



Original Research

Impact of patient safety on hospital prognosis: Association between adverse events and in-hospital mortality

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ABSTRACT

Introduction: Adverse events (AEs) involve a safety problem and compromise the quality of care, but evidence on how they affect the prognosis of patients is limited.

Objective: In this study, the relationship between the presence of AEs and in-hospital mortality among patients is analysed, and their characteristics are compared.

Material and methods: An observational study with a cross-sectional design was conducted in 32 hospitals of varying complexity in the Community of Madrid. The clinical history of 9,111 patients was analysed. Patients who were in the emergency room and those admitted to psychiatric units or centres were excluded. All hospitalisations were reviewed using the Harvard Medical Practice Study methodology for the detection and characterisation of AEs. The association between in-hospital mortality and the number of AEs was analysed with two multivariate models via logistic regression: 1) an explanatory model adjusted for confounders and 2) a predictive model of in-hospital mortality. A descriptive analysis of the differential characteristics of the AE was performed for the patients who died.

Results: In-hospital mortality was 5%, with a higher incidence of AEs in patients who died (29.8% versus 11.9%; $p < 0.005$). The presence of 1 AE (OR [95% CI]: 2.1 [1.6 to 2.7]) or ≥ 3 AEs (2.4 [1.1 to 5.1]) significantly increased the odds of mortality. In addition, the increase in the number of AEs was a predictor of mortality without a dose-response effect. The AEs that were most associated with in-hospital mortality were those related to care (15.5%; $p = 0.047$), and 15.3% of the AEs that occurred during ward care contributed to in-hospital mortality.

Conclusion: There is an association between AEs and in-hospital mortality. The presence of at least 1 AE implies a critical event in the patient's prognosis without a dose-response effect. Reducing AEs related to care in patients with comorbidities is positioned as an efficient strategy for improving health outcomes.

Introduction

The World Health Organization (WHO) defines an adverse events (AE) as any incident that occurs during medical care and causes unnecessary harm to the patient, whether physical, psychological or emotional.¹ Approximately one in 10 patients suffer from an AE in the hos-

pital setting, and more than 3 million people die each year as a result.² AEs increase the burden of disease and compromise the sustainability of the health system by generating extra financial costs in the form of prolonged hospital stays or the need for new procedures.^{3,4}

It is essential to measure AEs and determine their impact in order to design policies that reduce AEs. The Harvard Medical Practice Study

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(HMPS) methodology⁵ has been a pioneer in the detection and study of AEs. Several studies have subsequently replicated it in different countries,^{6–9} both through longitudinal designs¹⁰ and transversal methods,¹¹ making it the reference methodology. One of the main areas of study has been the impact of hospital AEs on patients and on the healthcare system. Thus, a meta-analysis by Panagioti *et al* in 2019 revealed that 48% of AEs prolonged hospital stay, required a new surgical intervention or contributed to in-hospital mortality.¹² Zhan *et al* reported that AEs increased hospital stays by an average of 1–11 days, requiring additional healthcare in almost all cases.¹³ Estimates made in Europe in 2022 value this annual extra cost at 1 million euros for each hospital with more than 500 beds.³

It is accepted that AEs increase in-hospital mortality and worsen the prognosis of patients. However, most studies have been limited to describing the frequency of patients with AEs who died during hospitalisation, with values ranging between 5% and 11%.^{10,14}

Therefore, the aim of the current study, included in the Study on Patient Safety in Hospitals of the Community of Madrid (ESHMAD),¹⁵ was to estimate, in a pioneering way, an adjusted measure of the association between the number of active AEs suffered by the patient and in-hospital mortality. In addition, the following were analysed: 1) the presence of AEs as a predictor of in-hospital mortality and 2) the differential characteristics of AEs in patients who died and their impact on hospital stay.

