


RESEARCH

The impact of ABCDE bundle implementation on patient outcomes: A nationwide cohort study

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Abstract

Background: The ABCDE bundle is a set of evidence-based practices to systematically reduce the risks of sedation, delirium, and immobility in intensive care patients. Implementing the bundle improves clinical outcome.

Aims and Objectives: To investigate the association between patient outcomes and compliance with bundle components ABC (analgo-sedation algorithms), D (delirium protocol), and E (early mobilization protocol).

Design: A Spanish multicentre cohort study of adult patients receiving invasive mechanical ventilation (IMV) for ≥ 48 h until extubation.

Methods: The primary outcome was pain level, cooperation to permit Medical Research Council Scale administration, patient days of delirium, and mobility. The secondary outcome was cumulative drug dosing by IMV days. Tertiary outcomes (ICU days, IMV days, bed rest days, ICU mortality, ICUAW) and independent variables (analgo-sedation, delirium, early mobilization protocols) were also studied.

Results: Data were collected from 605 patients in 80 ICUs and 5214 patient days with IMV. Two-thirds of the ICUs studied applied no protocols. Pain was not assessed on 83.6% of patient days. Patient cooperation made scale administration feasible on 20.7% of days. Delirium and immobility were found on 4.2% and 69.9% of days, respectively. Patients had shorter stays in ICUs with bundle protocols and fewer days of IMV in ICUs with delirium and mobilization bundle components ($P = 0.006$ and $P = 0.03$, respectively). Analgo-sedation protocols were associated with more opioid dosing

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($P = 0.02$), and delirium and early mobilization protocols with more propofol ($P = 0.001$), dexmedetomidine ($P = 0.001$), and lower benzodiazepine dosing ($P = 0.008$).

Conclusions: The implementation rate of ABCDE bundle components was very low in our Spanish setting, but when implemented, patients had a shorter ICU stay, more analgesia dosing, and lighter sedation.

Relevance to clinical practice: Applying some but not all the bundle components, there is increased analgesia and light sedation drug use, decreased benzodiazepines, and increased patient cooperation and mobility, resulting in a shorter ICU stay and fewer days of IMV.

KEYWORDS

delirium, early mobilization, mechanical ventilation, pain assessment, sedation

1 | INTRODUCTION

Pain, agitation, delirium, acquired muscle weakness, and lack of sleep are common, distressing symptoms in critically ill patients. Clinical guidelines recommend the use of the ABCDE bundle—an evidence-based multicomponent strategy to optimize Intensive Care Unit (ICU) patients' recovery and outcomes.^{1–6} The ABCDE bundle comprises the following components: (A) assess, prevent, and manage pain; (B) both spontaneous awakening trials (SAT) and spontaneous breathing trials (SBT); (C) choice of analgesia and sedation (considering drug metabolism, dose, titration, and discontinuation); (D) delirium: assess, prevent, and manage; (E) early mobility and exercise.

2 | BACKGROUND

Implementation of the ABCDE bundle has brought significant change to critically ill patient care. Patients are no longer deeply sedated, disconnected from their surroundings, and immobile; they are lightly sedated, and able to interact and exercise.^{7,8} Goals in patient care no longer focus exclusively on organic dysfunction but incorporate a long-term vision to cover the symptoms of critical illness—the back-end of critical care. These goals have led to a holistic approach to patient care, involving the integration and coordination of multidisciplinary ICU care teams.^{9–13}

Implementing the ABCDE bundle can improve survival,^{14–18} and reduce ICU and hospital stays,^{17,19} readmissions,¹⁹ delirium and coma,^{14,15,17,19,20} invasive mechanical ventilation (IMV) days,^{14,17,19} analgesia dosing,¹⁷ and the use of physical restraint.¹⁹

Although the evidence shows that the ABCDE bundle improves the patient outcomes mentioned above, implementing these strategies in clinical practice is complex and is approached differently across different countries and even in the same country.^{11–13,21–23} In Spain, for example, few ICUs have a physiotherapist in the ICU team. In addition, critical care nurses and respiratory therapists are yet to have established training specialties. Studies that have mapped the current implementation status of the ABCDE bundle in our setting^{24,25} show that only part of the first three components (ABC) are applied in practice. Incomplete implementation of ABC hampers DE acquisition, because good analgesia management

WHAT IS KNOWN ABOUT THE SUBJECT

- The use of ABCDE bundles improves analgesia practices and reduces patient delirium and immobility.
- The ABCDE bundles provide a bridge between current recommendations and clinical practice and improve ICU patient outcomes.

WHAT THIS PAPER CONTRIBUTES

- The study reveals a low bundle implementation rate in ICUs across Spain. Despite this, bundle components resulted in a shorter ICU stay and decreased mechanical ventilation days, greater use of analgesia, change in sedation strategies, decreased use of benzodiazepines, and increased use of dexmedetomidine and propofol.
- In protocols with analgesia algorithms, doses are titrated by physicians in Spain, and these protocols result in increased doses of opiates and benzodiazepine boluses.
- Delirium prevention and management protocols result in more cooperative patients, pain assessment feasibility, and decreased benzodiazepine use.
- Early mobilization protocols lead to improved patient mobility in bed or passive transfers, and decreased benzodiazepine use.

reduces delirium and facilitates interaction and mobilization.^{26–29} The first step to address these imbalances is to identify and prioritize the most deficient bundle components in our setting and those with the biggest impact on patient outcomes. The next step will be to analyse barriers, and a third phase will be to implement actions to improve compliance.

