# Incidence and impacts of pain in intensive care units: systematic review

Incidência e impactos da dor em unidades de terapia intensiva: revisão sistemática

lura Gonzalez Alves<sup>1,2</sup>, Rafaela Dias Bezerra<sup>1</sup>, Bianca Borges de Brito<sup>1</sup>

DOI 10.5935/2595-0118.20230084-en

# ABSTRACT

**BACKGROUND AND OBJECTIVES:** In Intensive Care Units (ICU), patients are exposed to multiple procedures that can be painful, and health professionals are not always aware of the pain in these patients. Inadequate pain assessment and management, in turn, has been associated with several adverse outcomes, including an increased rate of infection, prolonged mechanical ventilation, hemodynamic disturbances, delirium, and compromised immunity. Thus, this study aimed to summarize the scientific evidence about the incidence and impacts of pain in critically ill patients.

**CONTENTS:** A systematic review of observational studies (Pubmed and EMBASE databases) was performed with predetermined eligibility criteria. In the 32 studies included, it was identified that 10.1% to 61% of patients had pain at rest and 27.4% to 94% during procedures. In addition, there was evidence of improvement in patient outcomes after using validated instruments for pain measurement, including decreased length of ICU stay, duration of mechanical ventilation, mortality, delirium, adverse events, and disease severity.

**CONCLUSION**: Through the present study, it was observed that pain is a common phenomenon in ICU and that its identification and management constitute a realistic goal and depend on the evaluation. Furthermore, pain appears to be associated with worse clinical outcomes. Therefore, efforts must be made to provide comprehensive care for critically ill patients, aiming not only at their survival, but also at alleviating their suffering.

Iura Gonzalez Alves – ©https://orcid.org/0000-0003-2455-3788; Rafaela Dias Bezerra – ©https://orcid.org/0009-0002-4001-547X; Bianca Borges de Brito – ©https://orcid.org/0009-0002-3413-7956.

Bahian School of Medicine and Public Health, Medicine, Salvador, BA, Brazil.
 Federal University of Bahia, Physiotherapy, Salvador, BA, Brazil.

Presented on July 9, 2023. Accepted for publication on September 21, 2023. Conflict of interests: none – Sponsoring sources: none.

Responsible associate editor: Renato Leonardo de Freitas https://orcid.org/0000-0003-1799-5326

Correspondence to: Iura Gonzalez Alves E-mail: gonzalez.alvesin@gmail.com

© Sociedade Brasileira para o Estudo da Dor

**Keywords**: Association measure, Exposure risk or outcome, Intensive care unit, Pain, Pain measurement, Systematic review.

### RESUMO

JUSTIFICATIVA E OBJETIVOS: Nas Unidades de Terapia Intensiva (UTI) os pacientes são expostos a múltiplos procedimentos que podem ser dolorosos, e nem sempre os profissionais de saúde estão alertas para a dor nesses pacientes. A avaliação e o manejo inadequado da dor, por sua vez, têm sido associados a uma série de resultados adversos, incluindo aumento da taxa de infecção, ventilação mecânica prolongada, distúrbios hemodinâmicos, delírio e imunidade comprometida. Dessa forma, este estudo teve como objetivo sumarizar as evidências científicas acerca da incidência e dos impactos da dor em pacientes críticos. **CONTEÚDO**: Foi realizada uma revisão sistemática de estudos observacionais (bases de dados Pubmed e EMBASE) com critérios de elegibilidade predeterminados. Nos 32 estudos incluídos, foi identificado que de 10,1% a 61% dos pacientes apresentaram dor em repouso, e de 27,4% a 94% apresentaram dor durante os procedimentos. Além disso, houve evidências de melhora nos resultados dos pacientes após o uso de instrumentos validados para a mensuração da dor, incluindo diminuição do tempo de permanência na UTI, duração da ventilação mecânica, mortalidade, delírio, eventos adversos e gravidade da doença.

**CONCLUSÃO:** Através do presente estudo foi observado que a dor representa um fenômeno comum nas UTI e que a sua identificação e manejo constitui uma meta realista e dependente da avaliação. Além disso, a dor parece estar associada a piores desfechos clínicos. Sendo assim, deve-se voltar esforços para o cuidado integral ao paciente crítico, objetivando não só sua sobrevivência, mas também o alívio do seu sofrimento.

**Descritores**: Dor, Exposição risco ou desfecho, Medição da dor, Medida de associação, Revisão sistemática, Unidade de terapia intensiva.

# INTRODUCTION

The presence of pain is a common phenomenon among patients in intensive care units (ICUs). This is due to the severity and pathophysiology of the disease and as a result of the invasive therapies and procedures to which the patient is subjected<sup>1</sup>. Certainly, the cumulative effects of the physiological and behavioral aggression caused by carrying out procedures such as venipuncture, tracheal suctioning, change of decubitus, nasogastric tube, among others, can represent a painful and stressful time for the patient<sup>2,3</sup>.

In practice, assessing the pain experience in ICU environment is not a simple process, since most patients are unable to communicate due to the severity of their illness, or due to conditions such as mechanical ventilation (MV), sedation and a lowered level of consciousness<sup>2</sup>. Therefore, in this group of patients, it is important to consider the somatic and physiological equivalents of pain, which translate into specific signs and behaviors<sup>1</sup>. To this end, standardized tools for assessing pain in non-communicative and sedated patients have been developed. These include the Behavioral Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT), which aim to measure pain in ICU by focusing on three parameters: "facial expression", "upper limb movements", and "patient/mechanical ventilator interaction"<sup>2,5</sup>.

Although pain is reported as a frequent condition in the ICU and the tools to measure it are available, the inconsistent use of pain assessment scales in ICUs has resulted in a non-routine and inaccurate assessment of this vital sign and thus its inadequate control. At the same time, studies have identified that underdiagnosed pain can be associated with a series of adverse outcomes, including increased infection rates, prolonged MV, hemodynamic disturbances, delirium and compromised immunity<sup>4.5</sup>. Despite this, the scientific literature lacks an up-to-date systematic review that gathers information on the incidence of pain in ICU and its impact on important clinical outcomes. The aim of this study was to summarize the scientific evidence on the incidence of pain in ICU and the impact of implementing pain assessment protocols in the ICU.

# CONTENTS

A systematic review was carried out according to the criteria defined by the Reporting Guide for JBI Systematic Reviews (JBIS-RIR)<sup>14</sup>. Observational studies measuring the incidence of pain and the correlation of pain assessment in the ICU with clinical outcomes of critically ill patients were considered. The search was not restricted by language or year of publication and took place between March and June 2022 in the Pubmed and Embase databases. The last search, aimed at updating the results, was carried out in May 2023. The research question used to structure the investigation was based on the PECO acronym for observational studies, resulting in: (P) ICU patients, critically ill patient; (E) Pain exposure, pain assessment and pain measurement; and (O) Clinical outcome and results.

The following inclusion criteria were established for the selection of scientific articles: studies that presented data on the incidence of pain in ICU and/or presented the relationship/association/ correlation of pain with outcomes. Studies on pediatric and neonatal ICUs, studies validating pain scales and literature reviews were excluded.

### Search strategy

The keywords used were created using search terms from the Medical Subject Headings (MeSH), EMTREE and the Health Sciences Descriptors (DeCS): "ICU patient", "critically ill patient", "pain", "pain assessment", "pain management", "outcome", "clinical outcomes" and their synonyms. Two authors carried out the initial search and selected the titles and abstracts of the potentially relevant studies. Each abstract was independently assessed by two authors. If one of the authors considered the study to be relevant, the full article was obtained. The two authors independently analyzed the articles to select those to be included in the study. In the event of disagreement, the decision was made by consensus of the authors. A manual citation search was also carried out on the selected articles.

### Study selection and data extraction

An initial assessment was carried out based on the titles and abstracts of the articles, and those that did not meet the inclusion criteria were excluded. The articles collected were then read in full. First, all the articles selected were read, followed by a selective and analytical reading of the outcome points defined for this study. The information extracted from the articles was then recorded in order to organize and summarize the material.

To extract the results, a table was developed using Microsoft Office Excel, and the following information was recorded: authors, country/language, study population, average age, gender, pain incidence, pain assessment tool and clinical outcomes.

# RESULTS

The search strategy resulted in 12,967 articles. Of these, 32 met the eligibility criteria and were included in this review.

