

Current Practices in Sedation and Analgesia for Mechanically Ventilated Critically Ill Patients

A Prospective Multicenter Patient-based Study

Jean-Francois Payen, M.D., Ph.D.,* Gérald Chanques, M.D.,† Jean Mantz, M.D., Ph.D.,‡ Christiane Hercule, M.D.,§ Igor Auriant, M.D.,|| Jean-Luc Leguillou, M.D.,# Michèle Binhas, M.D.,** Céline Genty, B.Sc.,†† Carole Rolland, B.Sc.,‡‡ Jean-Luc Bosson, M.D., Ph.D.§§ for the DOLOREA Investigators|||

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Background: The authors conducted a patient-based survey of practices to fully describe the assessment and the management of pain and sedation of a large cohort of mechanically ventilated patients during their first week of intensive care unit (ICU) stay.

Methods: A total of 1,381 adult patients were included in a prospective, observational study in 44 ICUs in France. Pain and sedation assessment, analgesic and sedative use, and analgesic management during procedural pain were collected on days 2, 4, and 6 of the ICU stay.

Results: The observed rates of assessment on day 2 for sedation (43%) and analgesia (42%) were significantly smaller than that of use of sedatives (72%) and opioids (90%), also noted on days 4 and 6. The use of protocols/guidelines for sedation/analgesia in the ICU reduced the proportion of patients who were treated, although not evaluated. A large proportion of assessed patients were in a deep state of sedation (40–50%). Minor changes in the dosages of the main prescribed agents for sedation (midazolam, propofol) and analgesia (sufentanil, fentanyl, morphine, remifentanyl) were found across 6 days of the patient's ICU stay. Procedural pain was specifically managed for less than 25% of patients; during those procedures, the propor-

tion of patients with pain significantly increased from the baseline pain evaluation.

Conclusions: Excessively deep states of sedation and a lack of analgesia during painful procedures must be prevented. To facilitate systematic pain and sedation assessment and to adjust daily drug dosages accordingly, it seems crucial to promote educational programs and elaboration of protocols/guidelines in the ICU.

MOST patients admitted to an intensive care unit (ICU) for mechanical ventilation receive sedative and analgesic medications. They are integral parts of the complex management of these patients, to minimize patient discomfort and reduce the risk of agitation and accidental self-extubation. However, these medications can promote adverse consequences, including prolonged mechanical ventilation and ICU duration of stay.¹⁻³ To optimize the use of these medications, several review articles and guidelines have detailed their management for ICU patients.⁴⁻¹¹ Implementation of protocols regarding ICU sedation and analgesia led to benefits such as fewer ventilator days.¹²⁻¹⁵ Although research studies about pain and sedation in ICU have flourished, little is known about current practices. Questionnaires reported physicians' or nurses' preferences in the use of scoring systems for assessing pain and sedation and of sedative and analgesic drugs.¹⁶⁻²⁰ Such an approach may fail in reflecting what is really done at the patient's bedside, as recently pointed out.²¹ In addition, the rate of stated use of instruments for assessing sedation can range between 8% and 49% in Germany,^{17,18} and between 16% and 61% in Denmark.^{16,17}

Because there may be a substantial gap between the conception of guidelines, physicians' statements, and clinical practice, there is a need to document what is done daily in ICUs, to include those findings in further national guidelines.²² Current practices of pain and sedation in the ICU are limited to the use of medications.²³⁻²⁶ Although ICU patients are necessarily exposed to many procedures, the practice of analgesic management during procedural pain has been addressed in only one large study.²⁷ There are no data on the true rates of pain and sedation assessments in ICUs. Hence, there is a need to fully describe the practice of sedation and analgesia in the ICU to determine the impact of these guidelines on physicians' practice patterns. We conducted a large observational study of sedation and analgesia practices in several ICUs in France. Patient-

* Professor, Department of Anesthesiology and Critical Care, Albert Michallon Hospital, Grenoble, France. † Assistant Professor, Department of Anesthesiology and Critical Care, Saint-Eloi Hospital, Montpellier, France. ‡ Professor, Department of Anesthesiology and Critical Care, Beaujon Hospital, Clichy, France. § Assistant Professor, Department of Anesthesiology and Critical Care, Louis-Pradel Hospital, Lyon, France. || Assistant Professor, Department of Anesthesiology and Critical Care, Charles-Nicole Hospital, Rouen, France. # Assistant Professor, Department of Anesthesiology and Critical Care, Montsouris Hospital, Paris, France. ** Assistant Professor, Department of Anesthesiology and Critical Care, Henri Mondor Hospital, Créteil, France. †† Research Associate, ‡‡ Research Associate, Clinical Research Center INSERM 003, Albert Michallon Hospital, Grenoble, France. §§ Professor, Department of Biostatistics, Albert Michallon Hospital, and TIMC-IMAG, UMR 5525, Joseph Fourier University, Grenoble, France. ||| See appendix.

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Address correspondence to Dr. Payen: Département d'Anesthésie-Réanimation, Hôpital Albert Michallon, BP 217, 38043 Grenoble, France. jfpayen@ujf-grenoble.fr. Individual article reprints may be accessed at no charge through the Journal Web site, www.anesthesiology.org.

based data were repeatedly collected over 6 days of the patient's ICU stay. The purpose of this study was (1) to describe the assessment of pain and sedation during the first week of ICU stay, (2) to describe the management of painful procedures, and (3) to address whether daily drug dosages were adjusted according to patient requirements. We hypothesized that this approach would be useful in determining the impact of guidelines on physicians' practice patterns to develop appropriate educational program as well as future guidelines for the management of sedation and analgesia in the ICU.

