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ORIGINAL

Study of post-ICU mortality during 4 years (2006-2009). Analysis of the factors related to death in the ward after discharge from the ICU

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KEYWORDS
Critically ill patients;
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Abstract
Objective: To detect possible reasons for mortality of critical patients transferred from the ICU to the hospital wards and to analyze the possible attributable causes for such mortality.
Design: An observational study of prospectively collected data, analyzed retrospectively.
Population: Cohort analysis of 5328 with consecutive admissions to our ICU, whose evolution was followed up to hospital discharge or death.
Period: From January 2006 to December 2009.
Method: An analysis was made of differential significance of epidemiological, clinical-care, death risk estimate, coincidence between ICU admissions reasons and causes of death after ICU discharge, as well as limitation of health care effort incidence. Inappropriate ICU discharge was considered to exist if the death occurred during the first 48 hours after ICU transfer, without limitation of care effort.
Results: A total of 907 patients died (SMR = 0.9; 95% CI, 0.87-0.93), 202 of whom died after ICU discharge (3.8% of total sample and 22.3% of all deceased patients), ward length of stay being 12.4±17.9 days. No significant differences were found between deaths in the ICU or post-ICU deaths regarding infective complications appearing after admission to the ICU. Greater mortality was also not found in those re-admitted to the ICU after having been transferred to the ward. It was verified that the cause of death in the ward did not significantly coincide with the cause of admission to the ICU.
Discussion: Some mortality after ICU discharge is to be expected. Our data do not allow us to attribute this mortality rate to care deficiencies (inappropriate ICU discharges or deceased care in the wards). The reasons for this mortality have a varied and variable explanation. It mostly corresponds to an evolution of the patients differing from that expected when they were discharged from ICU.

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PALABRAS CLAVE
Paciente crítico;
UCI;
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Riesgo de muerte

Estudio de la mortalidad post-UCI durante 4 años (2006-2009). Análisis de factores en relación con el fallecimiento en planta tras el alta de UCI

Resumen
Objetivo: Detectar posibles razones de la mortalidad de los pacientes críticos trasladados desde la UCI a las plantas del hospital y analizar las potenciales causas atribuibles de esta mortalidad.
Diseño: Estudio observacional de datos prospectivos analizados retrospectivamente.
Muestra: Cohorte de 5.328 pacientes ingresados consecutivamente en nuestro SMI cuya evolución se sigue hasta el fallecimiento o el alta hospitalaria.
Período: Desde enero de 2006 a diciembre de 2009.
Método: Análisis de significación diferencial de datos epidemiológicos, clínico-asistenciales, de estimación de riesgo de muerte, de coincidencia de diagnóstico de causa de ingreso en UCI y de causa de fallecimiento y de incidencia de limitación de esfuerzo asistencial. Se consideró alta inadecuada de UCI si la muerte acontecía antes de las 48 h del traslado, sin limitación de esfuerzo asistencial.
Resultados: Fallecieron 907 pacientes (tasa estandarizada de 0,9; IC del 95%, 0,87-0,93) de los que 202 fallecieron tras el alta del SMI (el 3,8% de la población total y el 22,3% de los fallecidos); la estancia en planta post-UCI fue de 12,4 ± 17,9 días. No se detectaron diferencias significativas entre los fallecidos en UCI o tras la estancia en UCI respecto a complicaciones infectivas aparecidas tras el ingreso. Tampoco los reingresados en UCI tras el pase a planta presentaron una mayor mortalidad. Se comprueba que la causa de muerte en planta no es significativamente coincidente con la causa de ingreso en UCI.
Discusión: Cierta mortalidad de pacientes críticos tras el traslado desde UCI es un hecho habitual. Nuestros datos no permiten atribuir esta mortalidad a deficiencias asistenciales (altas inadecuadas o disminución de asistencia en planta). Las razones para esta mortalidad tienen una explicación variada y variable, y en su mayoría corresponden a evolución del paciente diferente de la previsible tras el traslado desde el SMI.

Introduction

On considering the healthcare effectiveness of Departments of Intensive Care Medicine (DICM), it is common practice to use an intermediate outcomes indicator such as mortality. The comparison between observed mortality and expected mortality is known as the "standard mortality rate" (SMR).

