Original article

Characteristics, incidence and temporal trends of sepsis in elderly patients undergoing surgery

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Background: **Despite increasing rates of surgery in the elderly, there is limited population-based information on sepsis in this age group. This study aimed to characterize the epidemiology and national trends of sepsis among elderly patients undergoing surgery in Spain.**

Methods: **This population-based longitudinal study of patients aged 65 years or older, undergoing surgery between 2006 and 2011, used data from the national hospital discharge database. Patients were identified by ICD coding. Primary endpoints were incidence and case-fatality rates of sepsis. Predefined age groups were examined. In-hospital mortality-related factors were assessed by means of exploratory logistic regression. Trends were assessed for annual percentage change in rates using Joinpoint regression analysis.**

Results: **A total of 44 342 episodes of sepsis were identified, representing 1·5 per cent of all 2 871 199 surgical hospital admissions of patients aged 65 years or older. The rates varied with age and sex. The in-hospital case-fatality rate was 43·9 per cent (19 482 patients), and associated with age, co-morbidity and organ dysfunction. Standardized rates of sepsis increased over time, with an annual change of 4·7 (95 per cent c.i. 1·4 to 8·5) per cent, whereas the case-fatality rate declined, with an overall annual change of −3·6 (−4·3 to −2·8) per cent. The decrease in mortality was more limited in patients with organ dysfunction and in the oldest age group.**

Conclusion: **Rates of sepsis are increasing among elderly patients undergoing surgery, whereas in-hospital case fatality, although common, is showing a decreasing trend.**

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Introduction

Sepsis is an important cause of morbidity, mortality and healthcare costs in patients undergoing surgery[1,2]. Several studies have indicated that the incidence of sepsis has increased in the general population[3–6] and in patients having surgery[7–9]. This is particularly evident in elderly patients, in whom the mortality rate is highest[10]. Surgery has become increasingly common among the elderly, and accounts for a large fraction of all operations performed in Western countries[11–13]. Increasing rates of surgery among elderly people have been recognized as a major component of growing healthcare costs[13].

There is limited population-based information on the incidence and mortality of sepsis among elderly patients undergoing surgery. Such knowledge is essential to assess the burden of the disease and for the proper distribution of limited health resources[14].

The use of nationwide databases makes it possible to identify changes over time in incidence, mortality and other epidemiological characteristics of sepsis. Such databases have been used widely to define the epidemiology of, and temporal trends in sepsis in general[3–6] and, albeit to a lesser extent, in surgical sepsis[7–9].

The aim of this study was to characterize the epidemiology of, and trends in sepsis among elderly patients undergoing surgery in Spain, by analysing the official administrative database of the National Health System.

Methods

An analysis of the official clinical–administrative Minimum Basic Hospital Discharge Data Set (MBDS) (Conjunto Mínimo Básico de Datos al Alta Hospitalaria) kept by the Ministry of Health, Social Services and Equality was conducted. The national MBDS records discharge data on

