medicina *intensiva*

SPECIAL ARTICLE

Analgosedation and delirium practices in critically ill patients in the Pan-American and Iberian setting, and factors associated with oversedation after the COVID-19 pandemic: Results from the PANDEMIC study

Carola Giménez-Esparza Vich [a,*], Felipe Martínez [b], Daniela Olmos Kutscherauer [c], Daniel Molano [d], Maria del Carmen Gallardo [e], Enrique Mario Olivares-Durán [f,g], Jesús Caballero [h], Rosa Reina [i], Manuela García Sánchez [j], Federico C. Carini [k,l], Comité de Analgesia, Sedación y Delirium de la Federación Panamericana e Ibérica de Cuidados Críticos y Terapia Intensiva (FEPIMCTI)[◇]

[a] *Servicio de Medicina Intensiva, Hospital Vega Baja, Orihuela, Alicante, Spain*
[b] *Facultad de Medicina, Escuela de Medicina, Universidad Andrés Bello, Viña del Mar, Chile*
[c] *Terapia Intensiva, Hospital Municipal Príncipe de Asturias; Profesora Asistente por Concurso de la Cátedra de Semiología UNC, Córdoba, Argentina*
[d] *Unidad de Cuidado Intensivo, Hospital de San José; Fundación Universitaria de Ciencias de la Salud, Bogotá, Colombia*
[e] *Unidad de Terapia Intensiva, Hospital Municipal La Merced, La Paz, Bolivia*
[f] *Unidad Médica de Alta Especialidad No. 1, Centro Médico Nacional del Bajío, Instituto Mexicano del Seguro Social, León, Mexico*
[g] *Departamento de Enfermería y Obstetricia Sede León; División de Ciencias de la Salud, Universidad de Guanajuato, Campus León, León, Mexico*
[h] *Servei de Medicina Intensiva, Hospital Universitari Arnau de Vilanova de Lleida, IRBLleida, Lleida, Spain*
[i] *Servicio de Terapia Intensiva, Hospital San Martín, La Plata; Docente Cátedra Terapia Intensiva, Facultad de Ciencias Médicas, Universidad Nacional de La Plata, Buenos Aires, Argentina*
[j] *Unidad de Cuidados Intensivos, Hospital Universitario Virgen Macarena, Sevilla, Spain*
[k] *Interdepartmental Division of Critical Care Medicine, University of Toronto, Ontario, Canada*
[l] *Unidad de Terapia Intensiva de Adultos, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina*

Abstract Oversedation has adverse effects on critically ill patients. The Analgosedation and Delirium Committee of the FEPIMCTI (Pan-American and Iberian Federation of Critical Care Medicine and Intensive Care) conducted a cross-sectional study through a survey addressed to ICU physicians: PANDEMIC (Pan-American and Iberian Study on the Management of Analgosedation and Delirium in Critical Care [feplmCti]).

Hypothesis: Worsening of these practices in the course of the pandemic and that continued afterwards, with further oversedation.

Objectives: Perception of analgosedation and delirium practices in Pan-American and Iberian ICUs before, during and after the COVID-19 pandemic, and factors associated with persistent oversedation after the pandemic.

Of the 1008 respondents, 25% perceived oversedation after the pandemic (95%CI 22.4–27.8). This perception was higher in South America (35.8%, *P* < .001). Main risk factor: habit acquired during the pandemic (adjusted OR [aOR] 3.16, 95%CI 2.24–4.45, *P* < .001). Main protective factor: delirium monitoring before the pandemic (aOR 0.70, 95%CI 0.50−0.98, *P* = .038).

The factors identified in this study provide a basis for targeting future interventions.

Prácticas de analgosedación y delirium en pacientes críticos de la región Panamericana e Ibérica y factores asociados a la sobresedación tras la pandemia COVID-19: resultados del estudio PANDEMIC

Resumen   La sobresedación tiene consecuencias negativas en pacientes críticos. Desde el Comité de Analgosedación y Delirium de la FEPIMCTI (Federación Panamericana e Ibérica de Medicina Crítica y Terapia Intensiva) diseñamos estudio transversal mediante encuesta dirigida a médicos/as de UCI: PANDEMIC [estudio Panamericano e Ibérico sobre manejo de ANalgosedación y DEliriuM en Cuidados Críticos (fepImCti)].

Hipótesis: Empeoramiento de dichas prácticas durante la pandemia que persistieron tras ella, con mayor sobresedación.

Objetivos: Percepción de prácticas de analgosedación y delirium en las UCI de la región Panamericana e Ibérica, antes, durante y después de la pandemia COVID-19 y factores asociados a persistencia sobresedación post-pandemia.

De los 1008 encuestados, 25% informó percepción de sobresedación tras la pandemia (IC95% 22.4%–27.8%), mayor en Sudamérica (35.8%, *P* < .001). Principal factor riesgo: hábito adquirido durante la pandemia (OR ajustado [aOR] 3.16, IC95% 2.24–4.45, *P* < .001). Principal factor protector: monitorización delirium (aOR 0.70, IC95% 0.50−0.98, *P* = .038) previo a la pandemia.

Estos factores identificados en el estudio ofrecen una base para dirigir intervenciones futuras.

Introduction

Sedation is a common practice in the Intensive Care Unit (ICU), though its overuse (doses higher than those needed by the patient) leads to oversedation with adverse effects such as increase duration of mechanical ventilation (MV), prolonged ICU stay, and delirium.[1,2] To minimize these adverse effects, the eCASH (early Comfort using Analgesia, minimal Sedatives and maximal Humane care) approach emphasizes early patient comfort, minimizing sedative use and promoting humane care.[3–5] The goal is to keep the patient awake, to minimize sedation and keep it as short as possible, and to avoid the use of benzodiazepines to improve the outcomes in the ICU.[6–8] Campaigns have been proposed to prevent oversedation in the ICU, to ensure patient comfort without compromising safety, and to improve the efficiency of bed management.[2]

Chamorro et al. recommended not to ''turn off the brain'' unless absolutely necessary, and for the shortest time possible, to avoid oversedation and its adverse effects.[9] A decrease in brain activity can alter neurotransmitter balance, increasing neuronal apoptosis and cerebral inflammation, which in turn can induce patient delirium and cognitive impairment. Thus, objective monitoring of the level of sedation is essential in patients requiring deep sedation.

