What makes hospitalized patients more vulnerable and increases their risk of experiencing an adverse event?

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Abstract

Objective. To analyze the relationship between the appearance of adverse events (AEs) and both patient comorbidities and the use of medical devices.

Design. Retrospective medical records review study.

Setting. Twenty-four Spanish public hospitals.

Participants. Clinical records of 5624 discharged patients.

Main Outcome Measure. Incidence of AEs.

Results. Patients aged >65 have 2.4 times the risk of experiencing an AE compared with those aged <65. The presence of certain comorbidities and devices (neoplasia, chronic hepatic alteration, cardiac insufficiency, coronary disease, high blood pressure, urethral catheterization, catheterization of a vessel, tracheostomy or stay of >7 days) were associated with developing an AE during hospitalization. There is a trend effect if we consider the number of comorbidities and the number of devices used. Thus, the risk of an AE in subjects who present no comorbidities was 3.2%, which rose to 9.9% in those with one intrinsic risk factor, 16.7% in those with two and 29.3% in those with three or more. Similarly, subjects without extrinsic risk factor experienced an AE in 4.4% of cases, which rose to 9.6% when there was one risk factor, to 13.4% when there were two and to 33.0% when there were three or more risk factors. The effect of some of these pathologies and that associated with age disappeared on adjusting in line with other variables.

Conclusions. The true risk resides in the number of exposures to potentially iatrogenic actions, rather than being intrinsic to age or the presence of certain comorbidities.

Keywords: patient safety, adverse events, medical errors, quality of care

Introduction

The frequency of adverse events (AE) associated with care, their effect on patients and their potential impact on health systems have been studied systematically [1]. But while the analysis of the causes of AE may provide solutions at a local level, this is not an appropriate approach for identifying risks, insofar as it does not take into account information from patients who do not experience AE. To identify risk factors related to the occurrence of certain AE would allow the development of strategies addressed to specifically susceptible populations.

In order to establish the risk associated with admission to hospital, researchers have carried out reviews of clinical records [2–7]. Thus, for example, the risk has been identified for patients admitted to intensive care [8, 9], for those undergoing surgery [10], for general medicine inpatients [11, 12], for those attended in accident and emergency [13] or for paediatric patients [14]. The more complex (device use) the care involved, the more likely an AE will be [6]. Likewise, a
prolonged hospital stay favors the appearance of AE [6, 7], though given that AE can prolong the stay it is not easy to accurately determine the risk involved.

The most widely studied risk factor is patient’s age. The Harvard Medical Practice Study (HMPS) [2], exploring the relationship between AE incidence and age groups, established a diagnosis-related groups (DRGs) classification according to the probability of experiencing an AE, taking into account the seriousness of the illness and the necessary device use, and found differences in the incidence on adjusting for both variables. The quality in Australian healthcare study (QAHCS) [3], like that carried out in New Zealand [5, 15], estimated the frequency of AE for each major diagnostic category (24 categories) by age groups. The Utah and Colorado study (UTCOS) [4] related age with DRGs according to complexity [16] and with the Charlson comorbidities index in the case of surgical AE [17]. As recommended in the HMPS [2], studies from other countries have also analyzed age as a risk factor [6, 7, 18, 19]. However, other risk factors have not been analyzed in a systematic way with the same intensity.

