



## SPECIAL ARTICLE

# Recommendations of the Working Groups from the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) for the management of adult critically ill patients<sup>☆</sup>



A. Hernández-Tejedor<sup>a,\*</sup>, O. Peñuelas<sup>b,c</sup>, G. Sirgo Rodríguez<sup>d</sup>, J.A. Llompарт-Pou<sup>e</sup>, E. Palencia Herrejón<sup>f</sup>, A. Estella<sup>g</sup>, M.P. Fuset Cabanes<sup>h</sup>, M.A. Alcalá-Llorente<sup>i</sup>, P. Ramírez Galleymore<sup>h</sup>, B. Obón Azuara<sup>j</sup>, J.A. Lorente Balanza<sup>b,c</sup>, C. Vaquerizo Alonso<sup>k</sup>, M.A. Ballesteros Sanz<sup>l</sup>, M. García García<sup>m</sup>, J. Caballero López<sup>n</sup>, A. Socías Mir<sup>o</sup>, A. Serrano Lázaro<sup>p</sup>, J.M. Pérez Villares<sup>q</sup>, M.E. Herrera-Gutiérrez<sup>r</sup>

<sup>a</sup> Hospital Universitario Fundación Alcorcón, Alcorcón, Madrid, Spain

<sup>b</sup> Hospital Universitario de Getafe, Getafe, Madrid, Spain

<sup>c</sup> CIBER de Enfermedades Respiratorias, Spain

<sup>d</sup> Hospital Universitario Joan XXIII, Instituto de Investigación Sanitaria Pere Virgili, Tarragona, Spain

<sup>e</sup> Hospital Universitari Son Espases, Instituto de Investigación Sanitaria de Palma (IdISPa), Palma de Mallorca, Spain

<sup>f</sup> Hospital Universitario Infanta Leonor, Madrid, Spain

<sup>g</sup> Hospital SAS de Jerez, Jerez de la Frontera, Cádiz, Spain

<sup>h</sup> Hospital Universitario y Politécnico La Fe, Valencia, Spain

<sup>i</sup> Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

<sup>j</sup> Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain

<sup>k</sup> Hospital Universitario de Fuenlabrada, Fuenlabrada, Madrid, Spain

<sup>l</sup> Hospital Universitario Marqués de Valdecilla, Santander, Spain

<sup>m</sup> Hospital Universitario Río Ortega, Valladolid, Spain

<sup>n</sup> Hospital Universitari Vall d'Hebron, Barcelona, Spain

<sup>o</sup> Hospital de Son Llàtzer, Palma de Mallorca, Spain

<sup>p</sup> Hospital Clínico Universitario de Valencia, Valencia, Spain

<sup>q</sup> Complejo Hospitalario Universitario de Granada, Granada, Spain

<sup>r</sup> Complejo Universitario Carlos Haya, Málaga, Spain

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Standardization;  
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**Abstract** The standardization of the Intensive Care Medicine may improve the management of the adult critically ill patient. However, these strategies have not been widely applied in the Intensive Care Units (ICUs). The aim is to elaborate the recommendations for the standardization

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\* Corresponding author.

E-mail address: [albertohmed@hotmail.com](mailto:albertohmed@hotmail.com) (A. Hernández-Tejedor).

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of the treatment of critical patients. A panel of experts from the thirteen working groups (WG) of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) was selected and nominated by virtue of clinical expertise and/or scientific experience to carry out the recommendations. Available scientific literature in the management of adult critically ill patients from 2002 to 2016 was extracted. The clinical evidence was discussed and summarized by the experts in the course of a consensus finding of every WG and finally approved by the WGs after an extensive internal review process that was carried out between December 2015 and December 2016. A total of 65 recommendations were developed, of which 5 corresponded to each of the 13 WGs. These recommendations are based on the opinion of experts and scientific knowledge, and are intended as a guide for the intensivists in the management of critical patients.

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## PALABRAS CLAVE

Estandarización;  
Paciente crítico;  
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intensivos

## Recomendaciones para el tratamiento de los pacientes críticos de los Grupos de Trabajo de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)

**Resumen** La estandarización de la medicina intensiva puede mejorar el tratamiento del paciente crítico. No obstante, estos programas de estandarización no se han aplicado de forma generalizada en las unidades de cuidados intensivos (UCI). El objetivo de este trabajo es elaborar las recomendaciones para la estandarización del tratamiento de los pacientes críticos. Se seleccionó un panel de expertos de los trece grupos de trabajo (GT) de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC), elegido por su experiencia clínica y/o científica para la realización de las recomendaciones. Se analizó la literatura publicada entre 2002 y 2016 sobre diferentes tópicos de los pacientes críticos. En reuniones de cada GT los expertos discutieron las propuestas y sintetizaron las conclusiones, que fueron finalmente aprobadas por los GT después de un amplio proceso de revisión interna realizado entre diciembre de 2015 y diciembre de 2016. Finalmente, se elaboraron un total de 65 recomendaciones, 5 por cada uno de los 13 GT. Estas recomendaciones se basan en la opinión de expertos y en el conocimiento científico y pretenden servir de guía para los intensivistas como una ayuda en el manejo de los pacientes críticos.

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## Introduction

The standardization of medical care through protocols and other tools forms part of the efforts to improve the quality of patient care. A series of quality indicators referred to the different processes in critical patient care were published in 2008. The publication comprised a total of 120 quality indicators covering all the areas and dimensions of Intensive Care Medicine.<sup>1</sup>

In 2010, the Spanish Ministry of Health developed a document, supported by the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (*Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias* [SEMICYUC]), in order to present the standards and recommendations for Intensive Care Units (ICUs) and thus contribute to improve the safety and quality of practice in critical care.<sup>2</sup> The SEMICYUC considers the quality of care to be a crucial element in the management of critical patients.<sup>3</sup> This strategy of standardizing activities in intensive care can help lower morbidity-mortality in the

ICU by reducing variations in practice and improving the general quality of patient care. In this context, standardized procedures for the placement of central venous catheters (Bacteremia Zero project, 2009), the application of strict hygiene of the hands, or the introduction of recommendations and interventions for preventing ventilator-associated pneumonia (Pneumonia Zero project, 2013), have been shown to reduce patient morbidity and healthcare costs.<sup>4,5</sup>

Standardization of most of the aspects referred to intensive care has an enormous potential for improving critical patient care<sup>6,7</sup>; however, despite the promising impact upon patient outcomes, such measures have not yet been adopted on a generalized basis.<sup>8</sup> The aim of the present document is therefore to transmit the recommendations for the standardization of critical care through a review of the available literature on the corresponding topics, carried out by 13 Working Groups (WGs) of the SEMICYUC, with a view to contributing to improve the safety and quality of clinical practice in critical patients.

## Methodology of the recommendations

### Conformation of the study group

In December 2015, the Expanded Steering Committee of the SEMICYUC, with the presence of the WG coordinators, decided to carry out this project with the purpose of defining and developing 65 recommendations (5 from each of the 13 WGs) of special interest in daily clinical practice. Six experts were chosen: a Director (MEHG) and 5 coordinators (GSR, OPR, JALP, AHT and EPH), with the task of adapting the style of the recommendations to the established norms. Each WG formed ad hoc working teams for development of the recommendations.

### Biomedical literature search and development of the recommendations

A literature search was made to develop these recommendations. Analyses were made of meta-analyses, randomized and observational clinical studies, systematic reviews and updates referred to adult critical patients found in MEDLINE, EMBASE reviews and the Cochrane Database of Systematic Reviews, covering the period from 2002 to June 2016, together with the opinions of the experts of each WG. Each WG established 5 recommendations of clinical relevance for the management of critical patients. The initial text and recommendations were forwarded to the intensivists pertaining to the respective WGs, with the aim of reaching consensus over the year 2016 on occasion of the different meetings of the WGs. Based on their contributions and the consensus reached in the meetings of the WGs, the final recommendations of the document were formulated on occasion of the National Congress of the SEMICYUC in 2016. The Editorial Committee carried out the final review of the document.

## Results

The recommendations referred to the management of critical patients developed by the respective WGs of the SEMICYUC are presented below.

### Bioethics Working Group

#### Recommendation 1: Avoid therapeutic futility

Through the use of invasive treatments, technological developments have made it possible to substitute vital functions and thus prolong life. However, it is not the purpose of Intensive Care Medicine to prolong life if doing so is not accompanied by the preservation of an acceptable quality of life of the patient.<sup>9</sup>

Limitation of life support treatment (LLST) forms part of end-of-life care in critical patients<sup>10</sup> and is based upon bioethical principles referred to respect for the person (autonomy and dignity) and beneficence (non-maleficence and fairness).

For this reason, from the ethical or legal perspective, health professionals are not obliged to satisfy demands for futile treatment measures.<sup>11</sup>

#### Recommendation 2: Whenever possible, decisions referred to the limitation of life support treatment should be made by consensus on a team basis

End-of-life decision making is difficult and normally arises from the care team. However, the patient and family must be informed and are to participate in decision making.<sup>12</sup>

Whenever possible, all the health professionals of the care team should take part in the deliberations in seek of consensus, including nursing staff<sup>13</sup> and professionals of other areas that may be of help in evaluating the prognosis and patient response to treatment. It is advisable to report the decision referred to LLST as a joint decision by the care team, not only as a decision by the supervising physician.

