

Trends in the presentation and management of traumatic spinal cord lesions above T6: 20-Year experience in a tertiary-level hospital in Spain

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Abstract

Objective: To analyze the changes in demographic and lesion characteristics of persons with acute traumatic spinal cord injury (ATSCI) above T6 over a period of 20 years, and to evaluate their impact on ICU resources use, length of stay and mortality.

Design: Retrospective observational study.

Setting: Intensive Care Unit (ICU) of the University Hospital Complex of A Coruña, Spain.

Participants: The study included 241 persons between 1998 and 2017 with an ATSCI above T6. For the purposes of the analysis, the overall study period was divided into three subperiods.

Results: Both the mean age of the people with ATSCI (49 vs. 51 vs. 57 years; $P = 0.046$) and the Charlson Comorbidity Index were higher during the last subperiod (mean: 1.9 ± 2.2 ; $P < 0.01$). The most frequent cause of the injury was falls, whose percentage increased over the years. The most common classification in the American Spinal Injury Association Impairment scale was grade A. An increase in the score of the Acute Physiology and Chronic Health Evaluation (APACHE II) score was observed (median: 9 vs. 10 vs. 15; $P < 0.01$). The length of stay in the ICU has decreased significantly over the years (30 ± 19 vs. 22 ± 14 vs. 19 ± 13 days). No significant differences were found between the rates of ICU or in-hospital mortality recorded over the three subperiods.

Conclusions: Despite the progressive increase in the age, comorbidity, and APACHE II, the length of ICU stay decreased significantly, with no associated changes in the mortality rates.

Keywords: Spinal cord injury, Acute spine trauma, Epidemiology, Mortality

Introduction

Epidemiological studies published in recent years describe changes in the epidemiology of acute traumatic spinal cord injury (ATSCI) characterized by a global decrease in its incidence and an increase in the number of fall-related injuries among elderly persons.^{1,2} age at injury onset and a greater frequency of falls has been described by several authors in different geographical areas.^{3,4}

In recent years, we have seen changes in the neuro- protection strategies applied in intensive care units (ICUs), whereby corticosteroid therapy is no longer used in most persons. New hemodynamic targets during the initial phase have been agreed upon (mean arterial pressure [MAP] of 85 mmHg during the first week), and early surgical treatment is recommended for those persons for which it is indicated.^{5,6}

In addition, the knowledge gained from other critical populations has allowed for identification of new indicators in the optimization of neurogenic shock, acute respiratory failure, and the need for tracheostomy associated with this condition. Furthermore, ICUs have progressively incorporated nosocomial infection prevention models that might contribute to the progno- sis of these persons.⁷

People with an ATSCI above T6 constitutes a more homogeneous subgroup of people with ATSCI who have a higher risk of organ dysfunction (neurogenic shock, need for respiratory support, etc.) and often require admission to the ICU. The respiratory and hemodynamic disorders experienced by these persons depend on the level and grade of the lesion. In C1–C2 lesions there is no effective musculature whatsoever, and C3–C4 injuries cause bilateral phrenic nerve paraly- sis in which case breathing is solely maintained by accessory muscles. Therefore, injuries above C5 often require early mechanical ventilation. Injuries below C5, on the other hand, cause complete intercostal and abdominal muscle paralysis. In contrast, lesions below T6 are usually not associated

with neuromuscular respiratory failure nor neurogenic shock. Thus, this people comprises a risk group for organ dysfunction that typically requires ICU admission.^{8–11}

Accordingly, understanding the epidemiological aspects of this entity is essential for planning priorities, identifying prevention guidelines, and allocating adequate health resources for its treatment. The limited literature available on this matter is mainly comprised of retrospective studies involving persons with ATSCI and few specifically analyze the subgroup of ATSCI persons admitted to the ICU.

Other authors have identified changes in the demographic and lesion characteristics of people with traumatic spinal cord injuries.^{2,12–16} Our aim is to confirm these changes in the group of persons with ATSCI above T6 requiring admission to the ICU and to assess the impact of this change on ICU resource use (need for multiorgan support and nosocomial complications), length of stay, and mortality (ICU and in-hospital) over two decades.

Materials and methods

We performed a retrospective, observational study of persons diagnosed with an ATSCI above T6 neurological level who had been admitted to the ICU of the University Hospital Complex of A Coruña, Spain (CHUAC, Complejo Hospitalario Universitario de A Coruña) over the 1998–2017 period. The CHUAC hospital is a referral center in the regional community of Galicia (Spain) for the treatment of persons with spinal cord injuries.

