

Factors predicting mortality in elderly patients admitted to a Moroccan medical intensive care unit

Jihane Belayachi, Mina El khayari, Tarek Dendane, Naoufel Madani, Khalid Abidi, Redouane Abouqal, Amine Ali Zeggwagh

Medical Intensive Care Unit, Ibn Sina University Hospital, Rabat, Morocco

Jihane Belayachi, MD

Mina El khayari, MD

Tarek Dendane, MD

Naoufel Madani, MD

Khalid Abidi, MD

Medical Intensive Care Unit, Ibn Sina University Hospital, and Laboratory of Biostatistics, Clinical and Epidemiological Research, Faculté de Médecine et de Pharmacie-Université Mohamed V, Rabat, Morocco

Redouane Abouqal, PHD, MD

Amine Ali Zeggwagh, PHD, MD

Corresponding author: Jihane Belayachi (be_jihane@yahoo.fr)

Introduction. There has been a notable increase in the incidence of elderly patients being admitted to intensive care units (ICUs), globally and in Morocco. Studies on the diagnosis and management of ICU patients often exclude subjects with multiple co-morbidities or those older than 80 years. However, as the world's population becomes increasingly old and ill, this subset will require ICU admission more frequently and their management will pose a serious challenge to the intensivists treating them. There are no studies in the current medical literature from low- or middle-income countries assessing the outcome of elderly patients admitted to ICUs. Specifically, little is known about the outcome of elderly patients admitted to ICUs in Morocco.

Aims. The aims of the present study were to analyse the characteristics of elderly Moroccan patients (aged ≥ 65 years) admitted to a medical ICU, and to identify factors predicting ICU mortality.

Methods. This was a retrospective study conducted in the medical ICU of a Moroccan university hospital. All elderly patients (≥ 65 years) with complete records were included, whatever their length of stay. Baseline characteristics, clinical parameters and severity of illness were recorded at admission. Patients were grouped according to their survival status using logistic regression analysis.

Results. During the study period, 1 072 patients were admitted to the ICU, of whom 16.6% ($n=179$) were aged >65 years and had complete records. Fifty-five per cent ($n=98$) were men. The median age was 70 years (interquartile range 67 - 75 years). The overall ICU mortality was 44.7%, and 64% of deaths occurred within 5 days of admission. On univariate analysis, the factors predicting mortality were alcohol misuse ($p=0.09$), pneumonia ($p\leq 0.001$), shock ($p=0.001$), dehydration ($p=0.007$), urine output ≤ 0.5 ml/kg/h ($p=0.003$), serum urea level >16.6 mmol/l ($p=0.01$), serum creatinine level >159 μ mol/l ($p=0.005$), and an abnormality on the chest radiograph ($p=0.01$). The Sequential Organ Failure Assessment (SOFA) score was the most accurate predictor of ICU mortality in this group of elderly patients, with an area under the curve (AUC) of 0.775 (standard deviation (SD) ± 0.036). The Acute Physiology and Chronic Health Evaluation II (APACHE II) score also performed adequately (AUC 0.757; SD ± 0.037), but the Simplified Acute Physiology Score II (SAPS II) and Logistic Organ Dysfunction System (LODS) scores were not useful in this group. Two parameters significantly associated with mortality risk were shock (odds ratio (OR) 11.5, 95% confidence interval (CI) 3.7 - 35.7; $p<0.001$) and pneumonia (OR 3.13, 95% CI 1.5 - 6.2; $p<0.001$).

Conclusion. Admission of aged patients to the ICU raises important medical, ethical, sociological and economic questions. Our findings suggest that severity of illness, shock and pneumonia on ICU admission were the independent risk factors associated with raised mortality, 64% of which occurred within 5 days of ICU admission.

S Afr J Crit Care 2012;28(1):22-27. DOI:10.7196/SAJCC.122

In recent years there has been a global increase in the incidence of elderly patients being admitted to intensive care units (ICUs).¹ This 'demographic transition' can be explained by both decreases in fertility and increased life expectancy. It has been predicted

that the elderly segment of the population will grow more rapidly than any other segment, and by 2050 the elderly population of the world will exceed that of the young for the first time in history.² This demographic revolution has also affected the Moroccan

population. Average life expectancy is clearly increasing (from 40 years in 1950 to 72 years in 2006), and it is expected that the total population aged >60 years will increase from 8% in 2009 to 15.4% in 2030. The proportion of the population aged >75 years had increased to 2.3% in 2009 and is predicted to be 3.8% in 2030.¹²

An increasingly old and ill population will require treatment in ICUs more frequently, and their management will pose a serious challenge to the treating intensivists. Early recognition of patients at high risk of mortality and other negative health outcomes is therefore needed, not only in order to plan care in advance and inform patients about prognosis and treatment, but also to control healthcare costs.

