initial 20% to 3% after implementation of interventions using stimulation, rehabilitation, and training exercises. However, some of the results in this field have differed. Skrobik et al. (2010) implemented a protocol that used nonpharmacologic and pharmacologic methods to manage pain, sedation, and delirium based on patients’ assessment scores, with results showing that the occurrence of delirium in critically ill patients was similar between the intervention and control groups. Another study (Bryczkowski et al., 2014) found no significant difference in the incidence of delirium between intervention and postintervention groups. The intervention included education and training, sleep promotion strategies, and a pharmacologic protocol to limit the administration of medications related to delirium. Hence, the authors of this study found insufficient evidence to support the best combination of interventions in the prevention and management of delirium in critically ill patients.

The findings of an increasing number of studies suggest an association between the duration of delirium and long-term cognitive dysfunction (Brummel et al., 2014). The study by Brummel et al. (2014) reported an association between the long-term deleterious effects of delirium and lower scores on the Awareness Questionnaire for motor–sensory function in a population of critically ill adult patients (p = .02). That study emphasized the importance of using effective strategies for the prevention of delirium to reduce functional disabilities among survivors of critical illness. Girard et al. (2010) found that cognitive impairment was more prevalent in patients whose delirium persisted for 3 or more days compared with those who were delirious for 1–2 days or were never delirious. However, the findings of that study were based on a non-ICU population. However, those trials did not conduct follow-up surveys of the ICU survivors with delirium during their ICU stays to evaluate their cognitive function. Consequently, it is unknown whether there were any differences in short-term cognitive function between the group receiving the multicomponent intervention strategies and the group treated with routine nursing care.

The “Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit” published by the American College of Critical Care Medicine include a “pain, agitation, and delirium (PAD) care bundle” (Barr et al., 2013). The guidelines integrate the best evidence on the optimal management of pain, agitation, sedation, and delirium. ICU-acquired delirium is a syndrome caused by the complicated and synergistic relationship between the precipitating and predisposing factors to which critically ill patients are exposed. Thus, strategies aimed at preventing delirium should focus on its multifactorial origins to be effective.

Considering the factors noted above, the authors of this study translated the PAD care bundle into Chinese and revised it based on the existing evidence. As a gap between evidence on the PAD care bundle and clinical practice was identified in our hospital, the authors then modified the elements of the PAD care bundle and reconstructed it.

The purposes of this study were to evaluate the effects of the PAD care bundle on the incidence of ICU delirium and the related clinical outcomes in mechanically ventilated patients and to explore the differences in short-term cognitive functions between the control and intervention groups of survivors longitudinally to 6 months after ICU discharge.

**Methods**

**Setting and Study Design**

This study, a randomized controlled trial with a 6-month follow-up, was conducted in two adult ICUs at Tianjin Third Central Hospital (a tertiary hospital). The two ICUs have 30 beds and admit patients with all types of surgical procedures and medical diagnoses. The medical ethics committee of Tianjin Third Central Hospital approved this study (TMKM20150130), and the study’s protocol was implemented in accordance with the Helsinki Declaration. Patients were informed of their rights and responsibilities and signed an informed consent form before being enrolled as participants.

**Participants**

Patients who were ≥ 18 years old, with mechanical ventilation expected for at least 72 hours, with a Richmond Agitation and Sedation Scale score ≥ 3 (eligible for delirium assessment), and were admitted to single-bed rooms in the ICU were eligible for inclusion. The exclusion criteria included presence of a preexisting condition interfering with the assessment of delirium (e.g., tetraplegia, impaired hearing or vision, dementia), mechanical ventilation ≥ 48 hours before ICU admission, a survival prognosis of less than 3 months, and a second admission during the study period. The patients receiving mechanical ventilation (N = 243) were divided randomly into two groups for the purposes of this study, which was conducted from January 2017 to February 2019. The patients in the control group (n = 120) received usual care, and those in the intervention group (n = 123) received the PAD care bundle. A computer was used to generate the random numbers used for group assignments. The participants received follow-up surveys at 3 and 6 months after their discharge from the ICU.