The ICU of the CHUAC admits people with ATSCI who require intensive care and ongoing treatment administered by staff specializing in intensive care and rehabilitation. The treatment plan is agreed upon and, once the persons' condition is stable, they are transferred to the specialized Spinal Cord Injury Unit (SCIU).

All adult (>18 years) with an ATSCI above T6 neurological level documented by specialist doctors of the SCIU were included in this study. Persons who (a) did not meet the above inclusion criteria, (b) were pregnant, (c) had “do not resuscitate” orders, and (d) another cause of shock (e.g. hemorrhagic) were excluded from the study. A total of 241 persons who met the established inclusion criteria were admitted to the ICU throughout the study period. This sample size allowed us to estimate population

characteristics with a 95% confidence interval (CI) margin of error that did not exceed 6.3%.

Variables relating to the persons' demographic characteristics (age and sex), comorbidities assessed with the Charlson Comorbidity Index (CCI), injury characteristics (cause of injury, neurological level, American Spinal Injury Association [ASIA] grade, level of spinal cord injury [SCI], ASIA motor score, polytrauma Injury Severity Score [ISS] on admission, Acute Physiology and Chronic Health Evaluation [APACHE II] score within the first 24 h of admission), the existence of a clinical condition of neurogenic shock (defined as a systolic arterial pressure <90 mmHg and/or a heart rate <50 bpm), the supportive therapy (fluids [fluid balance on the fourth day is defined as the difference between fluid intake and losses after four days], vasoactive drugs [noradrenaline, dopamine, dobutamine, adrenaline and isoprenaline sulfate, which are drugs that are routinely used in cases of shock], and mechanical ventilation), the medical (corticosteroids) and surgical treatment administered, the existence of nosocomial infectious complications (ventilator-associated pneumonia [VAP], urinary tract infection [UTI], or primary and catheter-related bacteremia [CRB]) and pressure ulcers (PUs), the length of stay (both in the ICU and the hospital itself), and the mortality (both ICU and in-hospital) were collected.

A descriptive analysis of all variables collected was performed. Quantitative variables were described as a mean \pm standard deviation, together with their median, and qualitative variables were reported as frequencies and percentages. Either parametric or non-parametric tests were used in the bivariate analysis, as appropriate.

The Kolmogorov–Smirnov test was used to analyze the normality of the data. Student's *t*-test, an Analysis of Variance (ANOVA), and either the Mann–Whitney *U* test or the Kruskal–Wallis test were used to analyze quantitative variables, as appropriate. The comparison of percentages was performed using a chi-square test.

Three subperiods (1998–2005, 2006–2011, and 2012–2017) were considered for the purpose of assessing the changes throughout the overall 20-year study period. Given that the intensive care physicians of our hospital started to perform percutaneous tracheostomies in 2004, we chose 2005 as the first cut-off point and attempted to ensure that the number of persons in each subperiod was as equal as possible. The 2012 cut-off point is related to the implementation of a change of strategy in the initial hemodynamic

management of these persons (MAP of 85 mmHg to ensure the spinal cord perfusion pressure).

Results

A total of 241 persons with ATSCI above T6 were admitted to the ICU of the CHUAC between January 1998 and December 2017. The mean (SD) age of the people, of whom 78% were men, was 53 (± 20) years and the median of their CCI was 0. The most frequent cause of the injury was a fall (41%), followed closely by a traffic collision (35%). ASIA impairment scale A was the predominant classification (52%), the median (IQR) APACHE II score was 12 (± 7), and 71% experienced neurogenic shock. The most frequent nosocomial infection was VAP (35%), followed closely by UTIs (33%). The mean (SD) stay of the persons in the ICU and the hospital itself was 24 (± 16) days and 189 (± 87) days, respectively. Almost a quarter (24%) of the persons comprising our study population passed away, with half of these deaths taking place in the ICU (Tables 1–4). A comparison of the three study subperiods (1998–2005, 2006–2011, and 2012–2017) revealed that the mean (SD) age of the persons increased from 50 (± 19) to 57 (± 19) years over the years, as did their CCI. In contrast, the sex ratio in the study population did not change over time and remained at around 3:1 (Table 1).