Definition of what is meant by "expected mortality" is more problematic, and raises two issues: How should it be estimated? At what time should it be considered? The first point is relatively easy to answer, since we have the so-called prognostic or death risk indicators – though these will not be dealt with in this study.

The second point is more complicated to answer. In establishing the prognostic probability of mortality, the authors have defined hospital discharge as the estimation timepoint. This classically has been the approach used in all the prognostic estimation systems[1] except the SAPS 3, which by definition establishes the point of analysis at 28 days from admission or at the time of hospital discharge (whichever comes first). Bearing this exception in mind, this means that the time of hospital discharge is considered for the analysis of effectiveness. It is therefore rather surprising to see the diversity of criteria used by different clinical investigators, who have coined the term "hidden mortality"[2,3] to define the possibility of patient death in conventional management wards after discharge from Intensive Care. This is possibly why a recent study analyzing these aspects was entitled "Unraveling post-ICU mortality".[4]

If what is meant by "hidden" is that the underlying cause is not known and may or may not be related to the reason for patient care in the DICM, then such nomenclature is acceptable. However, taking the term to mean that such mortality has not routinely been taken into account would be ignoring the existing documental evidence.

Underlying these considerations we have the possible answers to two very important questions: Was discharge from Intensive Care appropriate in time and manner? Did death occur due to the same cause or to some other cause, whether related or not? Some authors consider that the physiopathological and clinical instability of the patient at the time of discharge from the Intensive Care Unit (ICU) is the first mortality conditioning factor after moving the patient to a conventional ward.[5,6]

The aim of this study was to analyze the healthcare and diagnostic circumstances of a consecutive population of patients attended in a DICM, and who died in the conventional wards of the hospital after having been discharged from our Department.

Patients and methods

Corresponding to the period between 1 January 2009 and 31 December 2009, an analysis was made of the consecutive admissions to a 19-bed DICM in a teaching reference hospital.

The patient information was entered in a customized data management system (unit data management system, UDMS).

This information included demographic data (gender, age, origin at admission, type of patient: emergency or elective surgery, or non-surgical patient), epidemiological parameters (cause of admission according to IRS of the FRICE [Fund for Research on Intensive Care in Europe], specialty of origin at admission, pre-ICU, intra-ICU and post-ICU stays [expressed in days], readmission or not readmission, diagnosis at discharge from the DICM, mortality risk, presence of infection confirmed at admission or manifesting during stay in the ICU, and the presence or absence of multiorgan failure during stay in the DICM), and activity data (DICM healthcare procedures carried out during the stay, and the duration in days of some of these procedures – specifically ventilatory support and continuous extrarenal filtration techniques).

Readmission was defined as a new admission to the DICM in the course of the same stay in hospital, corresponding to a patient who had already been treated by the DICM. The mortality risk was estimated with the SAPS 3.

The intermediate healthcare outcome of the patients was expressed as mortality, distinguishing between death occurring during the stay in the DICM and mortality recorded after moving the patient to a conventional ward after the first admission. This means that the readmissions supervised by the DICM were excluded from analysis – being considered as single admissions.

The duration of the stays, in days, was established as follows: a) pre-ICU stay: days of stay in the hospital, from admission of the patient to entry to the ICU; b) stay in the ICU: from admission supervised by the DICM to first transfer to a conventional ward; and c) post-ICU stay: days elapsed between patient transfer from the DICM to a conventional ward and hospital discharge. To the effects of this study, we only express the post-ICU stay of the patients who died in the ward after being moved from the DICM.

"Early discharge" was considered in those cases in which death occurred less than 48 hours after discharge from the DICM, due to a cause "related" to or "coincident" with that leading to admission to the ICU – provided such discharge had not been agreed as a consequence of limitation of therapeutic effort (LTE) or as a death option in a less hostile environment and family setting. Review of the patient course in the conventional ward and of the attributed causes of death was carried out independently by two of the authors (ABM and SMF), and in the case of discrepancies, consensus was reached among three authors (RAC).

Continuous variables were expressed as the mean and standard deviation (SD), while discrete variables were reported as percentages or absolute numbers (patients or events). The statistical analysis was carried out using the SPSS version 15 statistical package (analysis of significance of the differences between non-paired continuous variables using the Student t-test) and the CIA 1.0 package (analysis of significance of the differences of proportions). Statistical significance was accepted for $p<0.05$.

