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Spinal infections in older people: an analysis of demographics, presenting features, microbiology and outcomes

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Spinal Infections In Older People

An Analysis of Demographics, Presenting Features, Microbiology and Outcomes

Introduction

Background

Spinal infections include vertebral osteomyelitis, septic discitis ('spondylodiscitis' when the two are coexistent), facet joint septic arthritis, and spinal epidural abscesses. Conventional teaching unifies these diagnoses by the presentation of back pain, fever, and elevated inflammatory markers. In the case of spinal epidural abscess, neurological deficits also typify the classical presenting symptomatology, but imply advanced disease [1-6]. However, clinical presentations may commonly be non-specific and not conform to these expected patterns [1, 2, 5, 7, 8].

Rates of general infection and sepsis increase with age [9], and also when considering spinal infections [9, 10]. Spinal infections are relatively uncommon, with incidence approximating 0.2 – 3.7/100,000 for spondylodiscitis and 2 - 20/100,000 hospital admissions for spinal epidural abscesses [10-12]. However overall incidence is proportionally higher in older than in younger patients, and is increasing [1, 10, 11, 13-15]. Delayed or missed diagnosis results in poorer outcomes, including significant morbidity, mortality, and functional impairment [1, 16-20].

Older people may be at higher risk of delayed diagnosis due to a higher prevalence of comorbidity, including degenerative back pain, which may cloud diagnostic thinking. Clinical assessment may be difficult because of pre-existing cognitive

impairment or intercurrent delirium, as well as atypical or subtler signs, symptoms and biochemical marker abnormalities [8, 9, 21]. Relatively few spinal infection studies specifically deal with older populations [8, 20, 22, 23]. Data on spinal infections in adults is similarly sparse [2, 7, 24-26]. There is therefore a need for contemporary, comparative data about the clinical patterns of spinal infections affecting older patients, to aid diagnosis and achieve better patient outcomes. This study aims to address this gap by comparing clinical presentations and outcomes between older patients and their younger counterparts, with the hypothesis that older patients present in a clinically atypical manner, and experience poorer outcomes.

Methods

Cases were identified for this retrospective cohort study at The Northern Hospital, a metropolitan centre with specialty infectious diseases and neurology consultation services, and no inpatient neurosurgical service. Ethics approval was obtained from hospital human research ethics committee (approval number ALR 15.2015).

Hospital records and the infectious diseases database were searched for cases of bacterial spinal infection ('spinal osteomyelitis', 'discitis', 'epidural abscess' and 'facet joint septic arthritis') between January 2008 and January 2015. Relevant cases had their electronic medical and/or paper files reviewed for clinical information regarding presentation, progress, investigations and outcomes. Clinical consistency with the attributed diagnosis was confirmed upon file review, and inclusion required an infective syndrome (symptoms, signs and investigations) consistent with a spinal infection, with corroborating magnetic resonance imaging (MRI) results

demonstrating discitis, vertebral infection, facet joint infection or epidural abscess, or computerised tomography (CT) clearly demonstrating vertebral osteomyelitis. Isolation of bacteria from a spinal biopsy, blood or urine cultures was not an absolute condition of inclusion, as culture-negative infections are relatively common [7, 27]. There was no formal hospital protocol for assessment and management of suspected spinal infections, and practice varied between clinicians. Generally, when the diagnosis was considered, blood cultures and spinal imaging were obtained. Depending on the neurological and imaging findings, empiric antibiotics were started. Biopsy was requested if blood cultures were unrevealing and the lesion was accessible. Study exclusion criteria were age below 18 years, or diagnosis not consistent with a spinal infection due to lack of supporting imaging.

Data collection included demographics and final diagnosis. Comorbidities used in the calculation of the Charlson Comorbidity Index were recorded [28]. Symptoms, signs and investigations within the first 24 hours of presentation were recorded, as well as any relevant microbiology results and imaging performed at later dates during the admission. “Older” was defined as age ≥65 years. Community-dwelling individuals were those living at home, either alone or with others. Discitis and osteomyelitis were considered one diagnostic entity (spondylodiscitis). Primary spinal epidural abscesses were those not associated with spondylodiscitis; secondary epidural abscesses were those clinically thought to have arisen from spondylodiscitis. If multiple vertebrae, or corresponding vertebral levels in the case of epidural abscess, were affected within one anatomical region, this was recorded as the appropriate category (e.g. L2-5 spondylodiscitis was categorised as ‘lumbar’). If spanning different regions in a contiguous or nonadjacent manner, this was categorised as

'multiregional' (e.g. levels L4-S2, or both C5-6 and L2-4 in the same patient). Microbiological diagnosis was based on either positive blood or spinal tissue cultures, as assessed by the treating infectious diseases physician.