Materials and methods

Study design

A multicentre observational study with a cross-sectional design was carried out in 32 hospitals in the Community of Madrid (eight with high complexity, 13 with medium complexity, six with low complexity, two support hospitals and three medium-stay hospitals). To construct the sample, each centre conducted a single cross-sectional assessment at the beginning of care activities on a designated day in May 2019. Patients who were in the emergency room and those admitted to psychiatric units or centres were excluded. The study was carried out according to the HMPS methodology with a review of medical records in two phases, using validated tools: 1) an AE screening phase through the screening guide adapted from the *Screening Review Form*;⁵ and 2) a phase of confirmation, classification and characterisation of the AEs, executed by the *Modular Review Form 2* (MRF2)¹⁶ applied to the positive records of the first phase. This phase was conducted when the patient was discharged or 1 month after screening to review all hospitalisations. The data were collected from the patient's clinical records by health professionals who received specific training in the review of AEs.¹⁷

Study variables

The dependent variable was mortality during hospitalisation. Based on the MRF2 protocol, the positive screenings of the first phase that met the following conditions were considered: 1) the AE was active during medical care, causing harm to the patient;¹ and 2) the damage was related to healthcare (a scale of 1–6 was applied, with '1' indicating minimal evidence or relationship and '6' total evidence; AEs being those with values ≥ 4).¹⁶ A new variable was created to categorise the number of AEs presented by each patient as 'Absence', '1', '2' or ' ≥ 3 '.

As independent variables, continuous, qualitative dichotomous and qualitative non-dichotomous variables were collected. The first group included age, total days of hospital stay, stay prior to screening, and additional days of stay due to AE. As qualitative dichotomies, the following were considered: 1) Patient demographics/comorbidities: sex, presence of cardiovascular disease, neoplasia, chronic obstructive pulmonary disease, immunodeficiency, liver cirrhosis, hypoalbuminaemia, pressure ulcers, reduced mobility and sensory deficits, renal failure (values of creatinine levels greater than 1.7 mg/dL at the time of admission), neutropenia (neutrophils $<1,000$), obesity (BMI >30 kg/m²) and active

smoking; 2) Instrumentalisation of clinical practice: history of surgical intervention during admission and presence on the day of screening of peripheral vascular catheters, central vascular catheters and urinary catheters. These variables were analysed individually and in combination, following the methodology of previous patient safety studies.^{10,18} Finally, as non-dichotomous qualitative variables, the type of hospitalisation service, the type of hospital ('Low-complexity acute care hospital', 'Medium-complexity acute hospital', 'high-complexity acute hospital', 'support hospital' and 'medium-stay hospital') and the variables related to AE were included. Hospital complexity was classified according to the National Health System Hospital Catalogue¹⁹ and the Hospitals 2022–2024 report from the Madrid Health Service Results Observatory.²⁰ Types of AEs were classified according to the MRF2 questionnaire,¹⁶ ensuring that all categories were mutually exclusive: 1) 'AEs related to care', referring to all incidents of damage derived from the nursing care of the patient during their hospitalisation (such as pressure ulcers [PUs], falls, and phlebitis); 2) 'AEs related to negative effects of medication', referring to all damage derived from a medication (such as nausea, diarrhoea and skin reactions); 3) 'AEs related to procedures', referring to all damage derived from any procedures (haemorrhage, pneumothorax, organ injury and suture dehiscence); 4) 'Healthcare-related infections', referring to any infectious process derived from care; and 5) 'Others' for those AEs that could not be classified into any previously mentioned category. For the definition of HAI, the criteria of the European Center for Disease Control in the European Point Prevalence Survey of Healthcare-associated Infections (EPPS) were used.^{18,21} The time of occurrence of an AE was classified as 'before admission', 'related to the admission process', 'during a procedure', 'after a procedure', 'during hospitalisation in the ward', or 'at the end of the hospitalisation'. With regard to the severity of the AE, the Conceptual Framework of the International Classification for Patient Safety of 2009 was applied,¹ with 'mild' being an AE that does not affect the management or duration of hospitalisation; 'moderate' being one that leads to readmission or additional days of hospitalisation; and 'severe' being one that leads to requirement for another surgery or that contributes to permanent disability or death.

Statistical analysis

Descriptive analysis included mean and median and standard deviation [SD] and interquartile range [IR]) for quantitative variables, and proportions for the qualitative variables. Bivariate analyses used *t*-tests or Mann–Whitney U tests for quantitative variables and chi-square or Fisher tests for qualitative ones, depending on whether they were parametric or non-parametric. P-values <0.05 indicated statistically significant differences.

Variables associated with in-hospital mortality were analysed using multivariate logistic regression with a backward selection method ($p < 0.05$), corrected for over-optimism by bootstrap and assessed with the Hosmer–Lemeshow test. All those that showed associations in the bivariate analysis were included.

