Spinal Fracture in Patients With Ankylosing Spondylitis

Cohort Definition, Distribution of Injuries, and Hospital Outcomes

Adam M. Lukasiewicz, MSc,* Daniel D. Bohl, MD,† Arya G. Varthi, MD,* Bryce A. Basques, MD,† Matthew L. Webb, AB,* Andre M. Samuel, BBA,* and Jonathan N. Grauer, MD*

Study Design. A retrospective cohort.
Objective. The aim of this study was to characterize spinal fractures in patients with ankylosing spondylitis.
Summary of Background Data. Patients with ankylosing spondylitis are susceptible to fractures of the spinal column, even from minor trauma. However, the literature describing patients with ankylosing spondylitis and spinal fractures consists largely of case reports and small case series. The purpose of this study is to better characterize fractures of the ankylosed spine, including the patient population, locations of fracture, and outcomes in a large, nationally representative sample.
Methods. All patients with diagnoses of both fracture of the spinal column and ankylosing spondylitis admitted between 2005 and 2011 were identified in the National Inpatient Sample (NIS). Patient demographics, fracture regions, and complications were characterized with descriptive statistics. The associations between injury characteristics and outcomes were assessed using Poisson regression.
Results. A total of 939 patients with ankylosing spondylitis admitted with a spinal fracture were identified in NIS. The average age was 68.4 ± 14.7 years, and 85% of patients were male. Cervical fractures were the most common (53.0%), followed by thoracic (41.9%), lumbar (18.2%), and sacral (1.5%). Spinal cord injury was present in 27.5% of cervical fractures, 16.0% of thoracic fractures, and 21.1% of cases overall. Fractures involving more than 1 region of the spine occurred in 13.1% of patients. Patients were treated with fusion in 49.9% of cases. In-hospital adverse events occurred in 29.4% of patients, and 6.6% of patients died during their admission.
Conclusion. More than 10% of patients had fractures in more than 1 region of the spine. There is a high risk of adverse events in this population, and 6.6% of patients died during their inpatient stay. These results provide clinicians with a better understanding of the distribution and the high morbidity and mortality of fractures in the ankylosed spine.
Key words: ankylosing spondylitis, distribution of injuries, national inpatient sample, spinal cord injury, spine fracture
Level of Evidence: 3
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Ankylosing spondylitis (AS) is a seronegative spondyloarthropathy that primarily affects the joints and ligaments of the spinal column. The disease usually develops around 25 years of age and affects men more than women.1–3 As the disease progresses, chronic inflammation of the spinal joints, ligaments, and intervertebral discs typically results in a classic “bamboo spine” in which the fused spine acts as a continuous, rigid axial support.4,5 Patients with AS are at a higher risk of spinal fractures than the general population, and even very low energy injuries can cause spinal fractures among patients with this disease.6 The increased risk of spine fractures in the AS population is generally thought to arise both from reduced vertebral bone quality and from amplified forces due to the rigid spine acting as a lever.7–9

Previous reports have found that the lower cervical spine is the most common site for fracture in the AS population,10,11 and that there is an increased risk of noncontiguous fractures in the AS population.12–16 Spinal fractures in patients with AS are also often unstable, 3-column injuries that are prone to displacement. Accordingly, the risk of spinal cord injury (SCI) is thought to be higher in patients with a spinal fracture in the context of AS, than the general spinal fracture population.17
AS is an uncommon condition, and although patients with the condition are at a higher risk of spinal fracture, less than one-fifth of patients have spinal fractures. As a result, most of the existing literature on the spinal fractures in this patient population is limited to relatively small case series; a meta-analysis of all case series of patients with spinal fracture and AS between 1980 and 2007 found a total of 345 patients. Studies included in this meta-analysis evaluated 4.5 patients on average, and the largest study included 37.

To better understand spinal fractures in patients with AS, we used a large, nationally representative cohort of patients from the National Inpatient Sample (NIS) to characterize the demographics and injuries of AS patients with spinal fracture. In addition, we examined the hospital course of these patients to describe and quantify the risk of mortality and general health adverse events.