Outcomes were classified as failure of medical treatment, or non-failure; patients who died or had a relapse of spinal infection were classified as failing medical treatment. Patients committed to medical management when neurosurgical management was initially thought unnecessary, but who later deteriorated and required surgical intervention, were also classified as failing medical treatment.

Descriptive analysis was conducted to compare the younger and older groups. Categorical variables were analysed using a Chi-squared test, or a Fisher's exact test for variable counts ≤5. Non-parametric (Mann-Whitney U) testing was used for the continuous variables that were non-normally distributed.

Time to event analysis was performed with death or failure of medical treatment considered as the outcome, with cases being censored after last contact confirming failure of medical treatment or non-failure. Multivariate cox regression analysis was performed, with manual forwards step-wise regression techniques employed due to the relatively small sample size. Only variables with p-values <0.2 on univariate analysis were considered in multivariate analysis.

Data were analysed using was STATA v12.1 (StataCorp 2011, College Station, TX: StataCorp LP), with a p-value cutoff of ≤0.05 considered to indicate statistical significance.

This work was partly supported by paid research time by the Northern and Austin Hospitals, Victoria, Australia, with no influence on study topic or design.

Results

Fifty-three patients met the appropriate inclusion and exclusion criteria. Three patients were excluded due to lack of supportive imaging and therefore possible alternative diagnoses.

Demographics and Baseline Characteristics

Details of baseline characteristics for the older and younger age groups are shown in Table 1. Ages ranged from 19 to 92 years, with a mean overall age of 64.7 years. 34 (64%) patients were classified as older, being age 65 or older. Mean ages were 75.9 years in the older group, and 44.6 years in the younger group. Ninety five percent of the younger and ninety four percent of the older groups presented from home. A male predominance in both age groups was noted. A higher Charlson Comorbidity Index was noted in older patients (p=0.013).

Type of spinal infection and anatomical level

The type of spinal infection was skewed towards concomitant spondylodiscitis and spinal epidural abscess in older patients, possibly suggesting a more advanced stage of disease with secondary epidural abscess formation. Primary spinal epidural abscess was more common in younger patients. Only one patient in the 65 and over age group did not have back pain; this was due to sensory impairment and an

infected stage 4 sacral pressure injury. Lumbar infections were the most common infection in both groups, but significantly more prevalent in the 65 and over age group (76% compared to 58%, p=0.008). Four cases of thoracic infections occurred in older patients, and instances of multilevel disease in the younger patients were due to spinal epidural abscess. The details of the type of spinal infection and anatomical level for each age group can be seen in Table 1.

Clinical Features and Investigations

Symptoms, signs and relevant investigation findings for the age groups are presented in Table 2. Median time to presentation was notably longer in older patients (13 vs 4 days, p=0.016). The classical features of fever, sweats, chills, and rigors were all less common in older patients. Hypotension was commoner in older people, and tachycardia similarly prevalent across both groups. Older patients were more likely to be on negatively inotropic agents such as beta-blockers, centrally acting calcium channel blockers and digoxin (18 patients [53%] vs 1 [5%]). Delirium was more common in the older cohort. Median inflammatory marker levels were all higher in older patients although there were no statistically significant differences. There were no meaningful differences in other biochemistry or haematology results. There were slightly more gram positive and negative infections in the older cohort, but this was offset by more culture-negative infections in the younger cohort. The most commonly isolated organisms were methicillin-sensitive and methicillin-resistant *Staphylococcus* aureus, with 5 (26%) cases in the younger cohort and 11 (32%) in older patients. Other gram positive organisms included *Staphylococcus epidermidis*, *Enterococcus faecalis,* and *Streptococcus anginosus*, *salivarius,* and *agalactiae*

species. Gram-negative organisms included *Escherichia coli, Pseudomonas aeruginosa*, *Pseudomonas stutzei, Klebsiella pneumoniae*, and *Propionibacterium acnes*. Anaerobes included *Clostridium perfringens*, *Propionibacterium acnes* and *Bacteroides* species. Polymicrobial infections ranged from mixed gram-positive isolates, gram-negative isolates with anaerobes, combinations thereof, or "mixed growth" on reports not further specified. All gram-negative infections were lumbar, with the exception of one thoracic *Klebsiella pneumoniae* discitis with epidural abscess.