To estimate the association between in-hospital mortality and the number of AEs, a multivariate explanatory model was developed by means of logistic regression adjusted for confounding variables, considering all those that modified the crude association by more than 10%.²² The confusion analysis can be found in the supplementary material in Table S1. For the statistical analysis, STATA version 18 software was used.²³

Results

Sample

9,111 patients met the inclusion criteria (Fig. 1). The mean age was 62.4 years (SD 25.7 years), 50.5% were women, and 72.2% (6,577) of hospital admissions were urgent, with 56.9% of patients admitted to

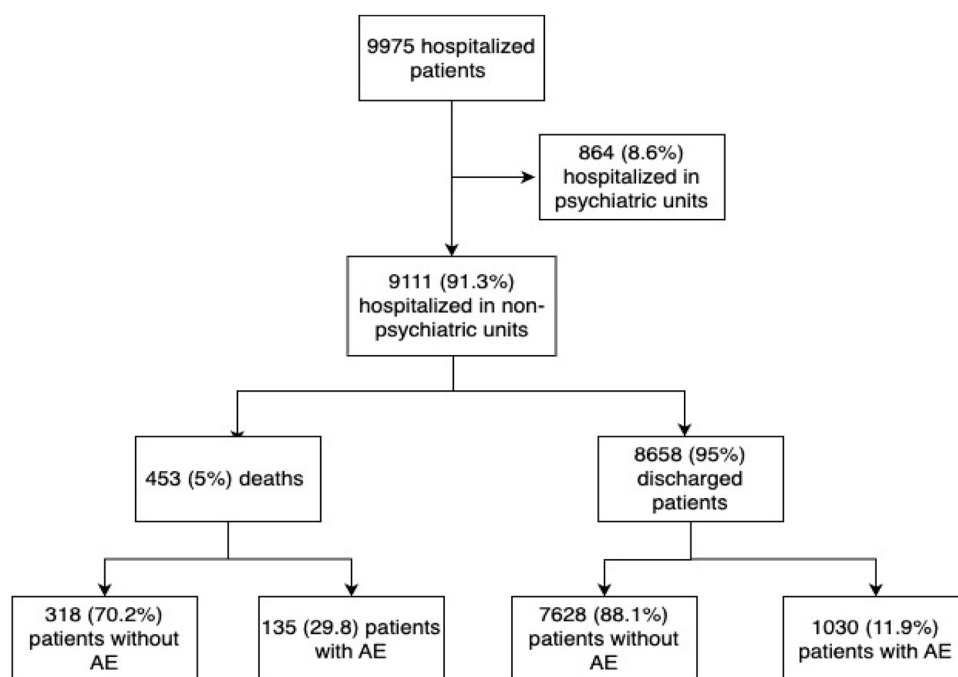


Fig. 1. Flow diagram.

medical specialties. The mean length of hospital stay prior to screening was 14.4 days (SD 42.8 days), with a median of 6 days (IQR: 1–44). Overall, 83.0% of patients (7,562) had ≥ 1 comorbidity and 80.9% (7,374) had ≥ 1 instrumentalisation factor in clinical practice. A total of 1,165 patients (12.8%) experienced ≥ 1 AE. The mean number of AEs was 0.16 per patient (0.38 among those who died during hospitalisation vs. 0.14 among who did not; $p < 0.005$).

In-hospital mortality was 5.0% (453 patients), with a mean age of 72.9 years (compared with 61.8 years in the non-deceased patients, $p < 0.001$). In patients with ≥ 1 AE, in-hospital mortality was 11.6% (compared with 4.0% of those without any AE; $p < 0.001$). With respect to the epidemiological characteristics, mortality was 12.8% in patients who presented ≥ 3 instrumentalisation factors of clinical practice (compared with 3.5% in those who did not; $p < 0.001$), 8% in patients who presented ≥ 3 comorbidities (compared with 0.5% who did not present them; $p < 0.001$) and 5.7% in men (compared with 4.3% in women; $p = 0.002$). Finally, in-hospital mortality was 14.9% in support hospitals and 11.1% in mid-stay hospitals (compared with 4.2% in medium- or high-complexity hospitals; $p < 0.001$), 13.2% in intensive medicine units (compared with 5.8% in medical units, 1.9% in surgical units; $p < 0.001$) and 3.4% in those who had surgery (compared with 5.6% among those who did not; $p < 0.001$) (Table 1).