2.1 | Aim and objectives

The aim of this study was to investigate the association between patient outcomes (pain level, level of cooperation, patient days with

delirium, patient days with physical restraint, level of mobility, drug levels of analgesia, sedatives, muscle relaxants, and antipsychotics, need for re-intubation or tracheostomy, ICU length of stay in days, IMV days, bed rest days, ICU mortality, and development of ICU-acquired muscle weakness (ICUAW)) and compliance with bundle components ABC (analgo-sedation algorithms), D (delirium prevention and management protocol), and E (early mobilization protocol).

2.2 | Design and methods

A 4-month, prospective, observational, multicentre cohort study was conducted in adult patients receiving IMV for at least 48 h in ICUs across Spain.

2.3 | Sample/participants

Based on the proportion of patients whose pain was assessed at least once per shift (929 of 1574 patients) found in a prior study by the ASCyD research group,²⁴ a confidence level of 95%, an estimated standard error of 4, and an expected loss to follow-up of 20%, the minimum sample size required was calculated to be 531 patients. Exclusion criteria were pregnant women, those referred to the ICU from other hospitals, patients with primary neurologic or neuromuscular pathology, those unable to walk (mobility aids allowed), recent limb amputees, users of orthopaedic devices, and patients with body mass index (BMI) >35.

2.4 | Data collection

Data were collected from day 3 of the ICU stay until extubation. The data collection procedure is described in Data S1.

2.5 | Research variables and measures

2.5.1 | Primary outcome

Pain level, level of cooperation, incidence of delirium and physical restraints, and level of mobility related to the implementation of bundle components ABC, D, and E.

Pain level

Pain level was calculated according to the number of patient days with pain out of total IMV patient days. In cooperative patients, pain was assessed by means of the numeric rating scale (NRS),¹ a self-reported pain scale ranging from 0 ("no pain") to 10 ("the worst imaginable pain"). In non-cooperative patients, pain was assessed by means of the behavioural indicators of pain scale (ESCID), a validated scale for non-communicative, mechanically ventilated medical and surgical patients,³⁰ whereby five items—facial musculature, movement, muscle tone, calmness, and IMV tolerance—are each scored on a scale of

0 to 2. The total score ranges from 0 (no pain) to 10 (worst pain). For both 10-point scales (NRS and ESCID), 0 represents absence of pain; 1 to 3 represent mild to moderate pain; 4 to 6 represent moderate to severe pain; and > 6 represents very severe pain. No score is understood as no pain assessment performed. ESCID³⁰ was internally reliable, with a Cronbach- α value of 0.85 (95% CI 0.81-0.88). Cronbach- α coefficients for ESCID domains were high, such that facial expression was 0.87 (95% CI 0.84-0.89), calmness 0.84 (95% CI 0.81-0.87), muscle tone 0.80 (95% CI 0.75-0.84), compliance with mechanical ventilation 0.70 (95% CI 0.63-0.75), and consolability 0.85 (95% CI 0.81-0.88).

Level of cooperation

To assess patients' level of cooperation, Hermans' standardized commands³¹ were applied, followed, if feasible, by a muscle strength assessment using the Medical Research Council sum-score (MRC sum-score). Specifically, every day a physiotherapist in the ICU assessed patients' level of cooperation with Hermans' five commands: (1) open and close your eyes; (2) look at me; (3) open your mouth and put out your tongue; (4) nod your head; (5) raise your eyebrows after I have counted to five. Each correct answer is worth 1 point. The commands may be repeated twice. Gentle physical stimulus (pinching the patient's skin) is allowed once to elicit a response.

Possible outcomes entered in the database were as follows:

- patient asleep;
- patient unable to follow commands;
- patient fully awake and cooperative (score of 5 out of 5). MRC assessment was feasible.

The MRC sum-score was repeated if feasible every 7 days until ICU discharge. If unfeasible, the patient's level of cooperation was reassessed every day until ICU discharge.

Patient days with delirium

This variable was calculated by the number of patient days with delirium (according to the nurse in charge) out of the total IMV patient days, rather than applying the confusion assessment method for the ICU (CAM-ICU), because only 22 ICUs out of 80 (27.5%) used a validated scale.²⁵

Patient days with physical restraint

Physical restraint was measured by the number of days that patients were restrained out of total IMV patient days, where physical restraint was defined as "any manual method, physical, or mechanical device, material, or equipment that immobilizes or reduces the ability of a patient to move his or her arms, legs, body, or head freely".¹

Level of mobility

Mobility was assessed using the ICU mobility scale (IMS),³² which measures mobility milestones in critically ill patients, and has been validated in our cultural setting.³³ The 10-point scale ranges from 0 (patient immobile, lying in bed) to 10 (independent ambulation). The IMS ranges are shown in Table S1.