Results

During the study period, a total of 5238 consecutive admissions to the DICM were registered, with a mean age of 60.5 ± 17.2 years and a male predominance of 67.2%. The mean duration of stay was 5.8 ± 10.2 days, and the SAPS 3-estimated mortality risk was 19.5 ± 21.2. A total of 191 of these patients were readmitted (for the posterior study of mortality and its causes we only considered the first admission supervised by the DICM). Most of the patients (4018 cases) were admitted due to nonsurgical causes. In 299 of these patients LTE was applied at some point during their stay in the ICU.

A total of 907 patients died (17.3%, corresponding to a SMR (actual versus predicted) of 0.9; 95%CI 0.87-0.93): 705 during the first stay in the ICU and 202 during the stay in the ward after discharge from the DICM (3.8% with respect to the global sample and 22.3% of the mortality among the patients considered in the study). The epidemiological data and their differential significance are detailed in Table 1.

Of the 191 readmissions (4.2% of the patients discharged alive from the DICM), only 8 deaths were recorded; both the mortality risk and the stay in the ICU were lower in the group of patients who died after discharge from the DICM than in those who died in the ICU during their first registered stay. Both indicators in turn were greater among the patients who survived.

On the other hand, the duration of stay in the ward, after discharge from the DICM, was 12.4 ± 17.9 days.

Table 2 reports the application of certain healthcare procedures in the groups of patients who survived and those who died (intra-ICU and after discharge from the ICU). It is important to note the different statistical significances upon comparing the application of one procedure or other, and of the duration of the application of some of them (mechanical ventilation and continuous renal replacement therapy).

On a complementary basis, Table 3 offers information on the presence of certain situations classically associated with an ominous prognosis. Thus, there are no statistically significant differences between the presence of infectious complications upon admission to the ICU, or manifesting during the stay, between the survivors and the patients that died – though such differences do exist between the survivors and the patients that died after discharge from the DICM. The same applies to the presence of pneumonia associated to mechanical ventilation.

Lastly, Table 4 reports the circumstances relating to death (as specified by the hospital discharge reports) after discharge from the ICU, and the cause of first admission to our DICM. The supplementary electronic material provided (at the end) refers to the causes and diagnoses associated to admission to the ICU, and the causes and diagnoses that appear in the hospital discharge report (after death).

Discussion

The aim of this study was to analyze the effects of a strategy for patient transfer to conventional hospital wards, based on both objective clinical and personal criteria, and to compare the results obtained with those found in the literature. However, as has been pointed out by Fernández,[7] it must be taken into account that knowing the mortality rates after discharge from the ICU at least theoretically allows us to lessen avoidable mortality – and this in turn forms part of a quality strategy.

Table 1 Demographic data

	Global	Live	Total deaths	Post-ICU deaths (percentage of total deaths)	p
Patients	5238	4331 (82.68%)	907 (17.31%)	202 (22.27%)*	
Males, %	67.2	67.6	68.2	64.9	a: NS; b: NS
Age (years)	60.5 ± 17.2	59.8 ± 17.3	66.9 ± 15.1	72.4 ± 11.8	a: < 0.05 (−0.04 to 0.02); b: < 0.05 (−0.04 to 0.09)
Type of patient					
Emergency surgery	526 (10.04%)	375 (8.65%)	151 (16.64%)	34 (16.83%)	a: < 0.05 (−0.1 to −0.05); b: < 0.05 (−0.13 to −0.03)
Elective surgery	694 (13.24%)	649 (14.98%)	45 (4.96%)	21 (10.39%)	a: NS; b: NS
Non-surgical	4.018 (76.7%)	3.307 (76.35%)	711 (78.39%)	147 (72.77%)	a: < 0.05 (−0.05 to −0.01); b: < 0.05 (−0.26 to −0.09)
Readmissions	191 (3.64%)	137 (3.16%)	54 (5.95%)	8 (3.96%)	a: NS; b: < 0.05 (−0.03 to −0.02)
Stays					
Pre-ICU	2.7 ± 8.1	2.3 ± 7.4	5.3 ± 12.2	7.2 ± 14.1	a: < 0.05 (−3.6 to −2.4); b: < 0.05 (−6 to −3.8)
ICU	5.8 ± 10.2	5.3 ± 9.5	8.8 ± 13.7	7.7 ± 12	a: < 0.05 (−4.24 to -2.76); b: < 0.05 (−3.76 to −1.04)
Post-ICU	–	6.6 ± 13.9	2.8 ± 9.5	12.4 ± 17.9	a: < 0.05 (2.05-4.75); b: < 0.05 (−7.79 to −3.01)
Mortality risk	19.5 ± 21.2	15.3 ± 16.7	45.2 ± 25	33.2 ± 22.1	a: < 0.05 (−31.2 to −28.6); b: < 0.05 (−20.3 to −15.5)
LTE	299 (5.71%)	43 (0.99%)	256 (28.22%)	23 (11.38%)	a: < 0.05 (−0.3 to −0.24); b: NS