### Instruments used to measure pain

Of the 32 studies included, 15 (46.8%) used the Behavioral Pain Scale (BPS) in their evaluations<sup>7,15-18,21,23,27,29,30,32,38,44-46</sup>. Of these, seven (46.6%) used the Numeric Rating Scale (NRS)<sup>7,18,21,29,20,32,46</sup> and two (14.2%) used the Behavioral Pain Scale-Non-Intubated (BPS-NI)<sup>21,29</sup>.

Of the studies analyzed, 10 (31.2%) used the Critical Care Pain Observation Tool (CPOT)<sup>10,19,25,27,31,33,37,39,42,45</sup>. Of these, three (30%) used NRS<sup>10,19,39</sup>.

Of all the studies included, only two (6.2%) used the Behavioral Indicators of Pain Scale (ESCID)<sup>20,26</sup> and only three (9.3%) used questionnaires to assess pain<sup>22,28,41</sup>. Of the latter three, only one also used NRS<sup>28</sup>. Only one study (3.1%) used the Edmonton Symptom Assessment Scale<sup>24</sup>. Three studies (9.3%) used the Visual Analogue Scale (VAS)<sup>32,41,42</sup>. The abstract of one study included in this review did not indicate the tool used to measure pain<sup>43</sup>. One of the studies included used non-behavioral tools to measure pain in the ICU<sup>40</sup>.

Additionally, it should be noted that only one study included in this review was carried out in Brazil<sup>44</sup> and used the BPS validated Brazilian version. In Brazil, there are currently two validated scales available in Portuguese, BPS and CPOT. In this sense, it should be noted that BPS has been well explored in terms of its properties for measuring pain in ICU, and CPOT has only one available validation study on critically ill patients in Brazil, thus requiring more studies to be developed in Brazil in order to assess the accuracy of this assessment tool<sup>46</sup>.



Figure 1. Flowchart of the article selection process

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

http://www.prisma-statement.org/

# INCIDENCE OF PAIN AT REST AND DURING PRO-CEDURES

### Behavioral Pain Scale (BPS)

Of the 32 studies included, 23 assessed the incidence of pain at rest and/or during routine ICU procedures. Of these, eleven (47.8%) used BPS in their assessments<sup>7,15-18,21,23,27,44.46</sup>. One of them used a 2-point increase score on BPS to detect their patients' pain, identifying mean scores of 3.82 at rest and 5.59 when turning<sup>27</sup>. Two studies defined pain as a BPS score>3, with between 33.2% and 61% of patients presenting pain at rest<sup>16,17</sup>. Pain behavior (BPS>3) was observed in 94% of the procedures evaluated, with a median BPS score of 617. Finally, the overall mean pre-procedure score was 3.43 (SD=0.67) and during procedures, 6.34 (SD=2.36)<sup>16</sup>.

It should be noted that one study considered a BPS score>3 as pain and BPS  $\geq$ 5 as significant pain<sup>44</sup>. Of the 201 observations, in 70 (34.8%) the patients had a BPS score≥5. In addition, in 91% of the observations during tracheal suctioning there was significant pain<sup>44</sup>.

On the other hand, one study considered a BPS score  $\ge 4$  as the cut-off point for diagnosing pain, with 98% of patients experiencing pain during physiotherapy sessions<sup>15</sup>. A single study considered a BPS score $\ge 5$  to detect "significant pain", and 33% of patients had significant pain at rest<sup>17</sup>. In addition, pain was significant (BPS $\geq$ 5) in 86% of the routine procedures evaluated (mobilization with turning and tracheal suctioning)<sup>17</sup>.

Four studies considered that a BPS score>5<sup>7,18,21,23</sup> was indicative of the presence of pain. One of them only used a BPS score>5 in their evaluations<sup>23</sup>. Two studies considered a BPS score>5, and also an NRS score>3 when the patient was able to self-report<sup>7,18</sup>. Thus, 51% of patients had pain (BPS>5 or NRS>3) at rest<sup>7</sup> and 42% during intervention<sup>18</sup>. A single study considered pain as a BPS>5, NRS>3 or BPS-NI>5 score, identifying 27.4% of patients with pain during rotation and 10.1% during rest<sup>21</sup>.

Only one study identified "severe pain" through a BPS>7 or NR>6 score, with an incidence equivalent to 36% in the group of patients who were not exposed to systematic pain assessment (intervention group) and 16% for patients in the group who received systematic pain assessment<sup>18</sup>. It is worth noting that in this same study, in the intervention group the risk of presenting pain was 1.44 (95% CI: 1.14 -1.81) and the risk of presenting agitation was 1.73 (95% CI: 1.15, 2.61), thus showing the protective effect of systematic pain assessment in the ICU for these outcomes.

In turn, one study considered BPS≥5 and CPOT≥3 as pain<sup>45</sup>. Pain signals increased significantly in both scales during inter-

ventions such as aspiration of bronchial secretions and repositioning of the patient (p<0.001). Signs of pain were observed in around 1/3 of the measurements<sup>45</sup>.

### Critical care pain observation tool (CPOT)

Seven of the 23 studies (30.4%) that assessed the incidence of pain used the CPOT scale in their evaluations<sup>10,19,25,27,37,39,45</sup>. One of them used a CPOT≥2 and/or *Bispectral Index* (BIS)≥88<sup>25</sup> score and found that 192 (90%) patients reported pain after aspiration and 38 (17%) after gentle touch. In turn, another study considered a CPOT score>2 or NRS>3 for pain<sup>19</sup>, and so the percentage of patients who experienced pain on at least one occasion was 33.8% at rest and 28.8% during bed baths. Twenty-four (20.3%) patients had inadequate pain management both at rest and during bed baths<sup>19</sup>.

One study<sup>10</sup> considered a CPOT score>3 or NRS>3 to diagnose pain. In this study, pain at rest was detected in 67 (27.6%) patients, 49 surgical and 18 non-surgical. On the other hand, pain during procedures was found 134 times (36.1%) in 52 (21.4%) patients, 29 (23.0%) surgical and 23 (26.5%) nonsurgical (p=0.523). In addition, another study considered a CPOT score≥3<sup>37</sup>. For cardiovascular ICU patients, it was observed that 28 of the 274 documented scores (10%) indicated the presence of pain<sup>37</sup>. Of the surgical and trauma ICU patients, 15% indicated the presence of pain<sup>37</sup>.

Another study selected for this study looked at the incidence of moderate to severe pain (NRS $\geq$ 4/CPOT $\geq$ 3) in a population of 711 critically ill adult patients from two hospitals in Finland<sup>39</sup>. In their results, 76% of the patients had moderate to severe pain during at least one of the 10 days they were monitored in ICU<sup>39</sup>.

Two studies used a CPOT score>5<sup>19,27</sup>. One of them considered a CPOT score>5 or NRS>6 to diagnose severe pain<sup>19</sup>. In this study, the incidence of severe pain at rest was 5.9%. Finally, one of the studies included in this review considered a CPOT score of 6-8 or NRS of 8-10 to indicate severe pain<sup>10</sup>. An NRS score>7 or a CPOT score>6 was recorded 25 times in 21 (10.3%) patients, 15 (11.9%) surgical and 6 (5.1%) non-surgical<sup>10</sup>.

# Behavioral indicators of pain scale (ESCID)

Two studies used the ESCID scale in their pain assessments<sup>20,26</sup>. One of them showed that patients undergoing painful procedures had increased scores during the application of the procedures, in relation to baseline measurements and measurements taken after the procedure<sup>20</sup>.

The second study, on the other hand, revealed a significant increase in the mean ESCID scores during the 3 days of evaluation and during the 3 moments of evaluation (tracheal aspiration)<sup>26</sup>.

# Visual analogue scale (VAS)

One study quantified pain using VAS<sup>22</sup>. In its results, pain was present in 47% of patients and the painful phenomena were distributed according to their frequency and intensity as follows: 23% of patients complained of tracheal aspirations (mean VAS 7.6), 19% of bladder tube insertion (mean VAS 6.5), 14% of team mobilizations (mean VAS 6.2), 14% of arterial punc-

438

tures (mean VAS 6) and 17% of venous punctures (mean VAS 4.5); other cases comprised 11% of patients<sup>22</sup>.

In this sense, the study<sup>41</sup> measured pain intensity in a cardiothoracic ICU using VAS and used questionnaires to assess patient satisfaction with pain management practices<sup>41</sup>. The average pain intensity in the sample studied was moderate (VAS≥4) and the responses to the questionnaire indicated that 96% of patients experienced effective pain control<sup>41</sup>.