**Pain, Agitation, and Delirium Care Bundle**

The PAD care bundle of interventions was implemented starting from the patient’s ICU admission until their discharge from the ICU, transfer to another medical center or ward, or death. This interdisciplinary, multicomponent, evidence-based protocol consisted of the following five major components.

**Pain monitoring and management**

Nurses assessed the patients for pain once every 3 hours using the Numeric Rating Scale for patients able to self-report and
the Critical-Care Pain Observation Tool (CPOT) for patients unable to self-report (Gomarverdi et al., 2019). Schedule IV opiates (morphine or fentanyl) were administered to patients in significant pain, as indicated by a score on the Numeric Rating Scale $\geq 4$ or CPOT $\geq 3$. Music therapy was offered to patients with mild pain.

**Light sedation and daily awakening**
Nurses assessed the patients for sedation once every 3 hours using the Richmond Agitation and Sedation Scale. Sedative and opiate infusions were stopped every morning at 8:00–9:00 a.m. The medications were restarted after the patient was awake and alert or, if agitated, at half the former rate, and the dose was adjusted to produce mild sedation (Richmond Agitation and Sedation Scale = −2 to 0). Physicians and respiratory therapists implemented the intervention.

**Early exercise**
Early exercise was guided using a four-level mobility protocol. The protocol was designed for critically ill patients, and the mobility level was determined by the patient’s level of consciousness and muscle strength (Li et al., 2018). The four levels of the mobility protocol were as follows: Level 1: for patients with disturbance of consciousness, nurses would help them turn over every 2 hours, change position, and perform passive exercise; Level 2: for patients who are conscious, nurses would cooperate with patients, guide and supervise active exercise, and help patients maintain a sitting posture and turn over; Level 3: for patients with muscle strength in their upper limbs (> Level 3), perform active exercise, and nurses would help them sit at the edge of the bed; and Level 4: for patients with muscle strength in their lower limbs (> Level 3), perform active exercise, and nurses would help them sit at the edge of the bed and move from the bed to a bedside chair for active joint exercise and even help them perform standing activities.

First, the exclusion of contraindications was conducted, changes in the patient’s condition were closely monitored during exercise, and the exercise was stopped when signs of fatigue were observed. The safety screening criteria for early exercise were as follows: respiratory system, FiO$_2$ > 60%; circulatory system, increasing doses of vasopressor infusions in the past 2 hours; myocardial infarction; arrhythmia; and injuries in which mobility is contraindicated (e.g., unstable fractures). The failure screening criteria included a decrease in mean arterial pressure, changes in signs or symptoms $\geq 5$ minutes, heart rate of $< 50$ or $> 130$ beats/minute, respiratory rate of $< 5$ or $> 40$ breaths/minute; systolic blood pressure $> 180$ mmHg, SaO$_2$ $< 88\%$, obvious man-machine confrontation, patient restlessness, or new arrhythmias.

Early exercise was performed for 20 minutes at a frequency of 3 times a day until the patient left the ICU. Physical therapists and nurses implemented the intervention.

**Sleep promotion**
The patients’ sleep period was designated as 22:00 to 4:00. During this period, the staff were asked to reduce potential disturbances to patients by clustering medical and nursing activities, reducing stimuli as much as possible, and taking measures to control light and noise levels. This was done by closing all doors, limiting vocal sounds, dimming the overhead lights, and turning off alarms as quickly as possible. The Richards–Campbell Sleep Questionnaire (RCSQ) was used to evaluate quality of sleep, with self-assessments scheduled after the first day in the ICU as well as on the fourth day and the day of ICU discharge. If a participant was unable to perform self-evaluations, the nurses assessed the sleep status. A higher score on the RCSQ indicated a better quality of sleep (Krotsetis et al., 2017).

**Delirium monitoring**
Nurses assessed the patients for delirium once every 8 hours using the Confusion Assessment Method for the ICU (CAM-ICU; Selim et al., 2018). Additional assessments were conducted when the participant’s level of consciousness changed.

