CLINICAL SCIENCE

Medical adverse events in elderly hospitalized patients: A prospective study

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OBJECTIVES: To determine the frequency of medical adverse events in elderly patients admitted to an acute care geriatric unit, the predictive factors of occurrence, and the correlation between adverse events and hospital mortality rates.

METHODS: This prospective study included 171 admissions of patients aged 60 years and older in the acute care geriatric unit in a teaching hospital in Brazil between 2007 and 2008. The following variables were assessed at admission: the patient age, gender, number of prescription drugs, geriatric syndromes (e.g., immobility, postural instability, dementia, depression, delirium, and incontinence), comorbidities, functional status (evaluated with the Katz Index of Independence in Activities of Daily Living), and severity of illness (evaluated with the Simplified Acute Physiology Score II). The incidence of delirium, infection, mortality, and the prescription of potentially inappropriate medications (based on the Beers criteria) were assessed during hospitalization. An observer who was uninvolved in patient care reported the adverse events.

RESULTS: The mean age of the sample was 78.12 years. A total of 187 medical adverse events occurred in 94 admissions (55%). The predictors of medical adverse events were undetermined. Compared with the patients with no adverse events, the patients with medical adverse events had a significantly longer hospital stay (21.41 ± 15.08 days versus 10.91 ± 7.21 days) and a higher mortality rate (39 deaths [41.5%] versus 17 deaths [22.1%]). Mortality was significantly predicted by the Simplified Acute Physiology Score II score (odds ratio [OR] = 1.13, confidence interval [CI] 95%, 1.07 to 1.20), the Katz score (OR = 1.47, CI 95%, 1.18 to 1.83), and medical adverse events (OR = 3.59, CI 95%, 1.55 to 8.30).

CONCLUSION: Medical adverse events should be monitored in every elderly hospitalized patient because there is no risk profile for susceptible patients, and the consequences of adverse events are serious, sometimes leading to longer hospital stays or even death.

KEYWORDS: Adverse Events; Elderly; Hospitalization; Risk Factor.

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INTRODUCTION

An adverse event (AE) is generally described as an unintended injury that 1) is caused by medical management rather than a disease process and 2) results in death, a life threatening illness, a disability at the time of discharge, an admission to the hospital, or prolongation of the hospital stay (1-4). Large retrospective studies in different countries have demonstrated that 3% to 50% of patients experience one or more AEs in the hospital and approximately 50% of these AEs may be preventable (1-9).

Hospitalized patients aged 65 years and older are at a higher risk of AEs than young adults (1,2,5-8,10-15). The incidence of AEs ranges from 5% to 58% in the elderly group (1,2,4,5,11,12,16-19). AEs increase the burden of already seriously ill elderly hospitalized patients and lead to functional impairment or death in 5% to 27% of cases (2,6,9,12,18,20). Patients who are injured as a result of medical error spend more time in the hospital (7,8,10,11,14-16,20) and have higher hospital costs (21,22). Several studies have attempted to identify the risk factors that are associated with the occurrence of AEs in hospitalized seniors, including the length of the hospital stay, number of comorbidities, admission to a psychiatric unit, severity of illness, level of consciousness, number of drugs prescribed, and functional status at the time of admission (11,12,16-18,20).

No potential conflict of interest was reported.

Studies to detect AEs vary in the methodologies that are used. Prospective observational studies have advantages over retrospective studies for estimating AEs because they can determine more events, particularly preventable ones, and are more reliable (21,23,24). Most studies evaluate AEs relative to all levels of care that are provided to the patients (e.g., nurse and physician care and system-related factors) without a thorough analysis of each specific level.

The aim of this prospective study was to determine the frequency of medical AEs in the admissions of elderly patients to an acute care geriatric ward and identify the predictive factors of AEs and the correlation between AEs and hospital mortality.

METHODS

Study design and subjects

This observational and prospective study included the admission of patients aged 60 years and older who had a minimum stay of 24 hours in the acute care ward of the geriatric unit at the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP) between April 2007 and June 2008.