Materials and Methods

This prospective, observational study was conducted from January 5, 2004, to January 31, 2005, with the participation of 43 ICUs in France and 1 ICU in Luxembourg. Each site had a minimum of 8 ICU beds, and individuals dedicated to this study, including a physician coordinator, one or two registered nurses, and, if possible, a physiotherapist. Before the start of the survey, a questionnaire was sent to each site to describe its own resources, its number of admissions in 2002, and the potential existence of protocols/guidelines and of dedicated education for pain and sedation management in the ICU. The Grenoble Institutional Ethical Committee approved the design of the study and, considering its observational nature, waived requirements for informed consent from the patients. Written information about this study was given to patients at their discharge from the ICU.

Patients were included if they were aged 15 yr or older and were admitted to the ICU for a foreseeable duration of mechanical ventilation of more than 24 h. Patients were excluded if they had severe brain injury on admission (defined by Glasgow Coma Scale score less than 9), if they required mechanical ventilation for less than 24 h, or if they had a delay in mechanical ventilation use exceeding 24 h after their admission to the ICU. For each patient, a set of variables was collected that included demographic characteristics, admission source, severity of illness as defined by Simplified Acute Physiology Score (SAPS) II and by an individual sequential organ failure assessment (SOFA) score of 3 or 4 (*i.e.*, moderate to severe organ failure),²⁸ patient's history, duration of mechanical ventilation, duration of stay in ICU, and patient outcome. If sedation or pain was assessed, investigators were asked to record which instrument was used and to record the level of sedation/analgesia that corresponded to a mean value of 2–4 assessments during a 24-h observation period. This information was collected on day 2 (D2), day 4 (D4), and day 6 (D6) of the patient's ICU stay. If sedatives or opioids were used during these periods, investigators were asked to record which drugs were chosen, their routes, their cumulative amounts

during each 24-h period (D2, D4, D6), and the reasons for administration. Information about the use of nonopioids and neuromuscular blocking agents was collected once each study day. Investigators were to record how they managed procedural pain from a list of procedures that had been previously established as painful: endotracheal suctioning, mobilization, wound care and dressing change, removal of chest tube, placement of arterial or central venous catheter, digestive endoscopy, bronchioendoscopy.^{27,29,30} Patient outcome, duration of mechanical ventilation, and duration of stay in the ICU were collected at the patient's discharge from the ICU. In the case of a prolonged ICU stay, the patient's data retrieval ended on day 31 (D31).

Patients were considered candidates for ventilatory weaning when they no longer had high-grade fever, hemodynamic instability, or severely altered consciousness, as well as by exhibiting adequate oxygenation with a fraction of inspired oxygen less than 50% and positive end-expiratory pressure less than 5 cm H₂O. Candidates for weaning were switched to pressure-support ventilation followed by daily spontaneous breathing trials on a T piece. The decision to extubate was based on simple bedside tolerance variables, including respiratory rate, oxygen saturation measured by pulse oximetry, and the use of accessory respiratory muscles during T-piece trials. This protocol was applied uniformly across all sites. There were no records of cognitive status impairment during weaning (*i.e.*, no assessment of delirium) or of patients' recollections after ICU discharge.

Each site had a dedicated individual who was asked to enter raw data into an electronic case report form, allowing an immediate and continuous process of monitoring of its completeness and correction (ClinInfo S.A., Lyon, France). The electronic case report form complied with Good Clinical and Methodological Practices (Code of Federal Regulations 21 part 11). To prevent excessive differences between sites in recruiting patients, each site could enter data for no more than six patients simultaneously. If six or fewer patients were enrolled, the study sample was chosen sequentially upon ICU admission; after the six-patient limit had been reached, no additional patient could be enrolled unless completing a previous patient's data file.

Descriptive statistics included frequencies and percentages for categorical variables, and medians and range (or interquartile range) for continuous-level variables. Inferential analyses included the chi-square test for heterogeneity, the McNemar test for paired data, and the Mann-Whitney test. Repeated measures of pain and sedation scores and of drug dosages were tested using the chi-square test for trend according to a linear model and analysis of variance after logarithmic transformation, respectively. Statistical significance was established at $P < 0.05$. All statistical analyses were performed using Stata version 8.0 software (Stata Corp., College Station, TX).

Results

Baseline Data

Of the 1,405 patients registered in the database, 24 were excluded because they had a severe brain injury on admission (11), no mechanical ventilation (5), or a delay in the mechanical ventilation use exceeding 24 h after admission (8). Therefore, a total of 1,381 patients at 44 active sites participated in the study. Sites affiliated with a university hospital and large sites affiliated with a community hospital were initially contacted *via* e-mail; among 49 sites that agreed to participate, 3 of them declined further to participate to the study, and 2 did not include patients. Active sites were primarily affiliated with a university hospital (34 of 44), had a median size of 12 ICU beds (8–31), and had a care team of 6 physicians (3–15) and 49 caregivers (26–134). These sites admitted a median number of 451 patients (209–2,324) in 2002. Of the 44 sites, 19 contributed data from less than 20 patients each, 19 from 20 and 50 patients, and 6 from more than 50 patients (maximum: 121 patients). No significant differences were found between the low-recruiter sites (< 20 included patients) and the other sites regarding their affiliation, resources, use of protocols, dedicated education for pain and sedation management in the ICU, age, and severity of illness of the patients admitted to these sites (data not shown). Baseline characteristics of the 1,381 patients on admission are shown in table 1. Outcome data were available from 1,378 patients (3 missing files).