In the event of discrepancies among professionals and/or patients or their representatives, it is advisable to consult and consider the recommendations of the Care Ethics Committee.<sup>14</sup>

#### Recommendation 3: Always inform the patient and/or relatives of the limitation of life support practices, and register them in the case history

The decisions referred to LLST are endorsed by our scientific society, form part of Good Clinical Practice, and are regarded as a quality standard.

The patient and family must participate in the decisions referred to LLST,<sup>12,15</sup> favoring shared decision making and their implication in the therapeutic and management plan.<sup>9</sup> Holding the family responsible for the decision made is to be avoided: maximum responsibility for LLST decisions corresponds to the care team.

In turn, the information supplied to the patients and/or relatives must be true, suited to their capacity to understand, and progressive, and addressing of the prognosis must be prudent and reasonable. The decisions are to be recorded in the case history, including the time of the decision, the participants in the decision, the actions agreed, and the information given to the patients and/or their representatives.

#### Recommendation 4: Shared decision making is to be based on the values of the patient, ensuring patient autonomy, and considering the living will document

The autonomy of the critical patient is to be protected, preserving the right to personal freedom. The patient values also must be taken into account. In those situations where the capacity to decide has been lost, the existence of a living will document is to be assessed, and its contents are to be respected.<sup>14</sup> In the absence of such a document, the patient values and preferences are to be explored through the relatives or representatives.

#### Recommendation 5: In decisions referred to the limitation of life support treatment, a palliative care plan should be established, designed to reduce patient suffering and facilitate accompaniment by the family

A palliative care plan is to be created<sup>12</sup> with the purpose of reducing patient suffering and improving quality of life.<sup>16</sup> This plan should include adequate assessment of the physical, psychological, social and spiritual needs of the patient and family.<sup>17</sup> The palliative care plan is to be agreed with the patient and/or family or representatives, and should be

reported to the care team. The possible evolutive outcomes are to be considered and explained to the patient and relatives. It is advisable to offer an environment that adequately protects intimacy.

### **Cardiological Intensive Care and Cardiopulmonary Resuscitation Working Group**

#### **Recommendation 1: Perform quality cardiopulmonary resuscitation maneuvers (European Resuscitation Council [ERC] 2015) and work in your center for the prevention of in-hospital cardiac arrest**

Cardiopulmonary resuscitation maneuvering (CPR) should be carried out following the international recommendations.<sup>18</sup> In this way, we can improve the prognosis of patients who have suffered cardiac arrest (CA). Care related to CA is one of the main responsibilities of the intensivist. Furthermore, the implementation of measures for preventing in-hospital CA based on vigilance and early alert systems contributes to lower its incidence.<sup>19</sup> Training in both CPR and in the prevention of CA should be encouraged among all the hospital staff.<sup>20</sup>

#### **Recommendation 2: Select optimum hemodynamic monitoring and consider ultrasound as a tool for improving quality of care and patient safety**

Hemodynamic monitoring is to be adapted to the characteristics of each individual patient. This will help optimize clinical management, evaluate response to the treatment provided, and (if noninvasive are used, where possible) avoid iatrogenic effects. Ultrasound in the critical patient and the use of protocols based on its use (e.g., FEEL, FEER, BLUE) are useful for the diagnosis of shock, CA or respiratory failure. Furthermore, such techniques can offer information of help in establishing the indication for invasive monitoring and selecting the most appropriate and safest device.<sup>21–23</sup>

#### **Recommendation 3: Early reperfusion in acute coronary syndrome is required. In case of ST-segment elevation (primary percutaneous coronary intervention >120 min), administer thrombolysis. In the absence of ST-segment elevation, decide the optimum moment for coronary intervention**

In the case of acute coronary syndrome (ACS), appropriate reperfusion for each individual patient is to be selected. The introduction of primary percutaneous coronary intervention (PCI) tends to obviate thrombolysis in patients with ACS and ST-segment elevation, in cases that stand to benefit from its administration.<sup>24,25</sup> In cases of ACS without ST-segment elevation, ischemic risk should be stratified in order to define the optimum timing of PCI.<sup>26</sup> It is advisable to establish multidisciplinary intervention protocols to afford appropriate reperfusion therapy adapted to the organization present in each hospital, Autonomous Community or region.

#### **Recommendation 4: Administer neurohormonal response blocking drugs in patients with heart failure**

Neurohormonal block has been shown to reduce mortality and the need for readmission.<sup>27</sup> In the absence of contraindications, treatment should be started as soon as possible with beta-blockers, angiotensin converting enzyme

inhibitors (ACEIs) or angiotensin II receptor antagonists (ARA II drugs), as well as with aldosterone receptor antagonists in patients presenting post-infarction heart failure (left ventricular ejection fraction [LVEF] <40%, diabetic or symptomatic) or with chronic heart failure secondary to severe ventricular dysfunction (LVEF <35%).<sup>28,29</sup>

#### **Recommendation 5: Provide perioperative atrial fibrillation prophylaxis in heart surgery patients**

Atrial fibrillation is the most common arrhythmia in the postoperative period of heart surgery, and increases patient morbidity–mortality, as well as the duration of stay and hospital costs. In the absence of contraindications, beta-blockers should be maintained before surgery, and should be introduced as soon as possible.<sup>30–32</sup> Optimum perioperative management is important in all patients undergoing heart surgery.

### **Nephrological Intensive Care Working Group**

#### **Recommendation 1: Patients at risk of suffering kidney damage are to be identified early, with due monitoring and the adoption of diagnostic-therapeutic measures to prevent such damage from developing**

Close monitoring is required of critical patients over 75 years of age, with heart disease, chronic renal failure or some previous episode of acute kidney injury (AKI) who receive nephrotoxic drugs or with clinically suspected hypovolemia (absolute or relative). Such monitoring should at least include repeated measurements of serum creatinine and hourly diuresis. Hemodynamic assessment is strongly advisable in order to define the need for additional fluid therapy, together with the adoption of diagnostic and therapeutic measures designed to avoid progression to advanced stage AKI (AKIN stages 2 and 3).<sup>33,34</sup> Such stages are associated to increased patient morbidity–mortality (both in the ICU and in hospital) extending over the middle to long term, with the consequent worsening of quality of life due to the development of cardiovascular processes (especially ischemic heart disease) and chronic renal failure with dependency upon ambulatory dialysis.<sup>35</sup>

#### **Recommendation 2: Avoid contrast-induced nephropathy, identifying patients at risk, affording hydration and minimizing the amount of contrast used**

Consideration is required of the following principal risk factors for the development of contrast-induced nephropathy (CIN): previous renal failure, diabetes mellitus, situations of renal hypoperfusion (heart failure, administration of diuretics), administration of nephrotoxic drugs, advanced age, and the volume and osmolarity of the administered contrast medium.<sup>36</sup> Intravenous hydration is the most effective preventive measure, together with avoidance of the aforementioned risk factors. The purpose of hydration is to maintain sufficient intravascular volume to increment renal perfusion, establish adequate diuresis prior to contrast administration, and avoid hypotension. The efficacy of administering sodium bicarbonate is no greater than that of isotonic saline solution, and N-acetylcysteine likewise has not been shown to afford benefit in preventing CIN.<sup>37</sup>

Exploration with contrast, when indicated, should not be avoided because of concerns about CIN.<sup>38</sup>

**Recommendation 3: Calculate the degree of acute kidney injury based on the RIFLE, AKIN or KDIGO scales**

Early detection of acute renal dysfunction is required. This will allow the definition of severity, assessment of the clinical course and the definition of when to start renal replacement therapy (RRT). It is advisable to monitor serum creatinine and diuresis, applying the RIFLE, AKIN or KDIGO scales. All three scales show good correlation to the prognosis, though AKIN and KDIGO are more sensitive. These definitions require a basal creatinine value (the most widely accepted criteria being: normal value or value closest to normal in the last 3 months, lowest value in the last 7 days, or value upon admission).<sup>34</sup> The determination of creatinine clearance over short time intervals (2, 4, 8 h) allows us to establish the glomerular filtration rate and establish drug dosing more precisely. The Cockcroft–Gault, MDRD or CKD-EPI formulas should not be used, since they are not valid in application to critical patients with AKI.<sup>39</sup>

**Recommendation 4: Consider the start of renal replacement therapy in patients with AKIN stage 3 acute renal dysfunction**

Renal replacement therapy should be started in patients diagnosed with AKIN stage 3 AKI, particularly in individuals with sepsis and multiorgan failure. The criterion for starting RRT based on creatinine (increment corresponding to triple the basal creatinine value or creatinine >4 mg/dl, with an acute increment of >0.5 mg/dl) is to be applied according to the clinical circumstances of the patient.<sup>40,41</sup> The criterion for starting RRT based on diuresis (diuresis <0.3 ml/kg/h in 24 h or anuria for 12 h) is to be applied provided adequate patient resuscitation has been achieved (in pre-renal conditions), or after application of the furosemide test in hyperhydration conditions.<sup>42</sup> Renal replacement therapy can be postponed in stable patients with isolated AKI in the absence of other types of organ failure, except in the presence of classical criteria for dialysis (pH < 7.20, K > 6.5 mEq/l, clinical complications related to uremia, acute lung edema, severe hyponatremia).

