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Epidemiological characteristics and impact of sepsis on survival after osteoporotic pelvic fracture in Austria

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We performed a retrospective nationwide register-based cohort study which included all in-hospital patients aged ≥ 50 with pelvic fracture (PF) between 2010 and 2018 in Austria. We identified patients who were hospitalized with sepsis within 180 days following a PF event. Aetiology of sepsis was divided by unspecified, gram positive, gram negative and other. Among 59,081 patients hospitalized with PF between 2010 and 2018 we identified 619 (1.05%) patients who were hospitalized with sepsis within 180 days following PF. The cumulative incidence risk of sepsis within 180 days after PF was significantly higher in males (1.4%, 95% CI 1.2%-1.5%) as compared to females (0.92%, 95% CI 0.83%-1.0%), $p < 0.001$. In the cohort of patients with sepsis, the one-year mortality was 50.4%. Mortality risk was greater for patients who developed sepsis, independently of age, sex and comorbidity status (HR 3.12, 95% CI 2.83–3.44, $p < 0.001$) as compared to patients without sepsis. With a very high one-year mortality risk among those who develop sepsis, our study emphasizes the substantial impact of sepsis on long term survival in fractured patients. These findings underscore the critical need for sepsis prevention and early detection and management to mitigate its detrimental effects on patient outcomes.

Pelvic fractures (PF) are common yet often underappreciated fractures[1,2]. While they constitute a relatively small percentage of all fractures (3–8% of total), they are associated with a notably high mortality rate[3–5]. The incidence of PF is increasing in European Union countries, alongside with ageing populations[6,7]. PF can result from both high- and low-energy trauma. In younger patients, these injuries typically occur as a consequence of high-energy trauma[8], whereas in older patients, they are usually associated with osteoporosis and more frequently occur due to low-energy trauma[9,10]. The annual incidence of PF in the older population is substantially higher than in the younger population[5,11,12]. It increases with advancing age and is most frequently observed among individuals aged of 70–80 years, with a higher prevalence in women than in men[13,14]. Beyond the age of 50 years, PF can be considered characteristic of osteoporosis and are associated with low bone mineral density[6,15,16].

An analysis of patients aged ≥ 50 years in Austria, hospitalized with PF between 2010 and 2018, revealed that standardized incidence rates increased for men by 10.0% and for women by 2.7%. In older adults, PF frequently leads to immobility, transient or permanent autonomy loss[17]. Remarkably, these fractures are characterized by a disproportionately high in-hospital mortality rate, despite older patients typically having less severe injuries compared to the younger patients[5]. Furthermore, the one-year mortality ranges from 9.5 to 27.0%[18–20].

Infectious complications and sepsis are common and expected complications following high-energy fractures. In patients with fractures, the occurrence of infection and sepsis significantly increases the direct treatment costs, approximately doubling the length of hospital stay[21] and increase mortality[22–24]. It is possible to predict a lower probability of sepsis in patients with low-energy PF due to the absence of severe trauma, open fractures and surgical intervention. At the same time, age, long-term immobilization and inpatient treatment represent risk factors for infections and sepsis. Elderly individuals are more susceptible to infectious diseases and display a worse prognosis and higher mortality, partially attributed to the decrease in immune responses that occurs with aging process[25].

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Although the international community has published several reports on pelvic ring fractures associated with osteoporosis, there is a notable absence of reports addressing the epidemiological characteristics of sepsis and its impact on mortality and treatment duration in patients with osteoporotic PF. There are limited publications that provide data on the etiological structure of sepsis in surgical patients with high-energy pelvic fractures[26,27] and severe trauma patients[28].

In light of the World Health Organization (WHO) resolution WHA70.7, titled "Improving the prevention, diagnosis and clinical management of sepsis"[29], the aim of this study was to determine the epidemiological characteristics and impact of sepsis on one-year mortality in the Austrian population of patients with PF aged ≥ 50 years, within the time frame from 2010 to 2018.

Methods

Setting and design

This was a retrospective nationwide register-based cohort study which included all patients with PF in Austria aged ≥ 50. Pseudonymized individual-level patients' data were obtained from social insurance authorities and the Federal Ministry of Labour, Social Affairs, Health and Consumer Protection in Austria.

Cohort of patients with pelvic fracture

We identified patients 50 years or older with inpatient hospitalization for a main or side diagnose of a PF between January 1, 2010 and December 31, 2018. The focus on this age group is based on the strong association between PF and osteoporosis. Pelvic fractures in older adults are frequently linked to low bone mineral density and other age-related factors, such as impaired balance and increased fall risk, which are characteristic of osteoporotic conditions. A PF event was defined by the following ICD-10 codes: S32.1 (Fracture of os sacrum), S32.2 (Fracture of os coccyges), S32.3 (Fracture of os ilium), S32.4 (Fracture of acetabulum), S32.5 (Fracture of os pubis), S32.6 (Fracture of ischium), S32.81 (Multiple fractures of pelvis with disruption of pelvic ring) and S32.89 (Fracture of other parts of pelvis). When selecting patients, we also adhered to current recommendations, no longer distinguishing between high and low trauma[15,30].

Sepsis within 180 days following pelvic fracture

We identified patients who were hospitalized with sepsis within 180 days following a PF event. All ICD-10 codes for sepsis are listed in the Supplemental Table S1.

We assessed the incidence of sepsis following a PF by examining the duration between hospital discharge post-PF and subsequent admission for sepsis within 180-day period. Next, we constructed a binary variable "sepsis within 180 days post-PF fracture" to delineate cases that manifested sepsis within the specified timeframe.

Etiology of sepsis was divided into four groups comprising following ICD-codes of sepsis: unspecified (A41.9, J95.0, T80.2, T81.4, R65.1, T88.0, R57.2, R57.8, R65.0, R65.9, G08), gram positive (A40.0, A40.1, A40.2, A40.3, A40.8, A40.9, A41.0, A41.1, A41.2), gram negative (A02.1, A39.2, A39.4, A41.3, A41.5, A21.7) and other (A32.7, A41.4, A41.8, A54.8, B00.7, B37.7) (Supplemental Table S1).

Length of hospital stay with PF and with a diagnosis of sepsis were tracked.

To assess the cumulative incidence of sepsis following PF, we utilized the *time to sepsis* as our primary metric. This was defined as the duration from the occurrence of the PF to one of the three possible endpoints: (1) an in-hospital stay due to sepsis, (2) death, (3) or the end of the follow-up period (censored). These distinct events allowed us to delineate and evaluate the risk associated with sepsis within our cohort, ensuring that competing risks, such as death before the onset of sepsis, were adequately considered in our analysis. The cumulative incidence function (CIF) was then employed to capture the probability of sepsis occurrence over time, adjusting for the death as a competing risk.

Incidence of hospitalizations with sepsis over studied period was calculated as new cases of sepsis in particular year divided by number of fractured patients at that year.

Mortality

We calculated 30-day and one-year mortality in a cohort of septic patients. *Survival time post-sepsis* was calculated from the date of time of hospital admission with sepsis until the date of death, the end of follow up (censored), whichever occurred first.

For differences in overall survival between septic and non-septic patients we calculated *survival time* from the admission date with PF until date of death or to the end of follow up on 08.03.2020. We used *time to sepsis* as a time-varying covariate.

Covariates

Data on demographics, vital status and comorbidities recognized on hospital discharges were present in a database.

We calculated the weighted Elixhauser scores using methods referenced in Behanova et al.[13].

Statistical analysis

Cumulative incidence of sepsis was estimated in the context of considering mortality as a competing risk. For assessing differences in CIF by sex, age group and sepsis etiology we applied Fine and Gray risk analysis[31].