2.5.2 | Secondary outcome

Drug levels of analgesia, sedatives, muscle relaxants, and antipsychotics (cumulative drug dosing by IMV days \times 100) associated with implementation of bundle components ABC, D, and E. Opioids were calculated with morphine equivalents, and benzodiazepines with midazolam equivalents (conversions are shown in Table S2).

2.5.3 | Tertiary outcomes

Need for re-intubation or tracheostomy, ICU length of stay in days, IMV days, bed rest days, ICU mortality, and development of ICUAW associated with implementation of bundle components ABC, D, and E.

The Medical Research Council sum-score (MRC sum-score) evaluates muscle strength, with a score ranging from 0 (no muscle contraction) to 5 (full strength). Physical examination of three muscle groups in each of the upper and lower limbs results in a composite or sum score of 60. ICUAW was diagnosed for values lower than 48 out of 60 at the first measurement (baseline MRC at first awakening).

2.5.4 | Independent variables

The following multidisciplinary protocols were considered as independent variables:

Protocols with analgo-sedation algorithms (components ABC in the bundle)

These protocols monitor sedation and agitation with a validated scale administered every 6 or 8 h, and they include daily sedation targets. Few include SAT, but all include the application of physician-led sedation and analgesia dosing algorithms.

Delirium prevention and management protocols (component D in the bundle)

These protocols encompass standardized assessments of delirium and pharmacological and non-pharmacological measures for delirium prevention and management. The second group of measures include sleep hygiene strategies, continuous reorientation (in time, place, and person), environmental measures, as well as family presence and participation.

Early mobilization protocols (component E in the bundle)

Early mobilization protocols provide algorithms to start mobilizing critically ill patients between days 2 and 5 of the ICU stay.

Detailed definitions and descriptions of the measurement tools and protocols are provided in Tables S3, S4, and S5.

2.5.5 | ICU-related variables

ICU-related variables were nurse-patient ratio, physiotherapist availability by number of hours, and percentage of IMV use.

2.5.6 | Patient-related variables

Patient-related variables were demographic data (age, gender, and BMI). The following indices and scores were applied: Charlson, Barthel, Acute Physiology And Chronic Health Evaluation II (APACHE II), and Sequential Organ Failure Assessment (SOFA). Respiratory variables were also collected, such as the use of artificial airways (endotracheal tube (ETT) or tracheostomy tube).

2.6 | Data analysis

Categorical variables were expressed as frequency and percentage, using Fisher or Chi-squared test for between-group comparisons. Quantitative variables were expressed as mean and standard deviation (SD) or median and percentile, as 25 to 75 or 10 to 90 percentile ranges, depending on the distribution, which was analysed with the Kolmogorov-Smirnov test for large sample sizes ($n \geq 30$) or the Shapiro-Wilk test for small samples ($n < 30$). Groups were compared using the Student *t* test or Mann-Whitney *U* test, depending on whether data followed a normal or non-normal distribution, respectively. Data were analysed using IBM SPSS Statistics 21.0 for Windows (SPSS Inc., Chicago IL, USA).

2.7 | Ethical and research approvals

The study was approved by the Ethics and Clinical Research Committees of the participating sites, a list of which can be found in Data S1.

3 | RESULTS

A total of 605 patients were studied from 80 ICUs, resulting in 5214 patient days with IMV. A flow diagram showing participants' enrolment and movement through the study is provided in Figure 1.