Morocco is a country of 32 million inhabitants in North Africa. The health budget makes up 1.1% of the gross domestic product and 5.5% of the central government budget.⁴ Morocco has inadequate numbers of doctors (0.5 per 1 000 people) and hospital beds (1.0 per 1 000 people), as well as poor access to treated water (82% of the population have poor access to treated water) and sanitation (75% of the population have poor access to sanitation). The healthcare system includes 122 hospitals, 2 400 health centres and 4 university clinics, but they are poorly maintained with inadequate capacity to meet the demand for medical care.⁴ Only 24 000 beds are available for the 6 million patients who seek care each year, including 3 million emergency cases.⁴ Morocco has two major health sectors, public and private, which are regarded as complementary rather than competitive. Patients may choose whether to attend primary or secondary public or private care. The majority of Moroccans in employment pay for health insurance, which covers most but not all health expenses in the public and private sectors. This health insurance remains valid after people reach pensionable age.

Many studies have evaluated the outcomes of elderly patients admitted to ICUs in Western countries,⁵⁻⁷ but little is known about outcomes of such patients admitted to ICUs in Morocco, an Arab country where cultural values and socio-economic standards differ from those in Western countries. The aims of the present study were to analyse the characteristics of elderly Moroccan patients (aged ≥65 years) admitted to a medical ICU, and to identify factors predicting death in the ICU.

Materials and methods

Study design and setting

The study was a retrospective analysis conducted in the medical ICU of Rabat University Hospital, a university hospital and the referral hospital for inhabitants of north-western Morocco. A clinical database of all consecutive admissions to a 12-bed medical ICU was collected for the 2-year study period from January 2005 to 31 December 2006. The 12-bed medical ICU admits approximately 550 patients a year, with an average age of 40 years. The unit is staffed by 6 senior physicians (who have worked in the ICU for more than 2 years) and 6 junior physicians (who have worked there for less than 2 years). Patients were admitted either from the emergency unit or from another department.

Inclusion and exclusion criteria

We included all patients aged ≥65 years, whatever their length of stay. Patients with incomplete records were excluded. Approval

for the study from the local ethics committees was discussed but not required.

Data collection

The following data were recorded for each patient: age, gender, co-morbidity, primary reason for the ICU admission, underlying disease, presence of infection, clinical and laboratory data required for determination of the severity of illness and organ dysfunction, and survival status (death or discharge from the ICU). Severe chronic diseases included chronic heart and respiratory disease, renal failure and cirrhosis of the liver. A history of smoking or alcohol use was also recorded. To assess health status on the first day in the ICU, severity of illness and organ dysfunction were measured using the Acute Physiology and Chronic Health Evaluation II (APACHE II),⁷ Simplified Acute Physiology Score II (SAPS II),⁸ Sequential Organ Failure Assessment (SOFA)⁹ and Logistic Organ Dysfunction System (LODS)¹⁰ scores. Dysfunction of 6 organ systems (cardiovascular, neurological, respiratory, coagulation, renal and hepatic) was assessed on day 1 using the SOFA score. The pre-sedation Glasgow Coma Scale was used to evaluate the level of consciousness in patients under sedation. Further data analysed included the use of mechanical ventilation and vaso-active drugs, and occurrence of an infection acquired in the ICU. Length of stay in the ICU was assessed as the number of days from admission to the ICU to discharge from the ICU. If a patient was readmitted to the ICU during the same hospitalisation, only data from the first admission were analysed. The main outcome measure used was survival status (death or ICU discharge).