30-day and one-year mortality in a cohort of septic patients were estimated using Kaplan-Meier survival curves. To evaluate statistical differences in survival distributions across sex, age group, and sepsis etiology we employed the log-rank test.

To evaluate the association between sepsis and all-cause mortality (between septic and non-septic patients), we used time-varying Cox proportional hazard regression to compute crude and multivariable adjusted hazard

ratios (HR) with 95% confidence intervals (CI). In the multivariable analysis we adjusted for age, sex, and EHI score. Additionally, we performed a sensitivity analysis to examine potential residual confounding of comorbidity. We repeated the analysis adjusting for specific comorbidities of the EHI index score instead of using EHI score.

Analysis were stratified by two age groups – 50–64 years old and ≥65 years old.

All statistical analyses were conducted using SPSS version 29 (IBM Corp., Armonk, NY, USA) and R Software[32].

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethical committee of the City of Vienna (Ethical approval number: EK 19-220-VK). As this is a retrospective study, the informed consent has been waived off by the Ethical committee of the City of Vienna.

Results

Baseline characteristics

The patient's flowchart is shown in Fig. 1. Among 59,081 patients hospitalized with PF between 2010 and 2018, 619 (1.05%) were hospitalized with sepsis within 180 days following PF. Of the septic cohort, 239 (38.6%) were males and 380 (61.4%) were females with a mean age of 77.1 (SD 10.5) years. No significant age difference was observed between patients with and without sepsis ($p=0.819$). Furthermore, the prevalence of male-sex was significantly higher in the sepsis group at 38.6% compared to 29.6% in the non-sepsis group ($p<0.001$). Additionally, patients within the septic cohort exhibited a higher comorbidity burden than those in the non-septic group. In terms of medication utilization prior to PF, the septic cohort had a significantly higher prevalence (for all $p\leq0.001$) of usage for antidepressants, antiepileptics, antiparkinson drugs, antirheumatic drugs, prednisolone, blood glucose lowering drugs, insulin, metamizole, opiates, platelet, proton pump inhibitors compared to the non-septic group (Table 1).

During the observation period, a total of 742 hospitalization events were recorded for 619 unique patients diagnosed with sepsis within 180 days post-PF. An upward trend was observed in the annual incident rate: starting from 1.2% in 2010. However, a decline to 0.8% was noted in 2014. The rate subsequently increased to 1.5% in 2016 and peaked at 1.6% in 2017. Yet, in 2018, another decline was observed, with the incidence rate dropping to 1.1% (Supplemental Table S2).

Epidemiology of sepsis and mortality after sepsis following PF

The etiological patterns of sepsis were similar in both age groups. Patients with negative culture predominated, accounting for 397 cases (64.1%): 59 (67.1%) in the 50–64 age group and 338 (63.7%) in the ≥65 age group. Gram positive microorganisms were confirmed in 92 cases (14.9%), with 16 (18.2%) in patients the 50–64 age group and 76 (14.3%) in the ≥65 age group. Gram negative microorganisms were found in 71 cases (11.5%): 7 (8.0%) in the 50–64 age group and 64 (12.1%) in the ≥65 age group). Additionally, 59 cases (9.5%) classified as "other" were confirmed in 6 patients (6.8%) aged 50–64 years and 53 (10.0%) in patient aged ≥65 years (Table 2).

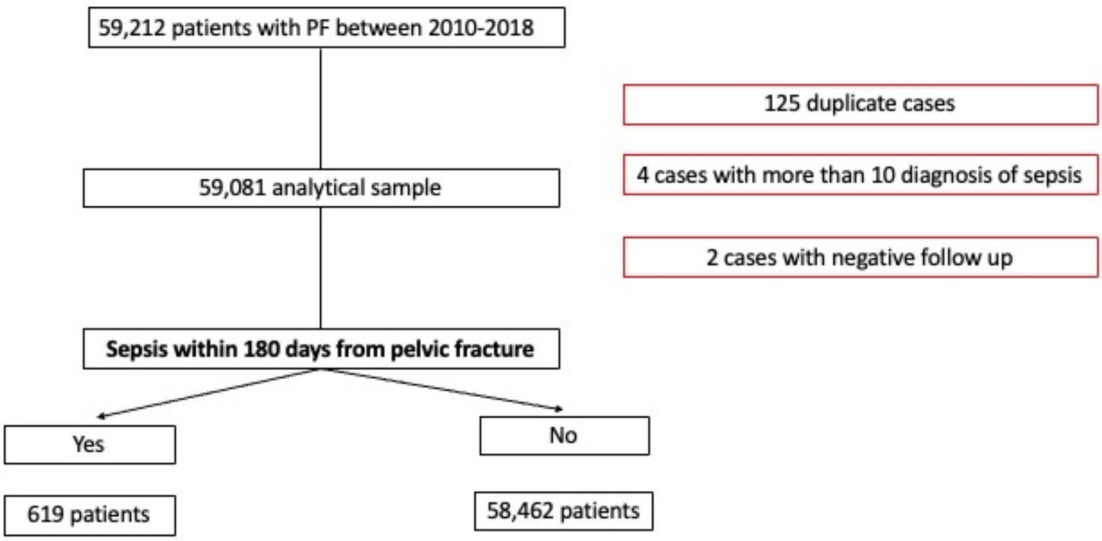


Fig. 1. Flowchart of patient's selection.

	Sepsis		
	No sepsis	Sepsis	
	58,462 (98.9)	619 (1.05)	p-value
Sex			< 0.001
Male	17,327 (29.6)	239 (38.6)	
Female	41,135 (70.4)	380 (61.4)	
Age, mean (SD)	77.22 (11.42)	77.12 (10.50)	0.819
Age category, N (%)			0.141
50–64	9644 (16.5)	88 (14.2)	
=>65	48,818 (83.5)	531 (85.8)	
Hospital stay with PF in days, Mean (SD)	12.8 (13.5)	25.6 (34.7)	< 0.001
Hospital-based comorbidities, N (%)			
AIDS/HIV	36 (0.1)	1 (0.2)	0.323
Alcohol abuse	2587 (4.4)	47 (7.6)	0.001
Blood loss anaemia	985 (1.7)	20 (3.2)	0.007
Cardiac arrhythmias	17,943 (30.7)	271 (43.8)	< 0.001
Congestive heart failure	12,770 (21.9)	238 (38.4)	< 0.001
Coagulopathy	2349 (4.0)	59 (9.5)	< 0.001
Chronic pulmonary disease	9158 (15.7)	161 (26.0)	< 0.001
Deficiency anaemia	3891 (6.7)	56 (9.0)	0.023
Depression	9802 (16.8)	135 (21.8)	0.001
Diabetes, complicated	5176 (8.9)	106 (17.1)	< 0.001
Diabetes, uncomplicated	9414 (16.1)	182 (29.4)	< 0.001
Drug abuse	992 (1.7)	20 (3.2)	0.007
Fluid and electrolyte disorders	10,425 (17.8)	171 (27.6)	< 0.001
Hypertension, complicated	2909 (5.0)	50 (8.1)	0.001
Hypothyroidism	5688 (9.7)	75 (12.1)	0.056
Hypertension, uncomplicated	34,635 (59.3)	423 (68.3)	< 0.001
Liver disease	5290 (9.1)	111 (17.9)	< 0.001
Lymphoma	932 (1.6)	27 (4.4)	< 0.001
Metastatic cancer	2108 (3.6)	29 (4.7)	0.158
Obesity	3385 (5.8)	85 (13.7)	< 0.001
Other neurological disorders	6599 (11.3)	100 (16.2)	< 0.001
Paralysis	837 (1.4)	26 (4.2)	< 0.001
Pulmonary circulation disorders	3938 (6.7)	77 (12.4)	< 0.001
Psychoses	708 (1.2)	6 (1.0)	0.713
Peptic ulcer disease, excluding bleeding	1012 (1.7)	13 (2.1)	0.439
Peripheral vascular disorders	8156 (14.0)	153 (24.7)	< 0.001
Renal failure	11,788 (20.2)	227 (36.7)	< 0.001
Rheumatoid arthritis/collaged vascular disease	2309 (4.0)	46 (7.4)	< 0.001
Valvular disease	7351 (12.6)	119 (19.2)	< 0.001
Solid tumour, without metastasis	7265 (12.4)	121 (19.5)	< 0.001
Weight loss	2010 (3.4)	42 (6.8)	< 0.001
Elixhauser index			< 0.001
< 0	3137 (5.4)	28 (4.5)	
0	17,392 (29.7)	59 (9.5)	
1–4	5790 (9.9)	51 (8.2)	
>=5	32,107 (54.9)	481 (77.7)	
Missing data	36 (0.1)	0 (0.0)	
Elixhauser score, Mean (SD)	8.01 (9.3)	13.7 (10.8)	< 0.001
Medications taken before PF, N (%)			
Antidepressants	23,443 (40.1)	292 (47.2)	< 0.001
Antiepileptics	8166 (14.0)	146 (23.6)	< 0.001
Antiparkinson drugs	5820 (10.0)	89 (14.4)	0.001
Antirheumatic drugs	38,822 (66.4)	454 (73.3)	< 0.001
Betamethasone	5224 (8.9)	69 (11.1)	0.065
Continued			