**Strategies for Implementation of the Pain, Agitation, and Delirium Care Bundle**
A multidisciplinary team, including registered nurses, physicians, respiratory therapists, physical therapists, and the administrative leadership, was established. The members of the team received training and education on delirium-related topics in three sequential stages. The content included the importance and meaning of the PAD care bundle, detailed steps for performing each bundle element, and the importance of adhering to the study’s protocol. Early exercise was implemented in conjunction with assessments of safety and success/failure criteria (developed from the existing literature; Balas et al., 2014). To ensure the reliability of the outcome assessment, four nurses who did not participate in the implementation of the interventions and were unaware of the intrinsic purpose of this study were trained to assess pain, sedation, and delirium. The intrarater reliability of the scales was 97% or higher. After the nurse in charge of the patient evaluated the patient’s PAD and provided patient care, these four nurses conducted a second evaluation of the same three variables. In case of inconsistent evaluations, doctors were invited to participate in a discussion about the discrepancies until the evaluations were consistent. Compliance with each bundle element was checked daily in each ICU by the administrative leadership during the study period.

**The Control Group (Usual Care)**
The following methods were adopted in the provision of usual care. Nursing staff implemented routine analgesia and sedation. Participant level of consciousness and degrees of analgesia and sedation were evaluated every 8 hours, and drug dosages were adjusted based on the doctor’s advice. Function was evaluated, and viscera, heart rate, blood pressure, central venous pressure, respiratory rate and rhythm, percutaneous blood oxygen saturation, and tidal volume were monitored. Airway management included the following procedures: An
endotracheal tube was secured with a dental pad and tape, and airway aspiration was performed based on the patient’s respiratory tone, blood oxygen saturation, and respiratory rate. Prevention of aspiration was achieved through continuous humidification with a ventilator humidifier to ensure the temperature of the upper airway was maintained between 37.0°C and 37.5°C. Patients were also observed for signs and symptoms of gastrointestinal dysfunction such as nausea, vomiting, abdominal distension, diarrhea, and constipation.

Data Collection
Data on 243 participants were analyzed from January 2017 to February 2019. The incidence of delirium was the primary outcome of this study, with secondary outcomes including delirium duration, ventilator time, ICU LOS, and 28-day ICU mortality. The following data were obtained from the participants’ medical records: age, gender, main reason for ICU admission, history of hypertension, severity of illness during the first 24 hours after ICU admission (as measured by Acute Physiology and Chronic Health Evaluation II [APACHE II] score), comorbidity of sepsis (before developing delirium), ventilator time, and ICU LOS. The duration of delirium was defined as the number of ICU days in which the patient’s CAM-ICU assessment was positive.

Cognitive function was assessed in this study using the Montreal Cognitive Assessment (MoCA) scale at admission and at 3 and 6 months after ICU discharge. The MoCA is a screening instrument that is used to assess multiple cognitive domains and may be completed in less than 10 minutes (Writing Group of Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment in China, Professional Committee on Cognitive Disorders, Branch of Neurologists, Chinese Medical Association, 2018). An adjustment for lower education is made for individuals with ≤ 12 years of education by adding 1 point to the total score. The total possible score is 30, with a total score < 26 indicating cognitive impairment. Patients were divided into a cognitively impaired group and a cognitively normal group based on their MoCA scores.

All of the scales used in this study were translated into Chinese by scholars and were shown to have good reliability and validity. A prior study of 608 critically ill patients reported

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**Figure 1**

Flowchart of Participants’ Enrolment and Follow-Up Processes

![Flowchart](chart.png)
a Cronbach's alpha coefficient and test–retest reliability of .795 and .950, respectively, for the CPOT (Gomarverdi et al., 2019). Selim et al. (2018) found the sensitivity of the CAM-ICU to be 96%; the Cronbach's alpha coefficient of the Chinese RCSQ was reported by Krotsetis et al. (2017) to be .84, and the sensitivity of the Chinese MoCA scale for screening cognitive impairment was found to be as high as 94% (Zhang et al., 2016).