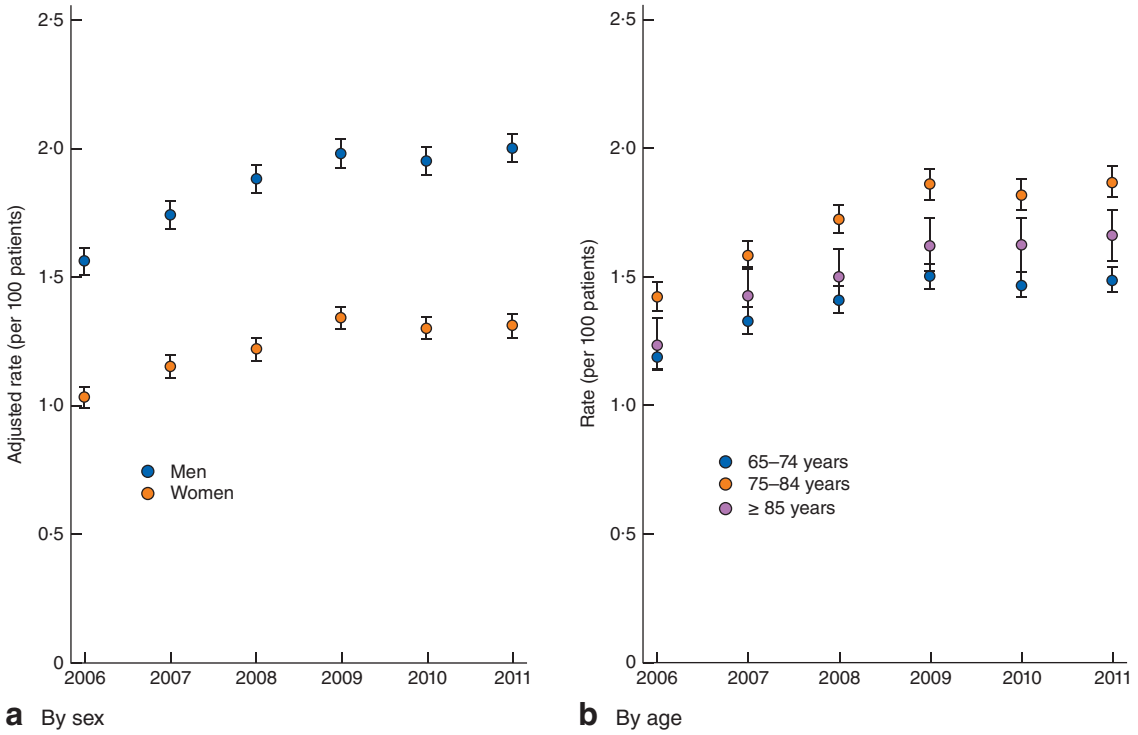

Fig. 1 Annual age-adjusted rates of sepsis for **a** men and women, and **b** predefined age groups across the study interval. Values are mean with 95 per cent c.i.

all episodes of hospital admission, coded according to the ICD, ninth revision, Clinical Modification (ICD-9-CM). These data are collected by clinical documentation units at all hospitals within the National Health System, then subjected to a validation process and consolidated in a single database. The information is considered to be representative of the national population, as the database includes information on over 97 per cent of all annual hospital admissions in Spain, a country with a universal public health system[15].

In the MBDS, each hospital admission is processed as a specific record and includes demographic information, ICD-9-CM codes (including the underlying diagnosis at discharge), 14 additional diagnoses and 20 related procedures, dates of admission and discharge, and type of admission. Data relating to admissions of adults in the study interval were also included from the Ministry of Health, Social Services and Equality[15].

Patient selection and definitions

The data were included from the MBDS for the interval from 1 January 2006 to 31 December 2011, and were grouped by calendar year. Based on previous studies, cases of sepsis were identified by secondary diagnoses[7] of ICD-9-CM codes for sepsis. To identify sepsis, formerly used codes[4–6,16] that define infection were used: 038 (038.0, streptococcal septicaemia; 038.1, staphylococcal septicaemia; 038.2, pneumococcal septicaemia; 038.3, septicaemia due to anaerobes; 038.4, septicaemia due to other Gram-negative organisms; 038.8, other specified septicaemias; 038.9, unspecified septicaemia); 003.1 (*Salmonella* septicaemia); 020.2 (septicaemic plague); 036.2 (meningococcal septicaemia); 036.3 (Waterhouse–Friderichsen syndrome); 054.5 (herpetic septicaemia); 098.89 (gonococcaemia); 112.5 (systemic candidiasis); 112.81 (candida endocarditis); 117.9 (other and unspecified mycoses); and 790.7 (bacteraemia). The ICD-9-CM code for sepsis, 995.91 (sepsis, systemic inflammatory response syndrome due to infectious process without organ dysfunction), and the code 995.92 (severe sepsis, sepsis with organ dysfunction), which were introduced in Spain in January 2004, were also included[15].

Of the identified records, episodes of hospital admission of patients aged 65 years or older with ICD-9-CM surgical procedure codes and surgical diagnosis-related groups (DRGs) were selected.

Primary outcomes included incidence and in-hospital case-fatality rate of sepsis. Demographics, co-morbidities, microbiological data and the presence of organ dysfunction were analysed, and these variables were examined in specific age groups (65–74, 75–84 and 85 years or older).

Co-morbidity was defined by using the Charlson Co-morbidity Index, as adapted and validated by Deyo and colleagues for ICD-9-CM[17]. For identification of specific microorganisms, code 041 was included as indicated by the ICD-9-CM coding manual, for the purpose of identifying bacterial agents in the case of diseases classified under the 'other' heading[15]. The specific codes used for organ dysfunction are shown in *Table S1* (supporting information).

The data used were sourced from anonymized records and were thus exempt from the need for informed consent[18].

Data analysis

Data were compared across predefined age groups, including demographic data, co-morbidities, organ dysfunction and mortality. The Charlson Co-morbidity Index was calculated as a continuous variable, and also as a categorical variable in four groups of increasing severity (0, 1–2, 3–4, more than 4)[19]. Case-fatality rates were calculated as the number of deaths divided by the number of patients with sepsis, expressed as a percentage.

Statistical analysis

Quantitative variables are presented as median (i.q.r.) as the data did not have a normal distribution. Association of qualitative variables was analysed by Pearson's χ^2 or Fisher's exact test. In-hospital mortality-related factors were identified using explanatory logistic regression. Variables with statistically significant results on bivariable analysis were included in the multivariable analysis. Results are presented as odds ratio (OR) with 95 per cent c.i. Variables with biological relevance, such as age and sex, and those related to hospital outcomes ($P < 0{\cdot}050$) were included in the model.