Data in parentheses: percentage with respect to the group of the column, except when indicated otherwise*.
a: significance of the difference between live and total deaths; b: significance of the difference between live and post-ICU deaths.
All significance values are expressed in relation to the value 0.05 (NS [nonsignificant] < 0.05 level of significance less (any value) than the mentioned value). Where pertinent, the value in parentheses corresponds to the 95%CI of the difference between proportions.

Table 2 Healthcare procedures

	Global	Live	Total deaths	Post-ICU deaths	p
OTI	1967 (37.75%)	1340 (30.93%)	647 (71.72%)	89 (44.05%)	a: < 0.05 (−0.43 to −0.37); b: < 0.05 (−0.36 to −0.22)
Tracheotomy	206 (3.85%)	145 (3.34%)	61 (6.76%)	11 (5.44%)	a: < 0.05 (−0.05 to −0.02); b: NS
MV	2405 (45.05%)	1684 (38.88%)	721 (79.93%)	116 (57.42%)	a: < 0.05 (−0.43 to −0.37); b: < 0.05 (−0.25 to −0.11)
CRRT	356 (6.69%)	190 (4.38%)	166 (18.4%)	31 (15.34%)	a: < 0.05 (−0.16 to −0.11); b: < 0.05 (−0.16 to −0.06)
Hemodynamic monitoring	547 (10.24%)	266 (6.14%)	281 (31.15%)	35 (17.32%)	a: < 0.05 (−0.28 to −0.27); b: < 0.05 (−0.16 to −0.06)
Transfusion	991 (18.56%)	620 (14.31%)	371 (41.11%)	56 (27.72%)	a: < 0.05 (−0.29 to −0.23); b: < 0.05 (−0.2 to −0.07)
Vasoactive drug support	2558 (47.92%)	1910 (44.1%)	648 (71.84%)	107 (52.97%)	a: < 0.05 (−0.31 to −0.24); b: < 0.05 (−0.16 to −0.02)
Days on MV	6.7 ± 11.2	5.9 ± 10.1	8.7 ± 13.5	8.2 ± 13.8	a: NS; b: < 0.05 (−3.75 to −8.48)
Days on CRRT	8.8 ± 10	7.1 ± 7.6	10.2 ± 11.3	9.4 ± 9.2	a: NS; b: < 0.05 (−3.38 to −1.22)

Data in parentheses: percentage with respect to the group of the column, except when indicated otherwise.
Days on CRRT: duration in days of the continuous renal replacement therapy of any kind; Days on MV: duration in days of ventilation support; OTI: orotracheal intubation for ventilation support; Hemodynamic monitoring: including invasive techniques (pulmonary artery flotation catheter) and less invasive techniques (PiCCO system); Vasoactive drug support: hemodynamic support with vasoactive amines; includes dopamine, noradrenaline, adrenaline or dobutamine (where applicable); Transfusion: red cell concentrates or whole blood; CRRT: continuous renal replacement techniques; MV: mechanical ventilation (both invasive and noninvasive).
a: significance of the difference between live and total deaths; b: significance of the difference between live and post-ICU deaths.
All significance values are expressed in relation to the value 0.05 (NS [nonsignificant] < 0.05 level of significance less (any value) than the mentioned value). Where pertinent, the value in parentheses corresponds to the 95%CI of the difference between proportions.