The patients were admitted directly from the emergency room, the intensive care unit, or were referred by a geriatric outpatient unit, day care hospital, homecare, or other specialty unit.

The acute care ward in the geriatric unit has 10 beds for elderly patients who present with pathologies that do not initially require surgery or admission to the intensive care unit. This ward is in HCFMUSP, which is a quaternary university teaching hospital with 2,200 beds located in São Paulo, the largest city in Brazil.

The patients were treated by a multidisciplinary health team whose members have been trained in gerontology, including geriatric physicians and residents, nurses, nutritionists, physical therapists, speech pathologists and audiologists, psychologists, occupational therapists, and social workers.

The patients who refused participation in the study and did not sign the informed consent were excluded. The study was approved by the HCFMUSP Ethics Committee and was in accordance with the Helsinki Declaration of 1975.

Procedures

The patient data were recorded by one of the authors (CS), a geriatrician who trained in detecting AEs during a geriatrics residency. This observer was not involved in patient care.

The data were obtained from the daily ward rounds and directly from patients or their caregivers using pre-defined questionnaires. If necessary, the observer had full access to the patients' charts.

The patient gender, age, data source (e.g., the patient or a caregiver), diagnosis of infection, and drugs currently in use (particularly medications considered inappropriate by the Beers criteria) (25) were reported upon admission to the geriatric ward. The occurrence of the following common geriatric syndromes were also assessed: dementia and depression (according to the Diagnostic and Statistical Manual of Mental Disorders 4th edition [DSM-IV] criteria), delirium (in accordance with the Confusion Assessment Method) (26), sphincter incontinency (defined as the involuntary loss of urine or feces in quantity and frequency sufficient to characterize it as a social and/or health problem), immobility (defined as the inability to change position in bed without help) and postural instability (defined as two or more falls in the previous year).

During the first 24 hours after admission, the Charlson Comorbidity Index (27), the Simplified Acute Physiology Score II (SAPS II) (28), and the Katz Index of Independency in Activities of Daily Living (29) were applied to evaluate comorbidities, illness severity and functional status, respectively. The validated scales that were used in the study were routinely applied to all of the patients in the geriatric unit. During the hospitalization period in the geriatric ward, the patients were evaluated daily by the multidisciplinary health team. The occurrence of infections, delirium and the prescription of potentially inappropriate drugs for the elderly (based on the Beers criteria) were observed. The length of stay in the geriatric unit and in-hospital mortality were recorded at the end of the hospitalization period. The Burden of Illness Score for Elderly Persons (30), which is a risk adjustment system for older individuals who are hospitalized, was calculated for each patient.

We defined a medical adverse event as an unintended injury or complication that resulted in disability and was caused by physician management rather than the patient's underlying disease process. Disability was defined as temporary or permanent impairment of physical or mental function. Major events were considered to be those events leading to an increased mortality risk. System-related events and events related to nursing care were not considered in the present study. Any event that did not show a clear cause-and-effect relationship to medical management and subsequent adverse clinical manifestation was not considered iatrogenic. Potentially harmful conditions were excluded if they did not involve injury to the patient. An intervention that resulted in many harmful outcomes was considered as a single AE. All of the events experienced by a patient were included. The AEs that occurred before the patient's admission to the geriatric unit were not considered, even if the patient was still suffering the consequences of the event.

The medical AEs were reported and briefly described by the observer. A commission, which included three experienced geriatricians who were not involved in the data collection or patient care, was formed to evaluate the AEs that were described by the observer in monthly meetings.

Statistical analysis

The data were analyzed using Student's T-test, the chi-squared test and Mann-Whitney U-test for continuous quantitative variables with normal distribution, categorical variables and qualitative ordinal variables, respectively. The significance level was set at 5%. A backward stepwise logistic regression model was conducted, the variables with p-values <0.10 in the univariate analyses were used to determine the predictors of in-hospital death. Odds ratios (OR) with CIs of 95% were calculated. The Nagelkerke's R-squared was used to determine the proportion of variation explained by the model. These analyses were performed using the SPSS statistical software, version 14 (SPSS, Inc., Chicago, IL).