Estimating the probability of suffering an infection from a surgical wound, a fall or phlebitis would permit us to design much more specific and appropriate strategies for addressing patient risk. The possibility of taking action in relation to the incidence of AE could be strengthened through knowledge of patients’ risk of suffering an AE related to factors such as diabetes, high blood pressure, obesity, using a urethral catheter or receiving assisted breathing. In the present study we asked ourselves: what role is played in the origin of AE by patient vulnerability, comorbidities, the device use and the prognosis of the illness responsible for the hospital admission? To this end, we analyzed the relationship between the appearance of an AE and, on the one hand, patient comorbidities, the device use and the diagnosis or others), hospital stay resulting from each AE, additional procedures and treatments as a consequence of AE, incapacitation or death, seriousness of the AE (mild: does not prolong the stay; moderate: prolongs the stay or results in admission; serious: results in a need for surgery, leads to incapacitation on discharge or is related to patient’s death) and avoidability of the AE. As care-related independent variables, we considered inpatient service (medical or surgical), type of admission (urgent or programmed), stay in days, surgical procedure [International Classification of Diseases, 9th revision and clinical modification (ICD-9CM)] and extrinsic risk factors (urethral catheter, peripheral vein catheter, central catheter, central catheter peripherally inserted, central vein catheter, parenteral feeding, enteral feeding, nasogastric catheter, esophageal gastric percutaneous catheter, tracheostomy, mechanically assisted breathing or immunosuppressive therapy); as illness-related independent variables: principal diagnosis (ICD-9CM code) and American Society of Anesthesiologists (ASA) risk [23]; as subject-related independent variables: age, sex and current intrinsic risk factors (coma, renal insufficiency, diabetes, neoplasia, chronic obstructive pulmonary illness, immunodeficiency, neutropenia, hepatic cirrhosis, drug addiction, obesity, malnutrition, pressure ulcers, malformations, cardiac insufficiency, coronary disease or high blood pressure).

For identifying possible AE we used a Screening Guide. This guide was similar to those used in the New York and UTCOSs, and was drawn up using consensus-based techniques as part of the ENEAS study [20]. Clinical records that met at least one of the 19 criteria of the screening guide reviewed by local nurses were examined in detail by two external medical reviewers (8 for the 24 hospitals). For the precise characterization of the AE we used the modular review form [21].

In order to assess the relationship between AE and health care, we used a scale of 1–6 that established the evidence of this relationship according to the reviewer’s judgment. We considered the AE as associated with the care for values of >3, following the model proposed in the study by Brennan et al. [2]. The same judgment was required for rating the avoidability of the AE. Agreement with technical supervision was determined by means of Kappa for each reviewer in a pilot study, and ranged from 0.43 to 0.87 in causality and from 0.27 to 0.84 in preventability. Discordances were discussed to resolve doubts. In order to compensate for the loss of AE that occurred after patient discharge, we included those AE that had occurred during a previous stay in hospital in the calculation of hospital incidence, in accordance with the scheme used by Brennan et al. [2].

As dependent variable, we considered the presence of AE (Category E–H in the National Coordinating Council for Medication Error Reporting and Prevention index for categorizing medication errors) [22] or incident (Category B–D). Other dependent variables were nature of the AE (associated with care, with a procedure, with nosocomial infection, with medication, with the diagnosis or others), hospital stay resulting from each AE, additional procedures and treatments as a consequence of AE, incapacitation or death, seriousness of the AE (mild: does not prolong the stay; moderate: prolongs the stay or results in admission; serious: results in a need for surgery, leads to incapacitation on discharge or is related to patient’s death) and avoidability of the AE. As care-related independent variables, we considered inpatient service (medical or surgical), type of admission (urgent or programmed), stay in days, surgical procedure [International Classification of Diseases, 9th revision and clinical modification (ICD-9CM)] and extrinsic risk factors (urethral catheter, peripheral vein catheter, central catheter, central catheter peripherally inserted, central vein catheter, parenteral feeding, enteral feeding, nasogastric catheter, esophageal gastric percutaneous catheter, tracheostomy, mechanically assisted breathing or immunosuppressive therapy); as illness-related independent variables: principal diagnosis (ICD-9CM code) and American Society of Anesthesiologists (ASA) risk [23]; as subject-related independent variables: age, sex and current intrinsic risk factors (coma, renal insufficiency, diabetes, neoplasia, chronic obstructive pulmonary illness, immunodeficiency, neutropenia, hepatic cirrhosis, drug addiction, obesity, malnutrition, pressure ulcers, malformations, cardiac insufficiency, coronary disease or high blood pressure).