Mortality

In the predictive model, an association was found with in-hospital mortality and presence of renal failure (OR [95% CI]: 3.41 [2.41 to 4.84], versus absence), cirrhosis (2.28 [1.42 to 3.34] versus absence), neoplasia (2.19 [1.78 to 2.78] versus absence), the increase in the number of AEs (1.57 [1.34 to 1.83] for each AE versus absence), sex (1.18 [0.96 to 1.44] for men versus women) and age (1.01 [1.00 to 1.02] for each year). Admission to surgical units was a protective factor (0.42 [0.36 to 0.77], versus being admitted to medical units), as was the presence of surgical intervention (0.70 [0.51 to 0.96] versus absence) (Table 2). The Hosmer–Lemeshow goodness-of-fit test was performed, with a result of $p = 0.869$.

Characteristics of AEs

Among the 9,111 patients, 1,165 experienced ≥ 1 AE, with a total of 1,432 AEs detected. The most frequent type of AE was HAI (38.3%),

followed by AE related to care (23.0%) and AE related to a procedure (21.5%). A total of 49.2% of the AEs occurred during the hospital stay, and 53.2% were moderate or severe. A total of 92.7% of the AEs required some type of additional assistance (observation or monitoring, additional tests or procedures, a longer hospital stay, other additional treatments or life support).

A total of 15.5% of AEs related to care were associated with in-hospital mortality (compared with 13.1% of HAIs, 9.6% of AEs related to negative effects of medication and 8.4% of AEs related to procedures; $p = 0.047$). Total 15.3% of the AEs that occurred during ward care contributed to in-hospital mortality (compared with 10.2% of the AEs that occurred before admission, 9.9% after a procedure and 9.8% of the AEs during a procedure; $p = 0.024$). A 19% of severe AEs occurred in patients with subsequent in-hospital mortality (versus 12.4% of mild AEs and 9.4% of moderate AEs; $p < 0.001$). A 21.9% of the AEs that required life support contributed to in-hospital mortality (versus 16.9% of those that only needed monitoring and 13.7% of those that required an additional test < 0.001) (Table S1).

Explanatory model of the association between AEs and in-hospital mortality

In the crude analysis, the OR (95% CI) for in-hospital mortality was 2.99 (2.37 to 3.76) for the presence of 1 AE, 3.10 (1.84 to 5.20) for the presence of 2 AEs, and 6.00 (2.97 to 12.10) for the presence of ≥ 3 AEs, compared with those with no AEs.

The number of comorbidities or instrumentalisation factors of clinical practice, the presence of surgical intervention, impaired mobility, hypoalbuminaemia, PUs, or urinary and vascular catheters act as confounding factors. According to the explanatory model adjusted for these variables, the risk of in-hospital mortality was 2.10 times higher for patients with 1 AE (OR [95% CI]: 2.10 [1.63 to 2.70]), 1.58 times higher for patients with 2 AEs (1.58 [0.89 to 2.80]) and 2.37 times higher for patients with ≥ 3 AEs (2.37 [1.10 to 5.14]) than that for patients without any AE (Table S2 and Fig. 2).

Discussion

A total of 9,111 hospitalisations were analysed in this cross-sectional study. An in-hospital mortality of 5% was found, with at least 1 AE in approximately one-third of the deceased patients. The presence of AEs

Table 1
Characteristics of the patients and episodes included in the study.