RESULTS

During the study period, there were 238 sequential admissions to the acute care ward of the geriatric unit. Of these, 47

patients refused to sign the informed consent. A total of 171 admissions were enrolled in the study; 101 female (59.1%). The mean age of the sample was 78.12±9.27 years. The patient characteristics are shown in Table 1.

In 94 admissions (55%), 187 medical AEs occurred during hospitalization. In 47.9% of the AEs, more than one event occurred, with an average of 2.01 events per admission. There were 103 major events. Examples of the frequent iatrogenic events are shown in Table 2.

Patient data, including the age, gender, data informant, presence of infection at the time of admission, geriatric syndromes, functional status, prognostic indexes, number of drugs prescribed, length of hospital stay, and hospital mortalities were analyzed for AE associations. The predictors of medical AEs during hospitalization in the geriatric ward were not observed in this study. The hospital stay length and in-hospital mortality rates were higher in the admissions with AEs (Table 1).

A model using in-hospital death as an endpoint was developed. The patient data informant, sphincter incontinency, immobility, diagnosis of infection at admission, SAPS II and Katz scores at admission, and occurrence of a medical AE were significantly related to death in a univariate analysis (Table 3). In a logistic regression, the SAPS II score (OR = 1.13, CI 95%, 1.07-1.20, $p<0.001$), Katz score (OR = 1.47, CI 95%, 1.18-1.83, $p = 0.001$), and occurrence of a medical AE (OR = 3.59, CI 95%, 1.55-8.30, $p = 0.003$) were predictors of death during hospitalization in the geriatric unit (Table 4). Nagelkerke's R-squared statistic was 0.40. The patients with major events were more likely to die during hospitalization than the patients with minor AEs (31 [47.7%] versus 7 [22.6%], $p = 0.019$).

DISCUSSION

The present study found that 55% of hospital admissions in a geriatric acute care ward were associated with a medical AE and no risk factors were associated with the occurrence of AEs. The length of hospital stay and in-hospital mortality rate were higher in the patients who were admitted with AEs. In-hospital deaths could be predicted based on the severity of illness measured by SAPS II, poorer functional status at admission, and the occurrence of an AE in the geriatric ward.

Although the frequency of AEs in the geriatric unit was high, it was in alignment with the rates for older patients that have been reported in the literature (1,2,4,6,11,12,16-20). Because of the nature of the prospective study design and the importance of determining a higher rate of AEs for quality improvement, we used a more inclusive AE definition than the major retrospective studies. We included injuries that did not necessarily result in prolonged hospital stays, disability at discharge, or death. Because most studies analyze AEs in general as opposed to medical adverse events, a comparison of the results of this study with other studies is difficult.

The prospective study design and the less restrictive definition of AEs could account for the high rate of complications. The study setting may be a contributing factor in that AEs have been reported to be more prevalent in teaching hospitals (7,9,31). The rate of AEs reported in studies in Brazil for all age groups ranges from 8% to 69% (32-34). In one retrospective and one prospective study from the same geriatric ward, AEs were less frequently reported than in the present study (43.7% and 25.9%, respectively) (18,20), which could be explained by the restricted population selected, including only those admitted to acute care instead of all of the geriatric ward patients. This group of patients tends to present with more severe illnesses and may be more susceptible to complications during hospitalization.

We did not find any risk factors that were associated with the occurrence of AEs. Other studies have reported that educational level, non-elective hospitalization, admission to a teaching hospital, hospital admission sector, functional status, severity of illness, associated comorbidities, level of consciousness, and the number of drugs prescribed at admission (7,10,11,13-18,20) were related to AEs during the hospital stay. However, most of these studies were

Table 1 - Patient characteristics with and without medical adverse events.