Deep sedation is a risk factor for the development of delirium during hospital admission.[10] Delirium, characterized by acute and fluctuating alterations in consciousness and the thinking process, is a common problem in the ICU, affecting up to 80% of all patients undergoing MV.[11–13] It is associated with a number of adverse effects including a prolongation of MV, increased mortality, long-term cognitive impairment, and an increased risk of functional disability.[14] Furthermore, patients who have received infusions of sedatives and opioids for prolonged periods are at a risk for iatrogenic withdrawal syndrome in the ICU and its associated problems.[15]

Against this background, the analgosedation and delirium guidelines of the American Society of Critical Care Medicine (SCCM) and the Pan-American and Iberian Federation of Critical Care Medicine and Intensive Care (FEPIMCTI) provide recommendations for the optimal management of analgosedation and delirium in critically ill patients.[16,17] The ABCDEF bundle of measures, developed by the SCCM (A: Assess, prevent and manage pain; B: Withdraw sedation and perform spontaneous breathing tests; C: Choice of analgesia and sedation; D: Assess, prevent and manage delirium; E: Early mobility and exercise; F: Family engagement and empowerment), provides an operational framework for implementing such recommendations, with ample evidence of their positive impact upon the outcomes of critical patients.[18,19] Despite the familiarity of these measures, their adoption is limited, and the COVID-19 pandemic has even further complicated their implementation, with a negative impact upon analgosedation practices.[20–25]

Based on the hypothesis that there was a worsening of these practices during the pandemic, with increased oversedation, and that such poor practices persisted after the pandemic, the present study was conducted to assess ICU physician's perceptions of analgosedation and delirium practices in the Pan-American and Iberian setting before, during and after the COVID-19 pandemic, and to identify the factors associated with persistent oversedation after the pandemic.

Patients and methods

Study design

A cross-sectional observational study involving a survey administered to physicians working in an adult ICU was conducted. An *ad hoc* questionnaire was developed for the study (see the Supplementary material).

The questionnaire was published online in a private password-protected server with access restricted to the principal investigators (Microsoft™ Forms; see Supplementary material).

Survey target population

The survey was targeted to healthcare professionals working in the adult ICUs of the region at the time of the study and also during the pandemic.

Distribution of the survey and invitation to participate

The invitation to participate was made iteratively through the online dissemination channels of the FEPIMCTI and its member societies, with the collaboration of the national coordinators. The survey was distributed by e-mail with the attached electronic link to the Microsoft™ Forms platform.

Sample size

The literature on sedation practices during the COVID-19 pandemic is limited. According to some reports and a previous study, it was estimated that the study would require 864 participants.[26,27] This sample size provided a 1.5% power with a two-sided 95% confidence interval to detect an estimated 10% incidence of perceived poorer sedation practices following the COVID-19 pandemic. The decision was made to increase the sample size by 15% (total of 1000 participants) to compensate for potential data loss.

Analytical strategy

A descriptive analysis was used to characterize the study sample by calculating the mean, standard deviation (SD), median and frequency. The 95% confidence interval (95%CI) was calculated for point estimates. Statistical significance was considered for $P < .05$. The inferential analysis in turn was based on the Student t-test and Mann-Whitney U test for the comparison of means, and the Fisher exact test for qualitative variables. The odds ratio (OR) was estimated to assess associations including the 95%CI. Logistic regression analysis was used to identify the relevant explanatory variables and control for confounding factors. Variables showing potential associations ($P < .15$) were entered in the multivariate model. The diagnostic ability was estimated from the receiver operating characteristic (ROC) curves, and goodness of fit was calculated using the Hosmer-Lemeshow statistic. The analyses were performed using the STATA® version 16.1 statistical package (StataCorp LP, 1996–2020).

Ethical particulars

The present study was evaluated and approved by the *Red Municipal de Bioética Clínica y Social* of the city of Córdoba (Argentina) and complies with the National Law on Personal Data Protection 25.326 (Republic of Argentina) for safeguarding the identity and data of the participants, and guaranteeing complete anonymity and confidentiality of the information. Informed consent was obtained from all the participants after receiving an explanation of the aims of the study and the time required to complete it.

Results

Sociodemographic characteristics of the participants and study sites

Sociodemographic data are presented in Table 1, and the distribution of countries to which the participants belonged is shown in Fig. 1, in order of perceived persistence of oversedation after the pandemic. This perception was greater among the professionals working in South America (35.8%), followed by the Iberian Peninsula (19.3%) and North America (15.5%).

According to the participants, there was less persistence of oversedation after the pandemic in those units with a higher nurse-to-patient ratio ($P = .02$) and with physiotherapists assigned to the ICU ($P = .009$).

Table 1 Sociodemographic characteristics of the study participants and centers.

Characteristics	No persistent deep sedation (n = 719)	Persistent deep sedation (n = 252)	Total (n = 1008)	P-value
Mean age (years, SD)	43.3 ± 10.8	42.1 ± 10.8	43.0 ± 10.8	.17 [1]
Geographical setting (n, %)				
North America	153 (21.3%)	28 (11.1%)	181 (18.6%)	
Central America and the Caribbean	24 (3.3%)	0 (0.0%)	24 (2.4%)	<.001 [2]
South America	296 (41.2%)	165 (65.5%)	461 (47.5%)	
Iberian peninsula	246 (34.2%)	59 (23.4%)	342 (33.9%)	
Working in university hospital (n, %)	547 (78.6%)	190 (77.9%)	737 (78.4%)	.86 [2]
Working in critical care training center (n, %)	396 (71.2%)	155 (74.5%)	551 (72.1%)	.42 [2]
Working in hospital with public funding (n, %)	572 (79.6%)	203 (80.6%)	775 (79.8%)	.79 [2]
Number of beds in the hospital (n, %)				
<200 beds	220 (20.6%)	73 (29.0%)	293 (30.2%)	
200–500 beds	307 (42.7%)	100 (39.7%)	407 (41.9%)	.37 [2]
>500 beds	192 (26.7%)	79 (31.4%)	271 (27.9%)	
Number of critical care beds in the hospital (n, %)				
<10 beds	164 (22.8%)	66 (26.2%)	230 (23.7%)	
10−20 beds	279 (38.8%)	77 (30.6%)	356 (36.7%)	.13 [2]
21–30 beds	126 (17.5%)	51 (20.2%)	177 (18.2%)	
>30 beds	150 (20.9%)	58 (23.0%)	208 (21.4%)	
Medical staff/patient ratio (n, %)				
1 every 4 patients	258 (46.4%)	80 (38.5%)	338 (44.2%)	
1 every 8 patients	236 (42.4%)	95 (45.7%)	331 (43.3%)	.07 [2]
1 every 12 patients	62 (11.2%)	33 (15.9%)	95 (12.4%)	
Nursing staff/patient ratio (n, %)				
1 every 1 patient	45 (6.3%)	13 (5.2%)	58 (6.0%)	
1 every 2 patients	473 (65.8%)	144 (57.1%)	617 (63.5%)	.02 [2]
1 every 3 patients	130 (18.1%)	55 (21.8%)	185 (19.1%)	
1 every 4 patients	71 (9.9%)	40 (15.9%)	111 (11.4%)	
Nursing staff specialized in critical care (n, %)	281 (39.1%)	99 (39.3%)	380 (39.1%)	>.99 [2]
With physiotherapist dedicated to critical patients (n, %)	382 (68.7%)	163 (78.4%)	545 (71.3%)	.009 [1]
Reference drugs in analgosedation and delirium available (n, %)	231 (32.1%)	78 (31.0%)	309 (31.8%)	.75 [2]
Music therapy available (n, %)	41 (7.4%)	14 (6.7%)	55 (7.2%)	.88 [2]
Occupational therapy available (n, %)	91 (16.4%)	47 (22.6%)	138 (18.1%)	.06 [2]
Clinical psychologist available (n, %)	238 (42.8%)	86 (41.4%)	324 (42.4%)	.74 [2]
Dedicated early mobilization team available (n, %)	204 (36.7%)	67 (32.2%)	271 (35.5%)	.27 [2]

IQR: interquartile range; SD: standard deviation.
[1] Student *t*-test.
[2] Fisher exact test.