	Sepsis		
	No sepsis	Sepsis	
	58,462 (98.9)	619 (1.05)	p-value
Dexamethasone	2740 (4.7)	36 (5.8)	0.181
Prednisolone	5441 (9.3)	107 (17.3)	< 0.001
Triamcinolone	6450 (11.0)	76 (12.3)	0.333
Blood glucose lowering drugs	7962 (13.6)	145 (23.4)	< 0.001
Insulin	2855 (4.9)	71 (11.5)	< 0.001
Bisphosphonates	14,139 (24.2)	135 (21.8)	0.186
Denosumab	1271 (2.2)	16 (2.6)	0.486
Metamizole	16,005 (27.4)	235 (38.0)	< 0.001
Methylprednisolone	1489 (2.5)	22 (3.6)	0.123
Opiates (weak)	15,960 (27.3)	229 (37.0)	< 0.001
Opiates (strong)	10,703 (18.3)	181 (29.2)	< 0.001
Platelet	14,568 (24.9)	216 (34.9)	< 0.001
Proton pump inhibitors	38,410 (65.7)	452 (73.0)	< 0.001

Table 1. Characteristic of patients with pelvic fractures.

		Age category, *N* (%)		
		50–64	≥ 65	Total
Sepsis		88 (14.2%)	531 (85.8%)	619
Sex	Males	44 (50.0%)	195 (36.7%)	239
	Females	44 (50.0%)	336 (63.3%)	380
Hospital days with first sepsis, mean (SD)		23.7 (29.3)	20.8 (27.1)	21.2 (27.4)
Hospital days with second sepsis, mean (SD)		28.1 (35.2)	22.0 (24.9)	23.0 (26.8)
Total hospital days with sepsis, mean (SD)		30.9 (43.1)	24.7 (33.1)	25.6 (34.7)
Etiology after first sepsis	Unspecified	59 (67.0%)	338 (63.7%)	397
	Grampositive	16 (18.2%)	76 (14.3%)	92
	Gramnegative	7 (8.0%)	64 (12.1%)	71
	Other	6 (6.8%)	53 (10.0%)	59
Etiology after second sepsis	Unspecified	10 (66.7%)	55 (74.3%)	65
	Grampositive	5 (33.3%)	14 (18.9%)	19
	Gramnegative	0	3 (4.1%)	3
	Other	0	2 (2.7%)	2

Table 2. Characteristics of patients with sepsis within 180 days after pelvic fracture.

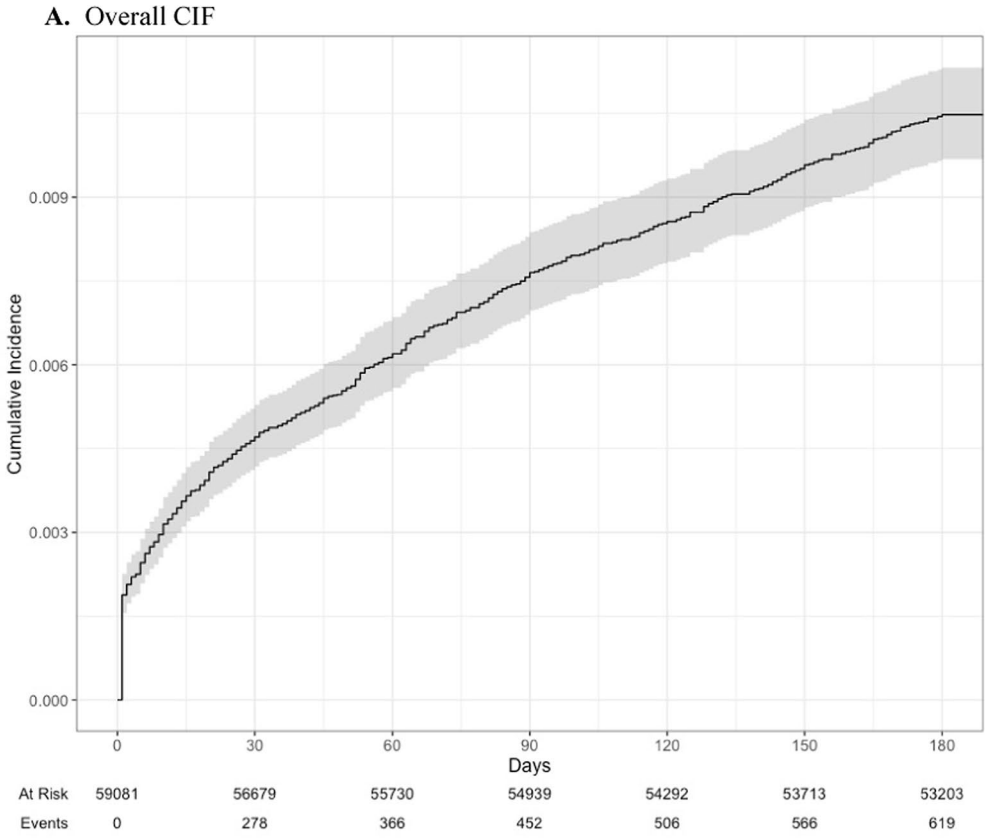
Staphylococcus aureus was the predominant causative agents of sepsis, identified in 55 cases (8.6%): 7 (8.0%) among patients aged 50–64 years and 48 (9.0%) in elderly patients. Streptococcus pneumoniae was isolated in 5 cases (0.9%), all of which were in elderly patients (Supplemental Table S3, Supplemental Fig. S1).

Incidence risk of sepsis by etiology within 180 days after PF was 1.05% (Fig. 2A–D). The cumulative incidence risk of sepsis 180 days after PF was significantly higher in males (1.4%, 95% CI 1.2%-1.5%) compared to females (0.92%, 95% CI 0.83%-1.0%), $p < 0.001$ (Fig. 2C). There were no significant differences in CIF by age group (Fig. 2D). In the cohort of patients with sepsis, the 7-day survival probability was 84%, the 30-day survival probability stood at 77.5%, and one-year survival probability was 49.59% (Fig. 3A). Survival probability significantly varied based on sepsis etiology. In terms of sepsis etiology groups, the lowest 30-days survival probability was seen in "Other" category (55.9%), followed by "Unspecified" at 65.7%, "Gram positive" at 73.9% and "Gram negative" at 90.1% (Fig. 3B). There were no sex differences (Fig. 3C). The one-year survival probability differed by age group; patients aged over 65 years had a reduced one-year survival probability of 47.1% (Fig. 3D). Frequency of sepsis in patients with fracture of the acetabulum or coccyx is presented in Supplemental Table S4.