We used chi-squared or Fisher’s exact test in the case of qualitative variables, including the chi-square test for trend and the Student’s t-test for quantitative variables. We carried out a multivariate analysis by means of likelihood-ratio forward stepwise logistic regression, controlling confusion and interaction phenomena, considering as dependent variable the presence of AE and all the independent variables mentioned above except umbilical catheter, procedure and main diagnosis of ICD codes. Statistical significance was considered for values of P < 0.05.
Confidentiality was ensured by means of a blind reporting system. The study was approved by the Aragón Committee of Ethics and Clinical Research.

Results

Of the 5624 patients, 1755 (32%) were screened out as possibly suffering AE. Of these, 501 were false positives of the screening guide. Another 191 patients had only experienced incidents (or near misses—events that did not result in injury or complication for the patient), so that the final total of patients identified as being injured in some way during hospitalization was 1063, the incidence of patients with healthcare-related AE (values >3 on the scale of evidence in causality) being 9.3% (525/5624); 95% CI: 8.6–10.1%. The incidence of patients with AE resulting from and detected during the hospital stay was 7.2% (406/5624); 95% CI: 6.5–7.9%.

The distribution of the different risk factors studied and the incidence of patients with some healthcare-related AE (including primary care and other care levels) on comparing groups taking into account intrinsic risk factors (or comorbidities), and the incidence of patients only with AE resulting from and detected during the hospitalization on comparing extrinsic risk factors (device use and other characteristics of care) are shown in Table 1.

Intrinsic risk factors

Mean age of subjects who experienced AE was 64.7 years (SD: 20.1), as against 52.3 years (SD: 25.0) for subjects without AE (P < 0.001). Patients aged >65 were more likely to develop AE than those aged <65 (14.4 versus 6.1%), so that the risk of experiencing an AE in older patients is more than double that for the younger ones (RR: 2.4). By gender, 10.2% of men versus 8.6% of women experienced an AE (P = 0.04). The presence of diabetes, neoplasia, chronic pulmonary illness, neutropenia or immunodeficiency, chronic hepatic alteration, obesity, hypoalbuminemia, pressure ulcers, cardiac insufficiency, coronary disease or high blood pressure increases the likelihood of experiencing an AE.

A total of 16.7% of subjects with the presence of some intrinsic risk factors (comorbidities) experienced an AE, as against 3.2% of subjects without risk factors (P < 0.001), a trend effect being found so that 9.9% of subjects with an intrinsic risk factor had AE, which rose to 16.7% for two risk factors and to 29.3% for three or more risk factors (P < 0.001). Figure 1 shows this trend.

The AE most commonly found in the study were those related to medication, which also were the most frequent among patients with almost any risk factors (Table 2). Worthy of note is the distribution of the AE in subjects with neutropenia or immunodeficiency, where the main problems were related to medication and not to health-related infection, in contrast to what is found in patients with obesity or chronic hepatic alteration.

Regarding the seriousness of AE, we analyzed ASA risk as an indicator of baseline health status of patients experiencing AE. In 446 patients, the distribution was in such a way that 13.7% were healthy, 26.7% had a mild illness, 49.8% had a functional limitation and 9.9% had a life-threatening condition. Seriousness of the AE was not related to patients’ ASA risk (P = 0.170).

However, on rating the role of principal-illness prognosis not conditioned by AE, 72.2% of subjects with AE recovered their baseline health status, 17.4% presented residual incapacitation on discharge and 10.4% presented terminal illness. In this case, seriousness of the AE was related to principal-illness prognosis (P = 0.012), in such a way that in cases with foreseeable residual invalidity on discharge, the percentage of serious AE was greater. The pattern in the other two groups was similar. Both the presence and absence of comorbidities (P = 0.002) and the total quantity of them (P = 0.001) were associated with seriousness of AE.