Analgosedation practices before the COVID-19 pandemic

Participant's perceptions of pre-pandemic analgosedation practices are reported in eTable 1 of the Supplementary material.

Targeted analgosedation (*P* = .001), pain monitoring with the ESCID scale (*P* = .014), analgesia monitoring by the nursing staff (*P* = .008), the preference for mild versus deep sedation (*P* = .007), dynamic and sequential sedation (*P* = .02), sedation level monitoring (*P* = .02), the frequency of sedation monitoring (*P* = .03), and the use of continuous electroencephalography to measure sedation level (*P* = .006) before the pandemic were associated with less perceived oversedation after the pandemic.

Pharmacotherapy in analgosedation before the COVID-19 pandemic

The most widely used analgesic and sedative drugs before the pandemic are shown in eTable 2. Fentanyl was the most commonly used analgesic for moderate to severe pain (58%), followed by multimodal analgesia (18.4%). Prescription of
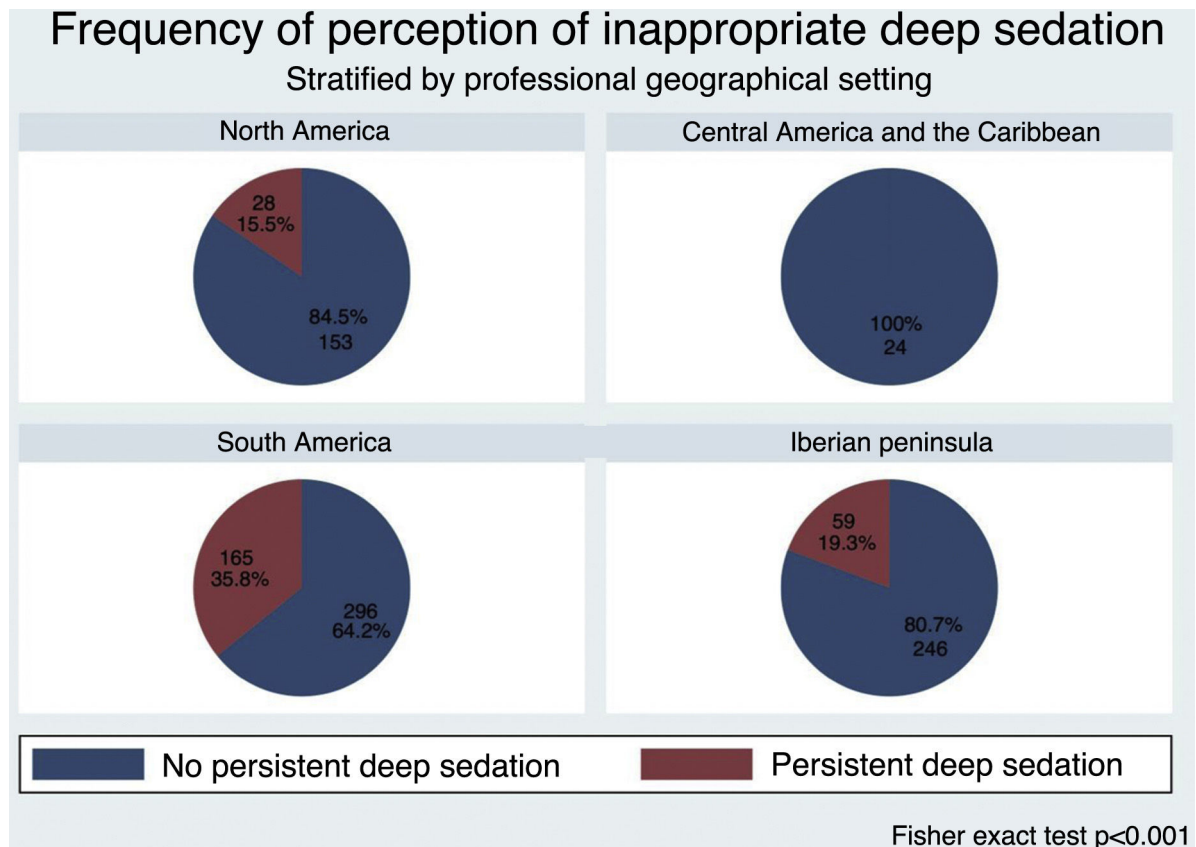
Figure 1 Frequency of perception of the participants referred to oversedation after the pandemic.

the latter before the pandemic was associated with a lower perception of persistent patient oversedation after the pandemic (P = .006).

The most commonly used drugs for superficial sedation were dexmedetomidine (39.8%), propofol (35.7%) and midazolam (22.6%), with an association being observed between the use of propofol and less perceived persistent oversedation after the pandemic (P = .007). In contrast, an association was observed between the use of midazolam and the perception of oversedation after the pandemic (P = .001).

The most commonly used drug for deep sedation before the pandemic was midazolam (59.9%), followed by propofol (37.2%).

General non-pharmacological and pharmacological delirium management before the pandemic

A total of 44% of the participants reported having delirium management protocols in place, and 75% reported actively assessing delirium before the pandemic, based on validated clinical scales (CAM-ICU and ICDSC) or the clinical impression. Of this 75%, a total of 74.1% used scales, implying that participants measured delirium using validated methods in 47.4% of the cases according to the perception of the participants (eTable3).

Over 70% of the participants reported using some of the measures in the ABCDEF bundle of recommendations for the prevention of delirium before the pandemic, with the associ-

ation observed between the use of several of these measures and other additional measures and the absence of persistent oversedation after the pandemic (eTable 3).

The drugs most commonly used for the prevention and treatment of delirium were dexmedetomidine (35.5%) and haloperidol (68.2%), respectively (eTable 4).

Changes in analgosedation and delirium management practices during the pandemic

Overall, 74.9% of the participants reported a change in analgosedation practices during the pandemic, and 69.9% reported that these changes persisted after the pandemic (Table 2). In turn, 60.1% felt that analgosedation and delirium management practices were worse during the pandemic than before the pandemic. The main reasons for these changes were reported to be work overload (71.9%) and the presence of staff without the necessary training or the necessary experience (70.8%). This latter aspect had a significant impact upon the perception of oversedation after the pandemic (P = .002) (eTable 5).

The most common changes during the pandemic were an increased use of inappropriate deep sedation and neuromuscular blockade (NMB) (76.5% and 73.8%, respectively), followed by an increased use of midazolam (65.8%) and less sequential or dynamic sedation (65.1%). Less monitoring of pain, sedation and delirium was also reported (41.2%, 35.3% and 40.2%, respectively). In addition, participants reported that more frequent use of midazolam and NMB continued

Table 2 Changes in analgosedation practices during and after the COVID-19 pandemic.