Evaluation of Sedation and Analgesia

Data regarding the assessment and the management of sedation and analgesia were obtained from 1,360 patient files on D2, 1,256 on D4, and 1,099 on D6. Overall, the number of sedation and analgesia assessments was significantly smaller than that of use of sedatives and opioids ($P < 0.01$) (table 2). This means that a large proportion of patients were not assessed while receiving treatment for sedation or for analgesia, *e.g.*, 45% (439 of 981) and 53% (648 of 1,219) on D2, respectively. Specific instruments for measuring both sedation and pain in the same patient were used for 28% of patients (383 of 1,360). The Ramsay scale and the behavioral pain scale (BPS)³¹ were the most frequently used instruments for evaluating sedation and pain, respectively (figs. 1A and B). The other instruments for measuring sedation were the Richmond Agitation-Sedation Scale and the Sedation-Agitation Scale, and for measuring pain, the visual analog scale, the verbal descriptor scale, and the numeric rating scale. Other instruments (*e.g.*, Harris scale, Glasgow Coma Scale score, Cook scale) and the Bispectral Index were of minor use (less than 10%). Significantly fewer patients were evaluated by using the BPS on each subsequent ICU day, whereas the visual analog scale and numeric rating scale became more frequently used ($P <$

Table 1. Demographic and Clinical Characteristics of the 1,381 Patients on Admission to the ICU

Age, median (range), yr	61 (15–98)
Weight, median (range), kg	73 (28–185)
Sex, n (% male)	899 (65)
SAPS II, median (range)	43 (6–112)
Admission source, n (%)	
Medicine	447 (32)
Unplanned surgery	446 (32)
Planned surgery	268 (19)
Trauma	166 (12)
Others	54 (4)
SOFA score 3 or 4 on admission,* n (%)	
Respiratory	842 (61)
Cardiovascular	834 (60)
Renal	251 (18)
Neurologic	160 (12)
Coagulation	126 (9)
Hepatic	88 (6)
Patient's history,* n (%)	
Chronic cardiac failure	300 (22)
Chronic respiratory failure	229 (17)
Cancer in progress	225 (16)
Diabetes	209 (15)
Regular intake of psychoactive drugs	151 (11)
Cirrhosis	141 (10)
Recent chemotherapy for cancer	87 (6)
Chronic renal failure	85 (6)
Stroke	82 (6)
Long-term intake of corticosteroids	62 (4)
Others	79 (6)
Duration of mechanical ventilation, median (range), days	8 (1–31)
Duration of ICU stay, median (range), days	12 (1–31)
Outcome,† n (%)	
Died in ICU	270 (20)
Transferred to surgical ward	556 (40)
Transferred to medical ward	242 (18)
Transferred to other ICU	101 (7)
Still in ICU on day 31	209 (15)
Tracheostomy	126 (9)
Reintubation	266 (19)

* The number of individual organ failures (sequential organ failure assessment [SOFA] score 3 or 4) and of patient's history exceeds the total number of included patients. † Outcome data were available from 1,378 patients.

ICU = intensive care unit; SAPS = Simplified Acute Physiology Score.

0.01); no such change was found regarding the sedation instruments (figs. 1A and B). A deep state of sedation was defined by a Ramsay score of 5 or 6, a Richmond Agitation-Sedation Scale score of -5 or -4 , or a Sedation-Agitation Scale score of 1 or 2 for a given patient during the 24-h epoch. This state of sedation was found in 57% (258 of 451) of assessed patients on D2, 48% (169 of 355) on D4, and 41% (109 of 266) on D6, and decreased over time ($P < 0.01$).

Use of Sedatives and Opioids

Midazolam was the agent most commonly used for sedation (65–70%), with propofol used 20% of the time. Sufentanil (35–40%) and fentanyl (30–35%) were the most frequently used opioids, with morphine (15–20%) and remifentanyl (10%) being used less often (figs. 2A and B). Other sedatives (clorazepate, flunitrazepam,

Table 2. Incidence (%) of Patients Being Assessed and Those Receiving Sedatives and Analgesics during the ICU Stay

	D2 (1,360 Patients)	D4 (1,256 Patients)	D6 (1,099 Patients)
Patients on MV	94	82	76
Sedation			
Assessment	43	36	31
Treatment	72*	56*	49*
Analgesia			
Assessment	42	39	37
Treatment with opioids	90*	80*	74*
Procedural pain			
Assessment	35	35	35
Treatment	22	21*	22*
Nonopioids	33	36	35

Day 2 (D2), day 4 (D4), and day 6 (D6) of intensive care unit (ICU) stay.

* $P < 0.01$ vs. proportion of assessed patients (chi-square test).