Incidence rates were estimated using the total number of National Health System hospital admissions with a surgical DRG code and involving patients aged 65 years or older, and were expressed per 100 patients. Age-adjusted rates were calculated by direct methods based on the 2008 surgical in-hospital population. Age-adjusted case-fatality rates were calculated by direct standardization based on 2008 data. Trends in surgical incidence and case-fatality rates for sepsis were quantified as the annual percentage

Table 1 General characteristics of the study population

	No. of patients ($n = 44\,342$)
Age (years)	
65–74	19 149 (43·2)
75–84	20 326 (45·8)
≥ 85	4867 (11·0)
Sex ratio (M : F)*	26 695 : 17 646
Principal diagnoses at admission	
Digestive diseases	13 341 (30·1)
Malignant neoplasms	9518 (21·5)
Circulatory diseases	7041 (15·9)
Trauma	2442 (5·5)
Charlson Co-morbidity Index	
0	10 699 (24·1)
1–2	20 576 (46·4)
3–4	8163 (18·4)
> 4	4904 (11·1)
Specific co-morbidities†	
Cancer	12 165 (27·4)
Diabetes	8888 (20·0)
Chronic heart failure	6578 (14·8)
COPD	5982 (13·5)
Chronic renal disease	4977 (11·2)
Liver disease	3386 (7·6)
Acute myocardial infarction	2681 (6·0)
Pathogens identified	16 755 (37·8)
Microbiological data†	
Gram-positive bacteria	11 859 (26·7)
Gram-negative bacteria	15 245 (34·4)
Fungus	1447 (3·3)
Unspecified septicaemia	15 374 (34·7)
Site of infection†	
Procedure-related	12 140 (27·4)
Bacteraemia	11 135 (25·1)
Abdominal	9470 (21·4)
Respiratory	6728 (15·2)
Central nervous system	375 (0·8)
Genitourinary	6190 (14·0)
Cardiac	518 (1·2)
Soft tissue	2187 (4·9)
Organ system dysfunction (no. of organs)	
0	11 649 (26·3)
1	11 475 (25·9)
≥ 2	20 225 (45·6)
Not specified‡	993 (2·2)
Type of organ system dysfunction†	
Respiratory	20 244 (45·7)
Cardiovascular	19 147 (43·2)
Renal	15 759 (35·5)
Hepatic	1436 (3·2)
Haematological	4066 (9·2)
Metabolic	2899 (6·5)
Neurological	3569 (8·0)
In-hospital death	19 482 (43·9)

Values in parentheses are percentages. *Data missing for one patient. COPD, chronic obstructive pulmonary disease. †Subgroups not mutually exclusive. ‡Organ dysfunction without number of organs specified.

Table 2 General characteristics of the population according to age

	65–74 years ($n = 19\,149$)	75–84 years ($n = 20\,326$)	≥ 85 years ($n = 4867$)	P‡
Sex*				< 0·001
M	12 588 (65·7)	11 962 (58·9)	2145 (44·1)	
F	6560 (34·3)	8364 (41·1)	2722 (55·9)	
Type of hospital admission*				< 0·001
Non-elective	13 598 (71·1)	15 888 (78·2)	4376 (90·0)	
Elective	5527 (28·9)	4417 (21·8)	488 (10·0)	
Major organ resection	5699 (29·8)	5929 (29·2)	1166 (24·0)	< 0·001
Charlson Co-morbidity Index				< 0·001
0	4294 (22·4)	5030 (24·7)	1375 (28·3)	
1–2	8813 (46·0)	9429 (46·4)	2334 (48·0)	
3–4	3575 (18·7)	3745 (18·4)	843 (17·3)	
> 04	2467 (12·9)	2122 (10·4)	315 (6·5)	
Specific co-morbidities†				
Cancer	5911 (30·9)	5342 (26·3)	912 (18·7)	< 0·001
Diabetes	3832 (20·0)	4126 (20·3)	930 (19·1)	0·174
Chronic heart failure	2461 (12·9)	3188 (15·7)	929 (19·1)	< 0·001
COPD	2414 (12·6)	2942 (14·5)	626 (12·9)	< 0·001
Chronic renal disease	1981 (10·3)	2342 (11·5)	654 (13·4)	< 0·001
Liver disease	1828 (9·5)	1341 (6·6)	217 (4·5)	< 0·001
Acute myocardial infarction	1175 (6·1)	1303 (6·4)	203 (4·2)	< 0·001
Pathogens identified	7762 (40·5)	7472 (36·8)	1521 (31·3)	< 0·001
Microbiological data†				
Gram-positive bacteria	5682 (29·7)	5212 (25·6)	965 (19·8)	< 0·001
Gram-negative bacteria	7029 (36·7)	6835 (33·6)	1381 (28·4)	< 0·001
Fungus	744 (3·9)	616 (3·0)	87 (1·8)	< 0·001
Unspecified septicaemia	6008 (31·4)	7323 (36·0)	2043 (42·0)	< 0·001
Polymicrobial infection	1454 (7·6)	1239 (6·1)	210 (4·3)	< 0·001
Site of infection†				
Respiratory	3327 (17·4)	2948 (14·5)	453 (9·3)	< 0·001
Bacteraemia	5210 (27·2)	4844 (23·8)	1081 (22·2)	< 0·001
Abdominal	4037 (21·1)	4402 (21·7)	1031 (21·2)	0·361
Genitourinary	2544 (13·3)	2876 (14·1)	770 (15·8)	< 0·001
Procedure-related	5984 (31·2)	5310 (26·1)	846 (17·4)	< 0·001
Organ system dysfunction				< 0·001
No	4991 (26·1)	5103 (25·1)	1555 (31·9)	
Yes	14 158 (73·9)	15 223 (74·9)	3312 (68·1)	
Type of organ dysfunction†				
Respiratory	9363 (48·9)	9345 (46·0)	1536 (31·6)	< 0·001
Cardiovascular	8211 (42·9)	9127 (44·9)	1809 (37·2)	< 0·001
Renal	6821 (35·6)	7404 (36·4)	1534 (31·5)	< 0·001
Hepatic	737 (3·8)	603 (3·0)	96 (2·0)	< 0·001
Haematological	1691 (8·8)	1965 (9·7)	410 (8·4)	0·003
Metabolic	1191 (6·2)	1392 (6·8)	316 (6·5)	0·040
Neurological	1684 (8·8)	1609 (7·9)	276 (5·7)	< 0·001
Invasive therapeutic measures				
Mechanical ventilation	7911 (41·3)	7559 (37·2)	944 (19·4)	< 0·001
Haemodialysis	2525 (13·2)	1969 (9·7)	123 (2·5)	< 0·001
In-hospital death	7638 (39·9)	9322 (45·9)	2522 (51·8)	< 0·001