METHODS AND MATERIALS
A retrospective cohort of patients admitted to a hospital between 2005 and 2011 for spinal fracture with a diagnosis of AS was identified in the NIS. The NIS is a large administrative database that captures a representative sample of all inpatient hospital stays in the United States each year. Patients with AS were identified by an International Classification of Diseases, Ninth Revision (ICD-9) code of 720.0. Patients with a spinal fracture were identified using ICD-9 codes in the 805 and 806 ranges, and only patients with a spinal fracture listed as their primary or secondary diagnosis were included.

Patient comorbidities were extracted from predefined variables in the NIS database, as well as ICD-9 diagnosis codes from the list of patient diagnoses. A modified Charlson comorbidity index (CCI), a measure of patient comorbidity burden, was calculated for each patient as described previously. Length of stay was extracted directly from the NIS database.

Spinal fractures were characterized by region (cervical, thoracic, lumbar, and sacral) and by SCI according to ICD-9 codes. Fractures in multiple regions of the spine were identified by the presence of ICD-9 codes documenting fractures in each of the involved regions.

Treatment details were discerned using ICD-9 procedure codes. Treatments were grouped into spinal fusion and other procedures. In the absence of a code indicating a surgical procedure, the patient was assumed to have been managed conservatively with a thoracolumbar brace, cervical collar, halo, or other nonsurgical treatment.

Demographics and spinal fracture distributions were examined using descriptive statistics. The associations between injury characteristics and length of stay were investigated with ordinary least squares multivariate regression. The associations between injury characteristics and mortality and adverse events during the inpatient stay were assessed using Poisson regression with robust error variance. This approach allows for an estimation of relative risk when the outcome is relatively common and odds ratios are not easily interpretable. Patient comorbidities and age were controlled for using CCI. Injuries were categorized as cervical, thoracic, lumbar, or multiregional. All calculations were performed using Stata 13.1 (StataCorp, College Station, TX). All tests were 2-tailed with significance at α equal to 0.05.

RESULTS

Patient Characteristics
In total, 939 patients with a diagnosis of AS admitted for a spinal fracture were identified in the NIS between 2005 and 2011. Patient characteristics are summarized in Table 1. The average age in this cohort was 68.4 ± 14.7 years (mean ± standard deviation), and 798 (85.0%) patients were male.

The most common comorbid conditions in this population were hypertension (541 patients, 57.6%), uncomplicated diabetes mellitus (199, 21.2%), fluid/electrolyte disturbances (195, 20.8%), chronic pulmonary disease (158, 16.8%), and nutrient-deficiency anemia (147, 15.7%). Approximately 50% of patients had a CCI of 3 or less.

The distribution of fractures along the spine is depicted in Figure 1 and Table 2. The cervical spine was the region most commonly fractured, with fractures in 498 patients (53.0%). Fractures in the thoracic spine were present in 393 patients (41.9%), fractures in the lumbar spine in 171 patients (18.2%), and fractures in the sacrum in 14 patients (1.5%). Fractures in multiple regions of the spine were present in 123 patients (13.1%). Ten patients had fractures in all regions of the spine. SCI occurred in 198 patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>%</th>
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<tbody>
<tr>
<td>Total</td>
<td>939</td>
<td>100%</td>
</tr>
<tr>
<td>Male</td>
<td>798</td>
<td>85.0%</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>4</td>
<td>0.4%</td>
</tr>
<tr>
<td>30–40</td>
<td>22</td>
<td>2.3%</td>
</tr>
<tr>
<td>40–50</td>
<td>94</td>
<td>10.0%</td>
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<tr>
<td>50–60</td>
<td>148</td>
<td>15.8%</td>
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<tr>
<td>60–70</td>
<td>185</td>
<td>19.7%</td>
</tr>
<tr>
<td>70–80</td>
<td>233</td>
<td>24.8%</td>
</tr>
<tr>
<td>&gt;80</td>
<td>253</td>
<td>26.9%</td>
</tr>
<tr>
<td>CCI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>97</td>
<td>10%</td>
</tr>
<tr>
<td>1</td>
<td>100</td>
<td>11%</td>
</tr>
<tr>
<td>2</td>
<td>148</td>
<td>16%</td>
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<td>3</td>
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<td>4</td>
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<td>5</td>
<td>108</td>
<td>12%</td>
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<tr>
<td>6+</td>
<td>140</td>
<td>15%</td>
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</table>