The most frequent causes of the ATSCI over the three subperiods were falls (41% vs. 30% vs. 47%) and traffic accidents (35% vs. 43% vs. 31%). ASIA impairment scale A was the most common classification, although the frequency of cases classified as grade D increased gradually over the years (4% in 1998–2005 vs. 27% in 2012–2017). The median (IQR) ASIA motor score increased from 19 points in the 1998–2005 subperiod, to 25 in the 2006–2011 subperiod, and, finally, to 50 in the 2012–2017 subperiod ($P < 0.001$).

Statistically significant differences were found between the median APACHE II scores recorded throughout the three subperiods (9 vs. 10 vs. 15). Similarly, the number of persons experiencing neurogenic shock also increased over time (55% vs. 70% vs. 81%) (Table 1).

A greater amount of vasoactive drugs were used during the last subperiod, the most frequent one being noradrenaline, whose use increased from 42% throughout the first subperiod to 98% during the last one. Aleudrina[®] (isoprenaline sulfate) was also used

more frequently during the last subperiod. In contrast, the amount of dobutamine administered remained the same throughout all three subperiods, and the administration of fluids decreased significantly and was more restricted over time (Table 2).

Support with invasive ventilation (IV) was required in 83% of the persons, with no significant changes being observed in the need for such support over time, whereas the use of non-invasive ventilation (NIV) decreased significantly over the study period (30% vs. 34% vs. 14%). More than half of the persons of our case series required a tracheostomy during all subperiods (58% vs. 54% vs. 58%), with the number of percutaneous tracheostomies increasing slightly over time with respect to the surgical ones (77% vs. 89% vs. 93%), although both procedures were performed at an earlier stage. Despite this, no changes were observed in the time elapsed between the start of the IV and the persons' decannulation (Table 2).

Surgery was indicated for the lesions in 32% of the cases during the first subperiod and in 61% of these over the 2012–2017 subperiod ($P = 0.001$) (Table 2). A decrease in the days elapsed until the conduct of the surgery was observed over time (median: 19 vs. 13 vs. 10 days; $P = 0.001$).

In contrast, the percentage of VAP increased from 27% to 42% over the study period. CRBs and PUs were also significantly more common during the last subperiod (Table 3). The length of the persons' stay in the ICU decreased over the study period from a mean of 30 days to 19 days, with no change being observed in the mean length of their overall hospital stay. No significant differences were observed either between the ICU and in-hospital mortality rates recorded throughout the three subperiods (Table 4).

Discussion

The results of our analysis of the population of persons admitted to the ICU with an ATSCI above T6 over the 20-year study period show epidemiological changes in this population toward a profile of persons of older age, with a greater number of comorbidities, a higher percentage of fall-related injuries, and mostly of male sex. In the late 1990s, ATSCI mostly affected 40-year-old men involved in traffic collision.² The mean age of the people with ATSCI above T6 who were included in our study is higher than that of other European and American populations of persons with ATSCI.^{2,13–16} The study performed by Li *et al.* in China also showed a significant change in the mean age

of these persons between 1999 and 2007 (45.1 ± 14.2 years) and 2008 – 2016 (51.6 ± 15.2 years).¹² These differences may be related to the demographic aging and low violence rates that characterize these healthcare area. The sex ratio of men to women in our case series (3.5:1) was similar to that reported in other studies,^{12,17–20} and the meta-analysis carried out by Kumar *et al.* evaluating the 2000–2016 period, in which an overall sex ratio of 3.37:1 in the global meta-analysis.²¹ The results of our study do not reveal significant changes in the ratio of male to female persons with this entity over the 20-year period, although some studies have suggested that the proportion of females with this condition has risen in recent years.¹³ The CCI increased (1.9) during the last subperiod of our study, possibly related to the aging of the population.²² Between 1996 and 2007, Furlan *et al.*²³ studied a population of persons with spinal cord injury (SCI) and a median age of 57 years, observing that 69% had no previous medical comorbidity (CCI = 0). Similarly, Beck *et al.*²⁴ analyzed the 2007–2016 period and reported a CCI of 0 in 70% of their case series comprised of persons with a median age of 50 years. Teunissen *et al.*,²⁵ in comparison, found a CCI of 1 in their analysis of a subgroup of persons with a median age of 69 years and a SCI secondary to ankylosing spinal fractures. The most frequent cause of ATSCIs above T6 in our setting were falls, with the results of our analyses proving the existence of a progressive increase of this injury mechanism over time. This information is very useful for the development of prevention programs. The rates of fall-related injuries recorded in our study are lower than those found in the study performed by McCaughey *et al.*,² who reported a mean incidence of this injury mechanism of 52% and an increase in the frequency of this type of injury from 42% to 60% over their study period (1994–2013). This increased percentage of fall-related injuries was also observed in other studies,^{1,2,12,15} although traffic accidents were the most common SCI mechanism worldwide in the meta-analysis performed by Kumar *et al.*²¹ when analyzing populations with a global median age of 40 years. Conversely, we observed a reduction in the percentage of traffic accidents as a mechanism responsible for the ATSCIs in our case series. A decrease in the rate of traffic accidents has been observed in recent years in Spain, probably in relation to the prevention campaigns (e.g. the entry into force of the points-based driver's license in 2006, the reform of the criminal code in 2007, and the implementation of the Road Safety Law in 2011).^{1,26} The launch of prevention campaigns and an increased public awareness may have also played a role in this fact. We did