Differences in mortality between patients with and without sepsis

The hazard of dying was greater for patients who developed sepsis within 180 days post-PF, independently of age, sex and comorbidity status (HR 3.12, 95% CI 2.83–3.44, $p < 0.001$). Their risk of death was more than three-fold increased compared to patients who did not develop sepsis (Table 3).

The sensitivity analysis adjusting for specific comorbidities instead of EHI score did not substantially change our results.



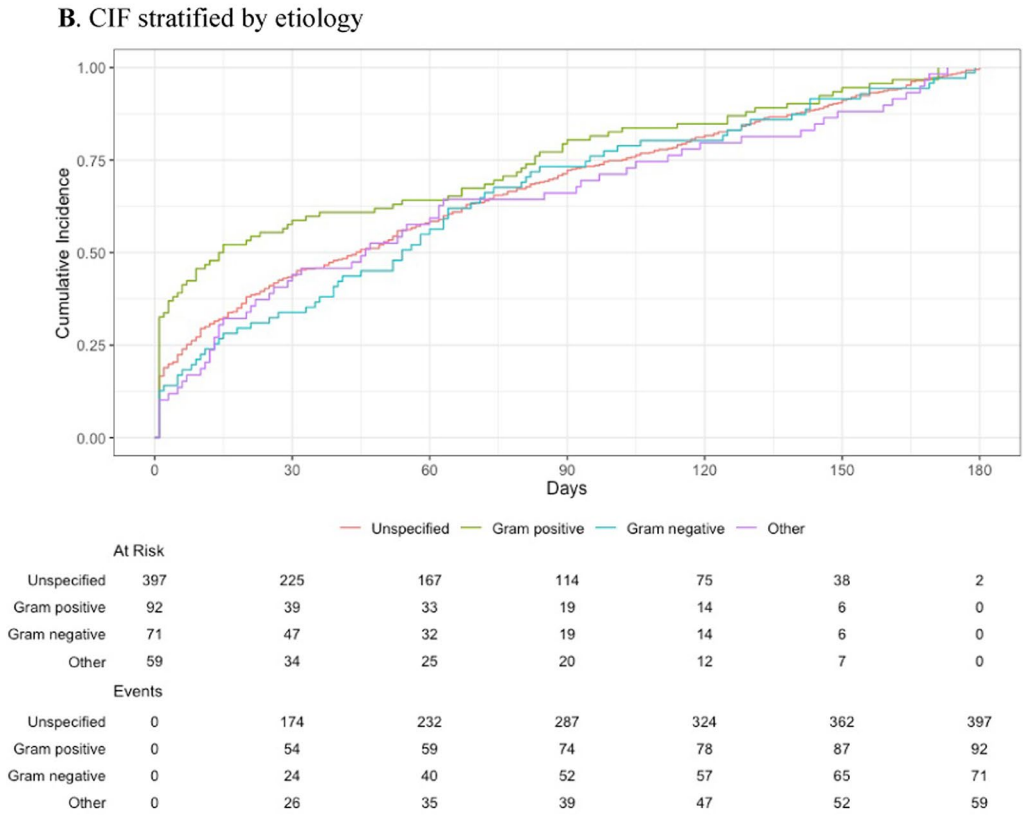
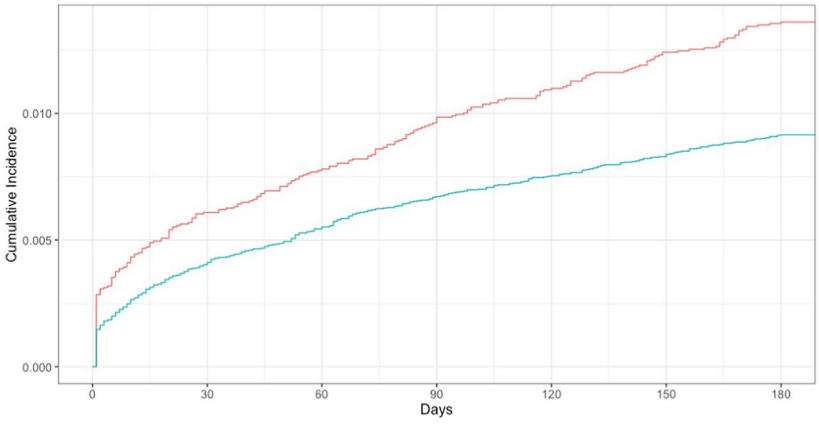


Fig. 2. Incidence risk (cumulative incidence function CIF) of sepsis within 180 days after PF in the presence of competing risk of death: overall CIF (**A**), stratified by etiology (**B**), sex (**C**), age group (**D**).

C. CIF stratified by sex

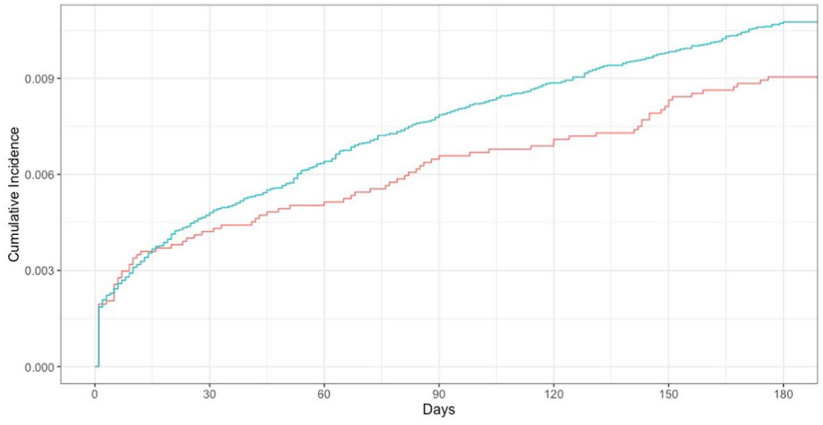


Males							
At Risk	17566	16587	16288	16031	15819	15631	15480
Events	0	107	137	173	193	218	239
Females							
At Risk	41515	40092	39442	38908	38473	38082	37723
Events	0	171	229	279	313	348	380

Characteristic	N	Day 7	Day 30	Day 60	Day 90	Day 180	p-value[†]
sex	59,081						<0.001
Males		0.39% (0.30%, 0.49%)	0.61% (0.50%, 0.73%)	0.78% (0.66%, 0.92%)	0.98% (0.85%, 1.1%)	1.4% (1.2%, 1.5%)	
Females		0.23% (0.18%, 0.28%)	0.41% (0.35%, 0.48%)	0.55% (0.48%, 0.63%)	0.67% (0.60%, 0.75%)	0.92% (0.83%, 1.0%)	