MV = mechanical ventilation.

levomepromazine, pentobarbital, haloperidol, hydroxyzine, cyamemazine, ketamine, clonidine) and opioids (tramadol, buprenorphine, nalbuphine, alfentanil)

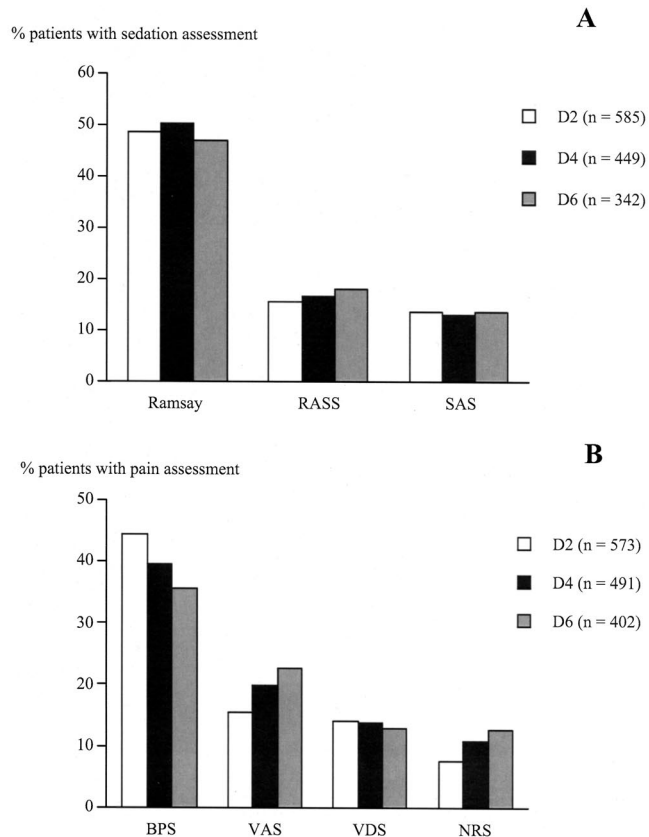


Fig. 1. Scales used for evaluating sedation (A) and pain (B) on day 2 (D2), day 4 (D4), and day 6 (D6) of the intensive care unit stay (% of assessed patients). Sedation was assessed using the Ramsay scale, the Richmond Agitation-Sedation Scale (RASS), and the Sedation-Agitation Scale (SAS). Pain was assessed using the behavioral pain scale (BPS), the visual analog scale (VAS), the verbal descriptor scale (VDS) and the numeric rating scale (NRS). Changes over time were significant for the proportion of patients assessed using BPS, VAS, and NRS (chi-square test for trend, $P < 0.01$).

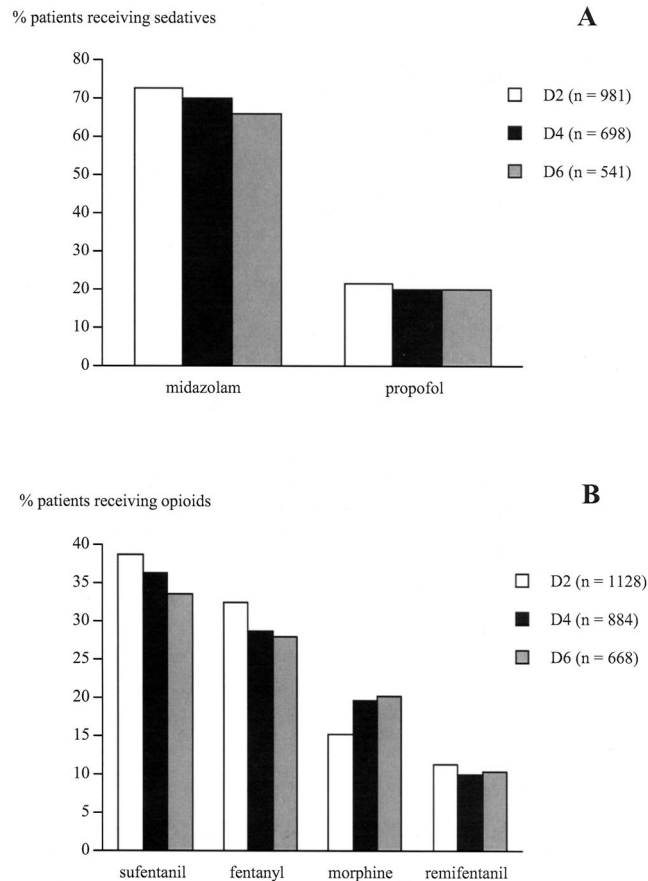


Fig. 2. Drugs used for sedation (A) and analgesia (B) on day 2 (D2), day 4 (D4), and day 6 (D6) of the intensive care unit stay (% of treated patients). Changes over time were significant for the proportion of patients receiving midazolam, sufentanil, fentanyl, and morphine (chi-square test for trend, $P < 0.05$).

were of minor use. A continuous intravenous infusion was the most frequent route of administering sedatives and opioids (> 90%). The main reasons given for prescription of continuous analgesia using opioids were for adaptation to the ventilator (84%) and the patient comfort (81%). A significant decrease in the proportion of patients receiving midazolam, sufentanil, and fentanyl was found over time ($P < 0.05$), whereas morphine administration increased significantly over the same period ($P < 0.01$) (figs. 2A and B). Considering those patients who received the same medication across their ICU stay, there were minor decreases in daily dosages of midazolam and sufentanil from D2 to D6 (table 3).