Statistical analyses

Statistical analyses were performed using the Statistics Package for Social Scientists (SPSS; Windows version 13.0. Continuous variables were presented as means (standard deviation (SD)) or as medians with 25th - 75th percentiles. Categorical variables were expressed as actual numbers and percentages. Characteristics of patients were compared using chi-square analysis for categorical variables and the *t*-test for continuous variables. Variables were assessed in the groups of patients stratified according to age (65 - 74 and ≥75 years) and survival status. Kaplan-Meier survival curves were used to visually compare the survival status of all elderly subjects stratified by length of stay. Receiver operating characteristic (ROC) curves were used to clarify the power of discriminant scores of gravity. The areas under the curves (AUCs) were calculated and compared using the non-parametric method of Hanley. Multivariate logistic regression analysis was applied to determine the independent contribution of clinical variables to the prediction of ICU mortality as a dependent variable. Variables that had a significant association with mortality to a value of $p < 0.05$ on univariate analysis were entered into a stepwise logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to estimate the independent determinants of ICU mortality. *P*-values <0.05 were considered significant for all tests.

Results

Characteristics of the study sample

During the study period, 1 072 patients were admitted to the ICU, of whom 200 were older than 65 years; 21 of these patients were excluded because of incomplete records, and the remaining 179 were enrolled into the study. Fifty-five per cent of these patients were male, and 78% were admitted via the emergency room. The

Table 1. Characteristics of elderly patients and comparison of subgroups according to survival status

	All patients (N=179)	Survivors (n=99)	Non-survivors (n=80)	p-value
Age (years), mean (SD)	72 (6)	71.7 (6)	71.7 (6)	NS
Gender, n (%)				NS
Female	81 (45.3)	48 (48.5)	33 (41.3)	
Male	98 (54.7)	51 (51.5)	47 (58.5)	
Severe chronic diseases, n (%)	108 (60.3)	59 (59.6)	49 (61.3)	NS
Chronic heart failure	36 (20.1)	16 (16.2)	20 (25)	
Respiratory failure	32 (18)	16 (16.2)	16 (20)	
Renal failure	6 (3.4)	3 (3)	3 (3.8)	
Cirrhosis	13 (7.3)	9 (9.1)	4 (5)	
Admission type, n (%)				NS
Emergency	141 (78.8)	76 (76.8)	65 (81.3)	
Other services	38 (21.2)	23 (23.2)	15 (18.8)	
Severity of illness, mean (SD)				
SAPS II score	35 (13)	32 (9.2)	38.5 (12.5)	<0.001
APACHE II score	15 (5.5)	12.7 (4.7)	17.7 (5.4)	<0.001
LODS score	5.6 (4.3)	4.4 (3.8)	7.2 (4.6)	<0.001
Most common reasons for admission to ICU, n (%)				
Infectious diseases	97 (54.2)	44 (44.4)	53 (62.6)	0.004
Respiratory diseases	37 (20.7)	19 (19.2)	18 (22.5)	NS
Metabolic diseases	42 (23.5)	26 (26.3)	16 (20)	NS
Cardiovascular diseases	25 (14)	11 (11.1)	14 (17.5)	NS
Cerebrovascular diseases	14 (7.8)	8 (8.1)	6 (7.5)	NS
Toxic diseases	7 (4)	5 (5.1)	2 (2.5)	NS
Most common causes of infectious diseases, n (%)				
Pulmonary	80 (44.6)	25 (25.3)	41 (51.3)	0.0001
Abdominopelvic	22 (12.4)	16 (16.2)	6 (7.6)	NS
Neurological	16 (8.9)	10 (10.1)	6 (7.5)	NS
Other	17 (9.5)	5 (5)	12 (15.1)	NS
Clinical parameters at admission to ICU				
Shock, n (%)	32 (17.9)	4 (4)	28 (35)	<0.001
Heart rate (beats/min), mean (SD)	102.2 (18.9)	98.8 (18.2)	106.4 (18.9)	0.007
Temperature (°C), mean (SD)	37.5 (0.9)	37.6 (0.9)	37.5 (1)	NS
Dehydration, n (%)	42 (23.5)	27 (27.3)	15 (18.8)	NS
Urine production (ml/24 h), mean (SD)	1 125 (755.5)	1 313 (792)	936 (670)	0.04
Biochemical measurements at admission to ICU, mean (SD)				
Bicarbonate (mmol/l)	24.9 (6.4)	25.3 (5)	24.3 (7.6)	NS
Urea (mmol/l)	10.7 (1.09)	0.9 (0.8)	1.2 (1.1)	NS
Creatinine (μmol/l)	179 (196)	173 (209)	187 (179)	NS
Protein (g/l)	62.1 (1.9)	62.2 (11.5)	62 (12.4)	NS
Glucose (mmol/l)	10.6 (9.5)	10.3 (9.5)	11 (9.4)	NS
White blood cells (×10 ⁹ /l)	21.1 (33.7)	23.4 (41)	18 (20.3)	NS
Haemoglobin (g/dl)	19.3 (19.8)	19.5 (3.5)	19.3 (4)	NS
Platelets (103/μl)	20.4 (12.6)	20.1 (13.2)	20.8 (11.9)	NS
Organ dysfunction on day 1, n (%)				
Cardiovascular	83 (46.4)	13 (13.1)	70 (87.5)	<0.0001
Impaired level of consciousness	90 (50.3)	52 (52.5)	38 (47.5)	NS
Arterial hypoxaemia	104 (58.1)	28 (76)	76 (95)	<0.0001
Uraemia or oliguria	73 (40.8)	38 (38.4)	35 (44.9)	NS
Thrombocytopenia	61 (34.1)	35 (37.6)	26 (35.6)	NS
Hyperbilirubinaemia	44 (24.6)	22 (45.8)	22 (51.2)	NS
Length of ICU stay (days), mean (SD)	6.6 (6)	6.9 (4.9)	6.3 (7.3)	NS
Mortality in ICU, n (%)	80 (40.7)	-	-	-