[†] Gray's Test

D. CIF by age group



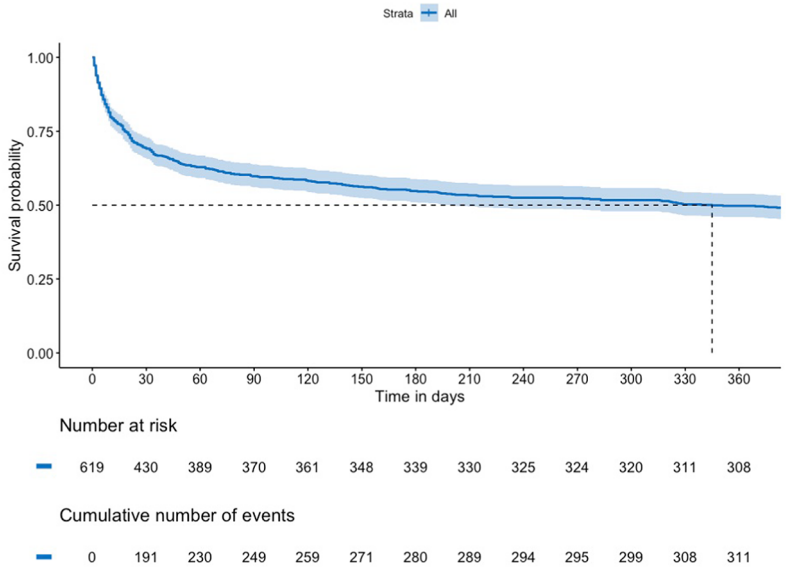
50-64							
At Risk	9732	9559	9521	9474	9449	9405	9379
Events	0	41	50	64	69	81	88
Above 65							
At Risk	49349	47120	46209	45465	44843	44308	43824
Events	0	237	316	388	437	485	531

Characteristic	N	Day 7	Day 30	Day 60	Day 90	Day 180	p-value[†]
Agecat	59,081						0.13
50-64		0.30% (0.20%, 0.42%)	0.42% (0.31%, 0.57%)	0.51% (0.39%, 0.67%)	0.66% (0.51%, 0.83%)	0.90% (0.73%, 1.1%)	
Above 65		0.27% (0.23%, 0.32%)	0.48% (0.42%, 0.54%)	0.64% (0.57%, 0.71%)	0.79% (0.71%, 0.87%)	1.1% (0.99%, 1.2%)	

[†] Gray's Test

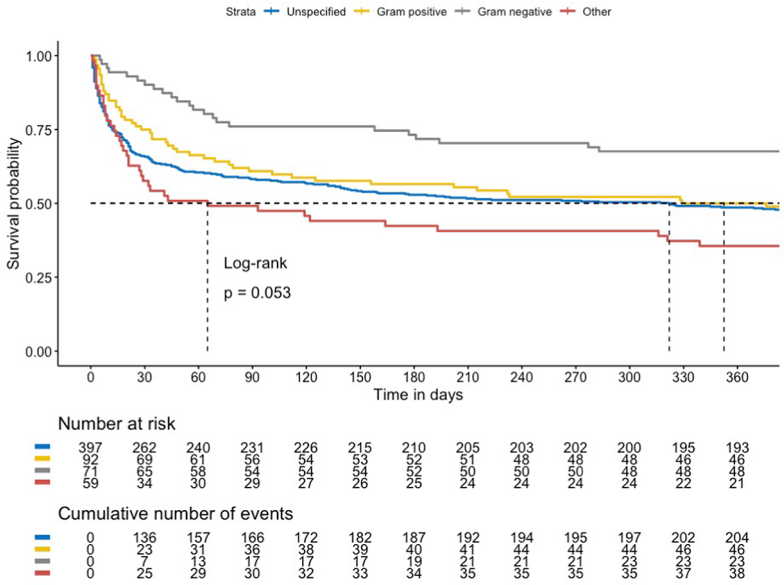
Figure 2. (continued)

A. one-year survival probability



Time in days	7	14	30	60	90	120	180	365
Survival probability	0.841	0.775	0.691	0.628	0.598	0.581	0.546	0.496

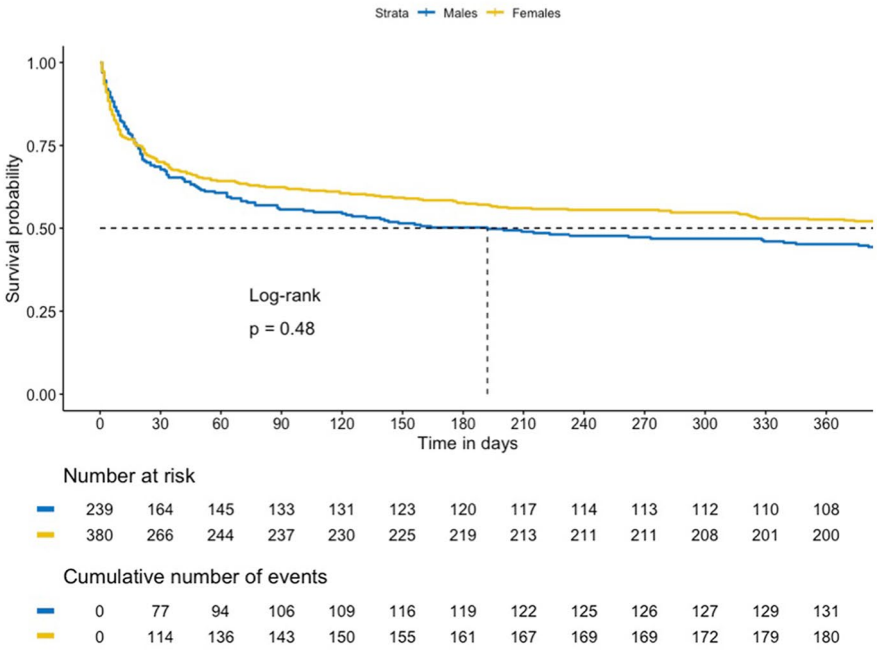
B. One-year survival probability by etiology status



Survival probability by etiology	Time in days 7	14	30	60	90	120	180	365
Unspecified	0.811	0.740	0.657	0.602	0.579	0.567	0.526	0.483
Gram positive	0.880	0.826	0.739	0.652	0.598	0.576	0.554	0.489
Gram negative	0.972	0.944	0.901	0.803	0.760	0.746	0.718	0.662
Other	0.830	0.729	0.559	0.491	0.474	0.440	0.407	0.356

Fig. 3. One-year survival probability in patients with sepsis (**A**), stratified by etiology of sepsis (**B**), by sex (**C**) and by age group (**D**).

C. One-year survival probability by sex



D. One year survival probability by age group

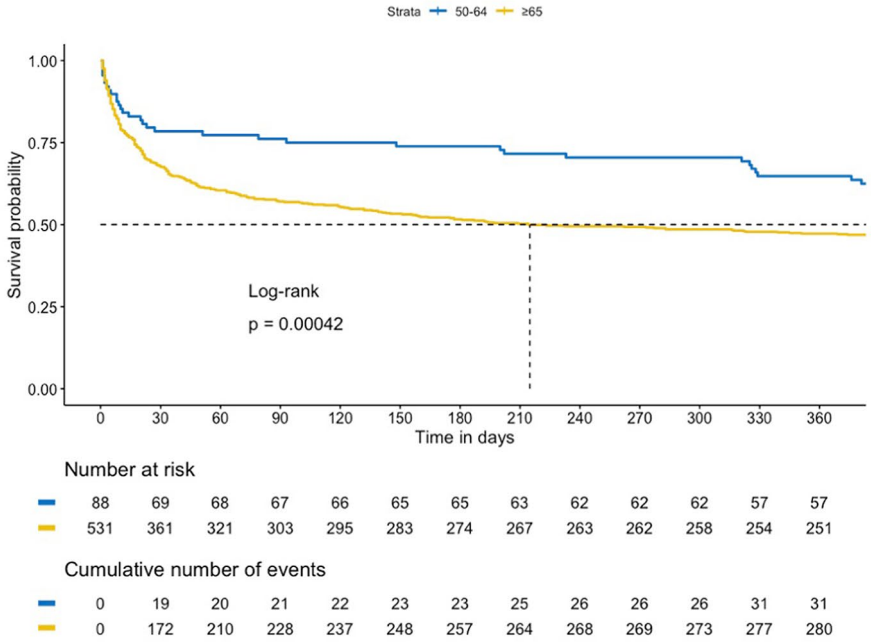


Figure 3. (continued)

Length of hospital stay and mortality of PF sepsis

The average length of hospital stay for patients with PF who did not develop sepsis 12.8 ± 13.5 days. This was significantly shorter than the 25.6 ± 34.7 days observed in PF patients who developed sepsis post-PF ($p < 0.001$).