Values in parentheses are percentages. *Data missing for some patients. COPD, chronic obstructive pulmonary disease. †Subgroups not mutually exclusive. ‡χ^2 test.

change with 95 per cent c.i. Linear-log regression models, assuming a standard Poisson distribution, were used[16,20]. This procedure enables testing of whether an apparent change in trend is statistically significant using a Monte Carlo permutation method[20].

Statistical analyses were performed using Stata® version 13 (StataCorp LP, College Station, Texas, USA) and the Joinpoint regression program version 4.2.0 (National Cancer Institute, Bethesda, Maryland, USA). $P < 0·050$ was considered statistically significant.

Table 3 Bivariable and multivariable risk analysis of risk factors for in-hospital death

	Odds ratio	
	Bivariable	Multivariable
Age (years)		
65–74	1·00 (reference)	1·00 (reference)
75–84	1·28 (1·23, 1·33)	1·27 (1·22, 1·33)
≥ 85	1·62 (1·52, 1·72)	1·87 (1·74, 2·01)
Sex		
M	1·00 (reference)	1·00 (reference)
F	1·07 (1·03, 1·11)	1·12 (1·07, 1·17)
Hospital admission		
Non-elective	1·00 (reference)	1·00 (reference)
Elective	0·81 (0·77, 0·85)	0·89 (0·85, 0·94)
Major organ resection		
No	1·00 (reference)	1·00 (reference)
Yes	1·55 (1·49, 1·62)	1·24 (1·17, 1·31)
Charlson Co-morbidity Index		
0	1·00 (reference)	1·00 (reference)
1–2	1·24 (1·18, 1·30)	1·38 (1·31, 1·47)
3–4	1·34 (1·27, 1·42)	1·57 (1·45, 1·70)
> 4	1·38 (1·29, 1·47)	1·80 (1·63, 1·99)
Specific co-morbidities*		
Cancer	1·07 (1·03, 1·12)	0·99 (0·93, 1·06)
Diabetes	0·84 (0·80, 0·88)	0·81 (0·76, 0·86)
Chronic heart failure	1·47 (1·40, 1·55)	1·14 (1·07, 1·21)
Pathogens identified		
No	1·00 (reference)	1·00 (reference)
Yes	0·37 (0·36, 0·39)	0·84 (0·80, 0·88)
Site of infection†		
Respiratory	1·71 (1·62, 1·80)	1·48 (1·40, 1·57)
Bacteraemia	0·18 (0·17, 0·19)	0·34 (0·32, 0·37)
Abdominal	1·72 (1·64, 1·80)	1·08 (1·02, 1·40)
Genitourinary	0·44 (0·41, 0·46)	0·52 (0·49, 0·56)
Procedure-related	0·72 (0·69, 0·75)	0·71 (0·68, 0·75)
Organ system dysfunction		
No	1·00 (reference)	1·00 (reference)
Yes	7·30 (6·90, 7·72)	4·84 (4·55, 5·14)

Values in parentheses are 95 per cent c.i. *For each condition, the reference group is patients without that condition. †For each site, the reference group is patients without infection at that site.