# Numeric rating scale (NRS)

One study used NRS and the International Pain Outcomes (IPO) questionnaire to find out about the subjective perception of pain in critically ill patients. The highest pain score reported among the 109 patients analyzed was  $5.59\pm2.72$ , while the lowest was  $2.13\pm2.03$  (p<0.001)<sup>28</sup>.

# Non-behavioral pain assessment tools

One study used three non-behavioral tools to detect pain after a nociceptive stimulus in critically ill patients unable to communicate. According to the pupillary pain index score, 44 patients (55%) had nociception while 23 (29%) and 18 (23%) had nociception according to the skin conductance algesimeter and the instantaneous analgesia nociception index, respectively<sup>40</sup>.

# Pain in the intensive care unit: a comparison of routine procedures

Three studies found no superiority for evoking pain among the painful procedures to which patients were exposed (mobilization with turning, endotracheal suction, placement and removal of drains, change of position and placement and removal of intravenous devices)<sup>17,10,20</sup>. In contrast, three studies found that some procedures could be considered more painful than others<sup>16,22,24</sup>. Thus, one of the studies identified higher mean BPS scores during patient repositioning (9.25±1.29), and lower scores during ophthalmic care (3.65±0.67)<sup>16</sup>. In addition, 23% of patients complained of tracheal aspirations (mean VAS 7.6), 19% of bladder tube insertion (mean VAS 6.5), 14% of team mobilizations (mean VAS 6.2), 14% of arterial punctures (mean VAS 6), 17% of venous punctures (mean VAS 4.5); other cases accounted for 11%<sup>22</sup>. One study found that the procedures associated with a higher perception of pain (ESAS scale) included endotracheal suction, endotracheal and nasogastric tubes, MV, arterial puncture and changing position in bed<sup>24</sup>.

# PAIN AND ITS ASSOCIATION WITH CLINICAL OUTCOMES

# Mechanical ventilation time

The implementation of a pain management algorithm resulted in shorter MV times in most of the included studies<sup>18,23,29,31-34,43</sup>. It is worth noting that this reduction in MV time varied significantly from 45.5 hours<sup>31</sup> to 55 hours<sup>18,29</sup>. In this sense, a prospective cohort compared the results of patients who were assessed for pain (BPS, VAS, NRS, Harris Scale, Verbal Descriptor Scale) with those of non-assessed patients<sup>32</sup>. The routinely assessed group had shorter MV duration (8 vs. 11 days; p<0.01). In addition, pain assessment was not significantly associated with lower chances of weaning from the ventilator (OR 1.40; 95% CI, 1.00 -1.98)32. When data before and after the implementation of protocols for the systematic management of analgesia, sedation and delirium<sup>34</sup> were evaluated, a reduction in MV time of an average of 1.58 days was identified<sup>34</sup>.

Another study included in this review analyzed 79 polytraumatized patients before and after the implementation of an acute pain quality management system<sup>43</sup>. In its results, the duration of invasive ventilation was lower (p=0.014) in the group after implementation of the intervention<sup>43</sup>.

On the other hand, one study compared the results of patients who received adequate pain monitoring (NRS and CPOT) with those who did not<sup>19</sup>. The duration of MV for the two groups was not statistically different<sup>19</sup>. This finding corroborates the findings of another study, which observed that critically ill patients in two ICUs, one cardiovascular and the other surgical-trauma<sup>37</sup>, showed no difference in MV duration before and after the implementation of systematic pain assessment by CPOT<sup>37</sup>. This was also observed in a study which found no clinically significant change in MV duration after the incorporation of pain assessment using the BPS scale in an adult ICU<sup>38</sup>.

These findings are in line with what was observed in a study on the impact of CPOT implementation on pain management and clinical outcomes in trauma ICU patients<sup>33</sup>. No statistical difference was found in MV duration between the 2 groups, however it was observed that almost half of the patients in the pre-implementation group (n=7) were ventilated for more than 96 hours, compared to only 4 patients in the post-implementation group<sup>33</sup>.

It is worth noting that one of the abstracts (banner presentation) included in this review analyzed data from critically ill patients before and after the implementation of a protocol to assess pain (Wong-Baker Faces and CPOT), agitation and delirium<sup>42</sup>. The average percentage of ventilator days was significantly higher in the group after implementation of the assessment protocol (80.4 vs 59.7, p<0.001)<sup>42</sup>.

## Time in the intensive care unit

It should be noted that most of the studies included in this review showed a significant reduction in the length of ICU stay after the implementation of systematic pain assessment. Thus, it was observed that in the intervention group there was a shorter ICU stay in different studies: median 2.6 days vs. 3.0 days, p= $0.04^{29}$  (pre vs. post BPS, BPS-NI and NRS), 211.5 ± 164.3 hours vs. 160.7 ± 125.7 hours, p= $0.038^{31}$  (pre vs. post CPOT), 18 vs.13 days; p< $0.01^{32}$  (pre vs. post BPS, EAV, NRS). ICU length of stay decreased from 6.3 to 5.35 days and hospitalization from 55 to 27 days after NRS implementation<sup>34</sup>. In this sense, one of the included studies explored the impact of CPOT implementation on pain management and identified a halving of ICU length of stay after CPOT implementation<sup>33</sup>. In line with this, one study observed a reduction in ICU length of stay (p=0.048) following the implementation of a pain management system  $^{43}$ .

In contrast to what has been shown so far, one study measured the impact of implementing systematic pain assessment in ICU patients (NRS and BPS)<sup>18</sup> and found no significant difference in the average length of ICU stay between the two groups<sup>18</sup>. These findings are in line with those of another study, which looked at critically ill patients before and after pain assessment using BPS<sup>38</sup>. ICU length of stay was similar in the two groups: 2.3 days (1.2-5.7) pre-implementation *versus* 2.6 days (1.1-6.8) post-implementation (z=1.3; p=0.18)<sup>38</sup>. Another selected retrospective study analyzed mechanically ventilated patients for more than 24 hours and found that the time spent in ICU was 9 days (4-17) in the group with BPS>5, compared to 6 days (4-12) in the control group (BPS≤5)<sup>23</sup>.

### Agitation

In different studies that measured the impact of implementing a pain management algorithm, patients in the intervention group had fewer agitation events (3% *versus* 6%, p=0.02, BPS and NRS)<sup>29</sup>. Similar results were observed in a study that identified a significantly lower incidence of agitation (RASS>1) and severe agitation (RASS>2) in the intervention group (systematic pain assessment with BPS and NRS) when compared to the control group: 29 vs. 12% (p. 002) and 18 vs. 5% (p. 002), respectively<sup>18</sup>.

In contrast, only one study found no significant difference in the incidence of agitation before and after the implementation of protocols for the systematic management of analgesia (NRS), sedation and delirium<sup>34</sup>.

### Sedation

A retrospective study compared patient outcomes before and after the implementation of a pain assessment/analgesia and sedation management protocol in an ICU<sup>31</sup>. Patients in "post" group had a lighter overall level of sedation than those in the pre-implementation group (CPOT). The median RASS during MV was 1.32 points higher in the post-implementation group, suggesting that the use of the pain assessment/analgesia management protocol was correlated with lighter overall levels of sedation (median RASS, -2.57 vs. -1.25, P=0.001)<sup>31</sup>. In contrast, another study found no significant difference in sedation levels before and after the implementation of protocols for the systematic management of pain (NRS), sedation and delirium<sup>34</sup>.

### Mortality

The use of behavioral pain assessment scales in ICU (NRS/ BPS) was associated with a reduction in mortality (OR [pain] = 0.365 [95% CI: 0.147-0.866], p = 0.022; OR [TISS - therapeutic intervention score system] = 1.137 [95% CI: 1.016-1.279], p = 0.026; OR [delirium] = 0.451 [95% CI: 0.220-0.924])<sup>30</sup>. In this respect, a prospective study evaluated a group of patients with adequate pain treatment and another with inadequate treatment (pain monitoring using NRS and CPOT)<sup>19</sup>. In the results, the ICU mortality rate was five (12.5%) for the inadequate treatment group and three (3.9%) for the adequate treatment group<sup>19</sup>.

Corroborating these findings, a study collected data from patients in an adult ICU before and after the implementation of protocols for the systematic management of analgesia (NRS), sedation and delirium<sup>34</sup>. The risk of 30-day mortality was 29.4% and 22.9% in the pre- and post-implementation cohorts, respectively<sup>34</sup>. Additionally, a retrospective study analyzed adult patients who received MV for more than 24 hours in ICU. The hospital mortality rate was 30% in the pain event group (BPS>5) and 9.9% in the control group (BPS  $\leq$ 5)<sup>23</sup>. The pain event group also had a 2.59 times higher risk of death<sup>23</sup>.