NS = not significant. Data are expressed as mean (SD) or number (n) and percentage (%).

median age was 70 years (interquartile range (IQR) 67 - 75 years). Sixty-five per cent of the patients were aged between 65 and 74 years, 31% between 75 and 84 years, and 4% ≥ 85 years. Severe chronic disease was present in 60.3% of cases. The most common severe chronic disease was heart failure (20.1%). The means SAPS II, APACHE II, LODS and SOFA scores were 35 (SD ± 11.3), 15 (SD ± 5.5), 5 (SD ± 3) and 5.6 (SD ± 4.3), respectively. Infectious and metabolic diseases were the most common medical diagnoses, and the leading cause of infection was pleuro-pulmonary in 44.6% of cases. Eighteen per cent of patients had clinical signs of shock at admission. Respiratory dysfunction at admission was common. Seventy-eight patients (43.6%) required assisted ventilation, 31.3% ($n=56$) on day 1 and 12.3% ($n=22$) beyond day 1. Seventy-eight patients received a vaso-active drug (18% at admission and 34.4% later on). Thirty-four patients developed an ICU-acquired infection, with pneumonia in 15.6%, urinary tract infection in 4.5% and bacteraemia in 1.7% of patients. The mean length of stay in the ICU was 6.6 (SD ± 6) days.

A comparison of all previous demographics and illness-related variables of the patients studied, divided into two groups according to their age (cut-off point 75 years), revealed no statistically significant differences. The characteristics of all the elderly patients and comparisons of subgroups according to survival status are shown in Table 1.

Factors predicting mortality

The global ICU mortality of the elderly patients was 44.7%, and 63.8% of those who died did so in the 5 days following admission (Fig. 1). However, the mortality rate in patients aged <70 years was not significantly different to that in those aged 70 - 75 years and >75 years. The Kaplan-Meier survival curve of ICU patients divided into the 3 age groups revealed no statistically significant differences in mortality rates (Fig. 2). On univariate analysis, the factors predicting mortality were heavy alcohol use ($p=0.09$), pneumonia ($p\leq 0.001$), shock ($p=0.001$), dehydration ($p=0.007$), urine output ≤ 0.5 cc/kg/h ($p=0.003$), serum urea level

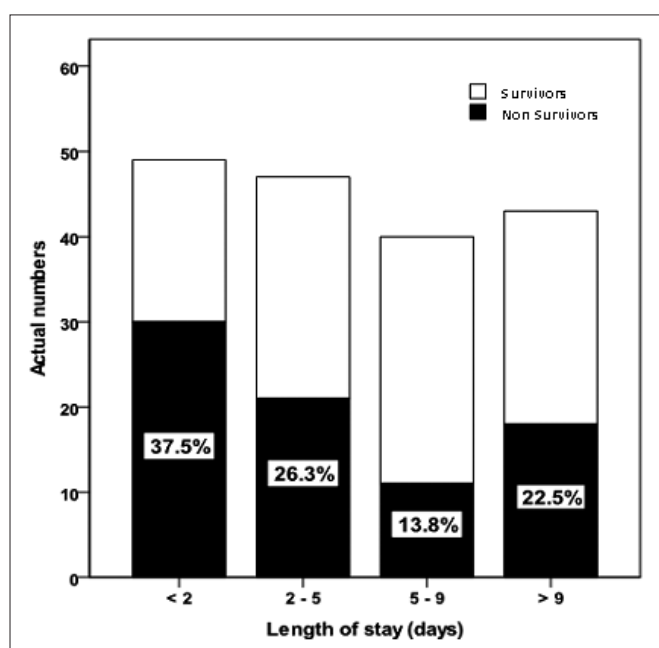


Fig. 1. Number and mortality of patients according to their length of stay in the intensive care unit.