**Recommendation 5: In critical patients, start renal replacement therapy adjusted to 30–35 ml/kg/h; adjustment should be dynamic according to the clinical course**

The recommended initial setting is 20–25 ml/kg/h. However, it must be taken into account that in many cases the applied RRT setting is not that prescribed, due to the periods of inactivity (mainly circuit coagulation and/or clinical indications). It is therefore advisable to start with 30–35 ml/kg/h, trying to reduce interruptions in therapy, in order to reach the optimum setting.<sup>34</sup> Furthermore, daily evaluation of the hemodynamic, metabolic and water balance situation of the patient is required in order to ensure dynamic adjustment of RRT. Such daily adjustment according to the clinical course of the patient ensures adequate management of water, solutes, electrolytes and acid-base balance. Likewise, it is advisable to adjust the patient medication to the intensity of RRT.<sup>43</sup>

**Infectious Diseases and Sepsis Working Group**

**Recommendation 1: Establish leaderships in the control of infection and in optimization of the use of antimicrobials in the ICU**

There should be professionals who lead control of infections acquired in the ICU and who facilitate optimization of antimicrobial use. Specifically, the tasks of these professionals are: vigilance of infections through registries; the development of infection prevention programs; updating of the empirical antimicrobial treatment protocols; evaluation and counseling on antimicrobial prescription; and care coordination in the infectious diseases setting with the nursing staff and other specialists implicated in patient care.<sup>44–46</sup>

**Recommendation 2: Foresee infections related to the use of devices in the ICU**

A systemic vision is required to address this objective. In this regard, prospective registry of the incidence of infections acquired in the ICU is recommended, participating actively in the ENVIN-HELICS registry.<sup>47</sup> Furthermore, it is advisable to implement the recommendations of the Bacteremia Zero and Pneumonia Zero projects—specifically, those referred to the application of specific and standardized measures for the insertion and maintenance of intravascular and artificial airway devices. In addition, an integral safety plan is required, with measures designed to promote safety habits in daily clinical practice.<sup>5,48</sup>

**Recommendation 3: Adopt a program for the control of multiresistant microorganisms based on the recommendations of the Resistance Zero project**

This program should focus on: (1) Evaluation of antibiotic treatment and interviewing of the prescribing physician. The choice of antimicrobial should be based on internal protocols and on the local epidemiological characteristics; the use of combination therapy where required; adequate posology; reduction of the drug spectrum according to the microbiological results obtained; the minimum duration of therapy; the use of broad-spectrum antimicrobials only when needed; and the adverse effects and interactions. (2) Control of the cross-transmission of multiresistant bacteria (MRB). Screening for MRB should be made upon admission in patients with risk factors. Weekly screening of all admitted patients is indicated. Carriers are to be correctly identified. The existence of a training program, with motivation and monitoring of hand washing must be regarded as crucial for controlling MRB. (3) Correct disinfection of the critical patient environment.<sup>49,50</sup>

**Recommendation 4: Ensure rapid and effective control of the infectious process in the critical patient**

In the event of infection, antimicrobial treatment should be started immediately. In practice, biological samples (both blood and from the site of infection) should be obtained for microbiological study (stains, rapid tests, culture and antibiogram), provided this does not result in excessive delays in administration of the antimicrobial. No other diagnostic test should delay the start of treatment.<sup>51,52</sup> Furthermore, control of the infectious site should be made wherever possible. This includes the drainage of accumulations, tissue

resection, the repair of disruptions and withdrawal of devices related to the infection.<sup>53</sup>

**Recommendation 5: In the case of septic shock, hemodynamic resuscitation is required, with the administration of broad-spectrum antibiotics in the first 6 h of patient care**

The following resuscitation objectives should be reached as soon as possible and always within the first 6 h of treatment of septic shock (independently of where the patient is located): mean blood pressure (MBP) > 65 mmHg, diuresis >0.5 ml/kg/h, central venous pressure (CVP) 8–12 mmHg or 12–15 mmHg in patients subjected to mechanical ventilation, lactate <36 mg/dl, and central venous oxygen saturation (ScvO<sub>2</sub>) ≥ 70%.<sup>54</sup> To this effect, the patient should be subjected to hemodynamic monitoring (using invasive devices and/or ultrasound control) and metabolic control (lactate and ScvO<sub>2</sub>).<sup>21</sup> Furthermore, broad-spectrum antibiotic treatment should be started as soon as possible, based on one or more drugs selected according to the characteristics of the clinical condition and of the patient. The prescribed treatment should offer good penetration of the site of infection, and is to be administered via the correct dosage and route.<sup>55</sup>

**Evaluation of Technologies and Research Methodology Working Group**

**Recommendation 1: The introduction and configuration of a clinical information system should be viewed as a standard of quality and management in the ICU**

Clinical information systems (CIS) are necessary tools for management of the information generated in the ICU, and afford improvements referred to safety, care quality, clinical management, research and teaching.<sup>56–58</sup> A CIS should allow the following: (1) connectivity with peripheral devices; (2) integration with the case history in the hospital and with the hospital applications (two-way information exchange); (3) drug prescription; (4) full clinical sheet configuration (with management of in- and out-puts, nursing interventions, diagnoses, procedures and calculation of scales, drafting of care plans and assessments, management of alerts and meta-alerts); (5) registry of the minimum basic data set (MBDS)(with codes and reports); (6) availability of a data exploitation and analysis tool; and (7) possibility of validating the entered information (security and error correction element: monitoring artifacts or wrong entries). In addition, it should be configurable by clinical administrators.

**Recommendation 2: Evaluate and acquire the technology for the ICU, supported by a multidisciplinary team including intensivists, following the standards of the SEMICYUC and evaluation agencies**

Cost evaluation for the incorporation of healthcare technologies should be based on both cost-effectiveness and cost-utility analyses and on the social perspective.<sup>59</sup> The professionals can contribute to the internal sustainability of the health system through correct use of the technology. The characteristics to be met by an evaluation are: safety, functionality, utility, applicability, reliability, cost (budget impact of introducing the technology with an appropriate

time horizon) and maintenance.<sup>60,61</sup> The evaluating committees should feature an intensivist with expertise in the evaluation of healthcare technology. On the basis of the above, the following is proposed: promotion of training in healthcare technology; development of standards referred to the most widely used technologies; detection and evaluation of emerging technologies; collaboration with sponsors of technological innovations; facilitation of expert participation in their development and evaluation; and generation of information through the creation of a public database of the unit costs of the resources and procedures derived from the adoption of new technologies.

**Recommendation 3: Start observational multicenter registries, supported by the SEMICYUC, complying with the legal and documental requirements**

The predominant scientific research format within the SEMICYUC corresponds to observational multicenter studies. Spanish legislation offers guarantees regarding the protection of patient rights and data in such studies.<sup>62–64</sup> The investigators therefore must know and respect such legislation. The recommended steps are: (1) request classification of the study by the Spanish Medicines Agency, defining the need for informed consent; (2) request approval of the study-registry by an accredited reference Clinical Research Ethics Committee (CREC); (3) request a favorable opinion from the rest of the CRECs of the implicated hospitals; (4) confirm approval of the centers in which the study-registry is carried out, by means of the signing of an agreement; and (5) submit a cost estimate to the CREC, specifying whether it is zero.

**Recommendation 4: Register the activity of the ICU by means of the MBDS-ICU generated by the SEMICYUC**

Clinical management systems allowing evaluation of the ICUs should be available.<sup>65,66</sup> The MBDS-ICU generated by the SEMICYUC comprises 20 items that ensure the availability of sufficient information, collected in a uniform and standardized manner, to allow analysis of the care processes of the ICU (thereby avoiding their omission within the hospital process).<sup>67</sup> Its use has clear advantages: (1) unification of criteria; (2) adequate classification of the care processes inherent to Intensive Care Medicine; (3) planning of the services provided (care, clinical management, teaching and research); (4) knowledge of the results and activities of the ICU; and (5) conduction of research, generation of new hypotheses, and the provision of a national perspective of the importance of Intensive Care Medicine.