Characteristics	No persistent deep sedation (n = 719)	Persistent deep sedation (n = 252)	Total (n = 1008)	*P*-value
Changes in analgosedation and delirium management practices during pandemic (n, %)	518 (72.0%)	209 (82.9%)	727 (74.9%)	.001 [1]
Persistence of changes in analgosedation and delirium management practices after pandemic (n, %)	379 (65.5%)	181 (81.5%)	560 (69.9%)	<.001 [1]
More frequent use of inappropriate deep sedation during pandemic (n, %)	498 (69.4%)	244 (96.8%)	742 (76.5%)	<.001 [1]
More frequent use of inappropriate NMB during pandemic (n, %)	498 (69.3%)	219 (86.9%)	717 (73.8%)	<.001 [1]
Persistence of more frequent use of NMB after pandemic (n, %)	30 (5.1%)	136 (56.9%)	166 (20.0%)	<.001 [1]
Less frequent use of sequential or dynamic sedation during pandemic (n, %)	437 (60.9%)	195 (77.4%)	632 (65.1%)	<.001 [1]
Persistence of less frequent use of sequential or dynamic sedation after pandemic (n, %)	57 (10.5%)	141 (62.1%)	198 (25.7%)	<.001 [1]
More frequent use of midazolam during pandemic (n, %)	430 (60.2%)	205 (81.7%)	635 (65.8%)	<.001 [1]
Persistence of more frequent use of midazolam after pandemic (n, %)	91 (16.9%)	146 (64.0%)	237 (30.9%)	<.001 [1]
More frequent use of inhaled sedation during pandemic (n, %)	122 (17.1%)	44 (17.5%)	166 (17.2%)	.92 [1]
Persistence of more frequent use of inhaled sedation after pandemic (n, %)	88 (26.0%)	36 (25.2%)	124 (25.8%)	.91 [1]
Most common inhaled sedative (n, %)				
Isoflurane	74 (43.8%)	29 55.8%)	103 (46.6%)	.15
Sevoflurane	95 (56.2%)	23 (44.2%)	118 (53.4%)	[1]
Reduced monitoring of pain during pandemic (n, %)	255 (35.5%)	144 (57.6%)	399 (41.2%)	<.001 [1]
Reduced monitoring of sedation during pandemic (n, %)	211 (29.4%)	131 (52.4%)	342 (35.3%)	<.001 [1]
Reduced monitoring of delirium during pandemic (n, %)	245 (34.3%)	142 (57.0%)	387 (40.2%)	<.001 [1]

NMB: neuromuscular blockade.
[1] Fisher exact test.

after the pandemic (30.9% and 20%, respectively). All of these changes significantly increased the perception of persistent oversedation after the pandemic (Table 2).

With regard to delirium, 51% of the participants reported less use of delirium prevention measures (ABCDEF bundle and other recommendations) during the pandemic which was associated with the perception of persistent oversedation. In decreasing order of frequency, the defects in applying such measures were: fewer attempts to withdraw sedation (43.7%), failure to prioritize mild sedation (40.1%), no adjustment of ventilatory parameters to avoid asynchronies (38.9%), less monitoring of delirium (31.2%), failure to prioritize non-benzodiazepine drugs (29.5%), lack of adequate analgesia (29.5%) and failure to use reorientation measures (television, clocks, etc.) (25%). All these aspects were asso-

ciated with a greater perception of persistent oversedation after the pandemic (Table 3).

Changes in analgosedation and delirium management practices after the pandemic

Overall, 25.9% of the participants felt that the patients were sedated more than necessary after the pandemic (95%CI 22.4%–27.8%) and 12.8% were of the opinion that the analgosedation and delirium management practices were poorer than before the pandemic – this being related to the perception of oversedation (*P* < .001). Both the persistence of the habits acquired during the pandemic and the presence of untrained staff were significantly correlated with the

Table 3 Changes in the management of delirium during the pandemic.

Characteristics	No persistent deep sedation (n = 719)	Persistent deep sedation (n = 252)	Total (n = 1008)	P-value
Reduced application of measures for the prevention of delirium (n, %)	333 (46.4%)	159 (64.4%)	492 (51.0%)	<.001 [1]
ABCDEF bundle				
Reduced guaranteeing of adequate analgesia (n, %)	184 (26.9%)	89 (36.9%)	273 (29.5%)	.004 [1]
Reduced sedation withdrawal attempts, spontaneous breathing tests and/or mild sedation protocols (n, %)	283 (41.4%)	121 (50.2%)	404 (43.7%)	.02 [1]
Reduced prioritization of mild sedation (n, %)	261 (38.2%)	110 (45.6%)	371 (40.1%)	.047 [1]
Reduced selection of non-benzodiazepines (n, %)	189 (27.6%)	84 (34.8%)	273 (29.5%)	.04 [1]
Reduced sequential and dynamic sedation (n, %)	162 (23.7%)	63 (26.1%)	225 (24.3%)	.49 [1]
Reduced monitoring of delirium (n, %)	196 (28.6%)	93 (38.6%)	289 (31.2%)	.005 [1]
Reduced early mobilization and rehabilitation (n, %)	264 (38.6%)	96 (39.8%)	360 (38.9%)	.76 [1]
Reduced family participation (n, %)	348 (50.9%)	110 (45.6%)	458 (49.5%)	.18 [1]
Measures beyond the ABCDEF bundle				
Less adjustment of ventilatory parameters for minimization of asynchronies (n, %)	248 (36.4%)	110 (46.0%)	358 (38.9%)	.01 [1]
Reduced early mobilization and rehabilitation (n, %)	293 (43.0%)	99 (41.4%)	392 (42.6%)	.70 [1]
Reduced withdrawal of unnecessary devices (n, %)	225 (33.0%)	94 (39.3%)	319 (34.7%)	.08 [1]
No avoidance of use of mechanical restraints (n, %)	188 (27.6%)	62 (25.9%)	250 (27.2%)	.67 [1]
Less facilitation of patient-family-healthcare staff communication (n, %)	283 (41.6%)	94 (39.3%)	377 (41.0%)	.59 [1]
Less participation of the family and flexibility of visiting hours (n, %)	271 (39.8%)	94 (39.3%)	365 (39.7%)	.94 [1]
Less avoidance of sensory barriers (n, %)	151 (22.2%)	46 (19.2%)	197 (21.1%)	.36 [1]
Less use of reorientation measures (n, %)	185 (27.2%)	45 (18.8%)	230 (25.0%)	.01 [1]
Less preservation of sleep-waking cycle (n, %)	193 (28.3%)	61 (25.5%)	254 (27.6%)	.45 [1]
Less use of early psychological interventions and neurocognitive stimulation (n, %)	133 (19.5%)	49 (20.5%)	182 (19.8%)	.78 [1]

[1] Fisher exact test.

perception of oversedation after the pandemic (*P* < .001) (eTable 6).

Multivariate analysis

When all of the above elements were entered into a multivariate logistic regression analysis, 7 variables retained a statistically significant association with the perception of oversedation after the pandemic. The most significant risk factor identified was the persistence of habits acquired during the pandemic, with an adjusted odds ratio (aOR) of 3.16 (95%CI 2.24–4.45, *P* < .001). Other factors were lack of staff training or experience (aOR 1.70, 95%CI 1.16–2.50, *P* = .007) and the use of midazolam for superficial sedation before the pandemic (aOR 1.47, 95%CI 1.03–2.11, *P* = .035) (Table 4).