### Statistical Analysis

Demographic data and clinical outcomes are presented in this study as mean, standard deviation (SD) for continuous variables, and frequencies and percentages for categorical variables. The independent samples t test or nonparametric Mann–Whitney test was used to compare continuous variables between the groups, and the chi-square test was used for categorical variables. Differences in the incidence of delirium between the control and intervention groups were analyzed after adjusting for age, gender, APACHE II score, history of hypertension, and the comorbidity of sepsis using logistic regression. All analyses were performed with SPSS Statistics Version 17.0 (SPSS Inc., Chicago, IL, USA). The level of statistical significance was set at $p < .05$ (two-sided).

### Results

#### Patient Characteristics

During the study period, 1,393 patients were admitted to the two target ICUs. Of the 270 patients who met the inclusion criteria, data from 243 were analyzed (Figure 1). Eight patients were excluded because they had received mechanical ventilation < 72 hours, and 19 were excluded because they...
had discontinued treatment. The 243 patients were followed for more than 2,184 days in the ICU to assess them for the development of delirium. The 120 patients in the control group were followed for 1,215 days, and the 123 in the intervention group were followed for 969 days. No significant differences were found in the baseline data between the control and intervention groups (Table 1).

Effect of the Pain, Agitation, and Delirium Care Bundle on Outcomes

Differences in sedative and analgesic drug doses and sleep quality scores between the groups were analyzed. The total and average doses of midazolam in the intervention group were lower than those of the control group (p < .001). No significant difference was found in the total dose of morphine or fentanyl between the two study groups (p > .05). The total RCSQ score of the intervention group was higher than that of the control group (p < .05; Table 2).

The intervention group had a significantly lower incidence of delirium than the control group (Table 2). After adjusting for gender, age, APACHE II score, history of hypertension, and comorbidity of sepsis, the PAD care bundle showed continued efficacy, indicated by the lower incidence of delirium (p = .028) and the decrease by nearly half of the odds of delirium (OR = 0.46, 95% CI [0.23, 0.92]). The PAD care bundle was also associated with a significant reduction in the duration of delirium (p = .005) and shorter ventilator time (p = .023) and shorter ICU LOS (p < .001). No significant difference was found in 28-day ICU mortality between the two groups (Table 2).

Effect of the Pain, Agitation, and Delirium Care Bundle on Outcomes at the Follow-Ups

Of the 243 participants, 186 survived to discharge. A further 12 were lost to follow-up at the 3-month follow-up, and a further seven were lost to follow-up at the 6-month follow-up. Therefore, 167 patients, including 83 men (49.71%) and 84 women (50.29%), completed both of the follow-up assessments. At the 3-month follow-up, 44.44% in the control group versus 29.07% in the intervention group had developed cognitive impairment, which indicated a significant intergroup difference. Furthermore, at the 6-month follow-up, 41.98% in the control group versus 27.91% in the intervention group had developed cognitive impairment (Table 3). Differences in cognitive function between the two groups of patients were found on each dimension of the MoCA scale at the 3- and 6-month follow-ups (Table 4).

Adverse Events

The PAD care bundle was found in this study to be tolerated by patients and safe for use. No severe adverse events such as

### Table 3

| Characteristic                        | Intervention Group (n = 86) | Control Group (n = 81) | p  |
|---------------------------------------|-----------------------------|------------------------|----|
|                                       | n  | %    | n  | %    |     |
| Gender (male)                         | 42 | 48.84| 41 | 50.62| .818|
| Age (years; M and SD)                 | 53.57  | 14.77| 51.34  | 12.65| .298|
| APACHE II score (M and SD)            | 19.24  | 6.11 | 18.75  | 5.39 | .584|
| Admitting ICU diagnosis               |    |      |    |      | .933|
| Pneumonia                             | 13 | 15.12| 16 | 19.76| .818|
| COPD                                  | 14 | 16.27| 12 | 14.81| .818|
| Postoperation                         | 16 | 18.60| 12 | 14.81| .818|
| Sepsis                                | 9  | 10.47| 8  | 9.88 | .818|
| Renal failure                         | 13 | 15.12| 15 | 18.52| .818|
| Other                                 | 21 | 24.42| 18 | 22.22| .818|
| Delirium during ICU stay              | 14 | 16.28| 25 | 30.86| .026|
| Cognitive impairment                  |    |      |    |      |     |
| 3-month follow-up                     | 25 | 29.07| 36 | 44.44| .039|
| 6-month follow-up                     | 24 | 27.91| 34 | 41.98| .056|