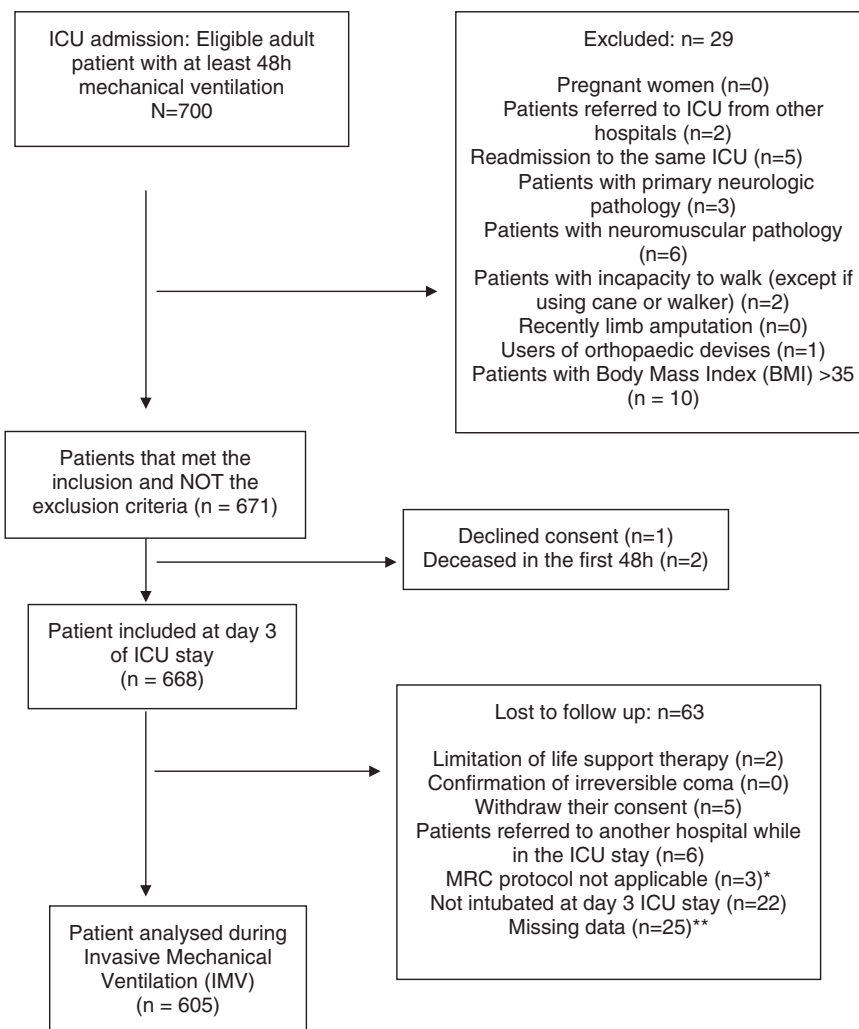
3.1 | Patient characteristics

Median age [25th-75th percentile] was 66 [54-74] years; women accounted for 182 (30.1%) of participants; and mean (SD) BMI was 26.9 (4.3). The most common diagnostic classification was "other medical diagnoses" with 269 (44.5%) patients, followed by sepsis with 120 (19.8%) and "other surgery" with 109 (18%) patients. Other diagnoses were heart surgery with 52 (8.6%) patients, trauma with 30 (5%), neurosurgery 14 (2.3%), and overdose with 11 (1.8%) patients.

3.2 | Bundle compliance

Of the 80 ICUs studied, 53 (66.2%) applied no protocols, 16 (20.0%) followed protocols with analgo-sedation algorithms (ABC), 12 (15.0%) implemented delirium prevention and management protocols (D), and

FIGURE 1 Flow chart of participants' movement throughout the study period.
*MRC protocol was not applicable because of the following reasons: two patients were under medical orders to not mobilize the lower limbs, and one patient developed aphasia during the ICU stay.
**The data were incorrectly added to the database and could not be recovered



*MRC protocol was not applicable due to the following reasons: 2 patients were under medical orders to not mobilize the lower limbs, and 1 patient developed aphasia during the ICU stay.
**The data were incorrectly added to the database and could not be recovered.

10 (12.5%) used early mobilization protocols (E). A total of 11 ICUs applied more than one protocol, such that 4 (5.0%) applied the ABCD bundle, 2 (2.5%) the ABCDE bundle, 4 (5.0%) the DE bundle, and 1 (1.2%) the ABCE bundle (see Table S5).

3.3 | Primary outcome

Of the 5214 IMV days analysed, pain was not assessed on 83.6% (95% CI 81.1-86.1) of days; it was assessed and found to be zero on 11.1% (95% CI 8.9-13.1) of days, mild to moderate on 3.2% (95% CI 2.1-4.2), moderate to severe on 1.9% (95% CI 0.8-2.8), and very intense on 0.2% (95% CI 0.08-0.5) of days. Patients' level of cooperation was sufficient to make the MRC feasible on 20.7% (95% CI 17.9-23.4) of days; delirium was identified on 4.2% (95% CI 2.8-5.5) of days, physical restraints were applied on 25.2% (95% CI 22.2-28.1) of days, and immobility (IMS of 0) was recorded on 69.6% (95% CI 66.6-72.7) of days (Table 1).

Of the 605 patients in the sample, 133 (22.0%) were admitted to an ICU that implemented a protocol with analgo-sedation algorithms

for dose management and adjustment (ABC). There were no significant differences between these patients and the rest of the sample regarding days with pain assessment, level of cooperation, incidence of delirium, or use of physical restraints (Table 2).

A delirium prevention and management protocol (D) was applied in 68 (11.2%) patients, and these patients had more pain assessments, a higher level of cooperation, and more MRC assessments; they had no lower incidence of delirium or greater mobility (Table 2).

An early mobilization protocol (E) was applied in 51 (8.4%) patients. These patients received more pain assessments, registering no differences in the level of cooperation, but more days of mobility with an IMS score of 1 to 2 (Table 2).

3.4 | Secondary outcome

The most common analgesic given as an intravenous infusion (IVI) was morphine, and as a bolus dose, paracetamol and metamizole. The most used sedative was propofol, and the most used muscle relaxant was cisatracurium (see Table S6).

TABLE 1 Level of pain, level of cooperation, incidence of delirium, and level of mobilization among patients receiving invasive mechanical ventilation (N = 605, 5214 patient days)

Level of pain	% patient days, 95% CI
Pain not assessed	83.6 (81.1 to 86.1)
Absence of pain (NRS/ESCID 0)	11.1 (8.9 to 13.1)
Mild-moderate pain (NRS/ESCID 1-3)	3.2 (2.1 to 4.2)
Moderate-severe pain (NRS/ESCID 4-6)	1.9 (0.8 to 2.8)
Very intense pain (NRS/ESCID 7-10)	0.2 (–0.08 to 0.5)
Level of cooperation	% patient days, 95% CI
MRC assessed	20.7 (17.9 to 23.4)
MRC not assessed; patient asleep	62.7 (59.7 to 65.7)
MRC not assessed; patient unable to follow commands	16.6 (14.4 to 18.8)
Incidence of delirium	% patient days, 95% CI
Delirium	4.2 (2.8 to 5.5)
Use of restraints	25.2 (22.2 to 28.1)
Level of mobility	% patient days, 95% CI
Immobile (IMS 0)	69.6 (66.6 to 72.7)
Active/passive mobility in bed (IMS 1–2)	29.2 (26.2 to 32.2)
Active/passive mobility out of bed (IMS 3–5)	1.1 (0.5 to 1.6)
Ambulatory (IMS ≥ 6)	0.1 (–0.02 to 0.2)

Abbreviations: ESCID, behavioural indicators of pain scale; IMS, ICU mobility scale; MRC, Medical Research Council sum-score; NRS, numeric rating scale.