Table 4 Multivariable regression model of risk factors for in-hospital death stratified by age

	Odds ratio		
	65–74 years	75–84 years	≥ 85 years
Sex			
M	1·00 (reference)	1·00 (reference)	1·00 (reference)
F	1·12 (1·05, 1·20)	1·11 (1·04, 1·19)	1·11 (0·98, 1·27)
Hospital admission			
Non-elective	1·00 (reference)	1·00 (reference)	1·00 (reference)
Elective	0·88 (0·82, 0·95)	0·93 (0·85, 1·01)	0·81 (0·65, 1·01)
Major organ resection			
No	1·00 (reference)	1·00 (reference)	1·00 (reference)
Yes	1·13 (1·04, 1·23)	1·25 (1·15, 1·35)	1·89 (1·58, 2·26)
Charlson Co-morbidity Index			
0	1·00 (reference)	1·00 (reference)	1·00 (reference)
1–2	1·50 (1·37, 1·65)	1·36 (1·25, 1·48)	1·11 (0·94, 1·32)
3–4	1·67 (1·48, 1·89)	1·54 (1·37, 1·74)	1·22 (0·96, 1·56)
> 4	2·12 (1·82, 2·45)	1·65 (1·42, 1·92)	1·23 (0·87, 1·76)
Specific co-morbidities*			
Cancer	0·97 (0·88, 1·07)	1·04 (0·95, 1·16)	0·95 (0·76, 1·19)
Diabetes	0·78 (0·71, 0·85)	0·83 (0·76, 0·90)	0·90 (0·75, 1·08)
Chronic heart failure	1·22 (1·10, 1·35)	1·06 (0·97, 1·16)	1·29 (1·08, 1·54)
Pathogens identified			
No	1·00 (reference)	1·00 (reference)	1·00 (reference)
Yes	0·83 (0·77, 0·90)	0·87 (0·81, 0·94)	0·68 (0·57, 0·82)
Site of infection†			
Respiratory	1·47 (1·37, 1·60)	1·50 (1·37, 1·63)	1·22 (0·98, 1·52)
Bacteraemia	0·36 (0·33, 0·40)	0·37 (0·31, 0·37)	0·32 (0·26, 0·40)
Abdominal	1·02 (0·94, 1·11)	1·12 (1·04, 1·21)	1·16 (0·98, 1·38)
Genitourinary	0·52 (0·47, 0·58)	0·52 (0·47, 0·57)	0·58 (0·48, 0·70)
Procedure-related	0·69 (0·64, 0·74)	0·74 (0·68, 0·79)	0·69 (0·66, 0·73)
Organ dysfunction			
No	1·00 (reference)	1·00 (reference)	1·00 (reference)
Yes	5·98 (5·39, 6·64)	4·75 (4·34, 5·20)	3·02 (2·60, 3·51)

Values in parentheses are 95 per cent c.i. *For each condition, the reference group is patients without that condition. †For each site, the reference group is patients without infection at that site.

Results

Incidence of sepsis

Of 258 897 episodes of sepsis in patients aged 65 years or older, 113 143 presented with ICD-9-CM surgical procedure codes; of these, 44 342 had a surgical DRG without sepsis code as principal diagnosis. These episodes accounted for 1·5 per cent of all 2 871 199 surgical hospital admission among patients aged at least 65 years across the 6-year interval, 1·9 per cent in men (26 695 of 1 436 472) and 1·2 per cent in women (17 646 of 1 434 727). For the defined age groups, rates were 1·4 per cent (19 149 of 1 370 734) at age 65–74 years, 1·7 per cent (20 326 of 1 181 339) at age 75–84 years and 1·5 per cent (4867 of 319 126) in patients aged 85 years or more.

There was a clear increase in sepsis from 2006 to 2011, from 1·3 per cent (5854 of 454 855) to 1·7 per cent (8281 of 497 183). The crude mean annual increase was 4·9 per cent. The standardized rate increased over the 6 years, with an annual change of 4·7 (95 per cent c.i. 1·4 to 8·5) per cent.

The incidence increased in women and in men, with a crude mean annual increase of 4·8 per cent for each. *Fig. 1a* shows the trends in standardized rates for men and women. In men, the standardized rate increased from 1·6 per 100 in 2006 to 2·0 per 100 in 2011, with an annual percentage change of 4·6 (95 per cent c.i. 1·5 to 7·8) per cent. For women, the standardized rate increased from 1·0 per 100 in 2006 to 1·3 per 100 in 2011, with an annual change of 4·6 (95 per cent c.i. 1·0 to 8·3) per cent.