Likewise, several factors were found to reduce the probability of perceived oversedation after the COVID-19 pandemic. These were the monitoring of delirium by medical staff before the pandemic (aOR 0.70, 95%CI 0.50−0.98,

Table 4 Multiple logistic regression analysis: factors associated with the persistence of oversedation after the COVID-19 pandemic (pseudo R^2 = 8.3%).

Variable	aOR	95%CI	P-value
Persistence of habits acquired during pandemic	3.16	2.24–4.45	<.001
Staff lacking training or experience	1.70	1.16–2.50	.007
Use of midazolam for superficial sedation before pandemic	1.47	1.03–2.11	.035
Medical staff monitoring appearance of delirium before pandemic	0.70	0.50–0.98	.038
Nursing staff monitoring analgosedation before pandemic	0.69	0.49–0.98	.038
Guaranteeing of sleep-waking cycle	0.68	0.49–0.96	.027
Use of targeted analgosedation before pandemic	0.66	0.45–0.98	.039
Constant (α)	0.40	0.24–0.67	<.001

aOR: adjusted odds ratio; CI: confidence interval.
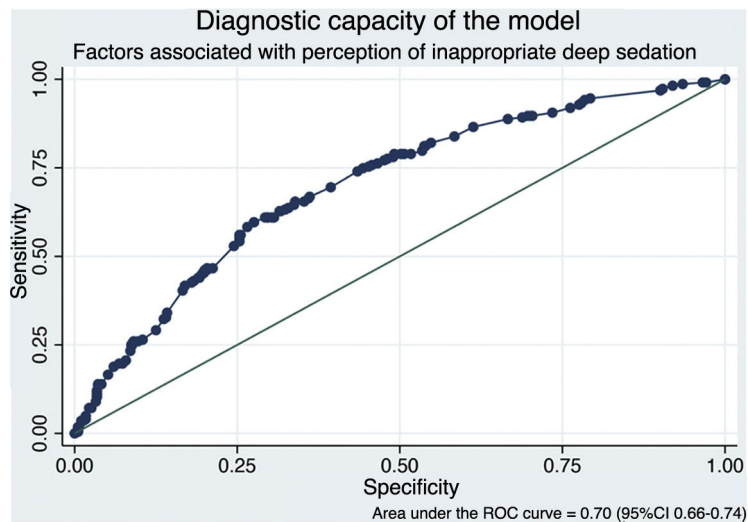
Figure 2 Receiver operating characteristic curve of the multivariate model.

P = .038); analgosedation monitoring by nursing staff before the pandemic (aOR 0.69, 95%CI 0.49−0.98, P = .038); ensuring the sleep-wake cycle before the pandemic (aOR 0.68, 95%CI 0.45−0.96, P = .027); and using a targeted analgosedation strategy before the pandemic (aOR 0.66, 95%CI 0.45−0.98, P = .039).

The full model had an area under the receiver operating characteristic (ROC) curve of 0.70 (95%CI 0.66−0.74), and showed adequate goodness of fit (Hosmer-Lemeshow P = .59). The full model is shown in Table 4, and the ROC curve is shown in Fig. 2.

Discussion

The COVID-19 pandemic led to the widespread use of deep sedation strategies in patients with acute respiratory failure requiring MV due to viral pneumonia and acute respiratory distress syndrome (ARDS).[28] This practice continued after the pandemic, although 25.9% of respondents considered that the patients were sedated more than necessary during this period. Other studies have reported similar findings. The main risk factor for post-pandemic oversedation, with an OR of 3.1, was found to be the continuation of the deep seda-

tion habits acquired during the pandemic, replacing previous strategies such as the ABCDEF bundle.

The literature highlights the dangers of oversedation, especially when used early, and continuing into the post-pandemic period.[29–31] Stephens et al. found early deep sedation in patients undergoing MV for COVID-19 with high benzodiazepine use was associated with increased mortality (aOR 3.44, 95%CI 1.65–7.17, P < .01).[26] These authors reported that approximately 70% of the COVID-19 patients undergoing MV received early deep sedation, which was associated with poorer outcomes including fewer ventilator-free days, longer hospital stay and increased mortality.

Additional factors described in other studies, such as the type of hospital (public or private), the number of hospital and ICU beds, or centers with university teaching and critical care training activities, were analyzed but not found to be associated with post-pandemic oversedation in the present study.[32–35] In contrast, the nurse-to-patient ratio and the presence of physiotherapists showed a significant association with oversedation, highlighting the importance of ensuring an adequate ratio of health care staff per patient, as reported in previous studies.[36]

An important and novel observation in our study was the important variability in perceived oversedation among the different geographic regions involved (P < .001). In this

regard, 35% of the participants in South America considered that patients were oversedated after the pandemic, compared to 19% in Europe and 15% in North America. These data, which are the first to describe these geographic differences, may reflect a lack of appropriate sedation protocols that prioritize mild sedation, inadequate implementation of the protocols, a lack of adequate monitoring, reduced availability of sedative drugs, and a lack of trained personnel.[1]

From the pharmacological perspective, global shortages and the need to use the available drugs led to overuse of benzodiazepines and opioids, especially midazolam (19% versus 32%, $P = .001$), which in turn was associated with post-pandemic oversedation. Oversedation with hypnotic benzodiazepines during the pandemic had a negative impact on patient prognosis, particularly in terms of length of stay and mortality after adjustment for the SOFA score.[33–35] The use of benzodiazepines in critically ill patients undergoing MV has been associated with adverse events such as delayed awakening and extubation, prolonged ICU and hospital stay, increased delirium, cognitive impairment and post-ICU syndrome.[37–39] Current recommendations emphasize the importance of prioritizing non-benzodiazepine drugs.[29,40–44]

Another important finding in our study was the association between analgosedation monitoring before the pandemic and the perception of oversedation after the pandemic, which again emphasizes the importance of monitoring in order to ensure adequate management of analgosedation. Analgesia onitoring by the nursing staff ($P = .008$), the monitoring of the sedation level ($P = .02$) and its frequency ($P = .03$), as well as the use of continuous electroencephalography ($P = .006$) before the pandemic were associated with less oversedation after the pandemic.

These data are consistent with current scientific evidence, which suggests that frequent monitoring of pain and sedation levels using validated scales on a frequent basis is considered to be essential in order to avoid oversedation and adverse events.[16] More recently, an expert consensus has recognized the utility of continuous electroencephalography to guide sedation in adult critically ill patients and recommends its use in all patients undergoing deep sedation (whether or not they are undergoing NMB), when clinical assessment is not possible.[45]

Another important factor in preventing oversedation and adverse events is adherence to the ABCDEF bundle.[46] In our study, adherence to the analgosedation protocol before the pandemic was 60%, rising to 80% for targeted analgosedation and to 90% for mild sedation protocols. These figures indicate a high degree of adherence compared with other studies.[47–49] These practices in turn were significantly correlated with lower perceptions of oversedation after the pandemic.[50–52]