During the first hospitalisation with sepsis, patients aged 50–64 years had an average stay of 23.7 ± 29.3 days. In contrast, patients aged 65 years and older had a slightly shorter average stay of 20.8 ± 27.1 days. For the second sepsis hospitalization, the duration was longer in the younger age group, with patients aged 50 to 64 years staying an average of 28.1 ± 35.2 days. Their older counterparts, those aged 65 and above, had an average stay of 22.0 ± 24.9 days. When considering the total duration of all-sepsis related hospitalizations, it amounts to an average of 25.6 ± 34.7 days (Table 2).

	Model 1		Model 2	
	Hazard ratio (95% CI)		Hazard ratio (95% CI)	
T_COV (sepsis)	3.46 (3.14–3.82)	$P<0.001$	3.12 (2.83–3.44)	$P<0.001$
Age			1.08 (1.08–1.08)	$P<0.001$
Male sex			1.52 (1.47–1.56)	$P<0.001$
CCI			1.032 (1.031–1.034)	$P<0.001$

Table 3. Mortality risk in patients with PF and its association with sepsis (sepsis was modelled as a time varying covariate). Model 1: crude, Model 2: adjusted for age, sex, Elixhauser comorbidity index.

Discussion

A recent global study reported 49 million cases and 11 million sepsis-related deaths in 2017, accounting for approximately 20% of all annual deaths globally[33]. Despite significant efforts in studying the problem of sepsis, there are still important data limitations and knowledge gaps in current estimates of the burden of sepsis. Most studies are intensive care- and hospital-based, limiting our understanding of community-acquired sepsis and the burden of long-term outcomes and sequelae in sepsis patients[34]. In this retrospective, nationwide, register-based cohort study, we analysed the epidemiology of hospital-treated sepsis and its impact on mortality in patient's aged ≥ 50 years with PF in Austria in 2010–2018.

The issue of infectious complications in elderly patients with low-energy PF has been underestimated. So far, this study represents the first comprehensive examination that provides detailed insights into the mortality, epidemiological factors, and etiological aspects among patient's ≥ 50 years with PF complicated by sepsis.

We found a sepsis incidence during 30 days after first PF of 0.46% and during 180 days as 1.05% (0.9% among patients 50–64 years old and 1.1% in patients ≥ 65 years). Notably, this incidence rate is expectedly lower than the in-hospital incidence of sepsis in patients with open PF (1.5%)[35] and within 30 days following geriatric surgery for hip fracture (2.4%)[36]. However, it is worth noting that the sepsis incidence in our study cohort was still relatively high, comparable to the 30-day sepsis incidence observed in patients following elective neurosurgery (0.87%)[37] and 0.7% after vertebroplasty or kyphoplasty for osteoporotic vertebral compression fractures[38]. Moreover, it has taken into account, that PF in patients 50 years and older mainly occur due to osteoporosis, and are usually treated conservatively, and not surgically.

Despite the fact that patients aged ≥ 65 years are at the highest risk for sepsis[39,40], our analysis revealed no significant age difference between patients with PF who developed sepsis and those who did not.

The cumulative incidence risk of sepsis within 180 days following PF was significantly higher in males compared to females. However, there were no sex differences in the one-year survival probability. Comorbidity is an important risk factor for infection up to 1 year after hip fracture surgery[41]. As anticipated, patients with sepsis exhibited significantly higher mean Elixhauser comorbidity scores along with a notably higher prevalence of almost all comorbidities than patients with PF not complicated by sepsis.

In an unexpectedly high proportion of patients, amounting to 66.4%, sepsis developed between 2 and 6 months after PF. It is plausible that the development of sepsis is facilitated by an initial inflammatory response triggered immediately following the bone fracture. This acute phase of inflammation may subsequently transition into a chronic phase that persists until the tissues are completely healed[42]. Moreover, it is known that even sterile trauma can induce alterations in post-traumatic immunity[43,44]. Long-term immobilization that accompanies PF contributes to the development of secondary complications such as pneumonia, urinary tract infections and bedsores[45]. Prolonged immobilization also increases the risk of developing sepsis several months after the fracture. The precise pathogenesis of sepsis development during the late phase of PF remains unclear and requires further research.

The duration of hospital treatment within our cohort of patients with PF and sepsis was notably lengthier, averaging at 25.6 ± 34.7 days. This duration exceeded that observed in septic patients in Germany in 2009–2017 (20.6 ± 20.8 days)[46] and, unsurprisingly, was considerably longer than the hospital stay for patients in our cohort without sepsis. This difference in hospital treatment duration demonstrates both an increased burden on the medical system and a substantial rise in the treatment costs associated with sepsis following PF.

The etiological structure of sepsis in patients aged ≥ 50 years old with PF has not been previously described. Our investigation revealed positive blood culture in 35.9% of cases, with a predominance of gram-positive infection, followed by a smaller number of confirmed gram-negative, anaerobic and fungal infection cases. In comparison, a Spanish population-based register study reported bacteraemia in 26.3% of septic patients, with variations ranging from 18.7 to 65.3% depending on the source of infection[39]. Our finding of 35.9% positive blood cultures sepsis after PF is positioned in the middle of the scale.

Annual mortality rate in Austrian patients with PF not complicated by sepsis is lower than that observed in other developed countries. Specifically, it is 4.0% among patients 50–64 years old and 13.2% in patients aged ≥ 65 years. For example, recent population-based study from the Germany reported a 1-year mortality rate of 25% in patients with PF aged ≥ 60 years between 2008 and 2010[47]. A Sweden study among patients ≥ 50 years found 1-year mortality after PF as 21% from 2001 to 2016 [48]. Furthermore, a recent UK study found in-hospital mortality to be 0.7% and 1-year mortality to be 16.9% among patients ≥ 60 years with conservatively treated PF[20]. The reasons for the lower mortality in patients with PF not complicated by sepsis in Austria are not entirely clear and require further research.

In contrast, the risk of death in the cohort with sepsis following PF increased by more than three-fold when compared to patients who did not develop sepsis. Our data indicate that the risk of mortality in patients with

sepsis post-PF critically depends on the etiology of sepsis, in addition to age, sex and comorbidity status. The highest 30-days mortality was observed in group of "Other" sepsis, followed by "Unspecified", "Gram positive" and "Gram negative". Notably, the majority of patients in the "Other" group were coded as "other specified sepsis". We assume that these included fungal and viral infections. These findings clearly indicate the need to improve the etiological confirmation, which, potentially, will help to optimize therapy, reduce the duration of hospital treatment and mortality[49,50].

Sepsis can exacerbate pre-existing conditions, lead to immune dysregulation, and cause multi-organ failure, all of which contribute to increased mortality rates. These mechanisms are complex and often interrelated, involving both direct effects of the septic process and indirect effects mediated by the host's immune response and comorbid conditions. The future studies could explore the contribution of individual factors such as treatment regimen, etiology, site of primary infection, immune response status, and comorbidities to sepsis-related mortality.