Table 3 Situations associated with an ominous in-hospital prognosis

	Global	Live	Total deaths	Post-ICU deaths	p
Infection upon admission to ICU	426 (7.98%)	256 (5.91%)	170 (18.84%)	34 (1.83%)	a: < 0.05 (−0.16 to −0.1); b: < 0.05 (−0.16 to −0.06)
Infection manifesting during stay in ICU	400 (7.49%)	258 (5.95%)	142 (15.74%)	27 (13.36%)	a: < 0.05 (−0.12 to −0.07); b: < 0.05 (−0.12 to −0.02)
Pneumonia associated to ventilation support	235 (4.4%)	157 (3.62%)	78 (8.64%)	18 (8.91%)	a: < 0.05 (−0.07 to −0.03); b: < 0.05 (−0.09 to −0.01)
Multiorgan failure	387 (7.24%)	102 (2.35%)	285 (31.59%)	21 (10.39%)	a: < 0.05 (−0.32 to −0.26); b: < 0.05 (−0.12 to −0.03)

The percentages with respect to a patients included in the group are shown in parentheses.
a: significance of the difference between live and total deaths; b: significance of the difference between live and post-ICU deaths.
All significance values are expressed in relation to the value 0.05 (NS [nonsignificant] < 0.05 level of significance less (any value) than the mentioned value). Where pertinent, the value in parentheses corresponds to the 95%CI of the difference between proportions.

Table 4 Circumstances of post-ICU mortality (n = 202)

Type of admission to ICU	
Emergency surgery	33
Elective surgery	21
Non-surgical	148
Type of discharge to ward	
Emergency surgery	33
Elective surgery	21
Non-surgical	148
Predicted death at discharge from ICU	
Yes	34
No	162
Possible	6
Cause of death after discharge from ICU related to admission to ICU	
Yes	171
No	31
Discharge death diagnosis coinciding with reason for admission to ICU	
Yes	50
No	152
Early discharge from ICU (stay under 48 hours)	
Yes	28
No	161
Yes, with foreseeable death	13
LTE during post-ICU stay in ward	
Yes	33
No	63
Not specified	106

It should be remembered that the post-ICU mortality rates reported in the literature, and the attributed causes of such mortality, are varied and more coincident in the causes and mechanisms of death than in the percentage incidence of patient mortality. Thus, Moreno[6] recorded a mortality rate of 8.6% among the patients transferred from the ICU, and identified as underlying factors of major importance a longer stay in the ICU, a greater mortality risk (SAPS 2), and the persistence of central neurological and renal functional instability. This author recommends postponing the transfer of patients with such characteristics until their discharge can be regarded as "safe". Some other post-ICU mortality rates have been cited by Goldhill (27%) as early as in 1998,[8] Beck (12.6%),[9] Fernández, on describing the Sabadell Score (9.6%[7] and 7%[10]), and Gordo, in patients receiving artificial ventilation support (19%[11] and 10%[12]).

Other authors have attempted to relate such mortality after discharge from the ICU to healthcare dependency factors: the need for a tracheostomy[11,13] or other indirect risk indicators such as the duration of stay in the ICU,[8,11] the weakening of patient physiological reserve,[14] the origin and type of patient (greater risk in clinical than in postsurgical patients),[15] and even the C-reactive protein concentrations.[16]

It is of note that almost all studies attempting to relate post-ICU mortality to some variable do so as a point and isolated observation, and only Daly[17] and Lapichino[15] (the latter involving bootstrap techniques) have attempted to establish validations posterior to the initial observation.

There are two possible reasons in particular for considering the causes of death in patients who survive their stay in the ICU and posteriorly die in the hospital ward. The first involves the question: Have we done everything as well as we should? Establishing healthcare effectiveness in the DICM involves a critical comparison between the observed and expected mortality data. Clearly, there may be many reasons for deviations of the real situation from the predicted situation, though some of them are related to the quality of the aforementioned medical care – either because the seriousness of the admitted patients is not adequate (either too much or too little), or because the care provided fails to meet the quality levels considered standard (e.g., if premature or untimely discharges have been decided).

The second reason is related to the fact of establishing relations between the attributed causes of death among the patients who die in the ward in comparison with the causes that justified admission to the ICU in the first place. If patients admitted to the DICM posteriorly die of the same disease, with or without limitation of therapeutic effort, the investigator must evaluate the reasons for discharge from the ICU and the adequacy of the decision, as well as the adequacy of the care received in the hospital ward. This is the case of Beck,[9] who examined the time relationship of the moment (time of day) of transfer from the DICM – identifying as the fundamental cause of death the quantitative difference in medical management between the ICU and the hospital ward. These observations in turn were reaffirmed by Duke.[18]