Note. APACHE II = Acute Physiology and Chronic Health Evaluation II; ICU = intensive care unit; COPD = chronic obstructive pulmonary disease.

### Table 4

| MoCA Scale | Intervention Group (n = 86) | Control Group (n = 81) | p    |
|------------|-----------------------------|------------------------|------|
|            | M   | SD | M   | SD |     |
| 3-month follow-up |    |    |    |    |     |
| Attention   | 5.80| 0.40| 3.96| 1.28| < .001|
| Orientation | 5.88| 0.32| 3.96| 1.25| < .001|
| Memory      | 3.92| 1.02| 2.20| 1.17| < .001|
| Visuospatial functioning | 4.32| 0.73| 2.08| 1.26| < .001|
| Naming      | 2.76| 0.51| 2.20| 0.85| < .001|
| Language    | 2.36| 0.69| 1.60| 1.02| < .001|
| Abstract thinking | 1.64| 0.56| 0.88| 0.77| < .001|
| 6-month follow-up |    |    |    |    |     |
| Attention   | 5.88| 0.32| 4.24| 1.11| < .001|
| Orientation | 5.92| 0.27| 4.16| 1.08| < .001|
| Memory      | 4.04| 0.87| 2.36| 1.13| < .001|
| Visuospatial functioning | 4.44| 0.64| 2.24| 1.24| < .001|
| Naming      | 2.84| 0.37| 2.32| 0.68| < .001|
| Language    | 2.44| 0.64| 1.76| 0.91| < .001|
| Abstract thinking | 1.72| 0.45| 0.96| 0.72| < .001|

Note. MoCA = Montreal Cognitive Assessment.
unplanned extubations or falling out of bed were reported. During the period of early exercise, a sudden increase in blood pressure (> 20% of the baseline pressure) occurred in nine patients, and four patients experienced a choking cough. During the waking period, seven patients experienced self-extubation and 16.26% experienced 20 adverse events. However, those events did not result in serious consequences because of timely management and resolution.

Discussion

Reviews and meta-analyses (Deemer et al., 2020; Devlin et al., 2018) indicate that multifaceted intervention programs are effective in improving clinical practices related to the assessment, prevention, and management of delirium and clinical outcomes in the ICU. However, further analyses were needed to determine whether the associations reported in these studies would have a causal relationship in our hospital setting. Considering the lack of randomized controlled trials evaluating the effects of interventions on the incidence of delirium and short-term cognitive function among mechanically ventilated patients in China, this study was developed and conducted using a randomized controlled trial design and blinded method to assess related clinical outcomes. In this study, the therapy applied for delirium after diagnosis was consistent. The delirium management flowchart on the wall reminded doctors and nurses to pay attention to differential diagnoses when a patient’s CAM-ICU assessment for confusion was positive as well as to pay attention to infection, acute metabolic disorders, trauma, central nervous system lesions, hypoxia, organ dysfunction, and toxins. The second key was to ensure implementation of the PAD care bundle. Training for all employees on the PAD care bundle (e.g., bedside teaching of interventions for early exercise to nurses) was necessary. The implementation of early exercise for delirium prevention was documented daily. During the study, the head nurse supervised and guided the implementation of the PAD care bundle.