Variable	All admissions (N = 171)	Without AE* (N = 77)	With AE (N = 94)	*p*-value†
Age, years, average±SD‡	78.12±9.27	78.10±9.18	78.14±9.39	0.981§
Female, n (%)	101 (59.1%)	46 (59.7%)	55 (58.5%)	0.871¶
Patient as informant, n (%)	80 (46.8%)	35 (45.5%)	45 (47.9%)	0.753¶
Time of hospitalization before admission to the geriatric unit, days, average±SD	6.08±13.93	5.27±15.27	6.77±12.73	0.493§
Sphincter incontinency, n (%)	109 (63.7%)	47 (61%)	62 (66%)	0.506¶
Immobility, n (%)	47 (27.5%)	19 (24.7%)	28 (29.8%)	0.456¶
Postural instability, n (%)	41 (24%)	20 (26%)	21 (22.3%)	0.580¶
Depression, n (%)	32 (18.7%)	12 (15.6%)	20 (21.3%)	0.342¶
Dementia, n (%)	51 (29.8%)	23 (29.9%)	28 (29.8%)	0.991¶
Delirium at admission, n (%)	61 (35.7%)	28 (36.4%)	33 (35.1%)	0.864¶
Infection at admission, n (%)	95 (55.6%)	45 (58.4%)	50 (53.2%)	0.492¶
CCI#, average±SD/Median	3.07±2.18/3	3.14±2.21/3	3.01±2.16/2.5	0.647**
SAPS II††, average±SD/Median	31.38±7.95/30	31.58±9.09/30	31.21±6.92/30	0.733**
Number of drugs at admission, average±SD/median	5.73±3.06/5	5.61±2.76/5	5.83±3.30/5	0.789**
Inappropriate prescriptions, using Beers criteria, n (%)	49 (28.7%)	21 (27.3%)	28 (29.8%)	0.717¶
Katz score at admission, average±SD/median	4.13±2.48/6	3.91±2.57/5	4.31±2.41/6	0.286**
Length of hospital stay, days, average±SD	16.68±13.24	10.91±7.21	21.41±15.08	<0.001§
BISEP‡‡, average±SD/median	3.30±1.44/3	3.19±1.42/3	3.39±1.45/3.5	0.407**
Deaths, n (%)	56 (32.7%)	17 (22.1%)	39 (41.5%)	0.007¶

*Adverse event, † comparison between patients with or without adverse events, ‡ standard deviation, § independent-sample T-test, ¶ chi-squared test, # Charlson comorbidity index, **Mann-Whitney U-test, †† Simplified Acute Physiology Score, ‡‡ Burden of Illness Score for Elderly Persons.

Table 2 - Frequent examples of medical adverse events.

Adverse events*	Number of events
Drug-related	82
Somnolence or delirium caused by opioids	8
Somnolence caused by neuroleptics	8
Acute renal failure caused by diuretics	8
Coumarin intoxication	3
Hypoglycemia caused by insulin	3
Others	52
Nosocomial infection†	61
Pneumonia	18
Urinary tract infection	12
Phlebitis in peripheral venous access	7
Central venous catheter infection	5
Unknown site	4
Pseudomembranous colitis	3
Others	12
Therapeutic procedures‡	36
Phlebitis in peripheral venous access	7
Pulmonary edema after fluid expansion or blood transfusion	5
Urinary tract infections related to indwelling catheters	5
Pneumothorax after central venous puncture	3
Rectal bleeding after enema	1
Others	15
Diagnostic procedures or mishaps	14
Complications related to colonoscopy	5
Contrast induced renal failure	3
Diagnostic mishap	2
Others	4
Miscellaneous	12
Delirium§	7
Procedure delay caused by physician mishap	2
Others	3
Surgical complications	9
Intra-abdominal or wound infection	3
Others	6

*An event can be classified in more than one category. For example, a central venous catheter infection is a nosocomial infection and a therapeutic procedure-related event.
†Infection acquired during hospital care 48 hours after admission.
‡Nonsurgical therapeutic procedures
§Delirium that started during the hospital stay in the geriatric ward and was apparently unrelated to drugs, therapeutic or diagnostic procedures.

Table 3 - Univariate analysis of in-hospital predictors of death.