	Total n = 9,111	In-hospital mortality n = 453	Hospital discharge n = 8,658	p value
Age ^a , mean (SD)	62.4 (25.7)	72.9 (17.8)	61.8 (25.9)	p < 0.001
Sex				
Men	4,544 (49.9)	258 (5.7)	4,286 (94.3)	0.002
Women	4,567 (50.1)	195 (4.3)	4,372 (95.7)	
Type of admission ^b				
Urgent	6,577 (72.2)	326 (5.0)	6,251 (95.0)	0.368
Scheduled	2,493 (27.4)	123 (4.9)	2,370 (95.1)	
Hospitalisation specialty				
Medical specialties	5,184 (56.9)	301 (5.8)	4,883 (94.2)	p < 0.001
Surgical specialties	3,123 (34.3)	60 (1.9)	3,063 (98.1)	
Intensive medicine	380 (4.2)	50 (13.2)	330 (86.8)	
Other	424 (4.6)	42 (9.9)	382 (90.1)	
Hospital type				
Low complexity	759 (8.3)	54 (7.1)	705 (92.9)	p < 0.001
Medium complexity	2,995 (32.9)	126 (4.2)	2,869 (95.8)	
High complexity	4,765 (52.3)	200 (4.2)	4,565 (95.8)	
Support	188 (2.1)	28 (14.9)	160 (85.1)	
Mid-stay	404 (4.4)	45 (11.1)	359 (88.9)	
Stay prior to screening				
0–2 days	2,241 (24.6)	41 (1.8)	2,200 (98.2)	p < 0.001
2–6 days	2,333 (25.6)	91 (3.9)	2,242 (96.1)	
6–15 days	1,994 (21.9)	126 (6.3)	1,868 (93.7)	
15–30 days	911 (10.0)	80 (8.8)	831 (91.2)	
≥30 days	922 (10.1)	105 (11.4)	817 (88.6)	
Unknown	710 (7.8)	10 (1.4)	700 (98.6)	
History of surgical intervention				
Absence	6,463 (70.9)	362 (5.6)	6,101 (94.4)	p < 0.001
Presence	2,648 (29.1)	91 (3.4)	2,557 (96.6)	
Number of comorbidities				
Absence	1,549 (17.0)	7 (0.5)	1,542 (99.5)	p < 0.001
1	1,419 (15.6)	27 (1.9)	1,392 (98.1)	
2	1,566 (17.2)	53 (3.4)	1,513 (96.6)	
≥3	4,577 (50.2)	366 (8.0)	4,211 (92.0)	
Number of instrumentalisation factors of clinical practice				
Absence	1,737 (19.6)	60 (3.5)	1,677 (96.5)	p < 0.001
1	5,388 (59.1)	199 (3.7)	5,189 (96.3)	
2	1,503 (16.5)	136 (9.1)	1,367 (90.9)	
≥3	483 (5.3)	58 (12.0)	425 (88.0)	
Adverse event				
Absence	7,946 (87.2)	318 (4.0)	7,628 (96.0)	p < 0.001
Presence	1,165 (12.8)	135 (11.6)	1,030 (88.4)	

^a72 missing.
^b43 missing data.
SD, standard deviation; p value.

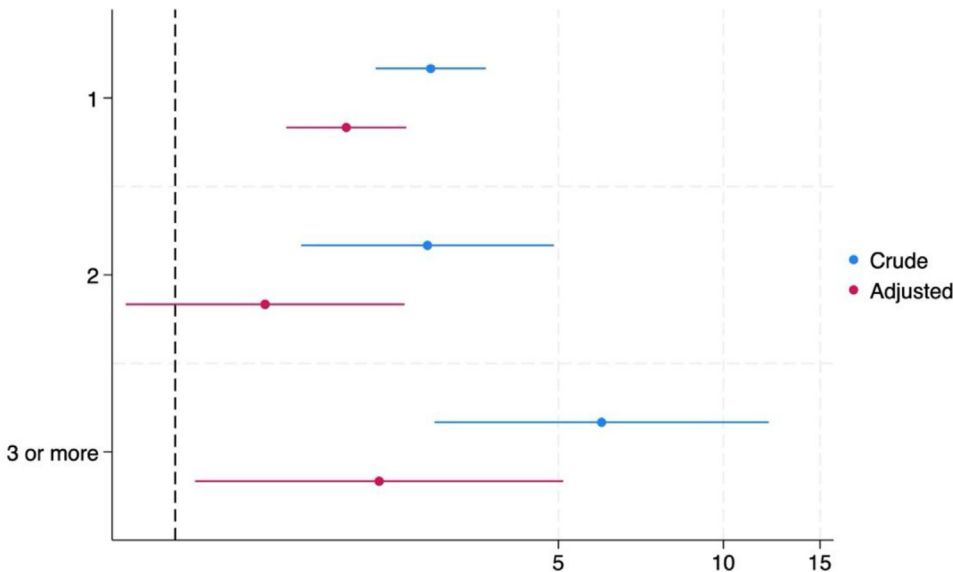


Fig. 2. Crude versus adjusted ORs for in-hospital mortality and the presence of 1 AE, 2 AEs or ≥3 AEs.

Table 2
In-hospital mortality predictive model during hospitalisation.