not identify any changes in the level of the injury or ISS over the study period. The percentage of persons with cervical lesions did not increase over the years; however, according to the data obtained in other case series,^{2,14} the percentage of lesions involving higher cervical levels (C1–C4) has increased with respect to those affecting lower levels (C5–C8). In contrast, the classification of the injuries according to the ASIA scale varied over the three study subperiods, and, although grade A injuries were the most frequent ASIA classification over all subperiods, a higher percentage of incomplete injuries and higher ASIA motor scores was recorded in recent years. We also identified some changes in the supportive treatment administered over the past two decades. During the last period, the use of vasoactive drugs was determined not only by the existence of hemodynamic instability, but also by the recommendation to achieve the target MAP that would allow for maintenance of adequate spinal cord perfusion pressure. The fluid balance during the resuscitation phase also decreased despite there being a higher percentage of persons with neurogenic shock, probably in relation to the implementation of a more accurate monitoring in the ICU. In addition, corticosteroid treatment and support with NIV have been replaced by other measures, but without resulting in an increase in the duration of the IV. NIV has failed to replace invasive support in the days immediately following the traumatic event in people whose pathology is characterized by neuromuscular paralysis, and its role in the weaning phase in this group of persons is not yet well defined.²⁷ Although tracheostomies are now performed earlier, this indicator is still improvable in a population of people with a predictable risk of requiring prolonged IV. We have not observed a significant increase in the rate of nosocomial infection, except for CRB, probably in relation to an increased use of hemodynamic monitoring devices despite the implementation of an infection prevention policy. There has also been a non-significant increase in the percentage of cases of VAP, particularly over the last period and greater than that published in other case series.^{28,29} Greater percentages are probably related to people requiring invasive respiratory support.³⁰

Finally, despite the above findings, the length of stay of the persons of our study population in the ICU decreased and their mortality rates did not vary. The mean length of hospital stay in the context of the treatment of an ATSCI above T6 varies greatly across countries, ranging between shorter stays of 20–75 days in the US (mainly due to the type of health system and the need to pay for this care) and Australia^{31–33} to longer

stays of 90–220 days.^{34,35} Although there are few published studies concerning the stay of persons with ATSCI in ICUs, González-Viejo *et al.*¹⁶ described a mean length of stay in a Spanish ICU of 12 days in cases of tetraplegia and of 15 days in cases of paraplegia between 1997 and 2009. However, the mean length of stay calculated over the last subperiod of our study is comparable to that of 17 days reported in a Canadian publication analyzing a series of people with an acute traumatic spinal cord injury hospitalized between 1997 and 2001.¹⁸ In the study performed by Lau *et al.*, the mean stay in the ICU was 13 days throughout the 2007–2017 period.³⁶ The length of stay in American ICUs of persons with ATSCI has also decreased significantly from a median stay of 26 days in 1974 to that of only 16 days over the 2005–2009 period.³⁷ The eleven-day reduction seen in the length of stay in the ICU between the first and the third subperiod of this study, together with the improvements in the initial care (for example, the improvement in the hemodynamic monitoring devices) and management (tracheostomy and implementation of protocols to control nosocomial infections) of persons with ATSCI, is also related to the ability to discharge tracheotomized persons who still depend on IV to the SCIU with a portable ventilator. The overall mean hospital and ICU mortality in our case series was 24% and 12%, respectively, with no significant changes being observed in these rates over time. These figures might seem high when compared with those reported in other publications;^{18,38} however, this can be explained by the fact that in our study we analyzed a subgroup of persons with a spinal cord injury above T6 (associated with a higher risk of dysfunction and death) and an elderly population with an inherently worse prognosis.³¹ Along these lines, Lubelski *et al.*³⁹ published a mortality rate of 21% in a population of people with cervical and upper thoracic injuries treated within the first 36 h of their onset. In our study, we analyzed a wide range of persons who had been admitted to the ICU. Although our hospital is a reference center at a regional level, because there is no regional registry available, our results may have been affected by the non-inclusion of persons who had died before receiving inpatient care or being transferred to our center. As this was a single-center case series, our study population was more homogeneous than that seen in standard care. Furthermore, the retrospective nature of our study may have resulted in an information bias. However, the completeness of the ICU records used to collect our data guarantees the reliability of the measurements collected. Finally, results could vary if different cutoffs were selected to define time periods.