Unlike what was observed in the aforementioned studies, other studies analyzed patients before and after the implementation of an analgesia protocol<sup>31</sup> and systematic pain

assessment (NRS and BPS)<sup>18</sup>, and none of them found significant differences in mortality rates between the groups (protocol *versus* no protocol).

### Delirium

One study evaluated ICU patients before and after the implementation of protocols for the systematic management of analgesia, sedation and delirium<sup>34</sup>. The number of patients presenting subsyndromic delirium was substantially lower in the post-implementation group (NRS), but delirium rates were similar (34.7% pre vs. 34.2% post). In contrast, another study analyzed critically ill patients before and after an assessment protocol implementation (Wong-baker and CPOT) for pain, agitation and delirium, and identified that delirium was more significant in the post group (82.1% vs. 0.85%, p<0.001)<sup>42</sup>.

Table 1. Measuring instruments and incidence of pain in intensive care unit patients

Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Chanques et al. <sup>7</sup>	230 clinical and surgical patients, median age (58 [50 -70]. 153 men.	France	A BPS score>5 or NRS>3 indicates pain.	The incidence of pain was 51%, with no significant difference bet- ween ST group and M group (52% vs. 50%; p- 0.78).	Trauma-surgical patients: The site of the injury is the main cause of pain at rest (present in 49%). Clinical patients: the back and limbs were the main causes of pain at rest (41%). The intensity of pain in clinical ICU patients is significantly higher than in surgi- cal trauma patients.
Everingham et al. <sup>15</sup>	Patients admitted to the ICU requiring MV and physiotherapy, 49 analyzed, NR, NR.	Finland	A BPS score≥ 4 indicates pain.	98% of patients felt pain during physiotherapy.	
Ayarah <sup>16</sup>	Mechanically ventilated Jordanian patients, 247 analyzed, 64 (18-88) years old, 189 men.	Jordan	A BPS score>3 indi- cates pain.	33.2% of the patients had pain at rest and 89.9% during the proce- dures. The overall BPS score during the procedure was 6.34±2.36. The pain score during the procedure was higher than the average pre- -procedure pain score.	The highest mean pain scores were observed during repositio- ning $(9.25\pm1.29)$ and the lowest scores were observed in patients who received ophthalmic care $(3.65\pm0.67)$ .
Robleda et al. <sup>17</sup>	Sedated critically ill pa- tients on MV, 70 analy- zed, 71 (62-79) years old, 45 men.	Spain	A BPS score>3 indicates pain and a score BPS≥5 indicates pain.	Pain behavior was observed in 94% of the procedures evaluated. In resting conditions, 61% of patients felt pain and 33% experienced significant pain. In 86% of the procedures, pain was scored as significant.	There were no significant differences in the BPS score between mobilization with a swivel and endotracheal suction (6 [5-8] vs. 7 [6-8]; $p= 0.146$ , respectively).
Chanques et al. <sup>18</sup>	Patients who stayed >24 hours in the ICU, 230 analyzed, 59 (48- 71) years old, 89 men.	France	Pain= BPS>5 or a level NRS>3. Severe pain=BPS>7 or an NRS level>6.	The incidence of pain and severe pain in the intervention group was 42% (p=0.002) and 16% (p=0.001), respectively.	
Damico et al. <sup>10</sup>	126 surgical and 117 non-surgical ICU pa- tients, 243 analyzed. Surgical: mean age 58.4±13.3, range 39-85 years, 78 men; Non- surgical: 55.3 (+- 15.6) range 24-86 years, 69 men.	Italy	Pain = NRS or CPOT > 3. Severe pain = NRS of 8-10 or CPOT of 6-8. Pain at rest = NRS or CPOT > 3.	NRS score > 7 or CPOT > 6 was re- corded in 10.3% of patients. 39.5% experienced at least one epi- sode of pain, either at rest or during procedures (RR = 1.7, CI = 1.2 -2.4; p = 0.0013); 9.5% had pain both at rest and during procedures. Pain at rest was detected in 27.6% of patients and during procedures in 36.1%.	The intensity of pain in surgical ICU patients is no different from that of non-surgical patients. Surgical patients had an increased risk of experiencing pain during only sedation administered without analgesia compared to non-surgical patients (RR = 5.6, CI = 3.2-9.9; p <0.001). No procedure was found to be more nocicartive than the others ( $n=0.23$ )

Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Thikom et al. <sup>19</sup>	Critically ill ventilated surgical patients, 118 analyzed, NR, NR.	Thailand	The cut-off point for inadequate treat- ment of is an NRS score>3 or a CPOT score>2 while the cut-off point for severe pain is an NRS score>6 or a CPOT score>5 at any assessment point.	33.8% of patients experienced inadequate pain management at rest and 28.8% during bed baths. Twenty-four (20.3%) experienced inadequate pain management both at rest and during bed baths. Of those who experienced inade- quate pain control at rest, the me- dian score (IQR) for the NRS was 5 (4.75, 5) and for the CPOT was 3 (3, 5). The incidence of severe pain at rest was 5.9%.	Overtreatment was found in two (1.7%) patients and their CPOT scores were each zero. Of the total of 708 evaluations, NRS was used as an instrument in 495 (69.9%) evaluations, while CPOT was used in 213 (30.0%). Of the 118 patients, 44 were assessed with NRS only, 17 were assessed with CPOT only and 57 were assessed with both NRS and CPOT (NRS 4 [1, 5], CPOT 2 [1, 5]).
López- Lopez et al. <sup>20</sup>	Non-communicative patients with severe trauma, 124 analyzed, mean age 45.93 years (SD=16.43), 96 men.	Spain	Behavioral Indica- tors of Pain Scale (ESCID) zero: No pain; 1-3: Mild to moderate pain; 4-6: Moderate to severe pain. to moderate pain; 4-6: moderate to se- vere pain; >6: very severe pain.	When undergoing painful pro- cedures on different evaluation days, patients showed an increa- se in pain scores during the appli- cation of the procedures in rela- tion to baseline measurements and those taken after the proce- dure. However, no increases in pain levels were observed when patients underwent the painless procedure at any of the three dif- ferent measurement times.	Aspiration and tracheal mobili- zation showed the same levels of pain at the three assessment times.
Olsen et al, <sup>21</sup>	Adult ICU patients from three units, 285 analy- zed, mean age 58.9 years (SD = 18.5), 191 men.	Norway	Pain is defined as NRS> 3, BPS>5 or BPS- -NI>5.	When pain was assessed regularly with pain assessment instruments, 10% of patients felt pain at rest and 27% felt pain during rotation. During the first 6 days, pain occurred in 5%-31.1% of patients. However, more patients had pain during rotation compared to rest (27.4% vs. 10.1%, $p < 0.001$ ). The first day was the day when most patients (13.4%) were in pain at rest. During the rotation, day 4 was the day when most patients (31%) felt pain.	Both at rest and during turning, the proportions of patients with pain were significantly higher for patients able to self-report pain, compared to patients not able to self-report pain (at rest, 20.8% vs. $3.1\%$ , p < 0.001; du- ring turning, $39.1\%$ vs. $21.5\%$ , p < 0.001).
Cazorla et al. <sup>22</sup>	Patients admitted to intensive care who had been mechani- cally ventilated for more than 24 hours, 70 analyzed, mean age 56.3 (19 to 91 years), 47.36% men.	France	VAS and a standar- dized questionnaire with 9 items and 20 questions.	Pain was present in 47% of pa- tients.	Painful phenomena were dis- tributed as follows in the study population, according to their frequency and intensity: 23% of patients complained of tra- cheal aspirations (mean VAS 7.6), 19% of bladder tube in- sertion (mean VAS 6.5), 14% of team mobilizations (mean VAS 6.2), 14% of arterial punctures (mean VAS 6), 17% of venous punctures (mean VAS 4.5), 11% of others.
Yamashita et al. <sup>23</sup>	Adult patients who re- ceived MV for more than 24 hours in the ICU, 151 analyzed, mean age 68.5±12.9 years, 66.9% men.	Japan	Pain event is defined as BPS > 5.	The median of the highest BPS was 4.0 (range 3.0 to 5.0). The overall incidence of patients with BPS $> 5$ was 19.9% (n =30).	

Continue...