**Recommendation 5: The use of experimental or non-consolidated techniques or treatments should be carried out in the context of studies or registries allowing adequate analysis of their efficacy**

Innovating or experimental treatments are to be used in the context of well-designed studies or registries.<sup>64</sup> The results (whether positive or negative) are to be published, in order to allow adequate assessment of efficacy, reduce the number of exposed individuals, and stimulate clinical research. Treatments of this kind (whether pharmacological or technological), which are external to the established standards, tend to generate interest, and their efficacy might be

subjectively overrated. Rigorous scientific analysis is therefore required, avoiding their indiscriminate and disorderly use.<sup>68</sup>

### Acute Respiratory Failure Working Group

#### Recommendation 1: Noninvasive ventilation should be used as first choice in patients with exacerbated chronic respiratory failure

Noninvasive mechanical ventilation (NIMV), added to habitual treatment for exacerbated hypercapnic chronic respiratory failure (HCRF) should be used, since it reduces the need for intubation, the duration of hospital stay, and mortality.<sup>69,70</sup> Over the last decade, NIMV has been increasingly used as a ventilatory support technique in patients with acute exacerbation of HCRF (arterial pH < 7.35 and hypercapnia).<sup>71</sup> The number needed to treat (NNT) for reducing orotracheal intubation is 5 patients (95% confidence interval [95%CI] 4–7 patients), and the NNT to reduce mortality is 8 patients (95%CI 6–3 patients).

#### Recommendation 2: Use protective mechanical ventilation in patients with acute respiratory distress syndrome: tidal volume 6–8 ml/kg (predicted body weight) and plateau pressure < 30 cmH<sub>2</sub>O

Patients with acute respiratory distress syndrome (ARDS) may develop complications in the form of ventilator-associated lung injury. Pulmonary protection ventilation strategies (tidal volume [Vt] 6–8 ml/kg predicted body weight, plateau pressure < 30 cmH<sub>2</sub>O) can benefit patients with ARDS, reducing mortality after 28 days and in-hospital mortality compared with ventilation strategies involving Vt ≥ 10 ml/kg.<sup>72,73</sup> Furthermore, it is advisable to adjust protective ventilation in order to maintain a driving pressure of ≤ 14 cmH<sub>2</sub>O, since patients with ARDS and a driving pressure of > 14 cmH<sub>2</sub>O suffer increased in-hospital mortality. However, strategies designed to establish optimum positive end-expiratory pressure (PEEP) in patients with ARDS (with the purpose of incrementing alveolar recruitment and avoiding hyperinflation) have not demonstrated a significant decrease in mortality, though they may improve lung function, shorten the duration of mechanical ventilation, and reduce the incidence of organ failure.<sup>74</sup>

#### Recommendation 3: Use prone decubitus in patients with acute respiratory distress syndrome and PaO<sub>2</sub>/FiO<sub>2</sub> < 150 mmHg

Early prone decubitus during mechanical ventilation is required in patients with ARDS presenting PaO<sub>2</sub>/FiO<sub>2</sub> < 150 mmHg. This strategy offers benefits compared with supine decubitus, since it is associated to lesser mortality after 28 days. It is advisable to use prone decubitus for at least 16 h and to suspend prone decubitus as soon as PaO<sub>2</sub>/FiO<sub>2</sub> > 150 mmHg with PEEP ≤ 10 cmH<sub>2</sub>O is reached.<sup>75–77</sup> The monitoring of adverse effects is necessary –the most frequent problems being pressure ulcers and tracheal tube obstruction.

#### Recommendation 4: Daily evaluation is required of the capacity of patients on mechanical ventilation to maintain spontaneous breathing

The possibility of suspending mechanical ventilation should be assessed on a daily basis by means of the spontaneous breathing test, since the duration of ventilation can be shortened as a result, with a reduction of costs, and without harming the patient. This test should be carried out using the internal protocols established by a multidisciplinary team.<sup>78</sup> It has been shown that the duration of mechanical ventilation in patients managed with standardized protocols decreases 25%, while the duration of weaning decreases over 75% and the ICU stay is shortened 10% compared with routine clinical practice.<sup>79,80</sup>

#### Recommendation 5: In patients subjected to mechanical ventilation, daily evaluation of the lowest necessary sedation dose is required

In patients subjected to mechanical ventilation, daily interruption of sedation or protocolized sedation using scales to secure mild sedation makes it possible to shorten the duration of ventilation, lessen the need for tracheostomy, and reduce ICU stay. Daily interruption of sedation or the use of protocolized sedation should be incorporated to the sedation protocols, which must make use of validated scales and are to be put into practice early (as soon as allowed by the patient clinical condition).<sup>81–83</sup> Furthermore, sedation protocols are not associated to adverse effects such as for example reintubation following self-extubation.

### Metabolism and Nutrition Working Group

#### Recommendation 1: Upon admission to the Intensive Care Unit, identify those patients with nutritional risk and a risk of developing refeeding syndrome

Although consensus is lacking regarding the optimum method for assessing nutritional risk, it is advisable to use the NUTRIC score to identify those patients that may benefit from intensive nutritional support. This score considers the following parameters: age, APACHE II, SOFA, comorbidities, days of stay until admission to the ICU, and optionally IL-6.<sup>84,85</sup> It is moreover advisable to compile a nutritional history, with anthropometric and biochemical parameters (protein, carbohydrate and lipid metabolism) at the time of admission. Refeeding syndrome (RS) is defined as the water-electrolyte alterations that develop secondary to intensive nutritional support in starved or severely malnourished patients. The syndrome can manifest with hypophosphatemia, arrhythmias, heart failure and respiratory failure. In patients at risk of suffering RS (alcoholism, oncological patients, fasting, loss of > 10% body weight in the last two months, denutrition, body mass index < 18 or > 40 kg/m<sup>2</sup>), the ionic deficits should be corrected before nutrition is started, administering intravenous thiamine the first three days, and initiating nutritional support at 50% of the calculated amount, followed by gradual increments.<sup>86</sup>

**Recommendation 2: Calculate the calorie/protein requirements adjusted to the stress factor and the evolutive phase of the patient, with re-evaluation on a daily basis or at least once a week**

Critical patients are in a hypermetabolic state. Their requirements are conditioned to the anthropometric parameters, the disease and severity of the lesions, and the existence of previous malnutrition.<sup>87</sup> It is advisable to calculate the calorie/protein requirements via indirect calorimetry or, alternatively, using predictive formulas adjusted to the stress factor, the disease and the evolutive phase of the patient (with re-evaluation on a daily basis or at least once a week).<sup>88</sup> Excessive or deficient nutritional support is known to increase the risk of infection, liver dysfunction and hyperglycemia, and moreover prolongs hospital stay. Most critical patients received less than the indicated protein supply. The recommended protein supply is 1.2–1.8 g/kg/day. Despite the presence of important nitrogen losses, it is not advisable to exceed 1.8 g/kg/day, except in special situations (obesity, continuous renal replacement therapy or polytraumatism).<sup>89</sup>

**Recommendation 3: Start early enteral nutrition in stable patients and consider complementary or total parenteral nutrition in the presence of digestive tract problems**

The early introduction of enteral nutrition (EN) is associated to a decrease in infectious complications and mortality in critical patients.<sup>90</sup> When a complete oral diet is not possible, and in the absence of contraindications, EN should be started in the first 24–48 h following admission to the ICU, once hemodynamic stability has been achieved (mean blood pressure  $\geq$  65 mmHg, vasopressors and lactic acid stabilized or descending). Parenteral nutrition (PN) is reserved for patients that cannot be fed through the digestive tube.<sup>91</sup> Enteral nutrition (trophic dose, 10–15 ml/h) and PN can be combined when digestive tolerance is not complete –reducing PN as EN gradually improves. Over-feeding is to be avoided, particularly when complementary PN is administered.<sup>92</sup>

**Recommendation 4: Monitor the parameters of adequate enteral and parenteral nutrition use, identify associated complications, and apply the interventional protocols**

The following should be checked in all critical patients receiving artificial nutrition: (1) compliance with the daily calorie and protein target (between 80% and 100% of the calculated requirements), with optimization of the measures to increase enteral supply (e.g., postpyloric tubes); (2) correct enteral tube positioning before starting EN, as determined by X-ray evaluation (distal tip of the tube located in the gastric antrum or transpyloric zone); (3) semi-raised patient positioning when receiving EN (patient chest angle  $>30^\circ$ ); (4) tolerance and protocolized management of the complications associated to the administration of EN (diarrhea, abdominal bloating, increased gastric residue, constipation, vomiting, regurgitation and bronchial aspiration) and PN (hyperglycemia, liver dysfunction, hypertriglyceridemia, catheter-related infection); and (5) periodic laboratory testing to adjust nutritional

support. Daily evaluation of: ions, blood glucose, renal function. At least once a week: liver function, triglycerides, nitrogen balance, prealbumin, retinol binding protein and albumin.<sup>93–95</sup>

**Recommendation 5: Maintain blood glucose levels of under 150 mg/dl with insulin therapy, using protocols that avoid blood glucose variability and hypoglycemia**

It is advisable to maintain blood glucose levels below 150 mg/dl with insulin therapy, using protocols that avoid blood glucose variability and severe hypoglycemia ( $<40$  mg/dl).<sup>96</sup> In critical patients, hyperglycemia is related to increased morbidity–mortality and infectious complications, and blood glucose variability is an independent mortality risk factor.<sup>97</sup> Strict blood glucose control (80–110 mg/dl) does not lower mortality and is not a safe practice (severe hypoglycemia). Some studies describe increased mortality even with moderate hypoglycemia ( $<60$  mg/dl).<sup>98</sup> It is advisable to measure the percentage of severe hypoglycemic episodes in order to adopt measures designed to reduce them. The standardization of insulin perfusion protocols improves efficiency and safety in blood glucose control.