This quantitative and qualitative difference in healthcare is the concept underlying in the inaptly termed "hidden mortality".[3] In 1999, Smith[19] insisted in reducing these changes in quantity and intensity of patient treatment, identifying the patients moved from the ICU to the ward who presented older age, higher mortality risk estimations, or who had required increased care efforts during their stay in the DICM. Similar orientations are provided by those studies which identify readmission to the ICU as corresponding to patients with an increased mortality risk and involving a greater care burden during their first stay in the DICM.[20] Campbell[21] stated that high post-ICU mortality observed without a simultaneous increase in the readmissions rate may be due to the fact that patient worsening has not been detected, or may occur due to causes different from those leading to first admission – considering that such readmissions are always associated to poorer outcomes in terms of mortality.[22]

The distinction between early and late readmissions was established by Chan,[23] who found that late readmission does not occur in relation to the first cause of admission to the ICU. Metnitz[24] in turn reported that early readmissions occur as a result of inopportune discharge from the ICU, and Ho[25] again identified a group of non-early readmissions (i.e., those taking place after 72 hours from discharge from the ICU) with a poorer mortality outcome with respect to the initial mortality risk and a poor physiological reserve (older age and a greater presence of comorbidities).[25]

However, the attributable causes of death among these patients, which are often unrelated to the reason for admission to Intensive Care, are not usually analyzed; conceptually, these are "different patients" – not patients whose survival outcome may be related to "early discharge" or inappropriate discharge from the DICM. This is the idea contained in the work of Braber,[4] which cites a post-ICU mortality rate of up to 10.3% in relation to longer stays, an increased estimated mortality risk and an increased demand for artificial ventilation support. Similar conclusions were drawn by Rivera,[26] on observing that the physiological reserve of patients who die in hospital after discharge from the ICU defines poorer quality of life and healthcare dependency than among the survivors. Ho[27] coincides with this "lack of similarity", while Lapichino stresses the worsening of physiological reserve.[15]

In contrast, other studies have established post-ICU mortality as variable, based on the subjective impression of the medical staff in charge of transfer to the ward (establishing patient recovery potential on the basis of personal experience), and have pointed to its intimate correlation to patient age.[7] This impression in turn was later reinforced[10] in a multicenter validation, on observing that post-ICU mortality varies between the 9% and 64% depending on the aforementioned subjective impression of the medical professional – though in this case the correlation to age was not confirmed, while an association to estimated mortality risk was identified. These changes with respect to the original description of the Sabadell Score make it possible to consider the variability of results and interpretations that can be related to variations in study design, sample size and the multicenter nature of the research, even when applying the same methodology.

On the other hand, the dependency of post-ICU mortality upon the level of care provided by the conventional hospitalization wards *a priori* does not appear questionable, unless voluntarily decided so, establishing limitation of therapeutic effort (LTE) criteria in certain patients considered to be in an irreversible situation or with few chances for survival. This is the strategy applied in the study published by Azoulay,[28] and which appears to be confirmed by our own series (albeit without statistical significance) – observing a larger proportion of restrictive care attitudes among the patients who die (Table 1), even during the stay in the ward, and moreover considering the scant presence in our setting of written LTE registries.

If death occurs due to other causes, attributing it to potential procedural or resource utilization strategy errors is questionable. In contrast, if death in the ward is related to the cause underlying previous admission to the ICU, then consideration is required of whether the patient has reached the end stage of the illness – accepting as reasonable the indication of limited therapeutic effort. Thus, Mayr[29] found the main causes of post-ICU mortality to be the presence of already known malignant tumors with a poor response to the initial treatment strategies, or the development of refractory heart failure that worsens again once the patient leaves the ICU.

Our series confirms the coexistence of some of the mentioned factors: the non-obligate association between early discharge and post-ICU mortality; the arguable relationship between the initial cause of admission to the DICM and the posterior attributed cause of death; the established presence of LTE in our policy towards patient transfer to the ward; and a high percentage concordance between the final outcome expected at discharge and the actual outcome recorded posteriorly.

In conclusion, we underscore that mortality among the patients after discharge from the ICU cannot be attributed to circumstantial inopportunity (in time and as refers to the patient situation); a large multicenter study is needed to adequately identify the causes of these deaths.

Conflict of interest

None of the authors have received payment or subventions of any kind for the conduction of this study. The authors declare no conflict of interest.

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