Table 1. Measuring instruments an	d incidence of pain in intensive	care unit patients - continuation

Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Nelson et al. <sup>24</sup>	Cancer patients treated in a medical ICU, 100 analyzed, mean age 65±14 (27-104) years, 65 men.	United States	Edmonton Symptom Assessment Scale (ESAS)	The majority of patients reported little or no pain or discomfort with most of the procedures.	Procedures associated with greater pain or discomfort for responders include endotra- cheal suction, endotracheal and nasogastric tubes, MV, arterial puncture and turning.
Shan et al. <sup>25</sup>	Adult patients with brain damage under- going MV, 400 analy- zed, median age 50 (37-62) years, 235 men.	China	CPOT and BIS were combined into 2 pat- terns to indicate pain as follows: CPOT $\geq$ 2 or BIS $\geq$ 88 after stimulation and also CPOT $\geq$ 2 and BIS $\geq$ 88 after stimulation.	There were 192 (90%) patients who reported pain after aspiration, while only 38 (17%) reported pain after gentle touch. In all patients, with or without self-reported pain, CPOT and BIS increased significantly after aspira- tion (p<.001), while they remained unchanged after gentle touch (p ranging from 0.06 to 0.14).	No significant differences were found in pre-stimulation CPOT and BIS values between the 2 stimulations (p ranging from 0.74 to 0.82), but all post-stimulation values were significantly higher after suction than after touch (all p<.001).
López- Lopez et al. <sup>26</sup>	Patients with moderate to severe head trauma, 27 analyzed, median age 38 (20-86) (IR 66) years, 18 men.	Spain	ESCID scale: ranges from zero to 10. 0 no pain; 1-3 Mild/mode- rate pain; 4-6 Mode- rate/severe pain; > 6 Very severe pain.	The average pain on aspiration of tracheal secretions, with a 95% CI over the 3 days of assessment, was $3.18 \pm 2.6$ (CI: $1.84-4.52$ ) on day 1, $2.59 \pm 2$ (CI: $1.56-3.62$ ) on day 3 and $3.9 \pm 2.3$ (CI: $2.76-5.13$ ) on day 6. In relation to the non-painful stimulus: day 1 $0.52 \pm 1.6$ ( $0.34-1.40$ ], day 3: $0.00$ and day 6: $0.29 \pm 0.4$ ( $0.05-0.53$ ).	When comparing the pain avera- ges obtained on the 3 evaluation days: days 1, 3 and 6, no sta- tistically significant differences ( $p = 0.243$ ) were found between the pain levels on the evaluation days. Regarding the pain score, depen- ding on whether or not surgery had been performed, no differen- ces were found.
lto et al. <sup>27</sup>	Patients on MV after surgery, 34 analyzed, median age 74 years (IQR=13.75), 20 men.	Japan	Increase > 2 in BPS: pain; CPOT>5: significant pain.	The average BPS scores were 3.82 at rest and 5.59 when turning. The average CPOT scores were 1.17 at rest and 3.18 when turning.	
López-Alfaro et al. <sup>28</sup>	Post-surgical ICU pa- tients, 109 analyzed, 62.92±15.54 years old, 66 men.	Spain	NRS: 0 (no pain) to 10 (maximum pain); Mild-moderate pain: 0 to 3. Moderate-se- vere pain: 4 to 6. Se- vere pain: ≥7; Ques- tionnaire IPO questionnaire to find out patients' subjective percep- tion of pain.	The highest pain score recorded was 4.47 $\pm 2.75$ , while the lowest was 0.69 $\pm 1.25$ . However, the highest and lowest pain scores reported by the patients were 5.59 $\pm 2.72$ and 2.13 $\pm 2.03$ , which showed significant differences (p<0.001).	Patients who reported that the pain made them very anxious or helpless were the ones who obtained the highest scores in the perception of greater pain, 7.35 $\pm$ 1.98 7.44 $\pm$ 1.85, respectively, with statistically significant differences (p = 0.001; p < 0.001). The highest pain scores were obtained in thoracic and cardiac surgery patients.
Rose et al. <sup>37</sup>	Critically ill patients from two ICUs. CPOT pre-implementation group: 189 analyzed, 133 men. Post-imple- mentation group: 184 analyzed, 133 men.	Canada	CPOT ≥ 3	For patients in the cardiovascu- lar ICU, the median CPOT was 0 (IQR 0-2), and 28 of the 274 do- cumented scores (10%) were 3 or more, indicating the presence of pain. For surgical and trauma ICU patients, the median score was 4 (IQR, 1-5), and 104 of the 693 sco- res (15%) were 3 or more.	
Elseoud et al. <sup>39</sup>	Adult critically ill pa- tients from two univer- sity hospitals in Finland, 711 analyzed, NR, NR.	Finland	Numeric Rating Scale (NRS) and Verbal Ra- ting Scale (VRS) used in communicative patients, and Critical Care Pain Observa- tion Tool (CPOT) in non-communicative patients (NRS≥4/ CPOT≥3/VRS≥mo- derate pain).	76% of the patients had moderate to severe pain during at least one of the 10 days of follow-up in ICU.	Age under 64, female gender and a history of chronic pain were as- sociated with a greater number of days in moderate to severe pain.

	-			-	
Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Fratino et al. <sup>40</sup>	Adult ICU patients, un- conscious (GCS < 9, with motor response < 5) and on MV, 80 analy- zed, 62 [53-71] years old, 59 men.	Belgium	Pupillary pain index (PPI) > 4, number of skin conductance fluctuations (NSCF) per second > 0.27 fluctuations/sec and instantaneous analgesia and noci- ception index IANI < 50 indicating noci- ception.	According to the PPI assessment, 44 patients (55%) had nociception, while 23 (29%) and 18 (23%) had nociception according to the alge- simeter and IANI assessment, res- pectively.	Clinical pain assessment was carried out at the start of the study using BPS. Among the 56 patients who did not receive Neuromuscular Blocking Agents (NMBAs), BPS increased from 3 [3-3] to 3 [3-4] after stimulation (p<0.01).
Meehan et al. <sup>41</sup>	Patients from a car- diothoracic ICU, 101 analyzed. Retrospec- tive group (n=51), NR, NR. Prospective group (N=50), NR, NR.	United States	VAS and Pain Relief Satisfaction Ques- tionnaires	Patients in the prospective group received significantly more analge- sia. Pain intensity was moderate (4 or more on VAS).	Women had higher overall scores on VAS than men, 4.57 versus 3.70. Responses from the Pain Relief Satisfaction Questionnaire indicated that 96% of patients experienced effective pain con- trol in the thoracic ICU.
Santos Oliveira et al. <sup>44</sup>	Severe patients una- ble to verbalize their perception of pain, 67 analyzed, 56 (36-74) years old, 47 (70.1%) men.	Brazil	BPS>3 shows the presence of pain and ≥5 indicates signifi- cant pain.	Of the 201 observations, 70 (34.8%) patients had BPS score ≥5. In 91% of the observations during tracheal aspiration there was a BPS≥5.	
Wojnar- Gruszka et al. <sup>45</sup>	ICU patients under MV and sedated, 81 analyzed, mean age 63.1±17.21, 47 (58%) men.	Switzer- land	Pain was defined as BPS≥5 and CPOT≥3 scores	Signs of pain increased significantly (p<0.001) during interventions in patients on both scales. Signs of pain were observed in about 1/3 of the measurements.	Patients undergoing deep seda- tion showed fewer signs of pain (p<0.05).
Dinse et al.47	Non-communicative cri- tical patients, 247 analy- zed. Septic (n=120): 65 (+/- 14.8) years old, 62% male. Non-septics (n=127): 65 (+/= 15.1) years, 67% men.	Germany	BPS and NRS	Patients in the septic group had a mean BPS score of 3 (3 to 5), while the non-septic group had a mean BPS score of 3 (3 to 7).	

	Table 1. Measuring	instruments and ir	ncidence of pain	ι in intensive care ι	nit patients - continuation
--	--------------------	--------------------	------------------	-----------------------	-----------------------------

NR = not reported; BIS = Bispectral Index; BPS = Behavioral Pain Scale; BPS-NI = Behavioral Pain Scale in non-intubated patients; CPOT = Critical-Care Pain Observation Tool; ESCID = Behavioral Indicators of Pain Scale; VAS = Visual Analog Scale; ESAS = Edmonton Symptom Assessment Scale; GCS = Glasgow Coma Scale; IANI = Instantaneous Analgesia Nociception Index; IPO = International Pain Outcomes Questionnaire; NRS = Numeric Rating Scale; NSCF = Number of skin conductante fluctuations; PPI = Pupillary Pain Index Score; SCA = Skin Conductance Algesimeter; VRS = Verbal Rating Scale; ICU = intensive care unit; MV = mechanical ventilation.