CCI indicates Charlson Comorbidity Index.
Two-thirds of SCI cases (137) were due to cervical spine fractures, and one-third (63) were due to thoracic spine fractures. Patients were treated with spinal fusion in 469 cases (49.9%).

The in-hospital adverse events associated with the above-described fractures are summarized in Table 3. Notably, 62 patients (6.6%) died. Regarding other adverse events, the most common were urinary tract infection (90 patients, 9.6%), intubation (80, 8.5%), acute kidney injury (66, 7.0%), and pneumonia (59, 6.3%). Overall, 29.4% of patients had an inpatient stay complicated by an adverse event. The mean length of hospital stay in this patient population was 9.0 ± 8.9 days, with an interquartile range of 4 to 11 (Fig. 2).

Table 4 summarizes the results of the multivariate analysis for analyses that controlled for gender and CCI. Relative to patients with cervical fractures, patients with thoracic fractures had reduced mortality (relative risk [RR] = 0.43, p = 0.014). The mortality associated with lumbar or multiple region fractures was not significantly different than that of cervical fractures. Patients with SCI were at a greater risk of mortality (RR = 3.45, P < 0.001), adverse events (RR = 2.18, P < 0.0001), and longer length of stay (6.3 days longer, P < 0.0001).

**DISCUSSION**

Patients with AS are at a high risk for spinal fracture, and often have unstable fractures with a high risk of SCI. As AS is a rare condition and spinal fracture is a relatively rare complication, the details of demographics, injuries, and outcomes in this population have not been well elucidated.
Although the demographics of the population in this study were generally similar to demographics in previous work using smaller case series, there were some differences. The average age in this study of 68.4 years was higher than the average age in most previously published case series examining this population. In those case series, the average age was usually between 50 and 60 years.20,24–26 The reason for this older than expected population is unclear and may reflect improving management of the disease course, thereby improving survival and delaying fractures.27,28 The proportion of female patients was roughly in the middle of the ranges reported in previous case series.20,29 The proportion of patients treated surgically in this study was also similar to previous results showing that slightly more than half of patients were treated operatively.20

The comorbidities in this population were particularly notable for the high prevalence of hypertension and pulmonary disease. Individuals with AS are known to have greater rates of hypertension, and increased cardiovascular mortality compared with the general population, possibly reflecting both the general inflammatory component of AS and the limitations on activity with arthritis.30,31 However, the prevalence of hypertension in this study was more than double the previous estimates, possibly reflecting the advanced disease state and poorer overall health in patients with AS complicated by spinal fracture. The high prevalence of pulmonary disease might be attributable to the pulmonary involvement of AS, which is thought to reduce lung volumes through both decreased chest expansion and inflammatory changes to the lung tissue itself.32

Previous work has largely emphasized that the cervical spine is the primary site of fracture in AS patients. In one recent meta-analysis of published case series, 78% of fractures were in the cervical spine.20 Although the cervical spine was the most common site of fracture in our study, cervical fractures were present in just slightly more than half of patients. The underlying cause of this mild discrepancy is unclear. Clinicians need to appreciate that although cervical fractures are common and concerning, thoracic fractures were present in about two-fifths of this population, and lumbar fractures were present in about one-fifth. Hence, the entire spine needs to be thoroughly evaluated in all AS patients with possible spinal fracture.