The patients who were admitted to an ICU that implemented a protocol with analgosedation algorithms for dose management and adjustment (ABC) received more opioids (remifentanyl IVI, and fentanyl bolus and tramadol in divided doses) and more metamizole as a bolus and divided dose alike. Likewise, they received more dexmedetomidine IVI, more midazolam boluses, and also cisatracurium IVI and rocuronium boluses (see Table S7).

Patients admitted to an ICU that implemented a delirium prevention and management protocol received more metamizole IVI, fewer fentanyl boluses, less benzodiazepine IVI and in bolus and more propofol and dexmedetomidine IVI (see Table S7).

Patients admitted to an ICU that implemented an early mobilization protocol received more remifentanyl, propofol, and dexmedetomidine (see Table S7).

3.5 | Tertiary outcome

Table 3 shows the nurse-to-patient ratios by type of protocol applied. The ICUs that applied analgosedation and mobilization protocols had more 1:2 nurse-to-patient ratios and very few shift-dependent ratios. On the contrary, ICUs with delirium and mobilization protocols had higher nurse-to-patient ratios of 1:3 and/or 1:4.

ICUs implementing an analgosedation protocol had higher rates of IMV than other ICUs, and they had more physiotherapy hours, younger patients, and a tendency towards lower comorbidity. In our sample, we found no differences in patient severity or mortality rate by bundle applied. In general, patients had shorter stays in ICUs that applied bundle protocols, and fewer days of IMV in ICUs that applied a delirium or mobilization bundle component (Table 3).

4 | DISCUSSION

We identified a low rate of implementation of the ABCDE bundle and a predominance of deep sedation and immobility in ICU patients in our setting, but despite this, there was a change in sedative and analgesia use and a shorter ICU stay when any part of the bundle was applied, and a reduction in IMV days when components D and E were applied.

Prevalence studies^{24,34–38} and other studies analysing bundle implementation in the ICU^{14–16,18,19,39} reveal a gap between recommendations and clinical practice itself. This study identified a low (20%) implementation of analgosedation protocols, far from the 40% to 60% implementation found by European surveys conducted among intensive care physicians^{21,36,37,40} and ICU nurses.^{24,41} The aims of analgosedation protocols include promoting light sedation and keeping patients awake and cooperative. This study found that just 20.7% of patients were alert and cooperative, whereas studies by Lee et al²⁰ and García-Sánchez et al³⁷ reported percentages of approximately 60%. However, Aragón et al³⁹ and Luetz et al³⁴ reported moderate to deep sedation in 98% and 74% of patients, respectively, and these prevalence figures are more similar to those found in this study, because 80% of our patients were unable to undergo MRC assessment because of lack of cooperation. In this study, protocols with analgosedation algorithms were not found to optimize aspects such as monitoring of pain and sedation, and did not lead to more alert and cooperative patients with less delirium and more mobility, and these aspects were indeed found by other authors.^{42–56} Incorrect implementation of recommendations could explain this difference.¹

Pain monitoring in this study (16.4%) was lower than the 30% rate reported by Luetz et al³⁴ in a study on ventilated patients, and a long way behind the 67.5% rate reported in the Spanish ASCyD project for patients with and without IMV.²⁴ The lower rate in our study is probably because we included only patients receiving IMV, who are often non-communicative. Indeed, Luetz et al³⁴ found that 70% of ICUs did not use any tool specifically developed for assessing pain in sedated patients, such as the behavioural pain scale. Hence, sedated patients are at higher risk for receiving insufficient analgesia. Other studies have reached the same conclusion regarding the low use of pain assessment tools in non-communicative patients.^{24,35,37,57}

Various authors^{58–60} concur that one of the largest barriers in pain measurement is the lack of implementation of analgesia protocols in ICUs, because these protocols incorporate validated scales for pain measurement scales. This barrier mainly affects non-communicative patients, a finding confirmed in our study. Phillips et al⁵⁸ used a

TABLE 2 Association of protocols for analgesation algorithms; delirium prevention and management; and early mobilization with pain assessment, level of cooperation, incidence of delirium, and level of mobilization in patients receiving invasive mechanical ventilation