Table 2. Main clinical outcomes reported by the selected studies

Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Olsen et al. <sup>29</sup>	ICU patients able to self-re- port or express pain beha- viors, 650 analyzed. Control group (n=252): mean age 52 (SD=± 20) years, 157 (62%) men. Intervention group (n=398): 60 (± 18), 265 (67%) men.	Norway	Pain events were de- fined as NRS scores >3 or BPS and BPS- -NI scores >5.	Disease severity was measu- red using the SAPS II score and agitation using the RASS scale.	Patients in the control group had shorter MV times, shorter ICU stays, fewer agitation events and significantly lower disease seve- rity.
Radtke et al. <sup>30</sup>	Patients with 3 or more days of hospitalization, 619 analy- zed. Pre-training group (n= 241): average age 54 (SD=20) years, 37 (60%) men. Pos- t-training group (n=228): 52(SD=18) years, 26(49%) men. Follow-up period group (n=150): 57(SD=19) years, 29(64%) men.	Germany	NRS was used to monitor pain in non- -intubated patients. For sedated patients, the BPS scale was used.	The RASS scale was used to monitor sedation. DDS (De- lirium Detection Score) was used to monitor delirium.	In ICU 2, the NRS/BPS measure was associated with a reduction in mortality.

Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Faust et al. <sup>31</sup>	Pre-implementation group: 65 adult MV patients, me- dian age 65 (55-73) years, 46 (70.7%) men. Post-implementation group: 79 adult MV patients, 63 (54.5 - 75) years old, 40 (50.6%) men.	USA	CPOT	SAPS II was calculated in all patients during the first 24 hours of MV to analyze the severity of the illness. Agita- tion was assessed by RASS.	The post-implementation group had a lower overall level of seda- tion, shorter MV time and shorter ICU stay. Mortality rates did not differ between the 2 groups.
Chanques et al. <sup>18</sup>	Patients who stayed >24 hou- rs in the ICU, 230 analyzed. Control group (n = 100): me- dian of age 58 (51 - 74) years, 64 (64%) men. Intervention group (n = 130): 59 (48-71) years, 89 (62%) men.	France	A pain event was de- fined by a BPS score > 5 or an NRS level > 3. Severe pain events were defined by a BPS score > 7 or an NRS level > 6.	Agitation was measured using the RASS scale. A agitation event was defined by RASS level >1. Severe agitation events were defined by RASS level > 2.	The intervention group showed a marked reduction in the du- ration of MV and in the rate of hospital-acquired infections. The incidence of agitation and severe agitation was significantly lower in the intervention group. There was no significant difference in the average length of stay and mortality in the ICU between the two groups.
Thikom et al. <sup>19</sup>	Critically ill surgical patients, 116 analyzed. Inadequate pain management group (n=40): mean age 63 (SD=±13.4) years, 21 (52.5%) men. Adequate pain treatment group (n=76): 67.2(SD=±19.7) years, 39 (51.3%) men.	Thailand	The cut-off point for inadequate pain treatment is an NRS score > 3 or a CPOT score > 2, while the cut-off point for se- vere pain is an NRS score > 6 or a CPOT score > 5 at any as- sessment point.	Severity of illness: APACHE II score; Agitation: Richmond Agitation-Sedation Scale (RASS).	The mortality rate was higher for the inadequate pain treatment group. The length of ICU stay, duration of MV and types of complications after 30 days were not statisti- cally different between the two groups.
Payen et al. <sup>32</sup>	Mechanically ventilated pa- tients, 1,144 analyzed. Group with pain assessment on day 2 of hospitalization (n=513): median age 59 (47-73) years, 429 (84%) men. Group wi- thout pain assessment on day 2 of hospitalization (n=631): 62 (46-74) years, 497 (79%) men.	France	BPS (49% of pa- tients), Harris Scale (19% of patients), VAS (14% of pa- tients), verbal des- criptor scale (12% of patients) and NRS (5% of patients).	SAPS II and SOFA were used to assess the severity of the illness. The Ramsay Scale, RASS, the Sedation-Agitation Scale and other instruments were used to assess sedation.	Patients assessed for pain on day 2 had a shorter duration of MV and a shorter ICU stay. Pain assessment was associated with greater chances of weaning from the ventilator and discharge from the ICU. No significant difference in mor- tality was found between the two groups of patients.
Arbour et al. <sup>33</sup>	Trauma ICU patients, 30 analyzed. Pre-implementation group (n=15): average age 54.53 (21.97) years, 14 men. Post-implementation group (n=15): 41 (21.99) years, 10 men.	Canada	Pre-implementation group: 2 or more behavioral indicators associated with pain. Post-implementation group: CPOT>2.	APACHE II score. When the APACHE II score was not available in the medical re- cord, it was calculated by the principal investigator based on vital signs and laboratory results from the first 24 hours after implementation.	Almost half of the patients in the pre-implementation group $(n = 7)$ were ventilated for more than 96 hours, compared to only 4 patients in the post-implementation group. The length of ICU stay seemed to halve after CPOT implantation.
Skrobik et al. <sup>34</sup>	Patients admitted to an adult ICU during 2 periods (pre- and post-implementation of the protocol), 1,214 analyzed. Pre group (n=610): NR, NR. Post group (n=604): NR, NR.	Canada	A numerical scale of zero to 10 points was used to assess pain.	RASS scale: comatose (-5), combative (+4); Intensive Care Delirium Screening Checklist (ICDSC): clinical delirium ( $\geq$ 4), subsyndromic delirium (> 0 and < 3) and ab- sence of delirium (0).	The occurrence of subsyndro- mic delirium was substantially lower in the post-implementation group, but delirium rates were similar between the two groups. There was a reduction in the risk of mortality, length of stay and MV time in the post-implemen- tation group. The average occur- rence of agitation did not differ between the cohorts.
Yamashita et al. <sup>23</sup>	Patients in MV>24 h, 151 analyzed, mean age $68.5 \pm 12.9$ years, $66.9\%$ male.	Japan	The pain event is de- fined as BPS>5.	Severity of illness: APACHE II score.	The mortality rate and duration of MV were significantly higher in the pain event group compared to the control group. The length of stay in the ICU did not differ between the groups.

Fable 2. Main clinica	al outcomes repor	ted by the selecte	d studies – continuation
-----------------------	-------------------	--------------------	--------------------------

Authors	Patient (diagnosis, number analyzed, age, gender)	Country	Pain measurement	Pain incidence	Additional results
Rose et al. <sup>37</sup>	Critically ill patients from two ICU, one cardiovascular (CVICU) and the other sur- gical-trauma (CRCU). CPOT pre-implementation group: 189 analyzed, 133 men. Pos- t-implementation group: 184 analyzed, 133 men.	Canada	CPOT ≥ 3	SOFA score.	In CRCU, decreased maximum SOFA scores were associated with increased documentation. In CVICU, the estimated me- dian length of ICU stay de- creased from 2.0 (IQR, 1.0- 5.0) days to 1.8 (IQR, 1.0-3.0) days (p=0.007); no difference was found in CRCU (median, 5.9; IQR, 2.9-13.6 days before and median, 7.0; IQR, 5.0-14.7 days after).
Williams et al. <sup>38</sup>	Patient on MV for at least 6 hours. Pre-implementa- tion group (n=369): 56 (39- 70) years old, 58% male. Post-implementation group (n=400): 56 (39-71) years, 67% male.	Colombia	BPS scale	APACHE II score.	ICU length of stay was similar in the 2 groups: 2.3 (1.2-5.7) days before implementation versus 2.6 (1.1-6.8) days af- ter implementation (z=1.3; p= 0.18). No clinically significant change in the duration of MV occurred after the introduction of the scales (median 24 hou- rs in the before group versus 28 hours in the after group; z= -1.5; p=0.13). The worst mean APACHE II score in the first 24 hours (t= -1.26; p=0.21) diffe- red little between the groups.
Onyenekwe et al. <sup>42</sup>	Patients intubated in an adult ICU, 1,673 analyzed. Pre- -protocol group (n=1,057), NR, NR. Post-protocol group (n=616), NR, NR.	NR	VAS or Wong-Baker FACES pain rating scale and CPOT.	Delirium was assessed with the Confusion Assessment Method for the ICU (CA- MICU).	The average percentage of ventilator days in which pain was assessed with any tool was significantly higher in the post group (80.4 vs, 59.7, p < 0.001). Delirium was also significantly more assessed in the post group (82.1% vs, 0.85%, p < 0.001).
Bãhmer et al. <sup>43</sup>	Polytraumatized patients, 79 analyzed, NR, NR.	Germany	NR		In the post-implementation group of the acute pain management system, the duration of invasive ventilation was shorter ( $p=0.014$ ) and there was a reduction in the length of stay in ICU ( $p=0.048$ ). The average pain intensity in the first 8 days was also higher in this group.