Extrinsic risk factors

Given that the information on extrinsic risk factors from other episodes and from other levels of care was not collected, we studied the relationship between these factors and the probability of experiencing an AE during the hospital stay and being detected during that stay. Thus, the incidence of patients with AE was greater in small hospitals (8.87, 95% CI: 6.25–11.49), of intermediate status in large hospitals (8.26, 95% CI: 7.13–9.39) and lesser in middle-sized hospitals (6.14, 95% CI: 5.26–7.01). In turn, it was higher in medical services (7.51, 95% CI: 6.47–8.55) than in surgical services (6.99, 95% CI: 6.11–7.88).

A total of 4648 patients (82.6%) had some extrinsic risk factors (invasive devices, such as peripheral vein catheter or urethral catheter). Accumulated total extrinsic risk factors was 7235. It was found that 8.2% of subjects with the presence of some extrinsic risk factors (Table 1) developed an AE, as against 2.6% of those without risk factors (P < 0.001); 80.3% of patients had peripheral vein catheter, and if we consider the patients who had some risk factor, the peripheral vein catheter was present in 97.2% of cases. Given the high proportion of subjects with a peripheral vein device, even in the absence of clinical need for this, we repeated the analysis, omitting this circumstance as a risk, and found that the effect was maintained.

Urethral catheterization of the patient, the catheterization of a vessel (non-peripheral), having a nasogastric catheter or a tracheostomy, receiving mechanically assisted breathing or immunosuppressive therapy and staying in hospital >1 week were associated with risk of experiencing an AE during the stay. We also found in this case a trend effect (Fig. 1), so that subjects without extrinsic risk factors had AE at a rate of 4.4%, which rose to 9.6% when there was one risk factor, to 13.4% when there were two risk factors and to 33.0% when there were three or more risk factors (P < 0.001).

In general, the AE most commonly found in patients using some risk device were nosocomial infections, in contrast to the case of individuals who experienced an AE during their hospital stay (Table 3).
On carrying out the multivariate analysis as an explanatory model of the fact of experiencing an AE during the hospital stay, we discovered that both size of hospital and type of department in which the patient is admitted, together with certain clinical factors, such as the presence of neoplasia, chronic hepatic alteration, cardiac insufficiency, coronary disease, high blood pressure, urethral catheterization, catheterization of a vessel, a tracheostomy or a stay of >7 days, were related to the occurrence of AE as shown in Table 4.
Discussion

We have shown that the presence of comorbidities and the use of devices increase the risk of AE. Until now, this approach had not been made. The other studies had considered only the possible confounding role of age on the frequency of AE, but we have analyzed the impact of certain diagnosis and use of catheterization on the probability of developing an AE.

The risk has been shown in the bivariate analysis. However, the effect of these pathologies and that which has been associated with age disappears on adjusting in accordance with other variables. Specifically, patients aged >65 are at 2.4 times more risk of suffering a healthcare-related AE than those aged <65. We confirmed that the effect traditionally associated with age (HMPS [2]: 2.19; QAHCS [3]: 1.89; UTCOS [4]: 1.89; New Zealand [5]: 1.70; and London [7]: 2.50) disappears on adjusting in accordance with other risk variables. This leads us to think that the true risk resides in the number of exposures to potentially iatrogenic actions, rather than being intrinsically related to age.

Similarly, the risk associated with the presence of chronic renal illness, diabetes, chronic pulmonary illness, neutropenia or immunodeficiency, obesity, hypoalbuminemia or pressure ulcers also disappears in the adjusted analysis, and this is possibly explained by the presence of risk devices use. Nevertheless, the effect of the presence of neoplasia, chronic hepatic alteration, cardiac insufficiency, coronary disease or high blood pressure is not explained by these variables. This may be due to the fact that we have not considered any exposure variable referring to the risk associated with use of medication—a risk which indeed results in the highest incidence of AE among patients presenting these pathologies.