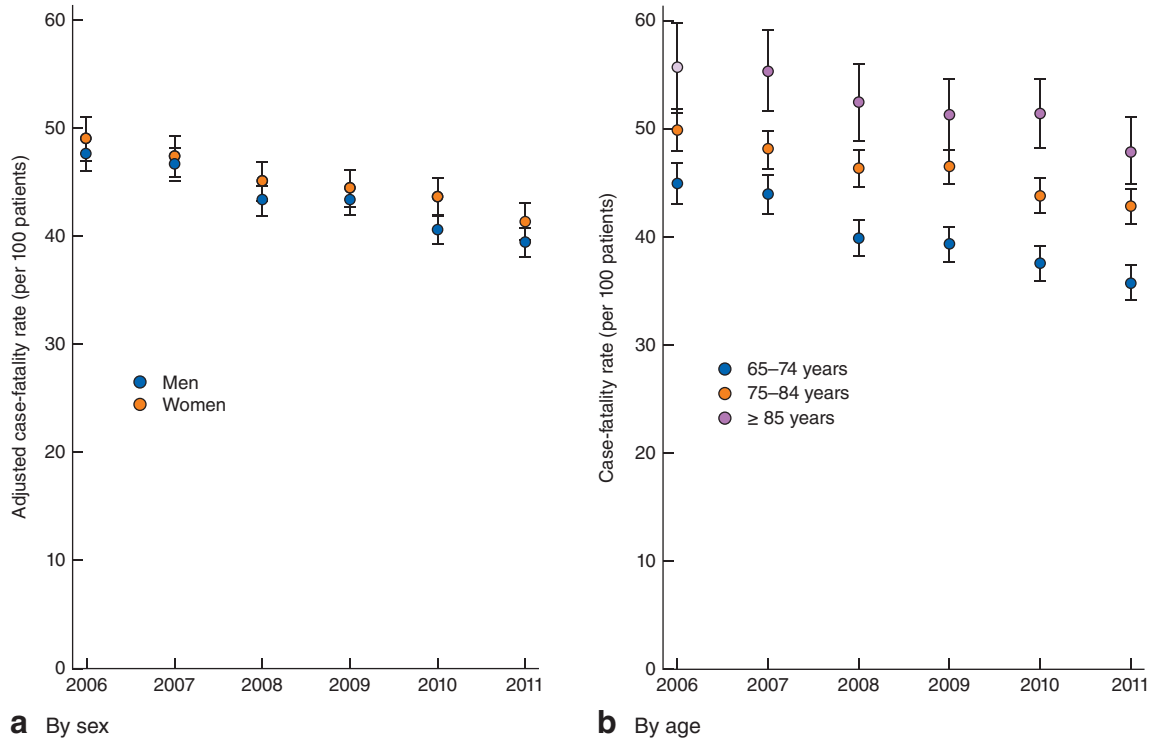

Fig. 2 Age-adjusted standardized in-hospital case-fatality rates for sepsis in **a** men and women, and **b** predefined age groups across the study interval. Values are mean annual rates with 95 per cent c.i.

The changes in incidence differed between age groups, with an estimated average annual increase of 4·0 per cent at age 65–74 years, 5·2 per cent at age 75–84 years, and 5·8 per cent for patients aged 85 years or older (*Fig. 1b*).

Demographic characteristics

Table 1 shows the general characteristics of the study population. The median age was 76 (71–81) years. Almost half of patients were aged 75–84 years, with a predominance of men. Some 10 699 patients (24·1 per cent) had a Charlson score of 0. The most frequent co-morbidities in the remaining patients were neoplasms, diabetes, cardiac insufficiency, chronic obstructive pulmonary disease and chronic renal disease. Underlying reasons for hospital admission were digestive diseases, cancer and circulatory diseases, and 12 794 patients (28·9 per cent) underwent major surgical resections.

At least one microorganism was coded in 16 755 sepsis episodes (37·8 per cent), the most frequent being Gram-negative bacteria, followed by Gram-positive bacteria. Infection was polymicrobial in 2903 episodes (6·5 per cent). The most frequent potential sources of sepsis were those associated with procedures, bacteraemia (in general) and those of abdominal origin.

Some 11 649 patients (26·3 per cent) did not present with acute organ dysfunction, whereas 11 475 (25·9 per cent) had single-organ dysfunction and 20 225 (45·6 per cent) presented with dysfunction of two or more organs. The percentage of patients with organ dysfunction rose across the study period, with an annual increase of 1·2 per cent. *Table 2* shows the demographic and clinical features in each of the predefined age groups.