NR = not reported; APACHE II = Acute Physiology and Chronic Health Evaluation II; BPS = Behavioral Pain Scale; BPS-NI = Behavioral Pain Scale in non-intubated patients; CPOT = Critical Care Pain Observation Tool; NRS = Numeric Rating Scale; RASS = Richard Agitation-Sedation Scale; SAPS II = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment; ICU = intensive care unit, MV ; mechanical ventilation.

### DISCUSSION

This study found that the incidence of pain in critically ill patients was significant, which suggests that the assessment of this variable is still neglected in highly complex environments. Between 10.1% and 61% of patients reported pain at rest, and between 27.4% and 94% reported pain during procedures. It was also found that the incidence of pain varied widely between the studies. There are several possible explanations for the large discrepancies, but it is likely that these differences are related to the profile of the populations studied and the types of procedures that induce pain. It should be noted that the present research included studies with populations of critically ill patients, however one of them did not restrict its sample to ICU patients, but also included patients on MV in the emergency room or red zone<sup>44</sup>.

This review found that some routine ICU procedures, such as endotracheal suction and decubitus changes, were analyzed as highly painful for patients. However, it is unclear whether the intensity of pain varies according to the procedure and, therefore, which procedure is the most painful.

This study also found that BPS was the most commonly used tool for measuring pain in non-communicative patients. Of the 32 studies included, 46.8% used this tool. This observation is similar to that reported by other studies, which showed that BPS is the most commonly used scale in non-responsive patients because it is highly accurate and easy to apply in critically ill patients<sup>37,38</sup>. Only one study included in this review chose to use non-behavioral tools to measure pain, considering that scales such as BPS and CPOT could underestimate nociception or be unreliable in patients unable to move, with brain damage or in whom pain can produce atypical reactions<sup>40</sup>. However, these non-behavioral tools still need further validation studies.

This review observed positive effects on the clinical outcomes of patients with adequate pain detection and management. Several studies analyzed reinforced this association, revealing that patients submitted to pain assessment protocols had better prognoses when compared to patients not submitted to these tools<sup>18,19,23,29-34,43</sup>. Only one study included in this review contradicted this trend<sup>42</sup>. In their results, MV time and delirium rates increased after the use of pain assessment protocols<sup>42</sup>.

Furthermore, the impact of pain assessment on patient outcomes had already been investigated in a systematic review published in 2015, which revealed data that seemed to indicate an association between pain assessment and improved clinical outcomes<sup>2</sup>. The present review, in turn, included a greater number of studies and went further in analyzing the incidence of pain in ICUs.

The limitations of this systematic review stem from the search strategy, which was restricted to the Pubmed and Embase databases, and the inherent limitations of the studies identified. The risk of bias of the studies included in this review was not assessed. In addition, it should be pointed out that the variation in the methods used to assess pain in ICU and the use of different cut-off points to identify this variable among the studies included may lead to a wide variation in pain incidence rates. At the same time, the scarcity of studies on this subject in Latin America is noteworthy, as only two studies included in this review were carried out in South American countries.

### CONCLUSION

The findings of this study highlighted that the BPS behavioral scale and the NRS self-report scale were the most commonly used to measure pain in ICU patients. Additionally, it was observed that the CPOT behavioral scale appeared as the second most used pain measurement instrument for non-verbal critical patients. BPS scores >3 or an increase of 2 points on this instrument were often considered to indicate the presence of pain in mechanically ventilated patients. A BPS score>5 was characterized as the presence of severe pain in the different samples studied. Considering all the studies included in this review, the presence of pain (at rest) ranged from 33.2% to 98% in the populations studied, highlighting that pain should be considered a prevalent problem in ICUs. In addition, it should be noted that several common procedures in ICU routines were considered to be painful procedures in the different studies (mobilization with turning, endotracheal suction, implementation and removal of drains and intravenous devices, and decubitus changes) and that some studies pointed to a more significant presence of pain in specific procedures, such as suction and insertion of drains/probes, compared to other procedures.

Finally, it should be noted that the identification and management of pain is a realistic goal and depends on the initial assessment. In the light of current evidence, it is possible to highlight, considering the studies included in this review, that the presence of pain in critically ill patients may be associated with worse clinical outcomes, such as increased mortality, length of stay and MV time. Thus, proper pain management in critically ill patients seems to have a positive impact (based on data from observational studies) on reducing MV time, length of hospital stay and mortality. This highlights the need for robust randomized controlled trials to establish a causal relationship between pain management in ICU and clinical and functional outcomes.

# **AUTHORS' CONTRIBUTIONS**

#### Iura Gonzalez Alves

Data Collection, Conceptualization, Resource Management, Project Management, Research, Methodology, Writing - Preparation of the Original, Writing - Review and Editing, Supervision, Validation, Visualization

### Rafaela Dias Bezerra

Data Collection, Research, Methodology, Writing - Preparation of the Original, Writing - Review and Editing, Visualization

# Bianca Borges de Brito

Data Collection, Research, Methodology, Writing - Review and Editing, Visualization

### REFERENCES

- Cade CH. Clinical tools for the assessment of pain in sedated critically ill adults. Nurs Crit Care. 2008;13(6):288-97.
- Georgiou E, Hadjibalassi M, Lambrinou E, Andreou P, Papathanassoglou ED. The impact of pain assessment on critically ill patients' outcomes: a systematic review. Biomed Res Int. 2015;2015:503830.
- Abdullayev R, Uludag O, Celik B. Analgesia nociception index: assessment of acute postoperative pain. Braz J Anesthesiol. 2019;69(4):396-402.
- Sakata RK. Analgesia e sedação em unidade de terapia intensiva. Rev Bras Anestesiol. 2010;60(6):653-8.
- Queiroz Sierra A, Ayres Ximenes Ponte Colaço M, Martins Soares Cruz B. Avaliação da dor em UTI adulta no Brasil através da "Behavioral Pain Scale": revisão sistemática. 43ª ed. Vol. 14. Rev Inspirar. 2017.
- Ribeiro AS, Santos JPN, Araújo DC, Santos ES, Magalhães FB, Pinheiro FG. Dor, agitação e sedoanalgesia em pacientes críticos internados em unidade de terapia intensiva. Farmacologia Aplicada à Enfermagem: Aspectos Teóricos e Práticos. 2020;27:74-86.
- Chanques G, Sebbane M, Barbotte E, Viel E, Eledjam JJ, Jaber S. A prospective study of pain at rest: incidence and characteristics of an unrecognized symptom in surgical and trauma versus medical intensive care unit patients. Anesthesiology. 2007;107(5):858-60.
- Kotfis K, Zegan-Barańska M, Szydłowski Ł, Żukowski M, Ely WE. Methods of pain assessment in adult intensive care unit patients - Polish version of the CPOT (Critical Care Pain Observation Tool) and BPS (Behavioral Pain Scale). Anesthesiol Intensive Ther. 2017;49(1):66-72.
- Pinheiro ARPQ, Marques RMD. Behavioral Pain Scale and Critical Care Pain Observation Tool for pain evaluation in orotracheally tubed critical patients. A systematic review of the literature. Rev Bras Ter Intensiva. 2019;31(4):571-81.
- Damico V, Macchi G, Murano L, Forastieri Molinari A. Incidence of pain at rest and during nursing procedures in ICU patients: a longitudinal observational study. Ann Ig. 2020;32(4):407-18.
- Latorre Marco I, Solís Muñoz M, Falero Ruiz T, Larrasquitu Sánchez A, Romay Pérez AB, Millán Santos I. Validación de la escala de conductas indicadoras de dolor para valorar el dolor en pacientes críticos, no comunicativos y sometidos a ventilación mecánica: resultados del proyecto ESCID. Enferm Intensiva. 2011;22(1):2-12.