Conclusions

To conclude, the results of our analysis of persons with an ATSCI above T6 requiring admission to an ICU over a 20-year period shows that an epidemiological change is taking place toward a profile of persons of older age, with a greater number of comorbidities, and a greater severity of the injury on admission as measured by the APACHE II scale. In addition, our study revealed changes in the supportive treatment of these persons in the ICU. Despite the above characteristics, the length of stay of persons with this entity in our ICU decreased, with no associated increases in the length of their overall hospital stay nor in their mortality rates.

Disclaimer statements

Contributors None.

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Conflicts of interest Authors have no conflict of interests to declare.

Statement of ethics

The study was approved by the Galician Clinical Research Ethics Committee (CAEIG, Comité Autonómico de Ética de la Investigación de Galicia) with authorization code: 2019/622.

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Table 1 Demographic and lesion characteristics over the three study subperiods.

	Total		1998–2005		2006–2011		2012–2017		P
Age (years)	53.2 (±20.1)	56.0	49.5 (±18.9)	49.0	51.3 (±21.4)	56.0	56.9 (±19.2)	60.0	0.046 []]
Charlson index	0.9 (±1.7)	0.0	0.1 (±0.3)	0.0	0.3 (±0.7)	0.0	1.9 (±2.2)	1.5	<0.001 [‡]
Sex									0.460 [†]
Male	187	77.6%	45	75.0%	62	74.7%	80	81.6%	
Female	54	22.4%	15	25.0%	21	25.3%	18	18.4%	
Injury mechanism									—
Fall	99	41.3%	18	30.0%	35	42.2%	46	47.4%	
Fall from a height	27	11.2%	8	13.3%	7	8.4%	12	12.4%	
Occupational accident	8	3.3%	0	0.0%	2	2.4%	6	6.2%	
Pedestrian collision	14	5.8%	7	11.1%	7	8.4%	5	5.1%	2.1%
Dive	7	2.9%	1	1.7%	5	6.0%	1	1.0%	
Traffic accident	85	35.3%	26	43.3%	29	34.9%	30	30.9%	
Neurological level									0.360 [†]
C1–C4	77	33.0%	22	39.3%	24	29.6%	31	32.3%	
C5–C8	93	39.9%	22	39.3%	29	35.8%	42	43.8%	
Thoracic (T1–T6)	63	27.0%	12	21.4%	28	34.6%	23	24.0%	
AIS grade									<0.001 [†]

A	117	51.8%	25	47.2%	55	68.8%	37	39.8%	
B	29	12.8%	10	18.9%	7	8.8%	12	12.9%	
C	46	20.4%	16	30.2%	11	13.8%	19	20.4%	
D	34	15.0%	2	3.8%	7	8.8%	25	26.9%	
ASIA motor score	35.9 (±26.9)	33.0	26.6 (±22.8)	19.0	31.9 (±24.1)	25.5	44.5 (±28.9)	50.0	<0.001‡
ISS	33.7 (±12.7)	29.0	33.8 (±11.9)	27.0	35.4 (±13.0)	29.0	32.2 (±13.0)	27.5	0.406‡
APACHE II score on admission	12.5 (±6.6)	12.0	11.0 (±7.3)	9.0	10.9 (±5.9)	10.0	14.8 (±6.0)	15.0	<0.001‡
Neurogenic shock	170	70.5%	33	55.0%	58	69.9%	79	80.6%	0.003†

Data are shown as *n* and a % or a mean ± standard deviation and median, as appropriate.

AIS: American Spinal Injury Association [ASIA] Impairment scale. ISS: Injury Severity Score.

APACHE II: Acute Physiology and Chronic Health Evaluation II.

†Chi-squared test.

‡ANOVA test.

allis test.

Table 2 Persons' treatment over the three study subperiods.