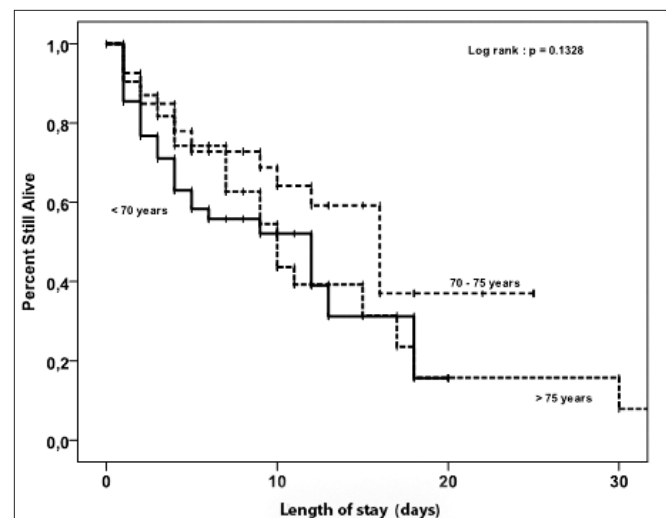


Fig. 2. Patient survival according to three age groups: ≤ 70 years, 70 - 75 years and ≥ 75 years.

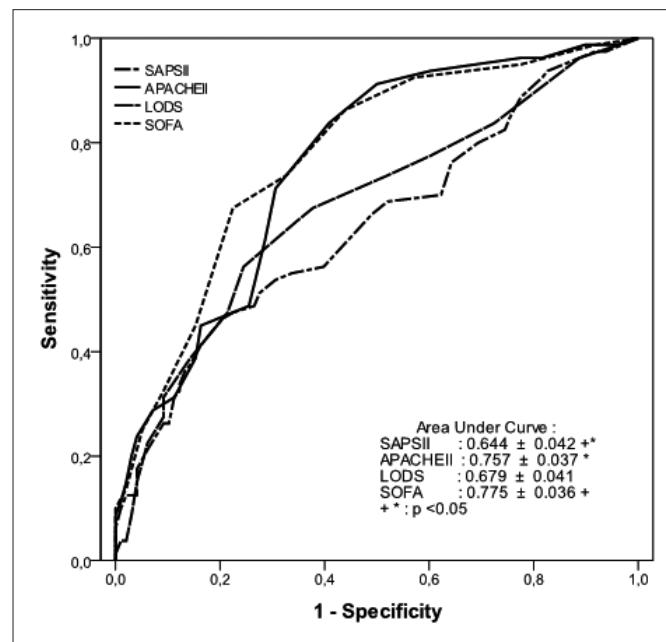


Fig. 3. Receiver operating characteristic (ROC) curves for 4 severity scores.

>16.6 mmol/l ($p=0.01$), and serum creatinine level >159 $\mu\text{mol/l}$ ($p=0.005$). Severity of illness as assessed by the APACHE II, SAPS II, and LODS scores also predicted mortality ($p<0.001$ for all). The SOFA and APACHE II scores had better ability to predict mortality than SAPS II, with AUCs of 0.775 (SD ± 0.036) and 0.757 (SD ± 0.037), respectively (Fig. 3). The results of multivariate analysis are shown in Table 2.

Discussion

The median age of our patients was 72 years, with a small proportion of very elderly (≥ 85 years); this reflects the Moroccan demographic profile. Severity of illness, shock and pneumonia on admission to the ICU were the independent risk factors of mortality. Many studies have evaluated elderly patients in ICUs in Western countries.⁵⁻⁷ This article reports the results of the first study analysing the characteristics and outcomes of older patients (aged ≥ 65 years) admitted to a medical ICU in Morocco. To our knowledge, no data from low- or middle-income countries have

Table 2. Multivariate analysis

Variables	β	OR	95% CI	p-value
Shock	2.45	11.5	3.7 - 35.7	<0.001
Pneumonia	1.1	3.13	1.6 - 3.2	<0.001

been reported, and our findings are more likely to be applicable to such countries than findings of studies in developed countries.