- López-López C, Arranz-Esteban A, Arias-Rivera S, Solís-Muñoz M, Pérez-Pérez T, Latorre-Marco I. Application of the Behavioural Indicators of Pain Scale in patients with traumatic brain injury. J Adv Nurs. 2020;76(7):1862-70.
- 13. Karcioglu O, Topacoglu H, Dikme O, Dikme O. A systematic review of the pain scales in adults: which to use? Am J Emerg Med. 2018;36(4):707-14.
- 14. JBI Manual for Evidence Synthesis. Aromataris E, Munn Z, editors. JBI; 2020.
- 15. Everingham K, Salisbury L, Lapinlampi P, Cornwall I, Frame F, Walsh T. Agitation
- and pain during physiotherapy in intensive care. Crit Care. 2010;14(Suppl 1):492.
  Ayasrah S. Care-related pain in critically III mechanically ventilated patients. Anaesth Intens Care. 2016;44(4):458-65.
- Robleda G, Roche-Campo F, Membrilla-Martínez L, Fernández-Lucio A, Villamor--Vázquez M, Merten A, Gich I, Mancebo J, Català-Puigbó E, Baños JE. Evaluación del dolor durante la movilización y la aspiración endotraqueal en pacientes críticos. Med Intensiva. 2016;40(2):96-104.
- Chanques G, Jaber S, Barbotte E, Violet S, Sebbane M, Perrigault PF, Mann C, Lefrant JY, Eledjam JJ. Impact of systematic evaluation of pain and agitation in an intensive care unit. Crit Care Med. 2006;34(6):1691-9.
- Thikom N, Thongsri R, Wongcharoenkit P, Khruamingmongkhon P, Wongtangman K. Incidence of inadequate pain treatment among ventilated, critically ill surgical patients in a Thai population. Pain Manag Nurs. 2021;22(3):336-42.
- López-López C, Pérez-Pérez T, Beneit-Montesinos JV, García-Klepzig JL, Martinez-Ureta MV, Murillo-Pérez MDA, Torrente-Vela SA, García-Iglesias M. Pain Assessment in Mechanically Ventilated, Noncommunicative Severe Trauma Patients. J Trauma Nurs. 2018;25(1):49-59.
- Olsen BF, Valeberg BT, Jacobsen M, Småstuen MC, Puntillo K, Rustøen T. Pain in intensive care unit patients-a longitudinal study. Nurs Open. 2020;8(1):224-31.
- Cazorla C, Cravoisy A, Gibot S, Nace L, Levy B, Bollaert PE. Perception par les patients de leur séjour en réanimation [Patients' perception of their experience in the intensive care unit]. Presse Med. 2007;36(2 Pt 1):211-6
- Yamashita A, Yamasaki M, Matsuyama H, Amaya F. Risk factors and prognosis of pain events during mechanical ventilation: a retrospective study. J Intensive Care. 2017;5:17.
- Nelson JE, Meier DE, Oei EJ, Nierman DM, Senzel RS, Manfredi PL, Davis SM, Morrison RS. Self-reported symptom experience of critically ill cancer patients receiving intensive care. Crit Care Med. 2001;29(2):277-82.
- Shan K, Cao W, Yuan Y, Hao JJ, Sun XM, He X, Li GY, Wang YM, Zhou JX. Use of the critical-care pain observation tool and the bispectral index for the detection of pain in brain-injured patients undergoing mechanical ventilation: A STROBE-compliant observational study. Medicine (Baltimore). 2018;97(22):e10985.
- 26. López-López C, Murillo-Pérez MA, Morales-Sánchez C, Torrente-Vela S, Orejana-Martín M, García-Iglesias M, Cuenca-Solanas M, Alted-López E. Valoración del dolor en la aspiración de secreciones traqueales en pacientes con traumatismo craneal mediante la Escala de conductas indicadoras de dolor (ESCID) [Pain assessment of tracheal suctioning on brain injury patients by pain behavioral indicator scale (ES-CID)]. Enferm Intensiva. 2014;25(3):114-21.
- Ito Y, Teruya K, Nakajima E. Evaluation of pain severity in critically ill patients on mechanical ventilation. Intensive Crit Care Nurs. 2022;68:103118.
- López-Alfaro MP, Echarte-Nuin I, Fernández-Sangil P, Moyano-Berardo BM, Goñi-Viguria R. Perception of pain in post-surgical patients in intensive care units. Enferm Intensiva. 2019.30(3):99-107.
- Olsen BF, Rustøen T, Sandvik L, Jacobsen M, Valeberg BT. Results of implementing a pain management algorithm in intensive care unit patients: The impact on pain assessment, length of stay, and duration of ventilation. J Crit Care. 2016;36:207-11.
- 30. Radtke FM, Heymann A, Franck M, Maechler F, Drews T, Luetz A, Nachtigall I, Wernecke KD, Spies CD. How to implement monitoring tools for sedation, pain and

delirium in the intensive care unit: an experimental cohort study. Intensive Care Med. 2012;38(12):1974-81.

- Faust AC, Rajan P, Sheperd LA, Alvarez CA, McCorstin P, Doebele RL. Impact of an analgesia-based sedation protocol on mechanically ventilated patients in a medical intensive care unit. anesthesia and analgesia. 2016;123(4):903-9.
- Payen JF, Bosson JL, Chanques G, Mantz J, Labarere J. Pain assessment is associated with decreased duration of mechanical ventilation in the intensive care unit. Anesthesiology. 2009;111(6):1308-16.
- Arbour C, Gélinas C, Michaud C. Impact of the implementation of the criticalcare pain observation tool (cpot) on pain management and clinical outcomes in mechanically ventilated trauma intensive care unit patients. J Trauma Nurs. 2011;18(1):52-60.
- Skrobik Y, Ahern S, Leblanc M, Marquis F, Awissi DK, Kavanagh BP. Protocolized intensive care unit management of analgesia, sedation, and delirium improves analgesia and subsyndromal delirium rates. Anesth Analg. 2010;111(2):451-63.
- 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(20):1471-7.
- Trogrlić Z, van der Jagt M, Bakker J, Balas MC, Ely EW, van der Voort PH, Ista E. A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes. Crit Care. 2015;19(1):157.
- Rose L, Haslam L, Dale C, Knechtel L, McGillion M. Behavioral pain assessment tool for critically ill adults unable to self-report pain. Am J Crit Care. 2013;22(3):246-55.
- Williams TA, Martin S, Leslie G, Thomas L, Leen T, Tamaliunas S, Lee KY, Dobb G. Duration of mechanical ventilation in an adult intensive care unit after introduction of sedation and pain scales. Am J Crit Care. 2008;17(4):349-56.
- 39. Elseoud WA. et al. Pain is a problem during critical care. In: 42º International Symposium on Intensive Care & Emergency Medicine. P093.40. Fratino S, Garré A, Garufi A, Hafdi S, Migliorino E, Stropeni S, Bogossian EG, Ndieugnou Djangang N, Albano G, Creteur J, Peluso L, Taccone FS. Evaluation of nociception in unconscious critically ill patients using a multimodal approach. Anaesth Crit Care Pain Med. 2023;42(2):101175.
- Meehan D, McRae M, Rourke D, Eisenring C, Imperial F. Analgesic administration, pain intensity, and patient satisfaction in cardiac surgical patients. Am J Crit Care. 1995;4(6):435-42.
- Onyeneke JC, Hanlon K, Peters M, Smoot CA, Jennings JH, Swiderek JL, Digiovine B. Introduction of sedation protocol for intubated patients in a medical intensive care unit. Am J Respir Crit Care Med 2018;197.
- 43. Böhmer AB, Mutert J, Poels M, Arends S, Lefering R, Gerbershagen MU, Wappler F, Joppich R. Pain intensity and treatment in patients with multiple trauma before and after implementation of a quality management system in acute pain therapy å€" a retrospective analysis. 2016;57:6-13.
- 44. Santos Oliveira L, Pimentel Macedo M, Silva S, Oliveira AP, Santos V. Pain assessment in critical patients using the Behavioral Pain Scale. BrJP. 2019;2(2):112-6.
- Wojnar-Gruszka K, Sega A, Płaszewska-Żywko L, Wojtan S, Potocka M, Kózka M. Pain Assessment with the BPS and CCPOT Behavioral Pain scales in mechanically ventilated patients requiring analgesia and sedation. Int J Environ Res Public Health. 2022;19(17):10894.
- Hora TC, Alves IG. Escalas para a avaliação da dor na unidade de terapia intensiva. Revisão sistemática. BrJP. 2020.3(3):263-74.
- Dinse CM, Bucher M, Burgdorff AM, Christel A, Flöther L. Pain management in surgical intensive care patients: a retrospective observational research. Medicine (Baltimore). 2022;101(46):e31297.