Outcomes

There were nine cases of failure of medical treatment in the older group, and one in the younger group. Of the older group, four died during the initial admission, three died after discharge, and two failed antibiotic therapy; one of these patients required transfer for neurosurgical intervention, and the other required an extended course of antibiotics alone. The younger patient who experienced failure of medical treatment also failed antibiotic therapy, requiring transfer for neurosurgical intervention. Two other younger patients were transferred to other hospitals for neurosurgical review in the first instance. Five older and six younger patients were lost to follow up after variable durations, which was accounted for in the time to event analysis. The time to death or failure of medical treatment analysis found a hazard ratio of 9.34 (95% Confidence Interval (CI): 1.23 to 71.12, p=0.031) for the older group compared to those aged less than 65 (Figure 1). Multivariate analysis indicated that radicular pain was the only other variable significantly associated with time to death or failure of medical treatment (HR 3.29, 95% CI: 1.02 to 10.58, p=0.046), with the HR for age 65 and over changing marginally with the addition of radicular pain into the multivariate

model (HR 8.98, 95% CI: 1.18 to 68.52, p=0.034). Median length of stay was 15 days (IQR 4 – 51) in the younger cohort, and 24 days (IQR 11 – 58) in older patients (p=0.182).

Discussion

Spinal infections can result in significant mortality and morbidity, and early diagnosis is a key part of management. This study demonstrates that older patients take longer to present to hospital, may have higher inflammatory markers, and less classical symptoms and signs. When they do present and are treated, they experience poorer outcomes. It is possible that factors known to be more likely in older adults such as chronic back pain, delirium or other cognitive impairment, and different immune responses may have contributed to these findings.

The demonstrated mean age supports the observed phenomenon of spinal infections being a disease of older people. The higher proportion of males being affected by spinal infections is consistent with rates reported in the wider literature [1, 5, 7, 8, 14-16, 19, 22]. Most patients presented from home, rather than other hospitals or aged care facilities. This may imply that institutionalised older people have lower rates of investigation and diagnosis in this regard. Consequently, they may either receive empirical treatment for an unspecified or misdiagnosed infection, or be managed with palliative intent. The statistically significant longer median time to presentation in the older patients is of interest, and reasons for delay in presentation were rarely documented in the medical records. Some patients received analgesia from their general practitioners for suspected degenerative back pain, but it was not possible to ascertain how many patients in total had sought primary care attention or experienced chronic degenerative back pain prior to presentation; the more frequent lumbar infections in the older group may suggest that this is a confounder in timely

diagnosis. Another possible reason for later presentation in older people may be that the onset of symptoms is more insidious.

Higher inflammatory markers at time of presentation in the older group may reflect longer duration and possibly more advanced stage of disease, especially if the higher rates of spinal epidural abscess associated with spondylodiscitis suggest secondary epidural infection. Only one case of spinal prosthetic infection implies referral bias, as most patients with complications relating to previous spinal surgery would likely return to the parent neurosurgical centre. Additionally, those spinal infections accurately diagnosed in the community may be referred directly to neurosurgical centres, and the relative frequency of this remains unknown in this study setting. Congruent rates of tachycardia between age groups, and more common hypotension in older patients may indicate severity of illness (again related to late presentation), this must be interpreted in conjunction with greater use of negatively inotropic and antihypertensive medication in older people. Other parameters that may be indicators of bony or generalised inflammation such as albumin and ALP did not show major abnormalities. Delirium was not routinely screened for clinically, and was likely under-recognised, especially in the more predisposed older group.

There were slight differences in microbiological findings. Higher rates of culture-negativity in the younger cohort may have been due to more aggressive initial antibiotic treatment prior to appropriate cultures, because of a more typical febrile presentation. An alternative possibility is that younger patients presenting earlier in the disease course do so before the development of secondary bacteraemia, resulting in lower blood culture yields. The most common gram positive organism

was *Staphylococcus aureus*, which is echoed in other studies [1, 3, 6-8, 10, 13-16, 22, 23, 25-27]. The predominance of gram negative organisms causing lumbar infection may represent seeding from overt or subclinical bladder or bowel infections, resulting in local haematogenous spread.