Mortality

The overall mortality rate was 43·9 per cent (19 482 patients); the rate increased progressively with age, being highest in the oldest group: 39·9 per cent (7638 of 19 149) at age 65–74 years, 45·9 per cent (9322 of 20 326) at age 75–84 years and 51·8 per cent (2522 of 4867) at age 85 years or older. Mortality was significantly higher in women than in men (OR 1·07, 95 per cent c.i. 1·03 to 1·11). There were notable differences according to the presence or absence of organ dysfunction. The mortality rate was 14·1 per cent (1645 of 11 649) in the group that did not develop organ dysfunction, but rose as high as 54·6 per cent

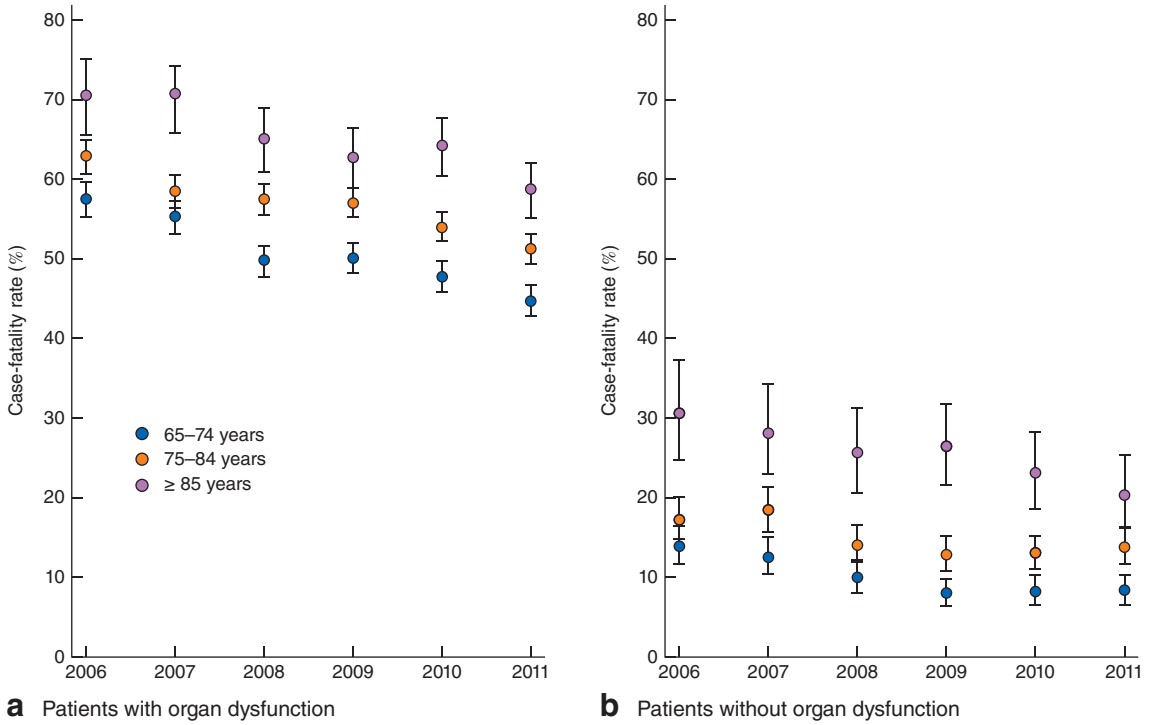

Fig. 3 Trends in in-hospital case-fatality rates for sepsis in **a** patients with organ dysfunction and **b** patients without organ dysfunction according to predefined age groups. Values are mean annual rates with 95 per cent c.i.

(17 837 of 32 693) in those who presented with organ dysfunction.

Multivariable regression analysis revealed that risk of death was significantly associated with increasing age, women, higher Charlson score, lack of identification of causative microorganism, respiratory or abdominal focus of infection, and development of organ dysfunction (*Table 3*). To account for interactions between age and several independent variables, a stratified logistic regression was performed for each age group, which showed that the influence of risk factors changed according to age (*Table 4*). Mortality was significantly higher in women than in men until the age of 84 years, but lost statistical significance in patients aged 85 years or older. The increase in the Charlson score also lost significance in the oldest age group. The impact of chronic heart failure on the risk of death was maintained in all age groups. Although major surgical resection was a mortality risk factor in all groups, the magnitude was clearly most pronounced in patients aged 85 years or older. The presence of organ dysfunction increased the risk of death (overall OR 4·84, 95 per cent c.i. 4·55 to 5·14), but the magnitude of its impact varied with age (*Table 4*).

The temporal analysis of in-hospital case fatality showed a decreasing trend. Age- and sex-standardized case-fatality rates showed a decrease from 48·2 per cent in 2006 to 40·2 per cent in 2011, with an overall annual change of −3·6 (95 per cent c.i. −4·3 to −2·8) per cent. The rate declined progressively in men and women alike (*Fig. 2a*). In men, the standardized case-fatality rate decreased from 47·7 per 100 in 2006 to 39·4 per 100 in 2011, with an annual change of −3·8 (−4·9 to −2·8) per cent. In women, the rate decreased from 49·1 per cent in 2006 to 41·3 per cent in 2011, with an annual change of −3·1 (−3·9 to −2·4) per cent.