The ICU mortality of elderly patients was 44.7%. Severity of illness, shock and pneumonia were associated with poor prognosis. Many investigations have shown that age alone is not associated with poor prognosis in the ICU.^{5,7,12} Other factors, including patient selection criteria, primary disease, co-morbidity, severity of illness and complications, significantly influence outcome.^{5,13-15}

Infectious disease was the leading cause of hospitalisation in our unit, irrespective of age.¹⁶ This could explain the predominance of infectious diseases, which were present in more than half of admissions (54.2%), and their causal relationship with mortality, especially from pneumonia. The incidence of pneumonia in the elderly is higher than in younger populations.¹⁷ As a result of a complex array of factors, the development of pneumonia in elderly patients differs from that in younger individuals.¹⁷ The most common cause of sepsis in elderly patients is respiratory tract infection, followed by genito-urinary tract infection.¹⁸ However, sepsis in the elderly may be more severe and present differently from that in younger patients.¹⁹

The SOFA and APACHE II scores demonstrated the best ability to assess severity of illness in elderly patients. The SAPS II score is significantly influenced by age and part of this score may be due to age-related points in this system.¹¹ Despite the weighting for age, SAPS II had the smallest AUC, indicating that it had the poorest predictive utility of the scores used.

Analysis of the three age groups revealed no significant differences in mortality rate. Across age categories, the Kaplan-Meier survival curves were remarkably similar. Mean ICU length of stay was 6.6 (SD 6) days for all admissions, and the figures for survivors and non-survivors were similar. While 64% of deaths occurred during the first 5 days after ICU admission, the patients died earlier during hospitalisation. This severe and rapidly fatal disease trajectory may be explained by delays in seeking medical care. The presenting symptoms of pneumonia in the elderly can be subtle and difficult to recognise.¹⁷ Fever is frequently absent, and delirium or alteration of functional physical capacity may be the only manifestations.¹⁷ Delay in seeking care can also be related to limited education, use of alternative medicine and financial constraints. Some patients may refuse to seek early medical care, attributing their deteriorating health to advanced age rather than reversible disease. Some elderly patients may also expect to die and be unwilling to receive treatment that will prolong the process.

In our elderly population, mortality rates were similar regardless of the age group. An increased incidence of sepsis with age, with the

mean age at which severe sepsis develops being around 60 years, has been reported.^{20,21} However, mortality rates associated with severe sepsis also increase with increasing age, with highest mortality in the very old (>85 years of age).^{21,22} The lack of significant differences between the groups of elderly patients in our study could be related to the small proportion of very elderly subjects.

Our study has several limitations. Firstly, it was conducted at a single institution with a specific case-mix of ICU patients. Secondly, no surgical patients were enrolled because of the specificity of our medical ICU. Thirdly, the study was retrospective, resulting in 21 patients being excluded because of incomplete records. Fourthly, there was a small proportion of very elderly patients. Finally, we did not assess the impact of pre-hospitalisation functional status.

Conclusion

Admission of elderly patients to the ICU raises important medical, ethical, sociological and economic questions. Our findings suggest that severity of illness, shock and pneumonia on admission to the ICU, but not age, were the independent risk factors associated with high death rates and earlier ICU mortality. Sepsis is an important cause of morbidity and mortality in the older population in our setting. Future longitudinal studies of long-term survival and functional status are needed to evaluate the effectiveness of critical care in the very elderly.

Author contributions. BJ participated in the study design, performed statistical analyses and drafted the manuscript. EM and DT acquired data. MN, AK and AR co-ordinated data. ZAA conceived the study, participated in its design, performed statistical analyses and data interpretation, and gave final approval of the manuscript. All authors read and approved the final manuscript.

Conflict of interest. The authors declare that they have no conflicting interests.