Adherence to the ABCDEF bundle varied across geographical settings. In this regard, the literature describes considerable heterogeneity in different studies, generally reporting poor adherence, with many barriers and facilitating factors.[52–54] The pandemic exacerbated the challenges, with work overload and a lack of qualified staff being the main barriers.[20] In 2019, Carboni Bisso et al. conducted a study to determine the scope and application of these measures in Argentina. The authors found that despite awareness of the bundle of measures, adherence to them was irregular.[55] The same group developed a similar ques-

tionnaire during the pandemic and found that the conditions of lockdown and work overload were critical in explaining the limitations in applying the ABCDEF bundle. These observations are consistent with our findings, which point to the important workload of the healthcare staff involved, the lack of experience in caring for critical patients, the fear of the isolation measures to avoid infection among the staff, and safety concerns such as self-extubation or orotracheal tube migration.[20] In the SAMDS-ICU study, Luz et al. evaluated the use of the bundle of measures before and during the COVID-19 pandemic, and found that many of the practices were not maintained during the pandemic. The main challenges to adherence to the measures were found to be work overload among the health care staff and a reduced presence critical care trained specialists.[21]

Lastly, the scarce use of validated scales to monitor delirium during the pandemic, and the decrease in preventive measures were associated with greater oversedation after versus before the pandemic (64.4% versus 46.4%, $P < .001$). Due to the high percentage of delirium diagnosed in COVID-19, with a 50%–60% incidence of hyperactive delirium in some series, we face an important increase in delirium associated with these inadequate sedation practices.[13,56] Recently Owen et al., in over 44,000 patients admitted to the ICU in Canada, reported that the adoption of the ABCDEF bundle reduced the incidence of delirium (two-month decrease of 0.34%, 95%CI 0.18−0.50, $P < .01$) from 33.48% (95%CI 29.64–37.31) in 2017 to 28.74% (95%CI 25.22–32.26) in 2019.[57] In our study, the main barriers facing prevention were a lack of family involvement in the care of the patient in the ICU, difficulties in monitoring analgosedation, and the increased benzodiazepine use, as already described in other studies.[58,59]

Our study has a number of limitations and strengths. Limitations include the subjectivity of the survey and the heterogeneity of analgosedation management in the different geographical settings. Also, we did not consider the professional hierarchy of the survey participants, which may have influenced the perception of medication use. On the other hand, although a considerable sample size was recruited, some of the participating countries showed a lower response rate, which limits the representativeness of our results.

With regard to the strengths of the study, we were able to secure the participation of many of the FEPIMCTI member countries, with local specialists caring for many patients with analgosedation before, during and after the pandemic. This provided relevant information on the factors influencing the changes in analgosedation practices in our setting.

We believe that knowledge of analgosedation and delirium management practices at the regional level is important for the development of local analgosedation and delirium expert committees or workgroups to discuss or endorse strategies for implementing the ABCDEF toolkit and promoting Zero Sedation.

Conclusions

Before the COVID-19 pandemic, the management of analgosedation was characterized by the predominant use of targeted protocols that favored priority on mild and dynamic

sedation in critically ill patients. During the pandemic the percentage of ICU patients receiving deep sedation increased. According to the physicians surveyed, this tendency to use deep sedation continued after the pandemic and was not always justified. The present study found that staff with little to no critical care training or experience, less monitoring of analgosedation, less nursing presence in the ICU, and habits acquired during the pandemic (especially the regular use of benzodiazepines and oversedation) were the main reasons for this perception of the post-pandemic situation. We need to resume socialization and retraining efforts in protocols and bundles of measures for safe patient sedation, and to reduce oversedation in the ICU.

Ethical responsibilities

The present study was evaluated and approved by the *Red Municipal de Bioética Clínica y Social* of the city of Córdoba (Argentina), and abides with the National Law on Personal Data Protection 25.326 (Republic of Argentina) for safeguarding the identity and data of the participants, and guaranteeing full anonymity and confidentiality of the information. Informed consent was obtained from all the participants after receiving an explanation of the aims of the study and the time required to complete it.

RESEARCH CARRIED OUT WITH THE SUPPORT OF: Comité de Analgesia, Sedación y Delirium de la Federación Panamericana e Ibérica de Cuidados Críticos y Terapia Intensiva (FEPIMCTI); URL: https://fepimcti.org/comite-de-expertos/sedacion-y-analgesia/).

Financial support

The present study has received no partial or total funding, or any type of grant or financial support.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.medine.2025.502123.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

References

1. Rasulo FA, Badenes R, Longhitano Y, Racca F, Zanza C, Marchesi M, et al. Excessive sedation as a risk factor for delirium: a comparison between two cohorts of ARDS critically ill patients with and without COVID-19. Life. 2022;12:2031, http://dx.doi.org/10.3390/LIFE12122031.
2. Caballero J, García-Sánchez M, Palencia-Herrejón E, Muñoz-Martínez T, Gómez-García JM, Ceniceros-Rozalén I, et al. Sobresedación Zero como herramienta de confort, seguridad y gestión en la unidades de cuidados intensivos. Med Intensiva. 2020;44:239–47, http://dx.doi.org/10.1016/j.medin.2019.09.010.
3. Vincent JL, Shehabi Y, Walsh TS, Pandharipande PP, Ball JA, Spronk P, et al. Comfort and patient-centred care without excessive sedation: the eCASH concept. Intensive Care Med. 2016;42:962–71, http://dx.doi.org/10.1007/s00134-016-4297-4.
4. Wang CT, Mao Y, Zhao L, Ma B. The impact of analgosedation on mortality and delirium in critically ill patients: a systematic review and meta-analysis. Intensive Crit Care Nurs. 2019;54:7–14, http://dx.doi.org/10.1016/j.iccn.2019.06.004.
5. Hyun DG, Ahn JH, Gil HY, Nam CM, Yun C, Lim CM. Longitudinal trajectories of sedation level and clinical outcomes in patients who are mechanically ventilated based on a group-based trajectory model: a prospective, multicentre, longitudinal and observational study in Korea. BMJ Open. 2023;13:e072628, http://dx.doi.org/10.1136/bmjopen-2023-072628.
6. Mehta S, Burry L, Cook D, Fergusson D, Steinberg M, Granton J, et al. Daily sedation interruption in mechanically ventilated critically ill patients cared for with a sedation protocol: a randomized controlled trial. JAMA. 2012;308:1985–92, http://dx.doi.org/10.1001/JAMA.2012.13872.
7. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med. 2000;342:1471–7 http://www.ncbi.nlm.nih.gov/pubmed/10816184
8. Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G. The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest. 1998;114:541–8, http://dx.doi.org/10.1378/CHEST.114.2.541.
9. Chamorro-Jambrina C, Chamorro-Falero C. Don't turn-off the brain. Med Intensiva. 2019;43:1–2, http://dx.doi.org/10.1016/j.medin.2018.07.011.
10. Patel SB, Poston JT, Pohlman A, Hall JB, Kress JP. Rapidly reversible, sedation-related delirium versus persistent delirium in the intensive care unit. Am J Respir Crit Care Med. 2014;189:658–65, http://dx.doi.org/10.1164/rccm.201310-1815OC.
11. Stollings JL, Kotfis K, Chanques G, Pun BT, Pandharipande PP, Ely EW. Delirium in critical illness: clinical manifestations, outcomes, and management. Intensive Care Med. 2021;47:1089–103, http://dx.doi.org/10.1007/s00134-021-06503-1.
12. Krewulak KD, Stelfox HT, Leigh JP, Ely EW, Fiest KM. Incidence and prevalence of delirium subtypes in an adult ICU. Crit Care Med. 2018;46:2029–35, http://dx.doi.org/10.1097/CCM.0000000000003402.
13. Pun BT, Badenes R, Heras La Calle G, Orun OM, Chen W, Raman R, et al. Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study. Lancet Respir Med. 2021;9:239–50, http://dx.doi.org/10.1016/S2213-2600(20)30552-X.
14. Girard TD, Jackson JC, Pandharipande PP, Pun BT, Thompson JL, Shintani AK, et al. Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. Crit Care Med. 2010;38:1513–20, http://dx.doi.org/10.1097/CCM.0b013e3181e47be1.
15. Bolesta S, Burry L, Perreault MM, Gélinas C, Smith KE, Eadie R, et al. International analgesia and sedation weaning and withdrawal practices in critically ill adults: the adult iatrogenic withdrawal study in the ICU. Crit Care Med. 2023;51:1502–14, http://dx.doi.org/10.1097/CCM.0000000000005951.
16. Devlin JW, Skrobik Y, Gélinas C, Needham DM, Slooter AJC, Pandharipande PP, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 2018;46:E825–73, http://dx.doi.org/10.1097/CCM.0000000000003299.
17. Celis-Rodríguez E, Birchenall C, Birchenall C, de la Cal MA, Carrillo R, Castorena G, et al. Guía de práctica clínica basada en la evidencia para el manejo de la sedoanalgesia en el paciente