Similarly, the case-fatality rate decreased in each age group, with an estimated specific mean annual decrease of 3·4 per cent at age 65–74 years, 2·4 per cent at age 75–84 years, and 2·3 per cent at age 85 years or older (*Fig. 2b*).

The decrease in mortality was far greater in the group without organ dysfunction than among patients with dysfunction (mean annual reduction 4·7 and 3·1 per cent respectively). *Fig. 3* shows the changes in mortality over the study by age group in patients with and without organ dysfunction. In patients without organ dysfunction, the estimated mean annual decrease was 6·7 per cent at age 65–74 years, 3·4 per cent at age 75–84 years and 5·6 per cent at age 85 years or older. Respective values in patients with organ dysfunction were 3·7, 3·1 and 2·8 per cent.

Discussion

This study used the nationwide database of hospital discharges in Spain to examine the epidemiological characteristics, and trends in the incidence and outcomes of sepsis in elderly patients undergoing surgery from 2006 to 2011. There was a remarkable increase in the incidence of sepsis, especially in patients aged 85 years or older. Conversely, a gradual decrease in case-fatality rates was seen over time, albeit more limited in patients with organ dysfunction and in the oldest age group.

The sepsis rate in the present study is lower than that reported in a population-based study[7] of all surgical admissions among patients aged 18 years or older in New Jersey from 1990 to 2006. In that investigation the sepsis rate was 3·7 per cent in adults aged 65 years or older. These differences may be explained by different populations and healthcare systems in the USA and Spain, as well as differences in study design. The clear increase in the incidence of sepsis observed here is in agreement with several population-based studies in adults after elective surgery[8,9] and in the general population[3–6,16]. However, specific reasons for this trend have not been clearly identified[21,22].

Even though the interpretation may be confounded in part by factors such as better diagnosis of sepsis, the introduction of specific ICD-CM-9 codes or other methodological issues[1,14,21], there are several possible reasons for a real increase in the incidence of sepsis in the elderly. The greater use of invasive procedures, immunosuppressive drugs and aggressive surgery in this population[1,4,22] may all have contributed to the increased incidence.

This study has shown a decreasing trend in case-fatality rates of sepsis over time. A number of population-based studies have shown a similar trend both in general sepsis[4,6,16,23] and in sepsis after surgery[7–9]. The results of a recent meta-analysis[24] showed a clear downward trend in sepsis-related mortality in the past two decades. Nevertheless, it has not been possible to identify the specific factors responsible for the decrease in mortality after sepsis[21,24].

The decline in case-fatality rates is especially relevant given the advanced age of the population analysed, the high percentage of patients admitted as an emergency and having major surgery, and the increased rate of organ dysfunction across the study interval. Of note, the decrease in mortality was less pronounced in the group of patients with organ dysfunction, and in patients aged 85 years or older.

The influence of age on the mortality risk was evident, with patients aged at least 85 years being at high risk. The presence of organ dysfunction increased the risk of death dramatically; organ failure in patients with sepsis had a cumulative effect on mortality. It is likely that the high degree of organ dysfunction could account for the high mortality rate in the population analysed. In agreement with previous studies[25,26], the decrease in case-fatality rates was smaller in patients with organ dysfunction than in those without. These data highlight the need for early diagnosis of sepsis to prevent organ dysfunction.

It must be acknowledged that early identification of sepsis in elderly patients poses a significant clinical challenge[1]. However, the implementation of sepsis educational programmes for health professionals[25] has improved patient outcomes and reduced mortality from sepsis[26,27].

The strength of the present study is the use of data from the official database of the Spanish National Health System. Data entry into this database is mandatory by law. The database covers over 97 per cent of the hospitals in Spain, and is subjected to regular audits to verify the adequacy and accuracy of the coding used[28,29]. This study followed the guidelines for publication of observational studies laid down in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative[30].

This investigation is subject to the limitations inherent to retrospective studies using administrative databases. There is a lack of details that are obtainable only from chart review, and the data do not allow causal inferences to be made. Data were not collected primarily for the purposes of research, and the accuracy of the codes could not be assessed for study purposes. Despite national rules and regulations governing the use of the ICD-9-CM coding system in Spain, such use may not have been uniform in all institutions, and there may have been some misclassification. However, an interval was selected in which the codes had not undergone changes in Spain. The Joinpoint analysis showed no inflection points, corroborating the absence of important changes or factors influencing the observed trends. The incidence and mortality of sepsis in the present study did not include mortality after hospital discharge[31,32], which makes the estimates conservative. The magnitude of the estimates underscores the importance of sepsis as a major problem in elderly patients undergoing surgery.

Sepsis is a common and frequently fatal condition. Data over time indicate that incidence rates of sepsis are increasing, whereas in-hospital case-fatality is showing a decreasing trend.

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 ICD-9-CM codes used to define organ dysfunction (Word document)