Variable	Survival (N = 115)	Death (N = 56)	*p*-value
Age, years, average ± SD*	77.96 ± 8.99	78.46 ± 9.89	0.738†
Female, n (%)	69 (60%)	32 (57.1%)	0.721‡
Patient as informant, n (%)	61 (53%)	19 (33.9%)	0.019‡
Time of hospitalization before admission to the geriatric unit, days, average ± SD	5.06 ± 13.83	8.07 ± 14.04	0.193†
Sphincter incontinency, n (%)	61 (53%)	48 (85.7%)	<0.001‡
Immobility, n (%)	24 (20.9%)	23 (41.1%)	0.005‡
Postural instability, n (%)	29 (25.2%)	12 (21.4%)	0.586‡
Depression, n (%)	22 (19.1%)	10 (17.9%)	0.841‡
Dementia, n (%)	35 (30.4%)	16 (28.6%)	0.803‡
Delirium at admission, n (%)	37 (32.2%)	24 (42.9%)	0.171‡
Infection at admission, n (%)	58 (50.4%)	37 (66.1%)	0.053‡
CCI§, average ± SD/median	2.96 ± 2.13/3	3.30 ± 2.28/3	0.415¶
SAPS II#, average ± SD/median	29.08 ± 6.74/29	36.11 ± 8.20/35	<0.001¶
Drugs at admission, average ± SD/median	5.85 ± 3.11/5	5.48 ± 2.99/5	0.555¶
Inappropriate prescription using Beers criteria, n (%)	36 (31.3%)	13 (23.2%)	0.272‡
Katz score at admission, average ± SD/median	3.50 ± 2.62/5	5.41 ± 1.52/6	<0.001¶
Length of hospital stay, days, average ± SD	16.83 ± 12.31	16.38 ± 15.08	0.832†
Adverse event, n (%)	55 (47.8%)	39 (69.6%)	0.007‡

*Standard deviation, † independent-sample T-test, ‡ chi-squared test, § Charlson comorbidity index, Mann-Whitney U-test, # Simplified Acute Physiology Score II.

Table 4 - A backward stepwise logistic regression of the predictors of in-hospital death.

		Coefficient	*p*-value	OR	CI 95%	
					Lower	Upper
Step 1	Patient as data source	0.898	0.086	2.456	0.880	6.850
	Sphincter incontinency	0.030	0.965	1.031	0.266	3.988
	Immobility	0.630	0.190	1.878	0.731	4.825
	Infection	0.588	0.158	1.801	0.796	4.076
	SAPS II	0.136	0.000	1.146	1.080	1.216
	Katz score at admission	0.430	0.010	1.537	1.108	2.131
	Adverse event	10.299	0.003	3.666	1.538	8.736
	Constant	-80.867	0.000	0.000		
Step 2	Patient as data source	0.895	0.084	2.448	0.887	6.753
	Immobility	0.634	0.181	1.885	0.745	4.773
	Infection	0.589	0.158	1.801	0.796	4.076
	SAPS II	0.136	0.000	1.146	1.080	1.215
	Katz score at admission	0.434	0.002	1.543	1.177	2.023
	Adverse event	1.300	0.003	3.669	1.540	8.738
	Constant	-8.870	0.000	0.000		
Step 3	Patient as data source	0.701	0.152	2.017	0.773	5.261
	Infection	0.575	0.163	1.777	0.792	3.986
	SAPS II	0.132	0.000	1.141	1.076	1.210
	Katz score at admission	0.471	0.001	1.602	1.226	2.092
	Adverse event	1.316	0.003	3.727	1.570	8.848
	Constant	-8.618	0.000	0.000		
Step 4	Patient as data source	0.651	0.178	1.918	0.744	4.945
	SAPS II	0.130	0.000	1.139	1.075	1.207
	Katz score at admission	0.476	0.000	1.610	1.236	2.096
	Adverse event	1.260	0.004	3.526	1.512	8.222
	Constant	-8.198	0.000	0.000		
Step 5	SAPS II	0.125	0.000	1.133	1.071	1.198
	Katz score at admission	0.384	0.001	1.469	1.181	1.827
	Adverse event	1.278	0.003	3.590	1.553	8.301
	Constant	-7.312	0.000	0.001		

retrospective and several were conducted in general hospitals and included all age groups.