	Protocol with analgesation algorithms			Delirium prevention and management protocol			Early mobilization protocol		
	yes N = 133 (22%)	no N = 472 (78%)	P value	yes N = 68 (11%)	no N = 534 (89%)	P value	yes N = 51 (8%)	no N = 554 (92%)	P value
Pain assessment (% patient days)	100 [50-100]	100 [0-100]	0.30	100 [0-100]	100 [37-100]	0.003	100 [0-100]	100 [26-100]	0.01
Pain not assessed									
Level of cooperation (% patient days)									
MRC assessed	0 [0-65]	0 [0-100]	0.77	10 [0-100]	0 [0-100]	0.01	0 [0-100]	0 [0-100]	0.72
MRC not assessed; patient asleep	80 [0-100]	73 [0-100]	0.35	75 [0-100]	75 [0-100]	0.46	78 [0-100]	75 [0-100]	0.97
MRC not assessed; patient unable to follow commands	0 [0-63]	0 [0-54]	0.35	0 [0-25]	0 [0-60]	0.01	0 [0-77]	0 [0-54]	0.24
Incidence of delirium (% patient days)									
Delirium	0 [0-5]	0 [0-0]	0.38	0 [0-0.6]	0 [0-0]	0.86	0 [0-0]	0 [0-0]	0.44
Physical restraint	0 [0-93]	0 [0-100]	0.78	0 [0-100]	0 [0-100]	0.64	0 [0-100]	0 [0-100]	0.53
Level of mobility (% patient days)									
Immobile (IMS 0)	100 [0-100]	92 [0-100]	0.05	87 [0-100]	93 [0-100]	0.46	50 [0-100]	94 [0-100]	0.009
Active/passive mobility in bed (IMS 1-2)	0 [0-92]	7 [0-100]	0.05	13 [0-100]	5 [0-100]	0.35	44 [0-100]	0 [0-100]	0.008
Active/passive mobility out of bed (IMS 3-5)	0 [0-0]	0 [0-0]	0.22	0	0 [0-0]	-	0 [0-0]	0 [0-0]	0.42

Note: Data are expressed as median [10th-90th percentile] and analysed with the Mann-Whitney U test. Abbreviations: IMS, ICU mobility scale; MRC, Medical Research Council sum-score.

TABLE 3 Patients' clinical data by bundle component implementation in the ICU

	ICU with protocol with analgesedation algorithms N = 133	ICU without analgesedation algorithms N = 472	ICU with delirium prevention and management protocol N = 68	ICU without delirium prevention and management protocol N = 534	ICU with early mobilization protocol N = 51	ICU without early mobilization protocol N = 554	
Nurse: patient ratio, n (%)		<0.001			<0.0001		<0.001
1:2	79 (59.4)	208 (44.1)	20 (29.4)	267 (50)	28 (54.9)	259 (46.8)	
1:3	19 (14.3)	99 (21)	32 (47.1)	83 (15.5)	20 (39.2)	98 (17.7)	
1:4	0 (0)	17 (3.6)	11 (16.2)	6 (1.1)	0 (0)	17 (3.1)	
Shift-dependent	5 (3.8)	59 (12.5)	5 (7.4)	59 (11)	0 (0)	64 (11.6)	
Patient-dependent ^b	30 (22.5)	89 (18.9)	0 (0)	119 (22.3)	3 (5.9)	116 (20.9)	
Percentage of IMV usage in the ICU ^{a,c}	42 [35-44]	29 [22-44]	22 [21-24]	41 [25-46]	24 [11-26]	40 [25-44]	<0.001
Physiotherapist hours per day available in the ICU ^{a,d}	6 [3-7]	5 [2-10]	5 [5-5]	5 [2-9]	5 [3-6]	5 [2-9]	0.5
Age in years ^a	62 [50-72]	67 [55-75]	69 [52-76]	65 [54-74]	67 [53-77]	65 [54-74]	0.9
Gender, female, n (%)	45 (33.8)	137 (29.1)	28 (41.2)	154 (28.9)	20 (39.2)	162 (29.3)	0.1
BMI, kg/m ^{2a}	27 [24-30]	26 [24-29]	26 [24-29]	26 [24-29]	27 [24-29]	26 [24-29]	0.5
Barthel at admission ^a	100 [100-100]	100 [95-100]	100 [100-100]	100 [95-100]	100 [100-100]	100 [95-100]	0.5
Charlson index ^a	4 [1-6]	5 [2-6]	5 [2-6]	4 [1-6]	4 [0-6]	4 [2-6]	0.8
APACHE II ^{a,e}	22 [18-26]	21 [17-27]	23 [19-29]	21 [16-27]	24 [19-28]	21 [26-27]	0.07
SOFA score (maximum during ICU stay) ^{a,f}	7 [6-9]	10 [7-12]	9 [8-10]	10 [7-12]	11 [8-13]	9 [7-12]	0.5
Re-intubation, n (%)	22 (16.5)	77 (16.3)	9 (13.2)	90 (16.9)	6 (11.8)	93 (16.8)	0.3
Tracheostomy, n (%)	29 (21.8)	136 (28.8)	16 (23.5)	148 (27.7)	11 (21.6)	154 (27.8)	0.3
Days of ICU stay ^a	12 [8-21]	15 [9-24]	12 [8-17]	15 [9-24]	13 [8-20]	15 [9-24]	0.04
Days of IMV ^a	5 [2-9]	6 [2-12]	4 [1-9]	5 [2-11]	5 [1-9]	5 [2-11]	0.03
Days of bed rest ^a	10 [7-17]	14 [8-22]	11 [8-17]	14 [8-22]	11 [7-17]	13 [8-22]	0.09
Death, n (%)	37 (27.8)	124 (26.3)	16 (23.5)	144 (27)	11 (21.6)	150 (27.1)	0.4
Patients with ICUAW n (%)	47 (35.3)	217 (46)	37 (54.4)	225 (42.1)	27 (52.9)	237 (42.8)	0.3

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; ICUAW, ICU-acquired muscle weakness; IMV, invasive mechanical ventilation; SOFA, Sequential Organ Failure Assessment score.