	Total n (%)	In-hospital mortality n (%)	OR	95% CI	p value
Adverse event					
By number of AEs	1,165 (12.8)	135 (11.6)	1.57	1.34 to 1.83	$p < 0.001$
Age*					
per year, mean (SD)	62.4 (25.7)	72.9 (17.8)	1.01	1.00 to 1.02	0.004
Sex					
Women	4,567 (50.1)	195 (4.3)	1.00	NA	
Men	4,544 (49.9)	258 (5.7)	1.18	0.96 to 1.45	0.10
Comorbidities**					
Kidney failure	209 (2.6)	57 (12.7)	3.41	2.41 to 4.84	$p < 0.001$
Mobility alteration	2,988 (37.7)	284 (63.5)	1.83	1.52 to 2.41	$p < 0.001$
Hypoalbuminaemia	1,464 (18.5)	178 (39.8)	1.53	1.22 to 1.91	$p < 0.001$
Neoplasia	1,997 (25.2)	192 (42.9)	2.19	1.78 to 2.78	$p < 0.001$
Cirrhosis	207 (2.6)	29 (6.5)	2.28	1.42 to 3.34	$p < 0.001$
Instrumentalisation factors of clinical practice**					
Urinary catheter	1,605 (19.2)	185 (41.9)	1.96	1.27 to 2.15	$p < 0.001$
Central venous catheter	1,068 (12.7)	119 (26.9)	1.64	1.12 to 2.05	0.003
Surgical intervention	2,648 (29.1)	91 (20.1)	0.70	0.51 to 0.96	0.024
Hospitalisation specialty					
Medical specialties	5,184 (56.9)	301 (5.8)	1.00	NA	
Surgical specialties	3,123 (34.3)	60 (1.9)	0.54	0.38 to 0.77	0.001
Intensive medicine	380 (4.2)	50 (13.2)	1.13	0.72 to 1.76	0.727
Other	424 (4.6)	42 (9.9)	2.14	1.48 to 3.10	$p < 0.001$
Cons			0.008		

*6 missing.

**Reference category of each risk factor, absence.

EA, adverse event; SD, standard deviation; p, p value; NA, not applicable; OR, odds ratio; CI, confidence interval.

was associated with doubling the risk of in-hospital mortality, adjusting for confounding variables. In-hospital mortality was more common in male patients who did not undergo surgery, who presented a greater number of comorbidities or instrumentalisations in clinical practice, or who were admitted to mid-stay or support hospitals. The presence of an AE was a predictor of in-hospital mortality. HAIs and those related to care were the most frequent types of AEs, the latter being the ones that contributed the most to in-hospital mortality.

Investigations of the impact of AEs on mortality have traditionally been carried out through descriptive analyses. Thomas *et al* in 2000 in Utah and Colorado reported that 6.6% of patients with AEs died,⁹ and Sousa *et al* in 2014 in Portugal noted that up to 10.8% of AEs occurred in patients who finally died.²⁴ Our study presents two novelties with respect to the previous evidence: 1) a complete individual analysis of the confounding variables was performed to estimate a precise measure of association, and 2) the role of the simultaneity of active AEs in the in-hospital prognosis was investigated. In this regard, our results suggest that the increased risk of in-hospital mortality doubles with the presence of the first AE (OR: 2.10), and is maintained with the presence of additional AEs, without observing a dose–response effect. The most similar result reported in the literature was reported by Martins *et al* in 2011, who estimated an OR of 9.5 for the presence of an AE and mortality in hospitalised patients, whereas the crude OR was 11.43 and the adjusted OR was 8.23 for avoidable AEs.²⁵ On the other hand, Haukland *et al* found an RR of 2.83 for the presence of AE and mortality in a retrospective record review.²⁶ These numbers are higher than those in our population, although, in our study, we considered all the AEs in a larger sample and analysed in depth the confounding factors that may affect this association. Our crude analysis also overestimated the association between the presence of AEs and in-hospital mortality.

In our study, the most severe AEs that required a greater degree of additional medical assistance were associated with higher mortality, which is consistent with the findings of other previous studies.²⁷ Although HAIs were the most frequent type of AE, the AEs with the greatest contribution to mortality were those related to care. This, in addition to the greater association with in-hospital mortality of AEs that occur

during ward care, suggests that their reduction is an efficient strategy for improving the prognosis of patients. Measures that manage to increase the ratio of nursing personnel per patient at risk or training have managed to reduce the frequency of AEs related to care and may have a significant impact on health outcomes.²⁸ Those related to procedures were the type of AE with the lowest associated mortality, which could be explained by their association with the selection for surgical interventions of those patients with a better previous prognosis.^{29,30,31}