adulto críticamente enfermo. Med Intensiva. 2013;37:519–74, http://dx.doi.org/10.1016/j.medin.2013.04.001.

18. Marra A, Ely EW, Pandharipande PP, Patel MB. The ABCDEF bundle in critical care. Crit Care Clin. 2017;33:225, http://dx.doi.org/10.1016/J.CCC.2016.12.005.

19. Pun BT, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, et al. Caring for critically ill patients with the ABCDEF bundle: results of the ICU liberation collaborative in over 15,000 adults. Crit Care Med. 2019;47:3–14, http://dx.doi.org/10.1097/CCM.0000000000003482.

20. Carboni Bisso I, Ávila Poletti D, Huespe I, Villalba D, Olmos D, Carini F. Adherencia al paquete de medidas ABCDEF durante la pandemia de COVID-19. Acta Colomb Cuid Intensivo. 2021;22:S55–61, http://dx.doi.org/10.1016/J.ACCI.2021.09.002.

21. Luz M, Brandão Barreto B, de Castro REV, Salluh J, Dal-Pizzol F, Araujo C, et al. Practices in sedation, analgesia, mobilization, delirium, and sleep deprivation in adult intensive care units (SAMDS-ICU): an international survey before and during the COVID-19 pandemic. Ann Intensive Care. 2022;12:9, http://dx.doi.org/10.1186/S13613-022-00985-Y.

22. Liu K, Nakamura K, Katsukawa H, Nydahl P, Ely EW, Kudchadkar SR, et al. Implementation of the ABCDEF bundle for critically ill ICU patients during the COVID-19 pandemic: a multi-national 1-day point prevalence study. Front Med (Lausanne). 2021;8:735860, http://dx.doi.org/10.3389/FMED.2021.735860/BIBTEX.

23. Negro A, Bambi S, De Vecchi M, Isotti P, Villa G, Miconi L, et al. The ABCDE bundle implementation in an intensive care unit: facilitators and barriers perceived by nurses and doctors. Int J Nurs Pract. 2022;28:e12984, http://dx.doi.org/10.1111/IJN.12984.

24. Frade-Mera MJ, Arias-Rivera S, Zaragoza-García I, Martí JD, Gallart E, San José-Arribas A, et al. The impact of ABCDE bundle implementation on patient outcomes: a nationwide cohort study. Nurs Crit Care. 2022;27:772–83.-L, http://dx.doi.org/10.1111/NICC.12740.

25. Giménez-Esparza Vich C, Alcántara Carmona S, García Sánchez M. Delirium in COVID-19. Practical aspects of a frequent association. Med Intensiva (Engl Ed). 2022;46:336–40, http://dx.doi.org/10.1016/j.medine.2022.04.007.

26. Stephens RJ, Evans EM, Pajor MJ, Pappal RD, Egan HM, Wei M, et al. A dual-center cohort study on the association between early deep sedation and clinical outcomes in mechanically ventilated patients during the COVID-19 pandemic: the COVID-SED study. Crit Care. 2022;26:179, http://dx.doi.org/10.21203/RS.3.RS-1389892/V1.

27. Braun A, Garner O, Staggers K, Velamuri K. Effects of the covid-19 pandemic on sedation practices and abcdef bundle compliance: a national survey of intensivists in the united states. Chest. 2022;161:A201, http://dx.doi.org/10.1016/J.CHEST.2021.12.233.

28. Wongtangman K, Santer P, Wachtendorf LJ, Azimaraghi O, Baedorf Kassis E, Teja B, et al. Association of sedation, coma, and in-hospital mortality in mechanically ventilated patients with coronavirus disease 2019-related acute respiratory distress syndrome: a retrospective cohort study. Crit Care Med. 2021;49:1524–34, http://dx.doi.org/10.1097/CCM.0000000000005053.

29. Shehabi Y, Bellomo R, Reade MC, Bailey M, Bass F, Howe B, et al. Early intensive care sedation predicts long-term mortality in ventilated critically ill patients. Am J Respir Crit Care Med. 2012;186:724–31, http://dx.doi.org/10.1164/rccm.201203-0522OC.

30. Shehabi Y, Chan L, Kadiman S, Alias A, Ismail WN, Tan MA, et al. Sedation depth and long-term mortality in mechanically ventilated critically ill adults: a prospective longitudinal

31. Pappal RD, Roberts BW, Mohr NM, Ablordeppey E, Wessman BT, Drewry AM, et al. The ED-AWARENESS Study: a prospective, observational cohort study of awareness with paralysis in mechanically ventilated patients admitted from the emergency department. Ann Emerg Med. 2021;77:532–44, http://dx.doi.org/10.1016/j.annemergmed.2020.10.012.

32. Kotfis K, Zegan-Barańska M, Żukowski M, Kusza K, Kaczmarczyk M, Ely EW. Multicenter assessment of sedation and delirium practices in the intensive care units in Poland - is this common practice in Eastern Europe? BMC Anesthesiol. 2017;17:120, http://dx.doi.org/10.1186/s12871-017-0415-2.

33. Dantas dos Santos K, da Costa Martins I, Alves Ferreira Gonçalves F. Characterization of the sedation and analgesia in intensive care unit: an observational study. Online Braz J Nurs. 2016;15:157–66 https://www.redalyc.org/articulo.oa?id=361453979006

34. Temesgen N, Chekol B, Tamirie T, Eshetie D, Simeneh N, Feleke A. Adult sedation and analgesia in a resource limited intensive care unit – a systematic review and evidence based guideline. Ann Med Surg. 2021;66:102356, http://dx.doi.org/10.1016/j.amsu.2021.102356.

35. Wood-Thompson DK, Enyuma COA, Laher AE. Procedural sedation and analgesia practices in the emergency centre. Afr J Emerg Med. 2019;9:8–13, http://dx.doi.org/10.1016/j.afjem.2018.09.003.