Strengths and limitations

Our study has important strengths. We present for the first-time data on the incidence, duration of hospital treatment, mortality and etiological structure of sepsis after PF in patients ≥ 50 years old in Austria, representing the region of Central and Eastern Europe. Large, national databases was available for nine years, providing long-term information. Using unique pseudonyms for patients, we were able to identify readmissions and hospital discharges with the same diagnosis, exclude them, and calculate the first cases of PF and sepsis during the observed period and hence avoid overestimation due to double counting. Finally, our study utilized the use of competing risk analysis in assessing sepsis incidence, and we employed a time varying exposure approach for our comprehensive mortality analysis. Due to disease coding limitations, we could not ascertain the number of sepsis cases caused by microorganisms such as Pseudomonas aeruginosa, Klebsiella pneumonia, Acinetobacter baumannii, Enterococcus spp. etc. Additionally, we could not elucidate the sepsis etiology in patients coded as "other gram-negative pathogens", "Sepsis caused by gram-negative pathogens", "Sepsis caused by anaerobes" or "other specified sepsis". Furthermore, due to the register-based of our study, we could not differentiate between sepsis resulting from post-operative infections, prolonged hospitalisations, community-acquired infections. It was also not possible to distinguish between stable and unstable fracture, nor were detailed data on specific surgical interventions, including internal fixation, available.

Our data were limited to calculate all-cause mortality, instead of specific mortality. Next, we could not determine the severity and duration of septic episodes. Also, data on lifestyle factors, socioeconomic situations, history of falls, frailty, and detailed clinical aspects of the PF (e.g., X-ray confirmation, bone mineral density measures) were not available. Furthermore, we lacked data on the individual patient treatment regimes, be they conservative or surgical. Additionally, important variables that may influence the risk of sepsis and mortality outcomes – such as lifestyle factors, socioeconomic status, and a detailed fall history-were not available.

It is important to note that, although acetabular fractures represent a distinct subset of pelvic injuries, we included them in our study to provide a comprehensive view of sepsis in pelvic fractures. However, due to the relatively low number of sepsis cases within the acetabular fracture subgroup, we did not perform a separate subgroup analysis, as this could have resulted in limited statistical power and potential overinterpretation of the data.

Conclusion

The present study is the first to report an assessment of the epidemiology and mortality of patient's ≥ 50 years old with PF complicated by sepsis in Austria in the last decade. The etiology of post-PF sepsis in Austria is characterized by a predominance of gram-positive microorganisms and a low level of anaerobic infection. Morbidity and mortality in patients with post-PF sepsis are associated with male gender and the number of comorbidities; mortality, in addition, is associated with older age. The findings highlight the need for more effective strategies for the in- and out-patient management of osteoporotic PF, as well as the prevention of infectious complications.

Data availability

The datasets generated and/or analysed during the current study are not publicly available due to the risk of indirect identification, where pseudonymized data could inadvertently reveal participants identities when cross-referenced with other public information, but are available from the corresponding author on reasonable request.

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References

1. Abdelrahman, H. et al. Patterns, management, and outcomes of traumatic pelvic fracture: Insights from a multicenter study. *J. Orthop. Surg. Res.* **15**, 249. https://doi.org/10.1186/s13018-020-01772-w (2020).
2. Smith, C. T., Barton, D. W., Piple, A. S. & Carmouche, J. J. Pelvic fragility fractures: An opportunity to improve the undertreatment of osteoporosis. *J. Bone Joint Surg. Am.* **103**, 213–218. https://doi.org/10.2106/jbjs.20.00738 (2021).
3. Buller, L. T., Best, M. J. & Quinnan, S. M. A nationwide analysis of pelvic ring fractures: Incidence and Trends in treatment, length of Stay, and Mortality. *Geriatr. Orthop. Surg. Rehabil.* **7**, 9–17. https://doi.org/10.1177/2151458515616250 (2016).
4. Kannus, P., Parkkari, J., Niemi, S. & Sievanen, H. Low-trauma pelvic fractures in Elderly finns in 1970–2013. *Calcif Tissue Int.* **97**, 577–580. https://doi.org/10.1007/s00223-015-0056-8 (2015).
5. Verbeek, D. O. et al. Pelvic fractures in the Netherlands: epidemiology, characteristics and risk factors for in-hospital mortality in the older and younger population. *Eur. J. Orthop. Surg. Traumatol.* **28**, 197–205. https://doi.org/10.1007/s00590-017-2044-3 (2018).