The outcome data supported the hypothesis that older patients had poorer outcomes, in keeping with a recent comparative analysis [20]. Similar hazard ratios for the statistically significant composite outcome of death or failure of medical treatment add validity to this finding. Available data demonstrated deaths and failure of medical treatment predominantly affecting the older group, at relatively early time points across the follow up period of the study. However, medium and long-term outcomes for the few patients transferred to other hospitals are not known. Patients were pre-emptively transferred to hospitals with a neurosurgical service if they had an epidural abscess and were potential surgical candidates, regardless of whether or not they had neurological complications. These transfers must also be considered when interpreting length of stay duration. Radicular pain was associated with poor outcome in a statistically significant manner; this likely implies neurological compromise caused by more advanced disease, which would also cause higher rates of systemic complications. The poorer outcomes and longer lengths of stay in older patients may well be a direct consequence of more advanced disease at time of delayed presentation, in combination with comorbidities and possible frailty.

Limitations

The relatively small sample size of the study limits its ability to detect and confirm small differences between the groups. In addition to referral bias and follow-up

limitations due to the lack of an inpatient neurosurgical service at our institution, the clinical features, microbiology and outcomes may be quite different in those undergoing neurosurgical intervention or with prosthetic infections. However, our study setting may likely reflect patterns and practice in other hospitals without a neurosurgical service. Those patients transferred to neurosurgical centres were censored from the Kaplan-Meier analysis, but it should be noted that their progress to surgery or possible ongoing solely medical treatment is unknown. Differences in presenting features did not reach statistical significance due to the study being underpowered to detect differences in this regard. This study also raises the issue of potential under-diagnosis of spinal infections, as one patient could not undergo MRI due to having metallic implants, but had clear CT findings of vertebral osteomyelitis. However, there may be patients with spinal infections who were excluded from this study due to having an MRI contraindication and consequently lacking definitive imaging findings.

Conclusions

Spinal infections should be considered as a differential diagnosis in anyone with new or increasing back pain. Basic investigations (full blood count, C-reactive protein) should be performed in the older patient with new or worsening back pain, even in the absence of classical infective symptoms and signs. Larger prospective studies are needed to confirm the above findings; a multi-centre centre approach, involving neurosurgical centres, would allow for a more representative sample of infections. Outcome data including function, pain and quality of life could also be explored. More detail about prior chronic back pain, recent contact with primary care, frailty, and premorbid and consequent cognitive impairment could also be elucidated.

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Figure Legends

Table 1 – Demographics, baseline characteristics, type and anatomical level of infection; n (%) unless otherwise indicated

SD – Standard Deviation; IQR – Interquartile Range; SA – septic arthritis; OM – osteomyelitis; SEA – spinal epidural abscess

Table 2 - Univariate Analysis of Symptoms, Signs and Investigations; n (%) unless otherwise indicated

SD – Standard Deviation; IQR – Interquartile Range; SBP – systolic blood pressure; CRP – C-reactive protein; WCC – white cell count; ALP – alkaline phosphatase.

Figure 1 – Kaplan-Meier Hazard Curves for the probability of death or failure of medical treatment across two age groups

Figures

Table 1 – Demographics, baseline characteristics, type and anatomical level of infection; n (%) unless otherwise indicated

	Age Group		p-value
	<65	**≥65**	
Demographics and Baseline Characteristics			
n (% of total)	19 (36)	34 (64)	
Male (%)	14 (79)	22 (65)	0.223
Living Arrangements			1.000
Community	18 (95)	32 (94)	
Aged care facility/subacute hospital	1 (5)	2 (6)	
Charlson Comorbidity Index, Mean ± SD	0.9 ± 1.6	2.1 ± 1.9	0.013
Median time to presentation, days (IQR)	4 (1-14)	13 (5-24)	0.016
Type of spinal infection			0.419
Discitis/OM	6 (32)	12 (35)	
Facet joint SA	1 (5)	1 (3)	
Primary SEA	5 (26)	4 (12)	
Discitis/OM with EA	4 (21)	14 (41)	
Facet joint SA with EA	2 (11)	3 (9)	
Spinal prosthetic infection	1 (5)	0	
Anatomical Level			0.008
Cervical	2 (11)	2 (6)	
Thoracic	0	4 (12)	
Lumbar	11 (58)	26 (76)	
Sacral/coccygeal	1 (5)	2 (6)	
Multilevel	5 (26)	0	