A significant decrease in the proportion of patients receiving sedatives and/or opioids during their ICU stay is shown in figure 3 ($P < 0.01$). Comparable changes were found for patients having respiratory and/or cardiovascular failure (sequential organ failure assessment score of 3 or 4) over the same period ($P < 0.01$), whereas there was no change in the proportion of renal, neurologic, hematologic, and/or liver failure (data not shown). For most patients, the presence of cardiovascular failure was associated with the use of sedatives (82%,

Table 3. Time Course Evolution of the Daily Dosages of Sedatives and Opioids for Patients Receiving the Same Medication during the ICU Stay

	No. of Patients	D2	D4	D6
Midazolam ($\text{mg} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$)*	284	1.6 (0.9–2.6)	1.6 (0.8–2.5)	1.4 (0.7–2.5)
Propofol ($\text{mg} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$)	44	31 (15–58)	25 (16–46)	26 (11–41)
Sufentanil ($\mu\text{g} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$)*	206	6.0 (3.5–9.5)	5.7 (3.4–10.0)	4.4 (2.6–9.7)
Fentanyl ($\mu\text{g} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$)	151	51 (31–71)	50 (31–71)	48 (27–74)
Morphine ($\text{mg} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$)	44	0.5 (0.3–0.7)	0.4 (0.3–0.6)	0.4 (0.2–0.6)
Remifentanyl ($\mu\text{g} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$)	39	160 (118–226)	152 (92–206)	150 (101–216)

Values are expressed as median and interquartile range. Day 2 (D2), day 4 (D4), and day 6 (D6) of intensive care unit (ICU) stay.

* $P < 0.01$ over time (analysis of variance after logarithmic transformation).

72%, and 68% on D2, D4, and D6, respectively) and of opioids (95%, 89%, and 84% on D2, D4, and D6, respectively). Similarly, the presence of respiratory failure was associated with the use of sedatives (81%, 72%, and 70% on D2, D4, and D6, respectively) and of opioids (90%, 85%, and 83% on D2, D4, and D6, respectively). Of the patients in a deep state of sedation (see definition above), there were 74%, 65%, and 55% with cardiovascular failure on D2, D4, and D6, respectively ($P < 0.01$ over time); the proportion with respiratory failure and deep sedation remained unchanged over the same period (53%, 57%, and 54% on D2, D4, and D6, respectively).

Other Drugs

Nonopioids were prescribed for 35% of patients (table 2), and included paracetamol (88% on D2) and nefopam (39% on D2). There were 9%, 7%, and 5% of patients receiving neuromuscular blocking agents in addition to sedatives and analgesics on D2, D4, and D6, respectively; of these, 70% of neuromuscular blocking agents use was cisatracurium. For the patients receiving neuromuscular blocking agents, there were no data on pain and sedation assessment.

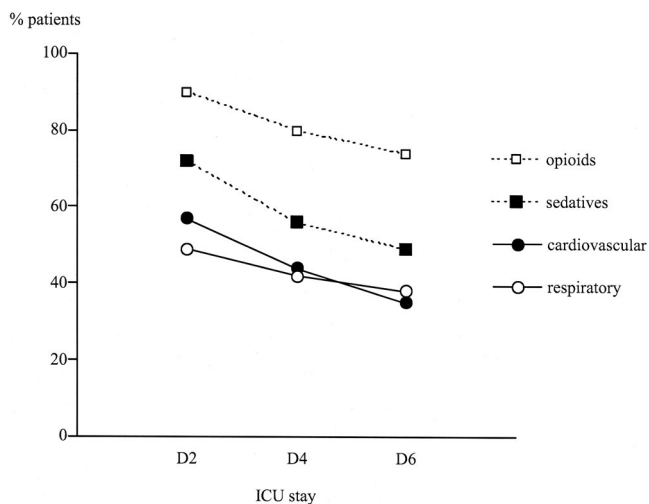


Fig. 3. Proportion of patients having respiratory and cardiovascular failures and of patients receiving sedatives and analgesics on day 2 (D2), day 4 (D4), and day 6 (D6) of their intensive care unit (ICU) stay. Changes over time were significant for all these proportions of patients (chi-square test for trend, $P < 0.01$).

Painful Procedures

In this study, endotracheal suctioning and mobilization during standard care were the most frequently reported painful procedures among the list of procedures. The proportion of patients receiving a specific pain treatment for the procedure was less than 25%, lower than the rate of pain assessments for the procedure (table 2). A bolus of opioids was primarily administered as the specific treatment during these procedures (70% of specific treatments). Pain was assessed before and during the procedure (endotracheal suctioning and mobilization) through use of the same pain instruments in 293 patients on D2, 259 patients on D4, and 198 patients on D6; there were significantly more patients with pain (defined by a BPS score of more than 4 of 12, a visual analog scale or a numeric rating scale score of more than 3 of 100 mm, or a verbal descriptor scale score of more than 1 of 4) during the procedure than before the procedure ($P < 0.05$) (table 4). Similar results were found when splitting the procedures: The proportions of patients experienced pain during endotracheal suctioning were 22%, 32%, and 31% using a BPS scale on D2, D4, and D6, respectively ($P < 0.01$ vs. before procedure).

Use of Protocols in ICU

A protocol/guideline for pain and sedation management was in place in 16 of 44 sites, and 23 sites organized dedicated education for pain and sedation management in the ICU. No site was conducting daily interruption of sedation. No differences were found between the 16 sites using protocols for pain and sedation management and the other 28 sites in terms of their affiliation, their number of caregivers and ICU beds, or the proportion of low-recruiter sites for the study (table 5). There was more dedicated education toward pain and sedation in sites using protocols ($P < 0.05$), and patients admitted to those sites were more likely to be assessed for pain and sedation, and during painful procedures on D2 ($P < 0.01$). Also, there were fewer patients in protocol sites that received drugs for sedation and analgesia than patients admitted to sites using no protocol ($P < 0.01$). These findings were also noted on D4 and D6 (data not shown).