**Neurointensive and Trauma Care Working Group**

**Recommendation 1: Severe trauma disease must be treated by specialized teams and in trauma care centers**

Severe trauma disease is a dynamic and complex clinical condition requiring an early and global management approach. Patients with severe trauma disease (Injury Severity Score [ISS]  $>15$ ) and/or severe traumatic brain injury (Glasgow Coma Score [GCS]  $\leq 8$ ) must be attended by a specialized medical team in which the intensivist plays a key role.<sup>99</sup> The aim is to secure a multidisciplinary approach in order to shorten the times referred to stabilization, diagnosis (imaging techniques) and treatment with damage control surgery, considering definitive patient transfer to duly accredited trauma care centers and/or ICUs. The scientific evidence points to trauma care centers as playing a crucial role—offering leadership, management, safety and quality control. Furthermore, such centers have been shown to be cost-efficient and lower patient mortality.<sup>100,101</sup>

**Recommendation 2: Administer tranexamic acid on an early basis in patients with traumatic hemorrhagic shock**

Tranexamic acid (TXA) is an antifibrinolytic agent that inhibits the conversion of plasminogen to plasmin – thereby avoiding dissolution of the fibrin clot. The CRASH 2 study reported improved survival in patients treated with TXA in the first three hours, with a 15% decrease in mortality due to bleeding, and a 15% decrease in mortality due to other causes.<sup>102</sup> Tranexamic acid is inexpensive and has few important side effects.<sup>103</sup> It is advisable to administer TXA forming part of resuscitation with damage control, as an intravenous dose of 1 g in 10 min, followed by a perfusion of 1 g over 8 h. Administration should be within the first three hours and



preferably earlier; its use in pre-hospital patient management is therefore contemplated.<sup>104</sup>

**Recommendation 3: Damage control surgery is indicated in patients with traumatic hemorrhagic shock**

Damage control surgery (DCS) is an abbreviated procedure designed to control bleeding, with priority being placed more on short-term physiological recovery than on definitive surgical repair in seriously ill patients with impaired physiological reserves. Damage control surgery comprises a series of elements: abbreviated surgery for bleeding control in the operating room; physiological optimization in the ICU (warming, hemodynamic and respiratory stabilization, and correction of the acid-base balance and coagulopathy); and finally secondary transfer (after 24–48 h) to the operating room for definite surgical treatment.<sup>105</sup>

This concept binds to resuscitation with damage control, which focuses on permissive hypotension and early blood product replacement with a view to avoiding the lethal triad: acidosis, coagulopathy and hypothermia. Damage control surgery has been associated to increased survival and a reduction of complications in patients with severe trauma and hemorrhagic shock.<sup>106</sup>

**Recommendation 4: Monitor intracranial pressure and cerebral perfusion pressure in patients with severe brain trauma (Glasgow coma score  $\leq 8$ ) and anomalous computed axial tomography (CAT) findings**

The scientific evidence warrants the use of intracranial pressure (ICP) monitoring as part of the management of patients with acute traumatic brain damage at risk of ICP elevation, based on the clinical and/or imaging findings (CAT alterations comprising hematomas, contusion, edema, herniation or compression of the basal cisterns).<sup>107,108</sup> The potential benefits of such monitoring include the early detection of increased intracranial injury, guidance for management, avoidance of the indiscriminate use of treatments to lower ICP, improved cerebral perfusion and better outcomes among those patients that respond to the measures for reducing ICP.

**Recommendation 5: In aneurysmal subarachnoid bleeding, administer nimodipine for the prevention of cerebral vasospasm**

Cerebral vasospasm is the main cause of late morbidity–mortality in subarachnoid bleeding of aneurysmal origin. Its intensity is directly related to the initial amount of extravasated blood. The presence of intracellular calcium is important for maintaining smooth muscle contraction, and is also a critical factor in the process of cell death. Calcium antagonists avoid calcium entry to the cell, blocking the calcium transport channels and thus preventing vasospasm and its main consequence: delayed cerebral ischemia.<sup>109</sup> Studies have shown that the administration of nimodipine (preferably via the digestive route) improves the functional prognosis and reduces morbidity secondary to delayed cerebral ischemia. Oral administration is safe (60 mg every 4 h during 21 days).<sup>110</sup>

**Planning, Organization and Management Working Group**

**Recommendation 1: Close quality healthcare activity knowing perceived satisfaction and quality among the patients and, if possible, among the relatives**

Satisfaction questionnaires should be used to know perceived quality and adopt measures designed to cover the needs and expectations of the patients and relatives.<sup>111</sup> Patients are the core consideration in critical care, and quality management should be based on their needs, expectations and perceptions. Furthermore, due to the clinical condition of these patients, the relatives become interlocutors of the healthcare team and act as representatives in decision making.<sup>112</sup> Many factors can condition the satisfaction of patients and their relatives: the seriousness of the patient condition, invasive diagnostic and therapeutic procedures, the complexity of decision making, uncertainty, the great emotional burden, the interaction of multiple professionals, the obligation to supply honest information about the situation, and environmental stress factors.<sup>113</sup>

**Recommendation 2: Transfer information and responsibility for patient care following a method that ensures the creation of a shared therapeutic plan**

Teamwork, the continuity of care and effectiveness are key factors for patient safety. The transfer of information should comprise the relevant clinical data and the current patient condition, information referred to decision making and pending procedures or interventions, and the information given to the patient and/or relatives.<sup>114</sup> Information moreover should be given in a pre-established place and time, on a routine basis, with clear identification of the staff in charge, and compiled in an accessible form.<sup>115</sup> The great frequency of information transfer, the severity and complexity of the patients, and the participation of different professionals in the daily work of the ICU make it necessary to ensure a clear, protocolized and disciplined exchange of information.<sup>116</sup>

**Recommendation 3: Learn and reduce the risk of repeated incidents and adverse events by performing a systematic analysis through the safety core of the ICU**

Incidents and adverse events are common in medical practice and are related to mortality, morbidity, and increased stays and resource utilization. They moreover lessen satisfaction among patients and their relatives. A safety core inherent to the ICU should be established with a view to promoting safety practices and analyzing the incidents and adverse events, providing the professionals with regular feedback.<sup>117</sup> Both analysis and feedback serve to train the groups in understanding the complexity of healthcare in the ICU. It must be remembered that the mechanisms or factors contributing to incidents that may seem insignificant are of the same nature as those that intervene in the most serious adverse events (sentinel cases).<sup>118,119</sup>

**Recommendation 4: Perform daily multidisciplinary rounds to align the clinical information with the practical aspects in management of the critical patient**

Professional activity in the ICU takes place in a changing environment, organized into processes that involve complex tasks, and which in turn are the responsibility of several professionals (teamwork). Such multidisciplinary rounds contribute to the following: (1) determination of whether the patient condition is reversible or not; (2) definition of treatment priorities and of the tasks required; (3) definition of the need to consult other specialists or perform complementary tests; (4) establish the patient mobilization options; and (5) define the key lines of information for the family.<sup>120</sup> Care quality decreases drastically if the professionals in charge of patient care do not share the information they have in order to jointly construct therapeutic horizons.<sup>121</sup> Better communication among professionals improves the prognosis of the critical patient.<sup>122</sup>

**Recommendation 5: Improve the quality of care, contribute to organizational learning, and open the door to new ways of clinical management, using the clinical information systems**

The current scenario referred to the guidance and management of organizations is set within the so-called "knowledge economy paradigm". This in turn is based on intangible resources and places priority on new forms of management fundamented upon the relevant role of knowledge and its strategic participation in the new value creation patterns.<sup>123</sup> In this scenario, clinical information systems (CIS) play a crucial role by allowing storage of the coded and structured information (making it retrievable, processable and shareable), improving the outcomes of the care process and increasing safety, while also consolidating the bases for clinical research.<sup>124</sup> Furthermore, CIS allow the optimization of workloads, contribute to organizational learning, and improve effective communication among the members.<sup>125</sup>

### Sedation and Analgesia Working Group

**Recommendation 1: Ensure the existence and compliance with a sedoanalgesia protocol in the ICU**

Each Unit should develop and apply a sedoanalgesia protocol, and keep it up to date. This protocol must be based on the best evidence available, should be established by consensus with the nursing staff, and should include the following: (1) the monitoring of pain (using the validated Visual Analog Scale [VAS], Numerical Rating Scale [NRS] and Behavioral Indicators of Pain Scale [ESCID]) and measures for its prevention and treatment; (2) monitoring of the level of sedation (using the validated Richmond Agitation and Sedation Scale [RASS] or Sedation-Agitation Scale [SAS]) and the algorithm for avoiding over-sedation; (3) the monitoring of delirium (using the validated Confusion Assessment Method for the ICU [CAM-ICU] or Intensive Care Delirium Screening Checklist [ICDSC]) and measures for its prevention and treatment; and (4) indications and monitoring of neuromuscular block. The pharmacological and non-pharmacological selection and adjustment algorithms must be agreed with the nursing staff and should include objectives referred to pain, sedation and/or delirium, indi-

vidualized for each patient.<sup>126,127</sup> These objectives are to be explicitly stated in the case history at least once a day, or whenever their modification is required.