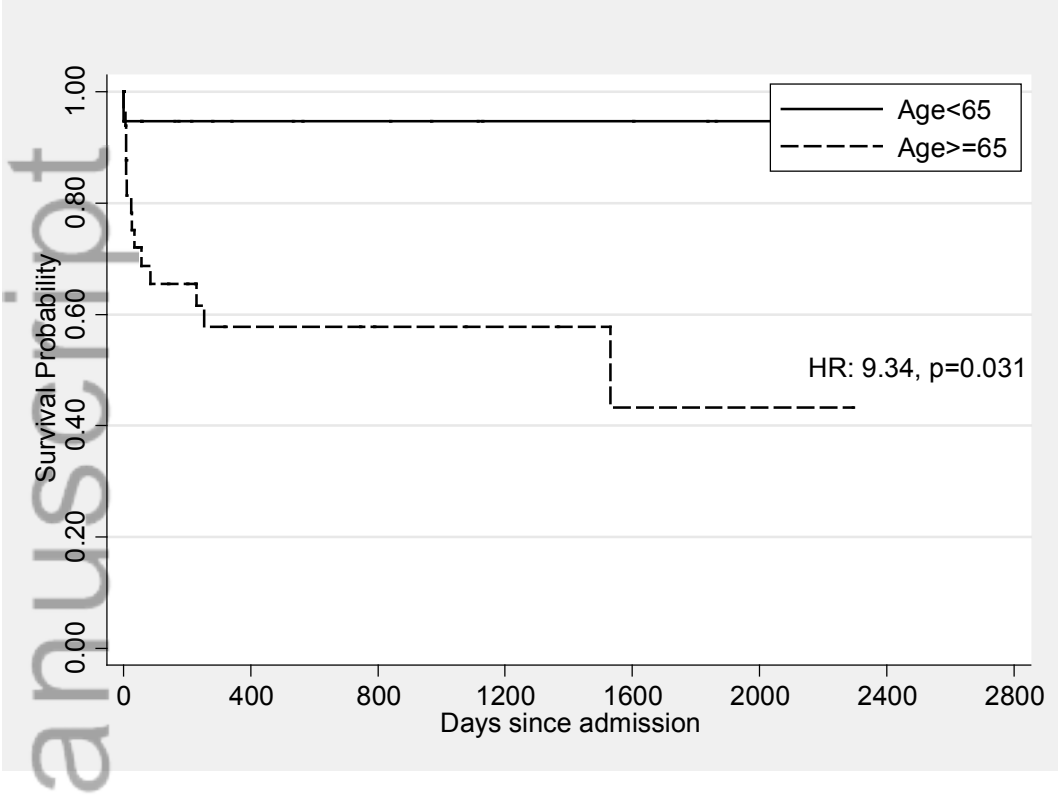
SD – Standard Deviation; IQR – Interquartile Range; SA – septic arthritis; OM – osteomyelitis; SEA – spinal epidural abscess

Table 2 - Univariate Analysis of Symptoms, Signs and Investigations; n (%) unless otherwise indicated

	Age Group		p-value
	<65	≥65	
Presenting Features			
Back pain	19 (100)	33 (97)	1.000
Documented fever (> 38°C)	12 (63)	13 (38)	0.095
Sweats/chills	13 (68)	16 (47)	0.134
Rigors	8 (42)	8 (24)	0.158
Tachycardia (heart rate >100/min)	6 (32)	12 (35)	0.784
Hypotension (SBP <90)	1 (5)	6 (18)	0.400
New neurological motor deficit	2 (11)	4 (12)	1.000
Radicular pain	2 (11)	5 (15)	1.000
Delirium	2 (11)	8 (24)	0.299
Investigations			
CRP, mg/L, Median (IQR)	114	166	0.282
WCC, $x10^9$, Median (IQR)	10	15	0.565
Neutrophil count, $x10^9$/L, Median (IQR)	7	11	0.425
Haemoglobin, g/L Mean ± SD	129.0 ± 18.6	122.9 ± 21.3	0.301
Platelet count, $x10^9$/L, Mean ± SD	302.0 ± 146.7	266.2 ± 131.6	0.367
Sodium, mmol/L, Mean ± SD	136.5 ± 4.1	135.8 ± 4.4	0.565
Albumin, g/L, Mean ± SD	32.1 ± 7.5	29.1 ± 6.0	0.120
ALP, units/L, Median (IQR)	88	103	0.274
Organism			0.525
Culture negative	8 (42)	8 (23)	
Gram positive	7 (37)	18 (53)	
Gram negative	2 (11)	6 (18)	
Anaerobic	1 (5)	1 (3)	
Polymicrobial	1 (5)	1 (3)	

SD – Standard Deviation; IQR – Interquartile Range; SBP – systolic blood pressure; CRP – C-reactive protein; WCC – white cell count; ALP – alkaline phosphatase.