In contrast to another study (20) that was conducted in the same geriatric ward and included elective and acute admissions in the analysis, the results of this study did not indicate that delirium, the number of drugs prescribed at admission, and the presence of postural instability predicted the occurrence of AEs. This result may be caused by the inclusion of a more heterogeneous group of patients in the previous study (acute and elective admissions). Another possibility is that the definition of AEs was restricted to medical adverse events in the present study.

The absence of predictors of medical AEs during the hospitalization of elderly patients suggests the hypothesis that the occurrence of these complications is not dependent on the condition of the patient at the time of admission. Although some events may be caused by latent errors and are not related to medical care, physicians must carefully assess their actions to protect patients from medical AEs.

Another important issue highlighted in this study is that medical adverse events led to longer hospital stays and were related to in-hospital deaths, which is similar to the results of previous research (7,8,10,11,14,16,18,33). The relationship between AEs and the length of hospital stay is not clear because it is not possible to determine if a longer hospital stay renders patients more susceptible to complications or if the AEs prolong the hospitalization.

A primary contribution of this study is that medical AEs are independent predictors of in-hospital death, even after adjusting for confounding factors. In a study performed in acute care hospitals, Meurer et al. found that the relative risk of death was 1.47 in patients with medical injuries, although the increased mortality risk associated with any medical injury disappeared after a logistic regression model was applied (14). The severity of illness as measured by the SAPS II and poor functional status based on the Katz score were also predictors of death, which is consistent with another study (35).

The present study had some limitations. Because the study was only performed in one hospital, the results may not be generalized.

The data regarding AEs are subjective and dependent on the judgment of the observer. To minimize this bias, all of the events were analyzed by a specialized commission, and those not considered as medical AEs were discharged. To prevent a misinterpretation of the events, the observer was not involved in patient care. Geriatricians are trained to avoid medical adverse events. Therefore, the number of events could be higher in other contexts.

It is difficult to separate AEs as a cause of morbidity or as an effect of the patients' comorbidities in observational studies using hospitalized patients. Another limitation is the exclusion of data regarding system-related AEs and the events that are related to nursing care, which decreases the reliability of the study.

Future studies should include additional variables, such as race, income, number of AEs and the occurrence of major AEs, to test for potential correlations and the predictors of mortality.

Patients are increasingly exposed to diagnostic and therapeutic procedures because of advances in medical practice, and iatrogenic illnesses must be considered as essential issues, particularly in older patients. Given that there is not a characteristic risk profile for patients who are susceptible to medical AEs, hospitalization and the actions of the health team are the most common reasons for occurrence. This study demonstrates that every elderly hospitalized patient is at risk for medical AEs. The consequences of AEs in older patients are extremely serious, which makes this subject relevant for further studies to better understand the mechanisms that could protect older in-patients from medical harm.

AUTHOR CONTRIBUTIONS

Szlejf C provided substantial contributions to the conception and design of the study, data acquisition, analysis and interpretation, drafting of the manuscript, and final approval of the manuscript. Farfel JM, Curiati JA and Jacob-Filho W contributed to the conception and design of the study and final approval of the manuscript. Couto Junior EB contributed to the analysis and interpretation of data. Azevedo RS contributed to the conception and design of the study, analysis and interpretation of data, critical revision of the article and final approval of the manuscript.

REFERENCES

1. Brennan TA, Hebert LE, Laird NM, Lawthers A, Thorpe KE, Leape LL, et al. Hospital characteristics associated with adverse events and substandard care. JAMA. 1991;265(24):3265-9, http://dx.doi.org/10.1001/jama.1991.03460240061028.
2. Wilson RM, Runciman WB, Gibberd RW, Harrison BT, Newby L, Hamilton JD. The quality in Australian health care study. Med J Aust. 1995;163(9):458-71.
3. Thomas EJ, Studdert DM, Burstin HR, Orav EJ, Zeena T, Williams EJ et al. Incidence and types of adverse events and negligent care in Utah and Colorado. Med Care. 2000;38(3):261-71, http://dx.doi.org/10.1097/00005650-200003000-00003.
4. Vincent C, Neale G, Woloshynowych M. Adverse events in British hospitals: preliminary retrospective record review. BMJ. 2001;322(7285):517-9, http://dx.doi.org/10.1136/bmj.322.7285.517.