**Recommendation 2: Monitor, foresee and adequately treat pain in the critical patient**

It is advisable to monitor, prevent and treat pain on a multidisciplinary basis, implicating all the health professionals that attend critical patients. Monitoring is recommended of the existence and intensity of pain using validated scales in both cooperative patients (VAS, NRS) and in uncooperative patients (Behavioral Pain Scale [BPS], ESCID, Critical Care Pain Observation Tool [CPOT]), at least once per nursing shift (ideally every 4 h) and 30 min after treating intense pain, to check the control achieved.<sup>128</sup> It is not advisable to base the monitoring of pain on the patient vital signs. Pain prevention is recommended, avoiding painful maneuvers and procedures as far as possible, and affording early and anticipated preventive analgesia before carrying out any necessary painful procedures. It is advisable to treat and keep the critical patient free of pain through multimodal analgesia, with priority focusing on analgesia before resorting to sedation.<sup>129,130</sup>

**Recommendation 3: Use sedation suited to each clinical situation, keeping it as superficial as possible through the use of monitoring systems**

Monitoring of the level of sedation and agitation using validated scales (SAS, RASS), performed at least once per shift, and drug adjustment to secure the prescribed level, are important elements in the management of critical patients.<sup>126</sup> This practice allows us to prevent and treat anxiety and facilitate patient adaptation, placing priority on non-pharmacological measures and drugs with a short half-life and a lesser capacity to induce delirium and/or addiction.<sup>131</sup> On the other hand, it is advisable to place greater priority on analgesia than on sedation, and to maintain the lowest necessary level of sedation at all times—with frequent reevaluation of the need for sedation. Attempts should be made to secure conscious sedation unless contraindicated (intracranial hypertension, severe ARDS, *status epilepticus* or the need for neuromuscular blockers).<sup>127</sup> In patients subjected to mechanical ventilation, the interruption of sedation and the possibility of weaning should be assessed jointly with the nursing staff on a daily basis.

**Recommendation 4: Foresee, detect and treat delirium in the ICU**

It is advisable to evaluate the presence of delirium in all adult patients admitted to the ICU for more than 24 h, at least once a day and when there is a change in mental state of the patient—except in individuals with a RASS score of under  $-3$  or equivalent, based on the use of validated scales (CAM-ICU or ICDSC).<sup>132</sup> The adoption of preventive measures is recommended particularly in patients with risk factors (prior dementia, arterial hypertension and alcoholism, seriousness of the disease, coma or the prior use of opiates and benzodiazepines), based fundamentally on non-pharmacological interventions such as early mobilization and sleep facilitation—controlling light, noise and nocturnal stimuli. In the case of drug treatment, the recommendation

is to prescribe haloperidol and/or atypical antipsychotics. In patients with delirium not related to alcohol or benzodiazepines, dexmedetomidine infusions are indicated for shortening the duration of delirium. Delirium is to be evaluated and treated before sedatives are used.<sup>133,134</sup>

**Recommendation 5: Neuromuscular blockers should be used at the lowest dose and for as little time as possible, monitoring the bispectral index (BIS) and train of four (TOF), with daily reevaluation of the indications and the appearance of complications**

The administration of neuromuscular blockers (NMBs) can be associated to serious complications; they therefore must be used with due attention to efficacy and safety. Such treatment is recommended in certain clinical situations, using the minimum effective dose and for as little time as possible, with reevaluation of the indications at least once a day and monitoring of the degree of block using a peripheral neurostimulator with TOF, in order to avoid unnecessary excessive doses. Before the use of NMBs and for the duration of block, the patient should receive analgesia and sedation, checking unconsciousness with monitoring of the BIS, which should be maintained between 40 and 60 (deep sedation).<sup>135,136</sup> It is essential to avoid possible complications associated to the use of NMBs, such as corneal ulcers, pressure ulcers, nerve damage and deformities due to compression and deep venous thrombosis. In addition, we must monitor the risk of ventilator disconnection and observe a high degree of suspicion of possible intercurrent problems (angina, acute abdomen, seizures).<sup>137</sup>

### Toxicology Working Group

**Recommendation 1: Ensure adequate airway protection before applying digestive tract decontamination measures in intoxicated patients**

The most common adverse events in patients subjected to digestive tract decontamination with activated charcoal are nausea and vomiting.<sup>138</sup> Such decontamination measures in patients with diminished consciousness and insufficient capacity to protect the airway entails a high risk of bronchial aspiration. The international clinical guides therefore contraindicate such measures if the airway has not been previously isolated through tracheal intubation.<sup>139,140</sup>

**Recommendation 2: Early use of renal filtration techniques is required in patients with lactic acidosis and a strong suspicion of association to metformin intoxication**

Metformin is not intrinsically toxic, but causes lactic acidosis and secondary shock if the lactate formed is not eliminated in cases of concomitant renal or liver failure. Renal replacement techniques (RRTs) are indicated for lactate clearance in patients with a strong suspicion of lactic acidosis associated to metformin (such situations usually not coinciding with overdose), in the presence of oliguria and when diuresis is not restored within the first hour.<sup>141</sup> There are no clear recommendations as to which RRT is best. We propose conventional hemodialysis in hemodynamically stable patients, and continuous hemofiltration in unstable patients. No data are available on peritoneal dialysis.<sup>142</sup> In the case of patients

admitted to the ICU, we advise hemodiafiltration on a very early basis until the lactate levels have normalized.<sup>143</sup>

**Recommendation 3: Start antidote and RRT early in patients with suspected alcohol and glycol intoxication**

Early antidote use together with RRT is indicated when severe alcohol and glycol intoxication is suspected. Toxic concentration in plasma need not be monitored.<sup>144</sup> The antidote is intravenous ethanol (fomepizole if available),<sup>145</sup> which inhibits the metabolism of methanol (MT) and ethyleneglycol (ETG), indicated in the presence of toxicologically or clinically suspected severity defined as: metabolic acidosis, high osmolar/anion gap values or altered consciousness; visual disturbances (MT); renal failure and hypocalcemia (ETG). Values of MT/ETG > 0.2 g/l also indicate administration of the antidote. In the case of serious clinical conditions, refractory acidosis (pH < 7.15–7.20), MT/ETG > 0.5 g/l or renal or liver failure, the start of RRT is advised (preferably high efficiency intermittent hemodialysis or continuous hemodialysis in the case of contraindications).<sup>146</sup> The antidote and RRT are to be suspended in the case of MT/ETG < 0.2 g/l and clinical remission/improvement. We advise the administration of sodium bicarbonate (until reaching pH > 7.20); intravenous thiamine 100 mg/12 h due to the high frequency of alcoholism (1 g if Wernicke encephalopathy is suspected), pyridoxine 100 mg/6 h in ETG, and calcium folinate or folic acid (50 mg/4 h during 24 h) in MT.

**Recommendation 4: Early intravenous administration of acetylcysteine is indicated in patients with suspected paracetamol intoxication (maintaining administration until liver function improves)**

Paracetamol is an antipyretic and analgesic drug that is fundamentally metabolized in the liver. The drug used to treat intoxication is N-acetylcysteine,<sup>147,148</sup> which is to be administered: (1) when a dose of >7.5 g or 150 mg/kg has been taken; (2) in cases exceeding 150 µg/ml of the Rumack–Matthew nomogram after 4 h; and (3) when the dose and/or timing of intake of the drug are not known. The administration protocol comprises a first dose of 150 mg/kg in 250 ml of 5% glucose saline solution over 30 min, 50 mg/kg in 500 ml of glucose saline over 4 h followed by 100 mg/kg in 1000 ml of glucose saline over 16 h. The aim is to afford early protection against the toxic metabolite, N-acetyl-p-benzoquinoneimine (NAPBQ), and alterations of the mitochondrial respiratory chain, which result in liver damage.<sup>149</sup> Our recommendation is to start treatment early and to maintain it until the liver cytolytic enzymes and prothrombin time have normalized.