Figure 1 – Kaplan-Meier Hazard Curves for the probability of death or failure of medical treatment across two age groups



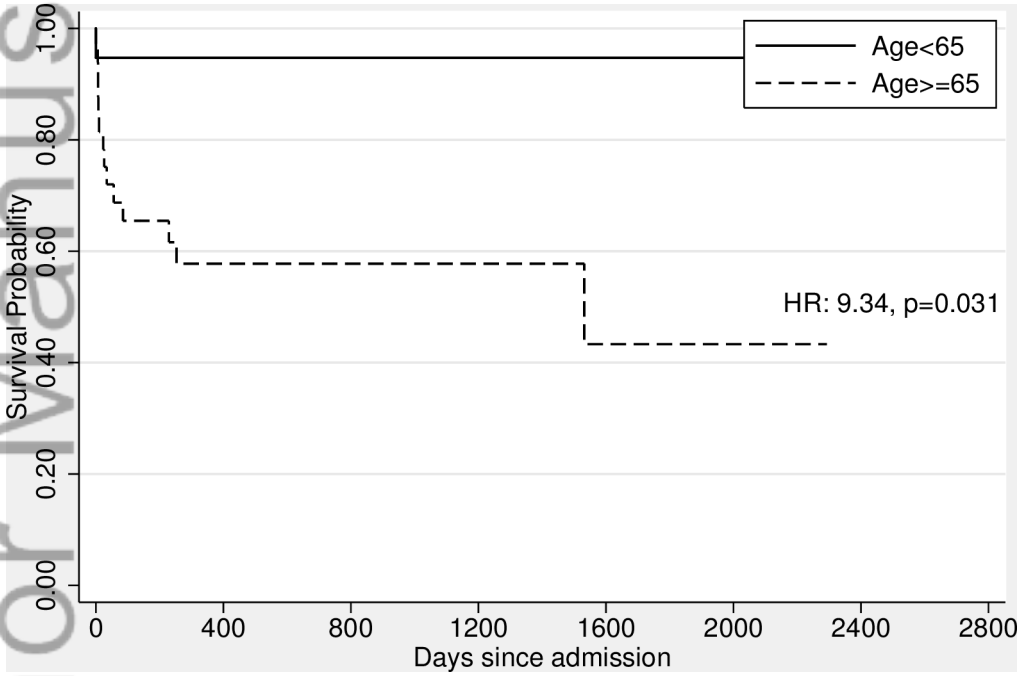


figure1

Spinal Infections In Older People

Abstract

Aims To explore differences in presentation and outcomes between younger and older patients with bacterial spinal infections.

Methods Clinical, microbiological and radiological information was collected for patients at a single metropolitan hospital with spinal infections (spondylodiscitis, vertebral osteomyelitis, septic discitis, facet joint septic arthritis, and spinal epidural abscess) between January 2008 and January 2015. Patients were excluded if under 18 years of age, or if clinical and imaging findings were inconsistent with the diagnosis. Presenting features, investigations and outcomes were compared for patients ≥65 (older) or <65 (younger) years old.

Results Of 53 identified patients, 34 (64%) were classified as older, with more males in both older (65%) and younger (79%) groups. Older patients presented later (median symptom duration 13 vs 4 days, p=0.016). Back pain was nearly ubiquitous. Older patients presented less commonly with fevers (38% vs 63%) and rigors (24% vs 42%), but more commonly with hypotension (18% vs 5%), delirium (24% vs 11%), higher median inflammatory marker levels, and variable microbiological findings, although these differences were not statistically significant. They had longer median lengths of stay (24 vs 14 days), and a higher likelihood of death or failure of medical treatment (HR 9.34, p=0.031). Radicular pain was associated with poor outcome (HR 3.29, p=0.046).

Conclusion Older patients with spinal infections present later, with higher inflammatory markers, and fewer typical infective symptoms and signs; these may contribute to poorer outcomes. A low threshold for promptly investigating older patients with new or worsening back pain should be held.

Spinal Infections In Older People

An Analysis of Demographics, Presenting Features, Microbiology and Outcomes

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Sanka Amadoru performed the data collection and study write-up.Craig Aboltins provided assistance with study design and supervision. Kwang Lim provided supervision. Mark Tacey provided the statistical analysis and advice. Kwang Lim, Craig Aboltins and Mark Tacey all provided input into the final manuscript and proofreading thereof. Estimated contributions are: Sanka Amadoru (65%), Craig Aboltins (15%), Kwang Lim (10%) and Mark Tacey (10%).

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