5. Leape LL, Brennan TA, Laird N, Lawthers AG, Localio R, Barnes BA, et al. The nature of adverse events in hospitalized patients.Results of the Harvard Medical Practice Study II. N Engl J Med. 1991;324(6):377-84.
6. Davis P, Lay-Yee R, Briant R, Ali W, Scott A, Schug S. Adverse events in New Zealand public hospitals I: occurrence and impact. N Z Med J. 2002;115(1167):U271.
7. Baker GR, Norton PG, Flintoft V, Blais R, Brown A, Cox J, et al. The Canadian Adverse Events Study: the incidence of adverse events among hospital patients in Canada. CMAJ. 2004;170(11):1678-86.
8. Aranaz-Andrés JM, Aibar-Remón C, Vitaller-Murillo J, Ruiz-López P, Limón-Ramírez R, Terol-García E. Incidence of adverse events related to health care in Spain: results of the Spanish National Study of Adverse Events. J Epidemiol Community Health. 2008;62(12):1022-9, http://dx.doi.org/10.1136/jech.2007.065227.
9. Zegers M, de Bruijne MC, Wagner C, Hoonhout LHF, Waaijman R, Smits M, et al. Adverse events and potentially preventable deaths in Dutch hospitals: results of a retrospective patient record review study. Qual Saf Health Care. 2009;18(4):297-302, http://dx.doi.org/10.1136/qshc.2007.025924.
10. Steel K, Gertman PM, Crescenzi C, Andreson J. Iatrogenic illness on a general medical service at a university hospital. N Engl J Med 1981;304(11):628-42.
11. Jahnigen D, Hannon RN, Laxson RN, LaForce FM. Iatrogenic disease in hospitalized elderly veterans. J Am Geriatr Soc. 1982;30(6):387-90.
12. Thomas EJ, Brennan TA. Incidence and types of preventable adverse events in elderly patients: population based review of medical records. BMJ. 2000;320(7237):741-4, http://dx.doi.org/10.1136/bmj.320.7237.741.
13. Forster AJ, Asmis TR, Clark HD, Al Saied G, Code CC, Caughey SC, et al. Ottawa Hospital Patient Safety Study: incidence and timing of adverse events in patients admitted to a Canadian teaching hospital. CMAJ 2004;170(8):1235-40.
14. Meurer LN, Yang H, Guse CE, Russo C, Brasel KJ, Layde PM. Excess mortality caused by medical injury. Annals of family medicine. 2006;4(5):410-6, http://dx.doi.org/10.1370/afm.553.
15. Madeira S, Melo M, Porto J, Monteiro S, Pereira de Moura JM, Alexandrino MB, et al. The diseases we cause: iatrogenic illness in a department of internal medicine. Eur J Intern Med. 2007;18(5):391-9.
16. Becker PM, McVey LJ, Saltz CC, Feussner JR, Jay Cohen H. Hospital-acquired complications in a randomized controlled clinical trial of a geriatric consultation team. JAMA. 1987;257(17):2313-7, http://dx.doi.org/10.1001/jama.1987.03390170069030.
17. Lefevre F, Feinglass J, Potts S, Soglin L, Yarnold P, Martin GJ, et al. Iatrogenic complications in high-risk, elderly patients. Arch Intern Med. 1992;152(10):2074-80, http://dx.doi.org/10.1001/archinte.1992.00400220090016.
18. Carvalho-Filho ET, Saporetti L, Souza MAR, Arantes ACLQ, Vaz MYKC, Hojaij NSL, et al. Iatrogenia em pacientes idosos hospitalizados. Rev Saude Publica. 1998;32(1):36-42.
19. Ackroyd-Stolarz S, Guernsey JR, MacKinnon NJ, Kovacks G. Impact of adverse events on hospital disposition in community-dwelling seniors admitted to acute care. Healthc Q. 2009;12 Spec No Patient:34-9.