6. Borgstrom, F. et al. Fragility fractures in Europe: Burden, management and opportunities. *Arch. Osteoporos.* **15**, 59. https://doi.org/10.1007/s11657-020-0706-y (2020).
7. Willers, C. et al. Osteoporosis in Europe: A compendium of country-specific reports. *Arch. Osteoporos.* **17**, 23. https://doi.org/10.1007/s11657-021-00969-8 (2022).
8. Giannoudis, P. V. et al. Prevalence of pelvic fractures, associated injuries, and mortality: The United Kingdom perspective. *J. Trauma.* **63**, 875–883. https://doi.org/10.1097/01.ta.0000242259.67486.15 (2007).
9. Court-Brown, C. M., Clement, N. D., Duckworth, A. D., Biant, L. C. & McQueen, M. M. The changing epidemiology of fall-related fractures in adults. *Injury* **48**, 819–824. https://doi.org/10.1016/j.injury.2017.02.021 (2017).
10. Holstein, J. H., Culemann, U. & Pohlemann, T. Working Group Mortality in pelvic fracture, P. What are predictors of mortality in patients with pelvic fractures? *Clin. Orthop. Relat. Res.* **470**, 2090–2097. https://doi.org/10.1007/s11999-012-2276-9 (2012).
11. Sterneder, M. et al. Insufficiency fractures vs. low-energy pelvic ring fractures—epidemiological, diagnostic and therapeutic characteristics of fragility fractures of the pelvic ring. *Z. Orthop. Unfall* **160**, 497–506. https://doi.org/10.1055/a-1394-6502 (2022).
12. Suneja, N., Kong, R. M., Tracey, O. C., Mallon, Z. & Tischler, E. H. Epidemiology of fragility pubic ramus fractures in the United States. *Geriatr. Orthop. Surg. Rehabil.* **13**, 21514593221097274. https://doi.org/10.1177/21514593221097274 (2022).
13. Behanova, M. et al. Pelvic fractures—an underestimated problem? Incidence and mortality risk after pelvic fracture in Austria, 2010–2018. *J. Clin. Med.* **11** https://doi.org/10.3390/jcm11102834 (2022).
14. Nanninga, G. L., de Leur, K., Panneman, M. J., van der Elst, M. & Hartholt, K. A. Increasing rates of pelvic fractures among older adults: The Netherlands, 1986–2011. *Age Ageing* **43**, 648–653. https://doi.org/10.1093/ageing/aft212 (2014).
15. Cummings, S. R. & Eastell, R. *Osteoporos. Int.* **31** 1023–1024 (2020).
16. Kocijan, R. et al. Perspectives on fracture liaison service in Austria: Clinical and economic considerations. *Front. Endocrinol. (Lausanne)* **15**, 1349579. https://doi.org/10.3389/fendo.2024.1349579 (2024).
17. Breuil, V., Roux, C. H. & Carle, G. F. Pelvic fractures: Epidemiology, consequences, and medical management. *Curr. Opin. Rheumatol.* **28**, 442–447. https://doi.org/10.1097/bor.0000000000000293 (2016).
18. Abernathy, B. R., Schroder, L. K., Bohn, D. C. & Switzer, J. A. Low-energy pelvic ring fractures: A care conundrum. *Geriatr. Orthop. Surg. Rehabil.* **12**, 2151459320985406. https://doi.org/10.1177/2151459320985406 (2021).
19. Fardellone, P. et al. The clinical and economic burden after an osteoporosis fracture in France: A nationwide population-based study. *Arch. Osteoporos.* **16**, 124. https://doi.org/10.1007/s11657-021-00976-9 (2021).
20. Ramser, M. et al. The impact of specific fracture characteristics of low-energy fractures of the pelvis on mortality. *BMC Geriatr.* **22**, 669. https://doi.org/10.1186/s12877-022-03223-z (2022).
21. Olesen, U. K. et al. The cost of infection in severe open tibial fractures treated with a free flap. *Int. Orthop.* **41**, 1049–1055. https://doi.org/10.1007/s00264-016-3337-6 (2017).
22. Hagiwara, A. et al. Predictors of severe sepsis-related in-hospital mortality based on a multicenter cohort study: The focused outcomes research in emergency care in acute respiratory distress syndrome, sepsis, and trauma study. *Med. (Baltim.)* **100**, e24844. https://doi.org/10.1097/md.0000000000024844 (2021).
23. Hoffman, S. E. et al. Spinal level and cord involvement in the prediction of sepsis development after vertebral fracture repair for traumatic spinal injury. *J. Neurosurg. Spine* 1–7. https://doi.org/10.3171/2021.12.Spine21423 (2022).
24. Morch, S. S. et al. The association between pre-operative sepsis and 30-day mortality in hip fracture patients-A cohort study. *Acta Anaesthesiol. Scand.* **62**, 1209–1214. https://doi.org/10.1111/aas.13160 (2018).
25. Salminen, A. Activation of immunosuppressive network in the aging process. *Ageing Res. Rev.* **57**, 100998. https://doi.org/10.1016/j.arr.2019.100998 (2020).
26. Kanakaris, N. K., Ciriello, V., Stavrou, P. Z., West, R. M. & Giannoudis, P. V. Deep infection following reconstruction of pelvic fractures: Prevalence, characteristics, and predisposing risk factors. *Eur. J. Trauma. Emerg. Surg.* **48**, 3701–3709. https://doi.org/10.1007/s00068-021-01618-y (2022).
27. Kellermann, F. et al. Advances in the treatment of implant-associated infections of the pelvis: Eradication rates, recurrence of infection, and outcome. *J. Clin. Med.* **12** https://doi.org/10.3390/jcm12082854 (2023).
28. Medam, S. et al. Risk factors for death in septic shock: A retrospective cohort study comparing trauma and non-trauma patients. *Med. (Baltim.)* **96**, e9241. https://doi.org/10.1097/md.0000000000009241 (2017).
29. Cassini, A. et al. Future directions and priorities in sepsis epidemiology research: a call for action. *Bull. World Health Organ.* **99**, 398–401. https://doi.org/10.2471/BLT.20.276709 (2021).
30. Leslie, W. D. et al. Fracture risk following high-trauma versus low-trauma fracture: A registry-based cohort study. *Osteoporos. Int.* **31**, 1059–1067 (2020).
31. Fine, J. P. A proportional hazards model for the subdistribution of a competing risk. *J. Am. Stat. Assoc.* **94**, 496–509 (1999).
32. R. *A Language and Environment for Statistical Computing* (R Foundation for Statistical Computing, Vienna, 2023).
33. Rudd, K. E. et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: Analysis for the global burden of disease study. *Lancet* **395**, 200–211. https://doi.org/10.1016/s0140-6736(19)32989-7 (2020).
34. Organization, W. H. Global report on the epidemiology and burden of sepsis: Current evidence, identifying gaps and future directions. 55 (2020).
35. Frane, N. et al. Risk factors for complications and in-hospital mortality: An analysis of 19,834 open pelvic ring fractures. *J. Clin. Orthop. Trauma* **11**, 1110–1116. https://doi.org/10.1016/j.jcot.2020.08.017 (2020).
36. Bohl, D. D. et al. Sepsis within 30 days of geriatric hip fracture surgery. *J. Arthroplast.* **32**, 3114–3119. https://doi.org/10.1016/j.arth.2017.05.024 (2017).
37. Pertsch, N. J., Tang, O. Y., Seicean, A., Toms, S. A. & Weil, R. J. Sepsis after elective neurosurgery: Incidence, outcomes, and predictive factors. *J. Clin. Neurosci.* **78**, 53–59. https://doi.org/10.1016/j.jocn.2020.06.015 (2020).
38. Kim, H. J. et al. Incidence and risk factors for complications and mortality after vertebroplasty or kyphoplasty in the osteoporotic vertebral compression fracture-analysis of 1932 cases from the American College of Surgeons National Surgical Quality Improvement. *Global Spine J.* **12**, 1125–1134. https://doi.org/10.1177/2192568220976355 (2022).
39. Lorencio Cardenas, C. et al. Trends in mortality in septic patients according to the different organ failure during 15 years. *Crit. Care* **26**, 302. https://doi.org/10.1186/s13054-022-04176-w (2022).
40. Martin, G. S., Mannino, D. M. & Moss, M. The effect of age on the development and outcome of adult sepsis. *Crit. Care Med.* **34**, 15–21. https://doi.org/10.1097/01.ccm.0000194535.82812.ba (2006).
41. Gadgaard, N. R. et al. Comorbidity and risk of infection among patients with hip fracture: A Danish population-based cohort study. *Osteoporos. Int.* https://doi.org/10.1007/s00198-023-06823-6 (2023).
42. Maruyama, M. et al. Modulation of the inflammatory response and bone healing. *Front. Endocrinol. (Lausanne)* **11**, 386. https://doi.org/10.3389/fendo.2020.00386 (2020).
43. Islam, M. N., Bradley, B. A. & Ceredig, R. Sterile post-traumatic immunosuppression. *Clin. Transl. Immunol.* **5**, e77. https://doi.org/10.1038/cti.2016.13 (2016).
44. Thompson, K. B., Krispinsky, L. T. & Stark, R. J. Late immune consequences of combat trauma: A review of trauma-related immune dysfunction and potential therapies. *Mil Med. Res.* **6**, 11. https://doi.org/10.1186/s40779-019-0202-0 (2019).
45. Tan, D., Wiseman, T., Betihavas, V. & Rolls, K. Patient, provider, and system factors that contribute to health care-associated infection and sepsis development in patients after a traumatic injury: An integrative review. *Aust. Crit. Care.* **34**, 269–277. https://doi.org/10.1016/j.aucc.2020.08.004 (2021).

46. Fleischmann-Struzek, C. et al. Epidemiology and costs of postsepsis morbidity, nursing care dependency, and mortality in Germany, 2013 to 2017. *JAMA Netw. Open* **4**, e2134290. https://doi.org/10.1001/jamanetworkopen.2021.34290 (2021).
47. Andrich, S. et al. Excess mortality after pelvic fractures among older people. *J. Bone Min. Res.* **32**, 1789–1801. https://doi.org/10.1002/jbmr.3116 (2017).
48. Lundin, N. et al. Epidemiology and mortality of pelvic and femur fractures-a nationwide register study of 417,840 fractures in Sweden across 16 years: Diverging trends for potentially lethal fractures. *Acta Orthop.* **92**, 323–328. https://doi.org/10.1080/17453674.2021.1878329 (2021).
49. Gupta, S. et al. Culture-negative severe Sepsis: Nationwide trends and outcomes. *Chest* **150**, 1251–1259. https://doi.org/10.1016/j.chest.2016.08.1460 (2016).
50. Lamy, B., Sundqvist, M., Idelevich, E. A. & Escmid Study Group for Bloodstream Infections and Sepsis. Bloodstream infections-standard and progress in pathogen diagnostics. *Clin. Microbiol. Infect.* **26**, 142–150. https://doi.org/10.1016/j.cmi.2019.11.017 (2020).

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Author contributions

Conceptualization and study design: A.S., J.Z., M.B. Supervision: A.S., J.Z., R.K., M.B. Data curation: B.R. Methodology: M.B. Validation: A.S. Data analysis and interpretation: A.S., M.B. Writing initial draft: A.S. Writing-review & editing: J.H., B.R., J.Z., R.K., M.B. All authors read and approved the final manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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