References

- Marik PE. Management of the critically ill geriatric patient. *Crit Care Med* 2006; 34:176-182. [http://dx.doi.org/10.1097/01.CCM.0000232624.14883.9A]
- United Nations. World Population Ageing: 1950-2050. New York: Population Division, Department of Economic and Social Affairs, United Nations, 2001. <http://www.un.org/esa/population/publications/worldageing19502050/> (accessed 6 June 2010).
- Démographie Marocaine: tendances passées et perspectives d'avenir. http://www.rdh50.ma/fr/pdf/rapport_thematique/Demographie/demographieA4corrigé.pdf (accessed 6 June 2010).
- World Health Organization. Country Cooperation Strategy for WHO and Morocco 2004-2007. http://www.who.int/countries/en/cooperation_strategy_mar_en.pdf (accessed 24 September 2010).
- Vosylus S, Sipylaitė J, Ivaskevicius J. Determinants of outcome in elderly patients admitted to the intensive care unit. *Age Ageing* 2005;34:157-162. [http://dx.doi.org/10.1093/ageing/afi037]
- De Rooij SE, Govers A, Korevaar JC, et al. Short-term and long-term mortality in very elderly patients admitted to an intensive care unit. *Intensive Care Med* 2006; 32:1039-44. [http://dx.doi.org/10.1007/s00134-006-0171-0]
- Sacanella E, Pe'rez-Castejo'n JM, Nicola's JM, et al. Mortality in healthy elderly patients after ICU admission. *Intensive Care Med* 2009;35:550-555. [http://dx.doi.org/10.1007/s00134-008-1345-8]
- Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818-829.
- 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;270:2957-2963. [http://dx.doi.org/10.1001/jama.1993.03510240069035]
- Vincent JL, de Mendonca A, Cantraine F. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. *Crit Care Med* 1998;26:1793-1800.
- Le Gall JR, Klar J, Lemeshow S, et al. The Logistic Organ Dysfunction system. A new way to assess organ dysfunction in the intensive care unit. ICU Scoring Group. *JAMA* 1996;276:802-810. [http://dx.doi.org/10.1001/jama.1996.03540100046027]
- Torres OH. Short- and long-term outcomes of older patients in intermediate care units. *Intensive Care Med* 2006;32:1052-1059. [http://dx.doi.org/10.1007/s00134-006-0170-1]
- Walther SM, Jonasson U. Outcome of the elderly critically ill after intensive care in an era of cost containment. *Acta Anaesthesiol Scand* 2004; 48:417-422. [http://dx.doi.org/10.1111/j.0001-5172.2004.00355.x]
- Bo M, Massaia M, Raspo S, et al. Predictive factors of in-hospital mortality in older patients admitted to a medical intensive care unit. *J Am Geriatr Soc* 2003;51:529-533. [http://dx.doi.org/10.1046/j.1532-5415.2003.51163.x]

15. Djaiani G, Ridley S. Outcome of intensive care in the elderly. *Anaesthesia* 1997;52:1130-1136.
16. Abidi K, Khoudri I, Belayachi J, et al. Eosinopenia is a reliable marker of sepsis on admission to medical intensive care units. *Critical Care* 2008;12:59. [<http://dx.doi.org/10.1186/cc6883>]
17. Torres A, El-Ebiary M, Riquelme R, et al. Community-acquired pneumonia in the elderly. *Semin Respir Infect* 1999;14:173-183.
18. Martin GS, Mannino DM, Moss M. The effect of age on the development and outcome of adult sepsis. *Crit Care Med* 2006;34:15-21. [<http://dx.doi.org/10.1097/01.CCM.0000194535.82812.BA>]
19. Gavazzi G, Krause KH. Ageing and infection. *Lancet Infect Dis* 2002;2:659-666. [[http://dx.doi.org/10.1016/s1473-3099\(02\)00437-1](http://dx.doi.org/10.1016/s1473-3099(02)00437-1)]
20. Yang Y, Yang KS, Hsann YM, Lim V, Ong BC. The effect of comorbidity and age on hospital mortality and length of stay in patients with sepsis. *J Crit Care* 2010;25:398-405. [<http://dx.doi.org/10.1016/j.jcrc.2009.09.001>]
21. Nasa P, Juneja D, Singh O, et al. Severe sepsis and its impact on outcome in elderly and very elderly patients admitted in intensive care unit. *J Intensive Care Med* 2011; 27:179-183. [<http://dx.doi.org/10.1177/0885066610397116>]
22. Curns AT, Holman RC, Sejvar JJ, et al. Infectious disease hospitalizations among older adults in the United States from 1990 through 2002. *Arch Intern Med* 2005;165:2514-2520. [<http://dx.doi.org/10.1001/archinte.165.21.2514>]