20. Szlejf C, Farfel JM, Saporetti LA, Jacob-Filho W, Curiati JA. Fatores relacionados com a ocorrência de iatrogenia em idosos internados em enfermaria geriátrica: estudo prospectivo. Einstein. 2008;6(3):337-42.
21. Weingart SN, McL Wilson R, Gibberd RW, Harrison B. Epidemiology of medical error. BMJ. 2000;320(7237):774-7, http://dx.doi.org/10.1136/bmj.320.7237.774.
22. Kohn LT, Corrigan JM, Donaldson MS, Editors. To Err is Human: Building a Safer Health System [on line]. 1st ed. Washington (DC): National Academy Press, 2000. Available at: http://www.nap.edu/catalog/9728.html. Acessed June 13th, 2012.
23. Thomas EJ, Petersen LA. Measuring errors and adverse events in health care. J Gen Intern Med. 2003;18(1):61-7, http://dx.doi.org/10.1046/j.1525-1497.2003.20147.x.
24. Michel P, Quenon JL, Sarasqueta AM, Scemama O. Comparison of three methods for estimating rates of adverse events and rates of preventable adverse events in acute care hospitals. BMJ. 2004;328(7433):1-5.
25. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults.Results of a US consensus panel of experts. Arch Intern Med. 2003;163(22):2716-24, http://dx.doi.org/10.1001/archinte.163.22.2716.
26. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the Confusion Assessment Method.A new method for detection of delirium. Ann Intern Med. 1990;113(12):941-8.
27. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83, http://dx.doi.org/10.1016/0021-9681(87)90171-8.
28. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA. 1993;270(24):2957-63, http://dx.doi.org/10.1001/jama.1993.03510240069035.
29. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged.The index of ADL: a standardized measure of biological and psychosocial function. JAMA. 1963;185:914-9, http://dx.doi.org/10.1001/jama.1963.03060120024016.
30. Inouye SK, Bogardus ST, Vitagliano G, Desai MM, Williams CS, Grady JN et al. Burden of Illness Score for Elderly Persons. Risk adjustment incorporating the cumulative impact of diseases, physiologic abnormalities, and functional impairments. Med Care. 2003;41(1):70-83, http://dx.doi.org/10.1097/00005650-200301000-00010.
31. Brennan TA, Hebert LE, Laird NM, Lawthers A, Thorpe KE, Leape LL et al. Hospital characteristics associated with adverse events and substandard care. JAMA. 1991;265(24):3265-9, http://dx.doi.org/10.1001/jama.1991.03460240061028.
32. Daud-Gallotti R, Novaes HMD, Lorenzi MC, Eluf-Neto J, Okamura MN, Velasco IT. Adverse events and death in stroke patients admitted to the emergency department of a tertiary university hospital. Eur J Emerg Med. 2005;12(2):63-71.
33. Daud-Gallotti R, Novaes HMD, Lorenzi MC, Eluf-Neto J, Okamura MN, Pizzo VRP. Adverse events in patients with community-acquired pneumonia at an academic tertiary emergency department. Infect Dis Clin Pract. 2006;14:350-9, http://dx.doi.org/10.1097/01.idc.0000227713.81012.ae.
34. Mendes W, Martins M, Rozenfeld S, Travassos C. The assessment of adverse events in hospitals in Brazil. Int J Qual Health Care 2009;21(4):279-84, http://dx.doi.org/10.1093/intqhc/mzp022.
35. Silva TJA, Jerussalmy CS, Farfel JM, Curiati JAE, Jacob-Filho W. Predictors of in-hospital mortality among older patients. Clinics. 2009;64(7):613-8, http://dx.doi.org/10.1590/S1807-59322009000700002.