As regards the risk associated with the type of care the patient receives, it is noteworthy that, in a similar way to that which occurs with patients’ age, being admitted to a surgical service increases the risk of experiencing an AE, which contradicts the findings of the preliminary analysis. As far as size of hospital is concerned, if we accept that it is exposure to health interventions and not other variables that explain the risk of experiencing AE, we would expect higher incidence in hospitals with more beds. On the other hand, it has been seen that classifying hospitals by size fails to capture the reality of the complexity of clinical practice, and all the more so taking into account that there are more and more highly specialized hospitals.

In studies of AE by means of clinical record reviews, the reliability represents a substantial limitation on interpreting the data [24–27], since the quality of the clinical records affects the final result. This may be another factor (in addition to the organization and health context) explaining the divergence of these

![Figure 1](Incidence of AE according to the number of intrinsic and extrinsic risk factors.)

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Nature of AE according to presence of intrinsic risk factors [values are n and % (row)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Related to non-invasive care</td>
</tr>
<tr>
<td>Age</td>
<td>&gt;65</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
</tr>
<tr>
<td>Chronic renal illness</td>
<td>Yes</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>Yes</td>
</tr>
<tr>
<td>Chronic pulmonary illness</td>
<td>Yes</td>
</tr>
<tr>
<td>Neutropenia or immunodeficiency</td>
<td>Yes</td>
</tr>
<tr>
<td>Chronic hepatic alteration</td>
<td>Yes</td>
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<tr>
<td>Obesity</td>
<td>Yes</td>
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<tr>
<td>Hypoalbuminemia</td>
<td>Yes</td>
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<tr>
<td>Pressure ulcers</td>
<td>Yes</td>
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<tr>
<td>Cardiac insufficiency</td>
<td>Yes</td>
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<tr>
<td>Coronary illness</td>
<td>Yes</td>
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<tr>
<td>High blood pressure</td>
<td>Yes</td>
</tr>
<tr>
<td>Total</td>
<td>50 (7.6)</td>
</tr>
</tbody>
</table>
results from those of the Canadian study [6] with regard to the relationship between the incidence of AE and size of hospital. Other limitations of this study reside in the fact that no information was gathered on extrinsic risk factors from other episodes, so that what was studied was the relationship between such factors and the likelihood of experiencing an AE as an inpatient, and being detected during that stay. We only studied AE that could be detected during the stay through clinical record review.

Patients’ stay is related to the risk of experiencing an AE, interpreting it in a bidirectional way, since not only does a prolonged stay increases the risk of developing an AE, but the patient may also remain in hospital longer as a consequence of the AE. Moreover, this association is independent of the presence of medical devices. This is an interesting finding, insofar as in principle, the device use is greater in the first days of the health care.

The larger the number of extrinsic risk factors, that is, the more the device use during the hospital stay, the greater the probability of suffering from an AE during the stay. The association between invasive procedures (especially catheters of different types and tracheostomies) is associated with the incidence of nosocomial infection, which accounts for the commonest type of AE in these patients.

We also found that seriousness of AE is not related to patient’s health status prior to admission (measured by the ASA risk, although this use has not been validated), but rather to principal-illness prognosis, which is what determines, together with comorbidities, the type of care the patient will receive.

Taking into account that the population admitted to Spanish hospitals is getting older (patients over the age of 65: from 34.22% in 1997 to 39.85% in 2007) [28], so that there is a trend towards a greater proportion of outpatient care, and to hospital care being more and more complex, it is likely that AE which occur in hospitals will become ever more serious if appropriate measures to control them are not taken. In parallel, the remaining levels of care (including primary care and outpatient care) will receive older and older patients with complex chronic conditions, and as we have seen, health care in these contexts is far from risk free [29, 30].

Many strategies of proven effectiveness are being developed for avoiding the appearance of AE. But as the incidence and nature of AE depend on the risk factors in patient, it is needed to target improvement actions on specific conditions or populations (>65), to bear in mind the contributory factors and to focus on minimizing the risks related to AE.

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