Table 4. Incidence (%) of Patients Having Pain as Assessed before and during Painful Procedure (Endotracheal Suctioning, Mobilization) with the Same Pain Instrument (BPS, VAS, VDS, or NRS) of Their ICU Stay

	D2 (293 Patients)	D4 (259 Patients)	D6 (198 Patients)
Before procedure			
BPS > 4	4	7	11
VAS > 30 mm	38	34	31
VDS > 1	30	29	23
NRS > 30 mm	24	19	24
During procedure			
BPS > 4	25†	29†	31†
VAS > 30 mm	62†	51*	48*
VDS > 1	43	40	38
NRS > 30 mm	34	44*	48*

Day 2 (D2), day 4 (D4), and day 6 (D6) of intensive care unit (ICU) stay.

* $P < 0.05$ and † $P < 0.01$ vs. before procedure (McNemar test).

BPS = behavioral pain scale; NRS = numeric rating scale; VAS = visual analog scale; VDS = verbal descriptor scale.

Discussion

The results of this large survey offer important insights into practices for sedation and analgesia in mechanically ventilated patients in France. This study reflects what is really done in ICUs, points out gaps between clinical practice and current recommendations, and could serve as a basis for the elaboration of national guidelines. Specifically, we found that assessment rates for pain and sedation were consistently lower than that of drug administration. This difference, however, was partially corrected with the use of protocols/guidelines for the management of pain and sedation. A large proportion of assessed patients were in a deep state of sedation and, whereas fewer patients received sedatives over time, no

major changes in their degree of sedation or in their sedative dosages occurred during the first week of ICU stay. In addition, there was limited attention directed toward management of procedural pain and, despite the frequent use of continuous administration of opioids, a significant proportion of patients had an increase in their level of pain during painful procedures. This is the largest study of ICU patient-based clinical practices to date that describes all aspects of sedation and analgesia during the ICU stay: assessment, drug use, and procedural pain.

This study measured current rates of pain and sedation assessments for ICU patients. That 40% of our patient sample was assessed for sedation or pain is in close agreement with that previously declared by French physicians in a European survey,¹⁷ but strongly contrasted with the 60–90% patients treated with sedatives or opioids. Recent questionnaires sent to ICU physicians in Germany, Canada, and Denmark revealed widely varying practice patterns regarding sedation monitoring and type of medications. The questionnaires did not address the relation between declared rates of assessment *versus* treatment for the patients.^{18–20} Despite publication of French and US guidelines for sedation and analgesia,^{10,11} our results indicate that practices of sedation and pain assessment have been disregarded for a majority of ICU patients, suggesting that impact of clinical trials and guidelines on physicians' practice patterns is quite low.

Such a discrepancy in the rate of assessment *versus* treatment is hardly conceivable regarding prescription of other drugs commonly prescribed in the ICU, such as vasoactive agents, antibiotics, and diuretics, which are based on assessments of physiologic status. There are several possible explanations about this discrepancy

Table 5. Impact of the Use of Protocol for Sedation and Analgesia Management among the 44 Participating Sites

	Use of Protocol (n = 16 Sites)	No Use of Protocol (n = 28 Sites)
University hospital, n (%)	12 (75)	22 (79)
ICU beds per site, median (range)	13 (8–31)	12 (8–24)
Caregivers per bed, median (range)	4.1 (2.7–5.6)	4.1 (2.0–7.5)
Low-recruiter sites, n (%)	5 (31)	14 (50)
Dedicated education, n (%)	12 (75)	11 (39)*
Patients on MV on D2, n (%)	602 (91)	672 (96)†
SAPS II, median (range)	41 (8–107)	44 (6–112)*
Sedation on D2, n (%)		
Assessment	370 (56)	215 (31)†
Treatment	451 (68)	530 (76)†
Analgesia on D2, n (%)		
Assessment	398 (60)	175 (25)†
Treatment with opioids	572 (87)	647 (92)†
Procedural pain on D2, n (%)		
Assessment	335 (51)	143 (20)†
Treatment	148 (22)	158 (23)
Nonopioids on D2, n (%)	217 (33)	230 (33)

Low-recruiter sites were defined as less than 20 patients included per site during the study. The number of patients in the intensive care unit (ICU) on day 2 (D2) was 660 in sites using a protocol and 700 in sites using no protocol.

* $P < 0.05$ and † $P < 0.01$ vs. "use of protocol."

MV = mechanical ventilation; SAPS = Simplified Acute Physiology Score.