In this study, the PAD care bundle was applied to nursing practices for analgesia and sedation of mechanically ventilated patients. The results, supporting the findings of previous studies, showed total and average doses of morphine and midazolam to be associated with shorter mechanical ventilation time, ICU treatment time, and total hospital LOS as well as a reduced incidence of delirium. One study found that mechanically ventilated patients who underwent daily interruption of sedation and early exercise required lower doses of benzodiazepines, had a lower incidence of delirium, and spent less time in the ICU and hospital (Li et al., 2018). A prospective before–after study in five ICUs conducted by Balas et al. (2014) integrated an intervention bundle with daily clinical care. This bundle, consisting of five key components, including Awakening, Breathing, Coordination, Delirium Monitoring/Management, and Early Exercise/Mobility, was named the “ABCDE bundle.” Their findings showed that the bundle of evidence-based interventions decreased the incidence and duration of delirium. We observed that the ICU LOS was shorter in the intervention group than in the control group, whereas Balas et al. found no significant difference in the ICU LOS between the two groups. Existing data indicate that delirium prevention and management require an integrated multidisciplinary approach with standardized care processes. In a study of over 15,000 ICU patients, complete implementation of an ABCDEF bundle consisting of the assessment, prevention, and management of pain; spontaneous awakening and breathing trials; choice of psychotropic medication; delirium monitoring and management; early mobility; and family engagement and empowerment reduced the likelihood of developing delirium (Pun et al., 2018).

Delirium has been found to be an independent predictor of cognitive dysfunction in ICU populations (van den Boogaard et al., 2012; Wolters et al., 2014). The importance of brain dysfunction in critically ill patients has received increasing recognition, and although the PAD/ABCDE bundle has been shown to affect delirium, its effect on cognitive function remains uncertain. The results of this study showed that short-term cognitive impairment occurred less often after ICU discharge in the participants managed with the PAD care bundle. The data showed that the intervention group experienced fewer days of delirium than the control group, which may be associated with better cognitive function at the 3- and 6-month follow-ups. Brummel et al. (2014) reported that patients who experienced longer duration of delirium during their ICU stay experienced more cognitive problems than their peers who experienced shorter episodes.

This study was potentially affected by several limitations. First, the sample population was small. Second, the interventions in this study were conducted by a multidisciplinary research team, and thus, it may not be plausible to presume that the high level of compliance with the PAD care bundle may be achieved by ICU staff alone, especially in light of known reluctance to apply a series of strategies to routine clinical care because of concerns about overwhelming healthcare staff. Third, the recommendation included in the new PAD guidelines regarding avoiding benzodiazepine use in patients at a high risk for delirium was not followed in this study. Benzodiazepines are still the most common sedatives used at most hospitals in China because dexmedetomidine is too expensive for most patients. Finally, a 3-month follow-up was used this study. Therefore, future studies using longer-term follow-up periods and larger samples of ICU patients should be conducted to test the results of this study.

Conclusions

The effectiveness and feasibility of the PAD care bundle, a selection of evidence-based, multifaceted interventions for preventing delirium and improving clinical outcomes in patients receiving mechanical ventilation, were assessed in this study. The participants who received the PAD care bundle presented a lower incidence and shorter duration of delirium as well as had shorter ventilator times and ICU LOS than
their control group peers, who received usual care. Furthermore, the intervention group showed higher cognitive function, as indicated by higher scores on the dimensions of the MoCA scale, at 6 months after ICU discharge. However, the PAD care bundle was not found to significantly affect 28-day ICU mortality.

Relevance to Clinical Practice
The findings indicate that the PAD care bundle, as a multi-component program targeting pain, agitation, sedation, and ICU delirium assessment and management, has the potential to improve clinical outcomes. However, adherence to the interventions continues to be a challenge. We recommend that the administrative leadership of ICUs adopt selected strategies (e.g., computerized or preprinted protocols, training and education, close communication and cooperation, checklists, and interdisciplinary teamwork) to achieve buy-in and performance of the interventions by staff.

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Data analysis and interpretation: DL, CFX, NC, YL, XDL
Drafting of the article: DL, LT, XPW, YFC
Critical revision of the article: LT, XPW

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