	Total		1998–2005		2006–2011		2012–2017		P
Fluid balance on the 4th day (L)	5.2 (±3.9)	4.9	7.0 (±3.1)	7.1	6.2 (±3.9)	6.3	3.1 (±3.4)	3.1	<0.001‡
Amines	173	71.8%	35	58.3%	52	62.7%	86	87%	<0.001†
Dopamine	49	28.3%	30	85.7%	13	25.0%	6	7.0%	<0.001†
Noradrenaline	140	80.9%	15	42.9%	43	82.7%	84	97.7%	<0.001†
Aleudrina® (isoprenaline sulfate)	12	6.9%	1	2.9%	5	9.6%	11	12.8%	–
Dobutamine	27	15.6%	7	20.0%	9	17.3%	11	12.8%	0.564†
Adrenaline	1	0.6%	1	2.9%	0	0.0%	0	0.0%	–
IV	202	83.8%	50	83.3%	70	84.3%	82	83.7%	0.985†
NIV	60	24.9%	18	30.0%	28	33.7%	14	14.3%	0.006†
Duration of the IV (days)	41.5 (±58.9)	23.5	45.6 (±51.7)	26	38.7 (±43.9)	25.5	41.3 (±73.2)	22.0	0.174‡
Duration of the NIV (days)	3.0 (±2.9)	2.0	4.4 (±3.7)	2.5	2.5 (±2.1)	3.0	2.2 (±2.9)	1.0	0.114‡
Tracheostomy	145	60.2%	35	58.3%	53	53.9%	57	58.2%	0.698†
Tracheostomy type									0.078†
Surgical	18	12.4%	8	22.9%	6	11.3%	4	7.0%	
Percutaneous	127	87.6%	27	77.1%	47	88.7%	53	93.0%	
IV start_ tracheostomy (days)	13.7 (±19.7)	10	22.5 (±37.1)	17.5	10.6 (±9.1)	8.0	11.1 (±7.3)	10.0	0.007‡
IV start_ decannulation (days)	88.3 (±79.5)	66.0	88.4 (±60.7)	70.0	80.5 (±49.6)	65.5	95.9 (±110.5)	64.0	0.867‡
Surgery	121	50.2%	19	31.7%	42	50.6%	60	61.2%	0.001†
Corticosteroids	131	54.4%	44	73.3%	70	84.3%	17	17.3%	<0.001†

Data are shown as *n* and a % or a mean \pm standard deviation and median, as appropriate.

Fluid balance on the 4th day (L): La diferencia entre el aporte y las pérdidas de fluidos (en litros) al 4^o día de evolución. IV: invasive ventilation.

NIV: non-invasive ventilation.

IV start_tracheostomy: time elapsed between the start of the intensive ventilation and the conduct of a tracheostomy. NIV start_decannulation: time elapsed between the start of the intensive ventilation and the decannulation.

†Chi-squared test.

‡Kruskall–Wallis test.

Table 3 Percentage of nosocomial complications over the three study subperiods.

	Total		1998–2005		2006–2011		2012–2017		P
	n	%	n	%	n	%	n	%	
VAP	84	34.9%	16	26.7%	27	32.5%	41	41.8%	0.130†
UTI	79	32.8%	20	33.3%	22	26.5%	37	37.8%	0.274†
CRB	22	9.1%	2	3.3%	3	3.6%	17	17.3%	0.001†
Primary bacteremia	11	4.6%	1	1.7%	5	6.0%	5	5.1%	0.443†
Pressure ulcer	21	8.7%	2	3.3%	2	2.4%	17	17.3%	< 0.001†

VAP: ventilator-associated pneumonia.

UTI: urinary tract infection.

RB: catheter-related bacteremia. red test.

†Chi-squared test.

Table 4 Length of stay and mortality rates over the three study subperiods.

	Total		1998–2005		2006–2011		2012–2017		P
In-hospital death	57	23.7%	15	25.0%	13	15.7%	23	23.5%	0.309†
Intra-ICU death	30	12.4%	10	16.7%	8	9.6%	12	12.2%	0.453†
Length of stay in the ICU (days)	23.8 (±15.8)	23	30.1 (±19.6)	26.0	21.8 (±13.9)	23.0	18.6 (±13.3)	18.5	0.001‡
Overall hospital stay (days)	188.8 (±86.9)	193.5	161.0 (±101.9)	167.5	165.9 (±96.5)	185.0	167.7 (±106.6)	178.0	0.870‡

Data are shown as *n* and a % or a mean ± standard deviation and median, as appropriate.

†Chi-squared test.

‡Kruskall–Wallis test.