when considering use of sedation and analgesia in the ICU. First, it is usually preferred to have patients sedated in the ICU, because this sedated state is believed to facilitate procedures, to prevent agitation and unplanned tube removal, and to protect against unpleasant memories of a life-threatening situation. The term "sedation in the ICU" is also confusing because it may incorporate the use of both analgesics and hypnotics, whereas pain (analgesia) and consciousness (sedation) are two separate entities. Therefore, sedatives and analgesics are still ordered on an as-needed basis, in lieu of assessments of the patient's specific drug requirements.²³ Second, there are no validated physiologic instruments to objectively measure sedation or pain levels in ICU patients. Assessment methods such as heart rate variability, lower esophageal contractility, changes in pupillary size, and bispectral analysis are still experimental: None have achieved acceptable validity and reliability for daily clinical use.^{9,32} Therefore, assessing sedation and pain must rely on the use of clinical scoring systems, which can be regarded as a time-consuming process by physicians and nurses. There are also significant limitations to current practices of pain assessment in noncommunicative patients. Third, routine assessments of pain and sedation are believed to have no visible impact on patient outcome, which may weaken the motivation of clinical teams in the use of instruments to measure sedation and analgesia as a standard of practice. However, implementation of drug administration algorithms directed by levels of sedation and analgesia was demonstrated to dramatically reduce ventilator days and duration of stay.^{12-14,33} Systematic assessments of pain and sedation could possibly have a similar impact on patient outcome by reducing the duration of mechanical ventilation and the rate of nosocomial infections.¹⁵ In our study, the use of protocols/guidelines in the ICU increased the rate of pain and sedation assessments, decreased the use of sedatives/analgesics, and was associated with more dedicated education for pain and sedation management (table 5). Accordingly, our findings strongly suggest that implementation of ICU protocols and increased education about pain and sedation can significantly help care teams in their efforts to follow national guidelines. An educational program should include the following sections: training for the measurement of pain and sedation using appropriate instruments, targeting a desired sedation level (*i.e.*, consciousness level) according to the patient's illness and his or her current condition, identifying painful procedures among those performed daily in the ICU, and using algorithms to adjust drug dosages at baseline and during those procedures. These points should be considered in the elaboration of educational programs and future recommendations for pain and sedation in the ICU.

In this study, as in other studies,¹⁷⁻²⁰ the Ramsay scale was used most commonly to assess sedation. It should be

noted, however, that the Ramsay scale was not designed for evaluating sedation in the ICU environment, and it has only exhibited fair properties of reliability and validity.³⁴ Whatever sedation instrument used (Ramsay scale, Sedation-Agitation Scale, Richmond Agitation-Sedation Scale), a large proportion of our patients were in a deep state of sedation and, whereas fewer patients received sedatives over time, no major changes in their sedative dosages occurred during the first week of ICU stay. This is in accordance with a recent German survey, showing a gap between the aimed level of sedation and that which was really obtained.²¹ Our findings indicate also that sedative/analgesic regimens were not adjusted, probably because a large proportion of patients were not evaluated to determine whether changes in drug dosages were necessary to maintain a level of consciousness compatible with nursing assessment of the patient's comfort and calmness. In regard to pain practices, we noted changes in pain instruments during the patient's ICU stay. The BPS scale, which was developed for uncommunicative patients,³¹ was used most frequently during the early days of ICU stay, whereas self-rating scales (visual analog scale, numeric rating scale) increased in use on subsequent days (fig. 1B). In a similar fashion, morphine increased in use as ICU days progressed. This change in type of assessment instruments and drugs most likely reflected an increase in the number of patients who were able to communicate verbally. If so, this reflected an adaptation of clinicians to the level of patient's consciousness since the proportion of patients receiving sedatives progressively decreased (table 2 and fig. 3). Because adequate pain assessment and management may depend primarily on whether the patient can communicate, a desired sedation level may be a vital aspect of ensuring patient comfort.

This study shows that fewer patients received sedatives and opioids over time. Interestingly, these changes paralleled the proportion of patients with cardiovascular and respiratory failures (fig. 3). Although causal relations between drug uses and patient outcomes cannot be determined from this observational study, these findings suggest that the use of sedatives and analgesics could account, in part, for the requirements of vasoactive agents for cardiovascular failure, as indicated by a sequential organ failure assessment score of 3 or 4. Indeed, a large proportion of patients with deep states of sedation level had cardiovascular failure and, to a lesser extent, respiratory failure. Neglecting a regular assessment of sedation to achieve desired sedation level may put patients at risk to receive inappropriate dosages of sedatives with concomitant effects on cardiovascular system.

For patients receiving the same medications over time, we did not find increased dose requirements in opioids. Therefore, we cannot provide support in favor of development of tachyphylaxis within 96 h of sufentanil use, as

previously suggested.²⁵ Although midazolam doses declined over time, drug effect may have increased over time with accumulation of active metabolites. We cannot make a comparison between sedatives such as propofol and midazolam, or opioids such as remifentanyl and other opioids regarding their impact on patient outcome (duration of mechanical ventilation, duration of stay, acquired complications) based on our study data. The choice of certain medications in this study most likely were influenced by many factors, including the severity of patient's illness, the foreseeable duration of mechanical ventilation, and the habits and resources of each site, as shown previously.¹⁸⁻²⁰ Future research should continue to address relations between drug type, amount, and important clinical outcomes.

We found a low incidence (less than 25%) of specific analgesic use during procedural pain, specifically suctioning and mobilization pain. In previous studies, pain intensity scores of 30-100 mm were rated by alert patients undergoing procedures, and some procedures were identified as the patient's most stressful ICU experiences.^{29,35} However, only one study fully described analgesic practices associated with common ICU procedures.²⁷ In that multisite study comprised of 5,957 adult patients, less than 20% of patients received opioids before and/or during six identified procedures, and 63% received no analgesics. Our results, derived from patients who underwent endotracheal suctioning and/or mobilization, were very similar. The finding that more patients had pain during painful procedures than before procedures (table 4) strongly suggests the lack of analgesia when the patient is subjected to noxious stimuli. Satisfactory levels of analgesia by continuous infusion of opioids during times without stimulation do not guarantee against pain reactions during procedures. The use of the BPS scale during painful procedures in noncommunicative patients is recommended to assess the adequacy of analgesia.³¹ Because more pain behaviors were noted in patients undergoing procedures than in those not undergoing procedures,³⁶ we recommend that pain be assessed in verbal and nonverbal patients during painful situations to increase the efficacy of analgesic interventions.