^aMedian [25th-75th percentile].

^bShift-dependent: the nurse-patient ratio varies by shift time and day, and is lower at night, weekends and on public holidays; Patient-dependent: the nurse-patient ratio varies by patient severity.

^cInvasive mechanical ventilation (IMV) usage formula: number of patients receiving IMV divided by the total patients in the ICU during the study period, multiplied by 100.

^dPhysiotherapist hours in the ICU: total physiotherapist hours in the ICU per day. Scheduled hours and the mean annual additional hours from referrals were included.

^eData only for 83 patients with sedation algorithms and for 217 patients without sedation algorithms; data for 26 patients with delirium management protocol and for 271 without; data for 23 patients with mobilization protocol and for 277 without.

^fData only for 11 patients with sedation algorithms and for 107 patients without sedation algorithms; data for 10 patients with delirium management protocol and for 105 without; data for 6 patients with mobilization protocol and for 112 without.

training programme to implement the Critical Care Pain Observation Tool (CPOT) scale, finding that health care professionals had problems understanding and using the scale, which led to redesigning the training programme. In view of these results, it appears to be important not only to use pain scales but also train staff how to use and integrate these scales in the context of an analgesia protocol.

The extremely low incidence of delirium (4.2%) found in this study is similar to the figures reported by Owen et al³⁸ for Europe (6%) and worldwide (9%) and similar to other studies in the Spanish setting.^{24,37} However, there is marked disparity compared with other studies that report an incidence ranging from 19% to 75%.^{14,16-20,34,61} In these studies, delirium was monitored by means of a standardized, validated scale.

The use of physical restraints (25.2%) in this study is similar to that reported by other studies in our setting^{24,37} and to restraint use reported among European nurses by Egerod et al.⁵⁷ However, higher restraint rates of 33% and 52% have been reported in the United States by Pun et al¹⁹ and in Canada by Burry et al,³⁵ respectively. The lower use of physical restraints in this study might be explained by the high prevalence of deep sedation and immobility, and associated contextual factors.⁶²

Patient mobility depends greatly on the level of cooperation. The low level of cooperation observed in our study among patients receiving IMV was associated with limited mobility. A study by Capell et al²⁶ reported higher mobility than that found in this study, and it also identified sedation as the main barrier to mobilization. As noted by Miller et al in a study on ABCDE bundle implementation,²⁹ the impact of early mobilization protocols depends on the implementation of earlier components in the bundle. Pain, sedation, coma, and delirium hamper early mobilization,^{26,28,29,63} and therefore these aspects should be taken into consideration when prioritizing improvement actions. The patients in this study were mostly mobilized in bed, as confirmed by other studies.^{26,63,64} Even in ICUs with early mobilization protocols, patients receiving IMV were still mobilized in bed, and this situation is again reflected in other studies.^{26,63-66} However, some studies have identified an association between bundle implementation and increased out-of-bed mobility,^{14,18} although a study by Bounds et al¹⁶ found a significant increase in patients in a sitting position after applying the bundle, while out-of-bed mobilization remained unchanged. Our results show little improvement in patient mobility, probably because of the few days that patients were found to be cooperative. One factor that may influence this finding is the absence of physiotherapists in critical care teams in our setting and the median of just 5 h per week of physiotherapy hours in ICUs with an early mobilization protocol.

We found that existing protocols implement standardized pain and sedation assessments, and drug algorithms based on a fixed target and predefined algorithms. These protocols are also widely implemented in the literature.^{42,44-56} Similarly, nurse-guided drug algorithms are widely reported to be effective,^{42,44-56} although in our setting, drug algorithms are physician-guided.²⁴ Despite limited adherence to the recommendations in these protocols, our study found greater use of opioids and dexmedetomidine to promote light

sedation, as corroborated in a study by Faust et al.⁴⁵ In our study, benzodiazepines were used more in boluses as rescue therapy to control agitation, and were always followed by IVI dose adjustments to attain the predefined target. However, IVI drug titration appears to have been performed incorrectly, because sedative doses did not decrease, unlike findings in other studies.^{42,44,45,47,48,50,53,54,56}

Bundle recommendations concerning choice of analgesic and sedative drugs prioritize analgesia, and encourage light sedation and avoidance of benzodiazepines because of their delirigenic effect.^{18,58} Unlike other authors' findings,^{37-39,67,68} our findings show that ICUs implement these recommendations, in line with several publications that show a decrease in benzodiazepine use and an increase in propofol and dexmedetomidine use.^{19,36,38,41,69}

Opioids, specifically morphine, were the most commonly used analgesics in this study, corroborating the findings of some studies,^{19,35,38,39,67,69} but contrary to others that found that fentanyl^{21,36,37,68} and remifentanyl⁴¹ are most prevalent. We observed that haloperidol was the most widely used drug to treat delirium, corroborating other authors' findings.^{21,37,39,67}

When delirium prevention and management protocols were applied in ICUs in this study, benzodiazepines were used less; and dexmedetomidine and propofol were used more. Studies by Trogrlić et al⁷⁰ and Lee et al²⁰ reported similar findings.