**Recommendation 5: Request evaluation by the Department of Psychiatry of those patients with attempted suicide, before deciding discharge from the ICU**

The frequency with which suicide attempts are repeated varies according to the literature source considered, but is high enough to warrant a thorough analysis, with the adoption of adequate preventive measures.<sup>150</sup> On the other hand, lethality assessment is difficult and lies beyond the competences of the intensive care professionals.<sup>151</sup> Likewise, a

large proportion of patients require subsequent follow-up or even admission by the Department of Psychiatry. Our recommendation is to request a psychiatric evaluation of all patients admitted to the ICU due to attempted suicide.<sup>152</sup>

### Transfusions and Blood Products Working Group

#### Recommendation 1: Consider a red cell concentrate transfusion threshold specific of the different populations of critical patients

The use of restrictive transfusion (hemoglobin  $\leq 7$  g/dl) reduces patient morbidity-mortality. In bleeding or septic patients or individuals with heart disease, a more permissive threshold is suggested (hemoglobin between 9 and 10 g/dl). In non-bleeding critical patients, almost all studies have shown that the transfusion of red cell concentrates with restrictive criteria reduces the transfusion index and rate, as well as the incidence of infections, with no associated increase in morbidity, hospital stay or mortality. However, some studies in non-bleeding critical patients with heart disease or non-bleeding critical patients with symptoms (angina, orthostatic hypotension or tachycardia) refractory to resuscitation fluid therapy suggest considering transfusion when the hemoglobin level drops to below 8 g/dl. In cardiac and gastrointestinal cancer surgery, as well as in patients with bleeding, sepsis or acute myocardial infarction, the literature warns of the risks of excessively restrictive thresholds and suggest a more liberal approach (hemoglobin under 9–10 g/dl).<sup>153–155</sup>

#### Recommendation 2: Avoid the transfusion of fresh frozen plasma in critical patients with active bleeding, despite alteration of the coagulation times

The transfusion of fresh frozen plasma (FFP) in the absence of active bleeding or high bleeding risk is not indicated, despite prolongation of the coagulation times. The transfusion of FFP should not be based on anomalous laboratory test results but on the risk and consequences of bleeding in the individual patient.<sup>156–158</sup>

#### Recommendation 3: Consider a platelet transfusion threshold specific of the different populations of critical patients

Prophylactic platelet transfusion is advised when: (1) the platelet count is  $<10 \times 10^9$  platelets/l, in order to avoid spontaneous bleeding in hypoproliferative thrombocytopenia; 2 the platelet count is  $<50 \times 10^9$  platelets/l and with a need for lumbar puncture or some non-neurosurgical procedure; or (3) the platelet count is  $<100 \times 10^9$  platelets/l before a neurosurgical or eye surgery procedure. Prophylactic transfusion cannot be disadvised when the count is  $<50 \times 10^9$  platelets/l and a central venous catheter is needed. Therapeutic platelet transfusion is advised: (1) in patients with active bleeding, in order to maintain levels  $>50 \times 10^9$  platelets/l; and (2) for maintaining a platelet count of  $>75 \times 10^9$  platelets/l in patients with active bleeding when bleeding fails to cease with lower values.<sup>159,160</sup> It is advisable to keep the count  $>100 \times 10^9$  platelets/l in patients with massive bleeding and brain traumatism. Therapeutic platelet transfusion cannot be disadvised in bleeding patients subjected to antiplatelet treatment.<sup>161</sup>

#### Recommendation 4: Transfuse blood components “unit by unit” (particularly red cell concentrates) in patients without active bleeding

The administration of red cell concentrates on a unit by unit basis, followed by reevaluation of the remaining needs after each transfusion, allows evaluation of the suitability of transfusion from the perspective of the volume administered (transfusion index). This index should be as low as needed to revert the situation giving rise to the indication of transfusion, or to reach a minimum safe level according to the clinical characteristics of the patient at the time. Each transfused unit increases the risk of a poorer clinical outcome for the patient. Consideration is required of the context of the situation, the patient environment (degree of monitoring), and the logistic problems for obtaining the red cell concentrates “when needed” (response time).<sup>162</sup> In the case of red cell concentrates, the AABB<sup>153</sup> has established a series of recommendations of help in deciding “when transfusion is needed”, while the recommendations of the update on the Seville Document<sup>154</sup> offer help in deciding “how much to transfuse”.

#### Recommendation 5: Revert anti-vitamin K anticoagulants with prothrombin complex concentrate in life-threatening situations or where urgent surgery is needed

Anticoagulation should be reverted once the indication has been established and considering the risk/benefit ratio of doing so. In addition, it should be carried out using the fastest method possible. The use of hemostatic drugs can increase the risk of thrombosis, which is already high in such patients (this being the reason why they are anticoagulated)—though the risk has been reduced by the current drugs.<sup>163,164</sup> Prothrombin complex concentrate (PCC) should be used due to its advantages with respect to the rest of the drugs used to revert anticoagulation. In effect, PCC quickly and effectively corrects plasma hemostasis, with almost immediate normalization of the coagulation times; it lacks the side effects of the blood products (volume overload associated to fresh frozen plasma, anaphylactic reactions, non-hemolytic febrile reactions, hemolytic reactions due to blood group incompatibilities and transfusion related acute lung injury [TRALI]); and does not pose risks of virus or prion transmission.<sup>161</sup>

### Transplantations Working Group

#### Recommendation 1: Offer the option of organ and tissue donation as an integral part of end-of-life care

Respecting the dignity of dying persons implies allowing them to decide the possibility of donating their organs and tissues, with due observation of personal autonomy and freedom to decide according to their own values.<sup>165</sup> Recognizing the right of the patient to decide how to die obliges us to explore his or her will to donate or not, and to respect the decision made. Donation should form part of end-of-life care, and this option must be considered in all patients who have died or are at the point of dying under conditions compatible with organ and tissue donation.<sup>166</sup> It is essential to spread the idea that organ and tissue donation forms

part of the services of the ICU, and is integrated within end-of-life care.<sup>167</sup>

**Recommendation 2: Guarantee the possibility of organ and tissue donation in all brain death patients**

The death of patients under neurological criteria inexorably occurs in the ICU due to the need for mechanical ventilation. The wish to donate organs and tissues on the part of all brain death (BD) patients is a right which all ICU physicians must respect and guarantee. Early detection and reporting to the transplant coordinator of all BD patients or patients with devastating neurological damage at risk of evolving toward BD should constitute a standardized process.<sup>168</sup> The transplant coordinator and intensivist in charge of the patient are the most adequate individuals for evaluating the potential donor, investigate the donation will of the deceased person, and ensure that this right is implemented under the best conditions possible. Adequate maintenance of the donor with a view to optimizing the donation process should form part of the services of the ICU.<sup>169,170</sup>

**Recommendation 3: Assess the possibility of controlled non-heart beating donation in patients where limitation of life support treatment is decided**

Controlled non-heart beating donation (CNHBD) is an important option for expanding organ donation in this country. In effect, its contribution has served to offset the decrease in donation rate as a result of fewer brain dead donors. Before starting a CNHBD program, there must be an adequate end-of-life care culture referred to critical patients and a consensus-based limitation of life support treatment (LLST) protocol. The intensivist must consider the possibility of donation when dealing with patients to be subjected to LLST.<sup>171</sup>

The CNHBD protocols are not technically complex and are open to any hospital.<sup>172</sup> These protocols comprise organ preservation and extraction: rapid surgery, in situ cold perfusion or normothermic abdominal perfusion with extracorporeal membrane oxygenation (ECMO). Each center should select the procedure suited to its own resources, or establish collaborations with supporting centers that possess adequate experience and technology.<sup>173</sup>

**Recommendation 4: Interview the relatives of patients with devastating brain damage not amenable to treatment, prior to brain death, to offer admission to the ICU**

The donation interview prior to BD is carried out in the case of patients with devastating brain damage where medical or surgical treatment is futile and death is expected to occur shortly. Consultation is made of the donation will of the patient, and where affirmative, permission is requested from the family to start or maintain intensive care allowing death to occur under conditions permitting BD donation.<sup>174</sup> The intensive care of organ donors must ensure adequate oxygenation and the preservation of potentially transplantable organs (mechanical ventilation, vasoactive drugs, etc.), and must be integrated within end-of-life care in the ICU—guaranteeing patient comfort and attention to the family during the entire dying process.<sup>175,176</sup>

**Recommendation 5: If allowed by the disease involved, include the possibility of tissue donation in the medical information given to the families of patients that die in the ICU**

The clinical use of human tissues is currently a therapeutic option within reach of all professionals, and significantly improves the quality of life of thousands of patients. The number of tissue transplants far outnumbers that of organ transplants (for every patient receiving an organ in Spain, 3.5 patients received tissue grafts). This increase in utilization has led to an increase in the demand for tissue donation (TD). Tissue donation exceeds the boundaries of organ donation, encompassing all patients dying of cardiac arrest. As a result, any in-hospital death may be regarded as an opportunity for TD.<sup>177</sup> The way to increase the detection of possible TDs is to ensure training and enhanced awareness among the health professionals. In this field, intensivists, as the central and sustaining reference in the Spanish donation and transplantation model, must lead the TD process.<sup>178,179</sup>

## Discussion

The critical patient management recommendations developed by the Working Groups of the SEMICYUC are fundamented on those aspects considered to be most relevant in the daily care of the patients admitted to the ICUs.

These recommendations seek to reduce variability in the management of critical patients, as well as to contribute to standardization of their care. The incorporation of these clinical practice recommendations may have beneficial effects upon clinical outcomes and patient safety.