There are some notable limitations to this survey of practices. Our results are derived from a convenience sample of hospitals that agreed to participate. Therefore, this survey of practices reflects what is done daily by the active 44 teams and cannot be uniformly transposed to all ICUs. Moreover, patients who participated were by convenience and dependent on the availability of investigators as well as on the number of simultaneously enrolled patients by each site. We aimed at collecting exhaustive information about practices for sedation and analgesia as well as at limiting an excessive difference between sites in the number of included patients. Although we used a limit to prevent excessive number of

simultaneously enrolled patients at each site, *i.e.*, six simultaneously enrolled patients, this limit was reached on only three occasions during the study period. Patients from the largest site were less than 10% of the studied population. The low number of missing values or errors in recording data (less than 3% throughout the study) and only 3 missing files among 1,381 patients conferred to the study results with a high degree of consistency. Although this survey cannot be considered representative and exhaustive of all patients admitted during the study period, this study was a full description of current practices during the first week of ICU stay for mechanically ventilated patients in multiple ICUs.

In conclusion, the results of this large observational study provide several insights that may help to improve our clinical practice and to draw up further national guidelines for analgesia and sedatives practices. Clearly, efforts should be directed to elaborate appropriate protocols/guidelines in the ICU to facilitate the regular use of sedation and pain scales, to enhance management of procedural pain, and to ensure the proper use of sedatives and analgesics. Such efforts could result in a vast improvement in patient comfort and clinical outcomes.

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Appendix: DOLOREA Investigators

Joachim Calderon, M.D. (Hôpital Cardiologique, Bordeaux, France), Laurent Beydon, M.D. (Centre Hospitalier Universitaire, Angers, France), Charles Cerf, M.D. (Hôpital Henri Mondor, Créteil, France), Philippe Barbe, M.D. (Centre Hospitalier, Chambéry, France), Stéphane Winnock, M.D. (Centre Hospitalier Universitaire, Caen, France), Mouldi Hamrouni, M.D. (Hôpital Louis Pasteur, Chartres, France), Dominique Guelon, M.D. (Hôpital Gabriel Montpied, Clermont-Ferrand, France), Stéphanie Artigues, M.D. (Hôtel Dieu, Clermont-Ferrand, France), Irène Messant, M.D. (Hôpital Général, Dijon, France), Elsa Brocas, M.D. (Centre Hospitalier Louise Michel, Evry, France), Pierre Lavagne, M.D. (Hôpital Michallon, Grenoble, France), Christiane Hercule, M.D. (Hôpital Cardiovasculaire et Pneumologique Louis Pradel, Lyon, France), Serge Duperret, M.D. (Hôpital Croix Rousse, Lyon, France), Khalid Berrada, M.D. (Hôtel Dieu, Lyon, France), Jean-Michel Grozel, M.D. (Centre Hospitalier Lyon Sud, Lyon, France), Gérald Chanques, M.D. (Hôpital St Eloi, Montpellier, France), Sarah Valette, M.D. (Hôpital Lapeyronie, Montpellier, France), Francine Bonnet, M.D., and Laurent Benayoun, M.D. (Hôpital Beaujon, Clichy, France), Adrien Decorps-Declere, M.D. (Hôpital Antoine Beclère, Clamart, France), Jacques Duranteau, M.D. (Hôpital Bicêtre, Le Kremlin-Bicêtre, France), Jean Mantz, M.D., and Hervé Quintard, M.D. (Hôpital Bichat Claude Bernard, Paris, France), Jean-Francois Timsit, M.D., and Bruno Mourvilliers, M.D. (Hôpital Bichat Claude Bernard, Paris, France), Christian Rathat, M.D. (Hôpital Avicenne, Bobigny, France), Rémy Gauzit, M.D. (Hôpital Jean Verdier, Bondy, France), Andrea Passard, M.D. (Hôpital Ambroise Paré, Boulogne-Billancourt, France), Jean-Paul Perez, M.D. (Hôpital d'Instruction des Armées, Clamart, France), Laurent Dubé, M.D. (Centre Hospitalier Universitaire, Angers, France), Michèle Binhas, M.D. (Hôpital Henri Mondor, Créteil, France), Anne-Claire Lukaszewicz, M.D. (Hôpital Lariboisière, Paris, France), Jean-Luc Leguillou, M.D. (Institut Mutualiste Montsouris, Paris, France), Laurent Jacob, M.D. (Hôpital Saint Louis, Paris, France), Sonia Elmetaoua, M.D. (Hôpital Tenon, Paris, France), Jean-Paul Bleichner, M.D. (Hôpital Ponchaillou, Rennes, France), Igor Auriant, M.D., and Gaëlle Demeilliers-Pfister, M.D. (Hôpital Charles Nicolle, Rouen, France), Philippe Mahul, M.D. (Hôpital Nord, St Etienne, France), Guy Freys, M.D. (Hôpital de Haute-pierre, Strasbourg, France), Pascale Sanchez, M.D. (Hôpital Purpan, Toulouse, France), Francois Lagarrigue, M.D. (Hôpital Trousseau, Tours, France), Bruno Raynard, M.D. (Institut Gustave Roussy, Villejuif, France), Emmanuelle Nalet, M.D. (Centre Hospitalier de la Région Annecienne, Annecy, France), Marc Feissel, M.D. (Centre Hospitalier Général, Belfort, France), Jérôme Baudot, M.D. (Centre Hospitalier Henri Duffaut, Avignon, France), and Marc Klop, M.D. (Clinique Sainte Thérèse, Luxembourg).