Patients with isolated thoracic injuries were at a reduced risk of mortality compared with patients with cervical injuries. However, patients with fractures in multiple regions had the same risk of mortality as patients with isolated cervical fractures. Although the risk of immediate mortality may not increase with multiple fracture sites, these additional fractures could cause substantial morbidity outside the primary hospitalization. Future work should establish the effect of multiple fractures beyond the initial hospital stay.

Although AS patients are known to occasionally have multiple distinct spine fractures,5,16,29 these injuries have not been well described. In this study, more than 10% of patients had an injury in more than 1 region of the spine. As ICD-9 coding only differentiates between broad regions of the spine, distinct but more closely related fractures—for instance, both upper and lower cervical vertebrae—could not be distinguished. Hence, the true proportion of patients with multiple, distinct fractures may well be higher. These results reinforce the idea that clinicians need to have a high suspicion of fracture throughout the spine in AS patients, even if a primary fracture site is found.

The risk of SCI in this study was substantial, with more than one-fifth of patients having a neurological deficit.

<table>
<thead>
<tr>
<th>TABLE 4. Injury Characteristics and Outcomes</th>
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<tbody>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>Factor</td>
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<tr>
<td>Fracture region (compared with cervical)</td>
</tr>
<tr>
<td>Thoracic</td>
</tr>
<tr>
<td>Lumbar</td>
</tr>
<tr>
<td>Multiple regions</td>
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<tr>
<td>Spinal cord injury</td>
</tr>
</tbody>
</table>

Bold indicates significance.

LOS indicates length of stay.
However, the rate of SCI here is lower than that of most previous studies, which have reported rates of SCI as high as 81% and 97%. This discrepancy may reflect the comparatively reduced proportion of cervical injury in our study, as, sensibly, no SCI associated with lumbar and sacral injuries was reported. Among patients with cervical fractures, only 28% of patients had recorded SCI. This result could reflect poor capture of SCI in the NIS database, a focus on the most clinically severe fractures in case reports, or both.

Although patients in this population with SCI will have poorer long-term functional outcomes, they are also at a greater risk of immediate mortality and morbidity, and they stay longer in the hospital. Clinicians need to be aware of the significant effect of SCI on immediate outcomes, and counsel patients appropriately.

The rate of complications in this study is in line with previous estimates of close to 30%. However, our study only included general health complications during the inpatient stay, and therefore likely substantially underestimates the true likelihood of adverse events in this patient population if the postoperative course after discharge were also considered. The mortality rate of 6.6% in this study was similar to most previous estimates, although less than rates considered. The mortality rate of 6.6% in this study was similar to most previous estimates, although less than rates from some smaller case series. However, as with adverse events, only mortality during the primary inpatient stay was captured, and the true mortality in the immediate postinjury period is likely far higher.

There are several limitations to this study. Detailed data on neurological status, both before and after the injury, were not available. Functional outcomes were also not available for this dataset. Although this study could evaluate patients for fractures in multiple regions of the spine, multiple cervical, thoracic, or lumbar fractures would not have been detected. Furthermore, ICD-9 coding does not specify fracture type or exact vertebral level, so these data were not available. As mentioned before, NIS data only cover the inpatient hospital stay. Hence, adverse events are likely higher in the immediate postinjury period.

In conclusion, patients with AS complicated by vertebral fracture are at a high risk for inpatient complications and mortality. Although the cervical spine is the most common location for spinal fractures, fractures in the thoracolumbar spine are more common than previously reported. SCI occurred in one-fifth of patients, and more than one-tenth of patients had a fracture in more than 1 region of the spine. Clinicians need to be vigilant for fractures throughout the spine when evaluating AS patients with suspected spinal fractures.

Sample between 2005 and 2011, this study examined the patterns of spinal fracture in this population.
- SCI occurred in 21.1% of patients, and 13.1% of patients had fractures in more than 1 region of the spine.
- In-hospital mortality in the population was 6.6%, and 29.4% of patients had an adverse event during the inpatient stay.

References