The limitations of the document include the fact that some of the recommendations are based on a low level of evidence. Other aspects related to critical patient care possibly might require future evaluation for inclusion in the series of recommendations on the management of critical patients. Monitoring of the adherence, degree of satisfaction, diffusion and impact of these recommendations should be independently evaluated by future studies. On the other hand, operational specifications caused us to select only five recommendations per Working Group. This required the document coordinating team to place priority on those recommendations considered to be most relevant and visible. In this regard, bias may have been introduced in drafting the manuscript. It is clear that there may be other recommendations in the management of critical patients. As a result, in future editions of the document some of them might be modified or suppressed, with the incorporation of other different recommendations.

In conclusion, the recommendations provided in this document hope to serve as a useful tool for improving the decision making process in critical patients admitted to the ICU. In no case has it been our intention to replace the decision capacity of the clinician in any given case. Application of the recommendations will also depend on the availability of means in each center or institution. On the other hand, new findings derived from clinical research may afford new evidence requiring a change in routine practice, and thus an update on the present recommendations.

## Ethical responsibilities

**Protection of people and animals.** The authors declare that this research has not involved experiments in humans or in animals.

**Confidentiality of data.** The authors declare that no patient data appear in this article.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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## Conflicts of interest

None.

## Annex. Participating authors

*Bioethics Working Group:* Olga Rubio-Sanchiz (Hospital Sant Joan de Déu, Althaia Xarxa Assistencial Universitària de Manresa) and Nuria Masnou (Hospital Universitari de Girona Doctor Josep Trueta).

*Cardiological Intensive Care and Cardiopulmonary Resuscitation Working Group:* Rocío Gómez López (Hospital Quirónsalud Miguel Domínguez), Andrés Carrillo López (Hospital Universitario Son Espases), Celina Llanos Jorge (Hospital Quirónsalud Tenerife) and Ana Ochagavía Calvo (Corporació Sanitària i Universitària Parc Taulí).

*Nephrological Intensive Care Working Group:* Francisco J. González-de-Molina-Ortiz (Hospital Universitari Mútua Terrassa), José Ros-Martínez (Hospital Clínico Universitario Virgen de la Arrixaca), Inmaculada de Dios-Chacon (Hospital de Son Llàtzer), Sonia Mas-Font (Hospital General Universitario de Castellón), Javier Maynar-Moliner (Hospital Universitario de Álava), Raquel Montoiro-Allué (Hospital Clínico Universitario Lozano Blesa), Antoni Roglan Piqueras (Hospital San Pau), Jose A. Sanchez-Izquierdo-Riera (Hospital Universitario 12 de Octubre), Gemma Seller-Pérez (Complejo Universitario Carlos Haya) and Teresa María Tomasa Irriguible (Hospital Germans Trias i Pujol).

*Infectious Diseases and Sepsis Working Group:* Xavier Nuvials Casals (Hospital Universitari Vall d'Hebron) and Borja Suberviola Cañas (Hospital Universitario Marqués de Valdecilla).

*Evaluation of Technologies and Research Methodology Working Group:* Eduardo Aguilar Alonso (Hospital Infanta Margarita), María Amparo Bodí Saera (Hospital Universitario de Tarragona Joan XXIII), Vicente Gómez Tello (Hospital Moncloa de Madrid), María Cruz Martín Delgado (Hospital Universitario de Torrejón) and Pedro Morrondo Valdeolmillos (Hospital Universitario Donostia).

*Acute Respiratory Failure Working Group:* Rafael Fernández Fernández (Althaia Xarxa Assistencial Universitària de Manresa), Federico Gordo Vidal (Hospital Universitario del Henares), Gonzalo Hernández Martínez (Complejo Hospitalario de Toledo, Hospital Virgen de la Salud), Marta López

Sánchez (Hospital Universitario Marqués de Valdecilla), Manuel Pérez Márquez (Hospital Universitario Rey Juan Carlos), Mariana Portillo Botelho (Hospital General Universitario de Ciudad Real), Isidro Prieto del Portillo and Ignacio Sáez de la Fuente (Hospital Universitario 12 de Octubre), Juan Pero Tirapu León (Complejo Hospitalario de Navarra), Juan Alfonso Soler Barnes (Hospital Morales Meseguer), Antonio Artigas Raventós (Hospital de Sabadell, Corporació Sanitària i Universitària Parc Taulí), Andrés Esteban de la Torre (Hospital Universitario de Getafe, CIBER de Enfermedades Respiratorias), Sonia López Cuenca (Hospital Universitario de Getafe), Arantxa Mas Serra (Hospital Moisès Broggi), Jordi Mancebo Cortés (Hospital de la Santa Creu i Sant Pau) and Pilar Ricart Martí (Hospital Universitari Germans Trias i Pujol).

*Metabolism and Nutrition Working Group:* María Luisa Bordejé Laguna (Hospital Universitario Germans Trias i Pujol), Juan Francisco Fernández Ortega and José Andrés Arboleda Sánchez (Hospital Regional Universitario Carlos Haya), José Acosta Escribano (Hospital General Universitario de Alicante), José Ignacio Herrero Meseguer (Hospital Universitari de Bellvitge), Juan Carlos Montejo González and Teodoro Grau Carmona (Hospital Universitario 12 de Octubre), Mónica Zamora Elson (Hospital General San Jorge), Luis Servià Goixart (Hospital Universitari Arnau de Vilanova), Pilar Martínez García (Hospital Universitario Puerto Real), Carlos Ortiz Leyba (Hospital Quirónsalud Sagrado Corazón), Alfons Bonet Saris (Clínica Girona), Sergio Ruiz Santana (Hospital Universitario de Gran Canaria Doctor Negrín), Carmen Sánchez Álvarez (Hospital General Universitario Reina Sofía), Jimena Abilés Osinaga (Hospital Costa del Sol), Encarnación Molina Domínguez (Hospital General Universitario de Ciudad Real) and Montserrat Casanovas Taltavull (Hospital de Igualada).

*Neurointensive and Trauma Care Working Group:* Luis Juan Terceros Almanza, Ignacio Sáez de la Fuente, Guillermo Morales Varas, Jesús Barea Mendoza, Carlos García Fuentes and Mario Chico Fernández (Hospital Universitario 12 de Octubre), Luis Servià Goixart (Hospital Universitari Arnau de Vilanova), Patricia López Fajardo (Hospital Universitario Nuestra Señora de la Candelaria), Rubén Herrán Monge and Pedro Enríquez Giraud (Hospital Universitario Río Hortega), Marilyn Riveiro Vilaboia (Hospital Universitari Vall d'Hebron) and Jesús Álvarez Fernández (Hospital Universitario de Getafe).

*Planning, Organization and Management Working Group:* María José Ferrer Higuera (Hospital Universitario Reina Sofía), Nieves Franco Garrobo (Hospital Universitario de Móstoles) and María Cruz Martín Delgado (Hospital Universitario de Torrejón).

*Sedation and Analgesia Working Group:* María José Jiménez and Cándido Pardo Rey (Hospital Universitario Clínico San Carlos), Ferrán Roche Campo (Hospital Verge de la Cinta), Manuela García Sánchez (Hospital Universitario Virgen Macarena), Carolina Giménez-Esparza Vich (Hospital Vega Baja Orihuela), Elena Ruiz-Escribano Taravilla (Hospital General Universitario de Albacete), Herminia Torrado Santos (Hospital Universitari de Bellvitge), Belén Estebanez (Hospital Universitario La Paz), Lorenzo López Pérez (Hospital Universitario Infanta Leonor), José Manuel Gómez García (Hospital General Universitario Gregorio Marañón), Chiara Caciono Reategui (Hospitales Madrid, Grupo HM) and

Miguel Ángel Romera Ortega (Hospital Universitario Puerta de Hierro).

*Toxicology Working Group:* Jaume Baldirà Martínez de Irujo (Hospital Universitari Vall d'Hebron), Ana María Ruiz Mena and Indalecio Morán Chorro (Hospital de la Santa Creu i Sant Pau), Alejandra Fernández Trujillo (Parc Sanitari Sant Joan de Déu) and Emilia Civeira Murillo (Hospital Clínico Universitario de Zaragoza).

*Transfusions and Blood Products Working Group:* Manuel Quintana Díaz and Abelardo García de Lorenzo (Hospital Universitario La Paz), Manuel Muñoz Gómez (Facultad de Medicina de Málaga), Gabriel Tirado Anglés (Hospital Royo Vilanova), Pilar Marcos (Hospital Universitari Germans Trias i Pujol), Santiago Ramón Leal-Noval (Hospital Universitario Virgen del Rocío), Juan Carlos Ruiz Rodríguez (Hospital Universitari Vall d'Hebron), Cristina Muñoz Esteban (Clínica Rotger).

*Transplantations Working Group:* Alberto Sandiumenge Camps (Hospital Universitari Vall d'Hebron), Juan José Egea Guerrero (Hospital Universitario Virgen del Rocío), Domingo Daga Ruiz (Hospitales Universitarios Regional y Virgen de la Victoria de Málaga), Eduardo Miñambres García (Hospital Universitario Marqués de Valdecilla), Juan José Rubio Muñoz (Hospital Universitario Puerta de Hierro), Francisco del Río Gallegos (Hospital Clínico de San Carlos).

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