Early mobilization protocols were associated with lower use of benzodiazepines and greater use of dexmedetomidine, as also found in a study by Lui et al.⁶⁴ These patients were not alert and cooperative, which represents one of the main barriers to mobilization.^{26,63} However, this study did find decreases in IMV time and ICU stay, which corroborates findings in other studies.^{64,65,71}

Regarding clinical variables, patients in ICUs that apply protocols have shorter ICU stays, which is reflected in the literature in terms of individual bundle component implementation^{1,42,43,65,72} and also general bundle implementation.^{17,19} Trogrlić et al⁷² conducted a systematic review on the effect of implementation strategies to assess, prevent, and manage ICU delirium, and these authors also reported shorter ICU stays after protocols were implemented, even when only a few strategies were used. The correlation observed in the present study between the existence of early mobilization protocols and the decrease in IMV days was also found in the meta-analysis by Zhang et al.⁶⁵

4.1 | Limitations

We were unable to analyse the Richmond agitation-sedation scale (RASS) results because the great majority were recorded in patients in ICUs implementing protocols with analgosedation algorithms. We compensated for this limitation by having a physiotherapist-led set of five standardized questions to decide if the MRC sum-score was feasible, whereby a cooperative patient's score would correspond to a RASS score of between -2 and 0. Despite this, a degree of subjectivity cannot be ruled out in the cooperation assessment, even though we applied Hermans' protocol to administer the five standardized questions.³¹

Because of the very low implementation of delirium scales,²⁵ delirium was instead identified subjectively by the charge nurse, which would explain the low rate observed, because hyperactive delirium is the main type identified through subjective assessment.

In our setting, SAT is an uncommon practice,^{25,37} and therefore we did not analyse the use of SAT or SBT as a strategy in bundle components ABC. The most recent recommendations¹ have found no differences between SAT and guided analgesedation protocols, and both strategies permit the maintenance of light sedation in patients.

4.2 | Implications and recommendations for practice

Applying some but not all the bundle components improves the quality of care and the clinical outcome of critically ill patients. We identify the implementation of strategies as a priority to overcome the structural and organizational barriers that hinder ABC bundle application, thereby achieving optimal pain monitoring in communicative and non-communicative patients alike, leading to effective analgesia and minimized use of opioids. Secondly, agitation-sedation and delirium monitoring should be reinforced, also applying protocols that avoid benzodiazepine use and promote light sedation, following nurse-guided algorithms to minimize and titrate analgesedation dosing. Finally, physiotherapists need to be incorporated into ICU teams to make early mobilization more efficient and effective.

5 | CONCLUSIONS

The implementation rate of bundle components was very low in our setting. However, we found that the use of bundle components in patients resulted in a shorter ICU stay, fewer IMV days, greater use of analgesia, and a change in sedation strategies, with decreased use of benzodiazepines, and increased use of dexmedetomidine and propofol. In protocols with analgesedation algorithms for dose management and adjustment, doses were titrated by physicians rather than nurses, and benzodiazepine bolus use was increased. Delirium prevention and management protocols resulted in more cooperative patients, pain assessment feasibility, and decreased benzodiazepine use. Early mobilization protocols led to improved patient mobility in bed or with passive transfers, and decreased benzodiazepine use.

In Spain, it is a priority in ICUs to promote the implementation of the ABC bundle with analgesedation protocols guided by nurses. In a second phase, the DE bundles should be implemented, together with a greater presence of physiotherapists.

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ETHICS APPROVAL STATEMENT

The research meets all ethical requirements.

PATIENT CONSENT STATEMENT

The research has been reviewed by the ethics committees of the health centres involved.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

All authors have given permission to reproduce the material in the manuscript.

AUTHOR CONTRIBUTIONS

Frade-Mera María Jesús, Raurell-Torredà Marta, Arias-Rivera Susana, Zaragoza-García Ignacio, Martí Joan Daniel, Gallart-Vivé Elisabet, San José Arribas Alicia, Velasco-Sanz Tamara Raquel, and Blazquez Martínez Eva: Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; Frade-Mera María Jesús, Raurell-Torredà Marta, Arias-Rivera Susana, and Zaragoza-García Ignacio: Involved in drafting the manuscript or revising it critically for important intellectual content; Frade-Mera María Jesús, Raurell-Torredà Marta, Arias-Rivera Susana, Zaragoza-García Ignacio, Martí Joan Daniel, Gallart-Vivé Elisabet, San José Arribas Alicia, Velasco-Sanz Tamara Raquel, and Blazquez Martínez Eva: Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Frade-Mera María Jesús, Raurell-Torredà Marta, Arias-Rivera Susana and Zaragoza-García Ignacio agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA AVAILABILITY STATEMENT

All data are available in the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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