Finally, the detection of AEs during hospitalisation was a predictor of mortality in a model that started with more than 15 epidemiological variables. In the predictive model, age; hospitalisation in medical specialties; the presence of kidney failure; impaired mobility; hypoalbuminaemia; neoplasia; cirrhosis; and PU or catheter use were also associated with increased in-hospital mortality. These risk factors have been described in the literature as poor prognosis conditions in hospitalised patients,³² together with the presence of a greater number of comorbidities.³³ These results suggest the need to direct strategies to reduce the frequency of AEs in this patient profile, fundamentally by improving ward care. Improvements in safety culture, increased notification of AEs and increased knowledge of adverse event prevention among healthcare professionals have the potential to reduce avoidable in-hospital mortality.³⁴

There are several limitations in our study. Its cross-sectional design does not allow us to establish causality, and we can only speak of an association between the different variables studied and in-hospital mortality. In addition, this design over-represents the AEs that prolong hospital stay (such as HAIs) owing to their greater probability of remaining active during the study date. However, this is also an advantage, as it ensures a high detection sensitivity of serious or prolonged-stay AEs, which are the ones that benefit the most from an in-depth analysis to implement future prevention strategies. Similarly, the use of cross-sectional designs for the identification and characterisation of AEs is widely accepted and has been used in many recent studies because of its high degree of efficiency.^{10,18,35} On the other hand, to minimise the possibility of missing data and ensure adequate quality of the data, a standardised, validated and robust methodology has been used, which,

together with a process of training reviewers, is capable of offering the highest degree of available evidence.^{3,17} Another limitation is that the data were collected prior to the COVID-19 pandemic; however, clinical practice has not changed substantially since then, and thus the findings remain applicable to current care settings.

Among the strengths of our study, we highlight the following: (1) the inclusion of a large sample of 9,111 patients, which ensures adequate statistical power; (2) the participation of 32 hospitals with different levels of complexity, providing good representativeness and optimal internal and external validity; (3) the application of a validated and internationally recognised methodology, which allows for high comparability across settings and over time; (4) the identification of a bundle of patient-related factors associated with a high risk of AEs, which enables the development of immediately applicable preventive measures and (5) the quantitative analysis of the effects of adverse events (AEs) on in-hospital mortality after adjustment for relevant epidemiological factors, demonstrating that even a single AE doubles the risk of death.

In this sense, a measure of association was obtained with an adjusted analysis between the presence of active AEs and in-hospital mortality. Although no dose–response effect has been found with an increase in the number of AEs, the existence of at least one of them already adversely affects the patient's hospital prognosis. These results are highly applicable to clinical practice and health management, as they suggest that AE prevention strategies could be especially effective in reducing in-hospital mortality and, therefore, in improving patient prognosis and quality of care in our centers.³⁶

Conclusions

The occurrence of at least 1 AE doubles the risk of in-hospital mortality, influencing the prognosis of the patient. The presence of a greater number of AEs maintains the risk but does not produce a dose–response effect. The most common AEs were HAIs and those related to care. However, the latter occurred more frequently in patients who died, positioning their reduction as an element with an exponential effect on improving patient prognosis.

The presence of AEs, advanced age, hospitalisation in a medical service, risk factors such as kidney failure, impaired mobility, hypoalbuminaemia, neoplasia, cirrhosis, PU and the presence of catheters are associated with increased in-hospital mortality. Establishing actions aimed at reducing the frequency of AEs in these patients is an appropriate strategy for improving health outcomes.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval and consent to participate

The study was approved by the Ethics Committee of Ramón y Cajal University Hospital (reference 057/19). Informed consent was not required, as the study complied with Regulation (EU) 2016/679 (General Data Protection Regulation, GDPR) and Spanish data protection law, meeting the exemption criteria based on the absence of direct intervention, full anonymisation of data, and the study's relevance to public health.

CRediT authorship contribution statement

Miriam Roncal Redin: Conceptualisation and Methodology, Formal analysis, Data curation, Funding acquisition and Writing original draft. **Diego San Jose:** Conceptualisation, methodology, Data curation, Formal analysis, Review and Editing and Supervision. **Cristina Díaz-Agero Pérez:** Review and Editing, Supervision and Project administration. **Jorge Vicente-Guijarro:** Data curation, Review and Editing and Supervision. **Paloma Moreno-Nunez:** Data curation, Formal analysis and Visualisation. **Alberto Pardo-Hernández:** Project administration and Supervision. **Jesus Maria Aranaz-Andres:** Conceptualisation, Review and Editing, Supervision and Project administration.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

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