36. Tsuyada H, Inoue S, Tsujimoto T, Ogawa T, Inada M, Kawaguchi M. Impact of nursing experience on cancellation of light sedation for mechanically ventilated patients in a setting of 1 : 2 nurse-patient ratio. Anaesthesiol Intensive Ther. 2019;51:210–7, http://dx.doi.org/10.5114/AIT.2019.87359.

37. Alcántara Carmona S, Chamorro-Jambrina C. Current role of midazolam in sedation of the ventilated critically ill patient: in favour. Med Intensiva. 2024;48:174–6, http://dx.doi.org/10.1016/j.medine.2023.12.003.

38. Caballero J, García-Sánchez M, Giménez-Esparza Vich C. Current role of midazolam in the sedation of the ventilated critically ill patient: against. Med Intensiva. 2024;48:177–9, http://dx.doi.org/10.1016/j.medine.2023.10.015.

39. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA. 2009;301:489–99, http://dx.doi.org/10.1001/jama.2009.56.

40. Celis-Rodríguez E, Díaz Cortés JC, Cárdenas Bolívar YR, Castorena Arellano G, Hernández A, Ceraso D, et al. Evidence-based clinical practice guidelines for the management of sedoanalgesia and delirium in critically ill adult patients. Med Intensiva. 2020;44:171–84, http://dx.doi.org/10.1016/j.medin.2019.07.013.

41. Fraser GL, Devlin JW, Worby CP, Alhazzani W, Barr J, Dasta JF, et al. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials. Crit Care Med. 2013;41 9 Suppl 1:S30–38, http://dx.doi.org/10.1097/CCM.0b013e3182a16898.

42. Rengel KF, Hayhurst CJ, Pandharipande PP, Hughes CG. Long-term cognitive and functional impairments after critical illness. Anesth Analg. 2019;128:772–80, http://dx.doi.org/10.1213/ANE.0000000000004066.

43. Lee H, Choi S, Jang EJ, Lee J, Kim D, Yoo S, et al. Effect of sedatives on in-hospital and long-term mortality of critically ill patients requiring extended mechanical ventilation for ≥ 48 hours. J Korean Med Sci. 2021;36:1–11, http://dx.doi.org/10.3346/JKMS.2021.36.E221.

44. Nanwani-Nanwani K, López-Pérez L, Giménez-Esparza C, Ruiz-Barranco I, Carrillo E, Arellano MS, et al. Preva-

lence of post-intensive care syndrome in mechanically ventilated patients with COVID-19. Sci Rep. 2022;12:7977, http://dx.doi.org/10.1038/s41598-022-11929-8.

45. Rasulo FA, Hopkins P, Lobo FA, Pandin P, Matta B, Carozzi C, et al. Processed electroencephalogram-based monitoring to guide sedation in critically ill adult patients: recommendations from an international expert panel-based consensus. Neurocrit Care. 2023;38:296, http://dx.doi.org/10.1007/S12028-022-01565-5.

46. Desantis M, Lichtenstern C, Hagenlocher JP, Bruckner T, Weigand MA, Kalenka A, et al. Implementation of a spontaneous awakening/spontaneous breathing trial protocol in a surgical intensive care unit: a before and after study. Minerva Anestesiol. 2023;89:306–15.-L, http://dx.doi.org/10.23736/S0375-9393.22.16806-9.

47. DeMellow JM, Kim TY, Romano PS, Drake C, Balas MC. Factors associated with ABCDE bundle adherence in critically ill adults requiring mechanical ventilation: an observational design. Intensive Crit Care Nurs. 2020;60:102873, http://dx.doi.org/10.1016/J.ICCN.2020.102873.

48. Boehm LM, Vasilevskis EE, Dietrich MS, Wells N, Ely EW, Pandharipande P, et al. Organizational domains and variation in attitudes of intensive care providers toward the ABCDE bundle. Am J Crit Care. 2017;26:e18–28, http://dx.doi.org/10.4037/AJCC2017297.

49. Boehm LM, Dietrich MS, Vasilevskis EE, Wells N, Pandharipande P, Ely EW, et al. Perceptions of workload burden and adherence to ABCDE bundle among intensive care providers. Am J Crit Care. 2017;26:e38–47, http://dx.doi.org/10.4037/ajcc2017544.

50. García-Sánchez M, Caballero-López J, Ceniceros-Rozalén I, Giménez-Esparza Vich C, Romera-Ortega MA, Pardo-Rey C, et al. Prácticas de analgosedación y delirium en Unidades de Cuidados Intensivos españolas: Encuesta 2013-2014. Med Intensiva. 2019;43:225–33, http://dx.doi.org/10.1016/j.medin.2018.12.003.

51. Veiga VC, Rojas SSO. Analgosedation and delirium in intensive care units in Brazil: current status. ASDUTI study. Rev Bras Ter Intensiva. 2018;30, http://dx.doi.org/10.5935/0103-507X.20180025.

52. Rojas V, Romero C, Tobar D, Alvarez E, Aranda R, Bugedo G, et al. Analgesia, sedation, neuromuscular blockade and delirium management practices in Chilean intensive care units. Rev Med Chil. 2021;149:864–72, http://dx.doi.org/10.4067/s0034-98872021000600864.

53. Nin Vaeza N. Prácticas de analgosedación y delirium en las UCI españolas. Med Intensiva. 2019;43:195–6, http://dx.doi.org/10.1016/j.medin.2019.01.002.

54. Morandi A, Piva S, Ely EW, Myatra SN, Salluh JIF, Amare D, et al. Worldwide survey of the «Assessing pain, Both spontaneous awakening and breathing trials, choice of drugs, delirium monitoring/management, early exercise/mobility, and family empowerment» (ABCDEF) bundle. Crit Care Med. 2017;45:e1111–22, http://dx.doi.org/10.1097/CCM.0000000000002640.

55. Carboni Bisso I, Carini F, Huespe I, Terraza S, Giannasi S, San Román EI. Encuesta argentina sobre el conocimiento y la aplicación del paquete de medidas abcdef. Rev Arg Med. 2019;7:84–9.

56. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. N Engl J Med. 2020;382:2268–70, http://dx.doi.org/10.1056/NEJMC2008597.

57. Owen VS, Sinnadurai S, Morrissey J, Colaco H, Wickson P, Dyjur D, et al. Multicentre implementation of a quality improvement initiative to reduce delirium in adult intensive care units: an interrupted time series analysis. J Crit Care. 2024;81:154524, http://dx.doi.org/10.1016/j.jcrc.2024.154524.

58. LaHue SC, James TC, Newman JC, Esmaili AM, Ormseth CH, Ely EW. Collaborative delirium prevention in the age of COVID-19. J Am Geriatr Soc. 2020;68:947–9, http://dx.doi.org/10.1111/jgs.16480.

59. Kotfis K, Williams Roberson S, Wilson JE, Dabrowski W, Pun BT, Ely EW. COVID-19: ICU delirium management during SARS-CoV-2 pandemic. Crit Care. 2020;24:176, http://dx.doi.org/10.1186/s13054-020-02882-x.