


Factors Associated With Major Complications and Mortality During Hospitalization in Patients With Ankylosing Spondylitis Undergoing Surgical Management for a Spine Fracture

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Abstract

Study design: Retrospective study.

Objectives: To analyze factors associated with major complications (MC) in patients with ankylosing spondylitis (AS) undergoing surgical management for a spine fracture.

Methods: Included were all persons with spine fractures and AS in a tertiary health care center between 2003 and 2019. Clinical data and MC were characterized with descriptive characteristics. Multivariable analyses were used to find factors associated with MC.

Results: In total, 174 traumatic fracture incidents in 166 patients with AS were included, with a mean patient age of 70.7 ± 13.1 years. The main reason for spine fracture was minor trauma (79.9%). Spinal cord injuries (SCI) were described in 36.7% of cases. The majority of patients (54.6%) showed more than one fracture of the spine, with cervical fractures being the most common (50.5%). Overall, the incidences of surgical site infection, implant failure, nosocomial pneumonia (NP), and mortality were 17.2%, 9.2%, 31%, and 14.9%, respectively. ICU stay > 48 hours was associated with MC (including death). Posterior approach for spondylodesis, ICU stay > 48 hours and cervical SCI were related to MC (excluding death). Age > 70 years, NP and Charlson comorbidity index > 5 points were associated with in-hospital mortality.

Conclusions: Patients with AS and surgical treatment of spine fractures are at high risk for MC. Therefore, our results might give physicians better insight into the incidence and sequelae of major complications and therefore might improve patient and family expectations.

Keywords

ankylosing spondylitis, complications, factors, fractures, outcome, spine

Introduction

Due to the unstable nature of spine fractures in patients with ankylosing spondylitis (AS), surgical treatment is the first line of choice, with superior clinical outcomes when compared to conservative treatment and immobilization.^{1,2} However, complication rates and elevated mortality rates after surgical management are significantly higher in patients with AS compared to normal spine trauma patients without preexisting bony

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abnormalities.³⁻⁵ Some authors have tried to explain this based on increased age, number of comorbidities or AS-related osteoporosis and decreased vital capacity, with possible risk of pulmonary complications.⁶⁻⁸

While there is increasing interest in better understanding the major complications (MC) of patients with AS undergoing surgical management for a spine fracture, there remains limited research in the area. Most of the existing literature on spinal fractures in patients with an ankylosed spine is limited to studies and reviews that grouped AS and diffuse idiopathic skeletal hyperostosis (DISH) as ankylosing spinal disorders (ASD).^{1,3,5,9-15} Some of these studies described a significant association between mortality and increased age, number of comorbidities, and minor trauma, but they included patients with conservative as well as surgical management of these 2 disease entities.^{5,10,11} Other researchers were able to show treatment results of large patient populations with AS by using extracted data from predefined variables in national databases.^{2,4,6,7,16} Their data showed significantly higher rates of surgical site infection (SSI), nosocomial pneumonia (NP) and total medical complications in surgically treated patients with AS compared to patients without AS or demonstrated that increased age, male gender, increased rates in the Charlson comorbidity index (CCI), cervical spine fractures, spinal cord injury (SCI), and NP are predictors of mortality after conservative or surgical management in patients with AS.^{2,4,7}

However, the current literature lacks information with respect to factors that may be associated with MC, such as SSI, implant failure (IF), NP, and death, in patients with AS during hospitalization. Furthermore, no monocentric data of a large patient population with AS undergoing surgical management for a spine fracture over a long observation period have been described to the best of our best knowledge. The purpose of the present study was: (1) to show the incidences of SSI, IF, NP, and death; and (2) to examine factors associated with these MC in patients with AS undergoing surgical management for a spine fracture.

Our hypothesis was that: (1) MC in patients with AS are common after surgical management; and (2) several factors in the patients and spine fracture characteristics, as well as surgical management data, will be associated with MC, which might be important for the treating physicians to provide prognostic information and to improve patient and family expectations.

Methods

Study Design and Selection Criteria

This retrospective, monocentric study was performed at a department of general and trauma surgery and a department of spinal cord injuries (SCI) in a university, tertiary health care center. It was approved by the local ethics committee (no. of approval 20-6845-BR). Patients were identified from the institute databases using the keywords “fracture” and “spine” and “AS” or “spine fracture” and “AS.” Demographic data, clinical findings, distribution of fractures, SCI, surgical treatment,

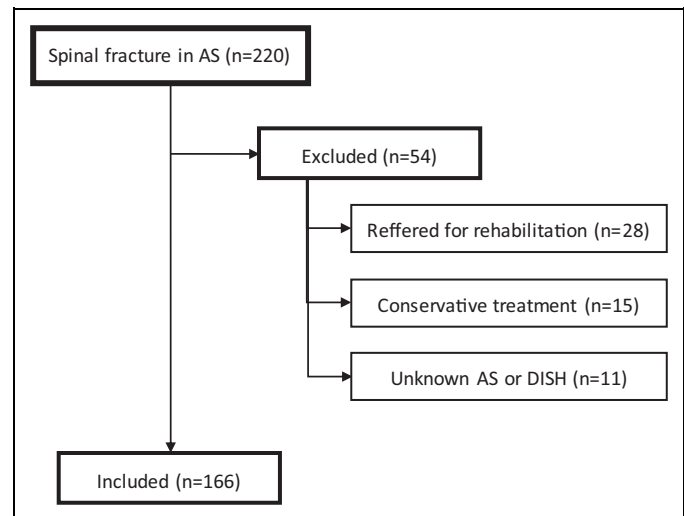


Figure 1. Flow diagram showing results of patient search. Abbreviations: AS ankylosing spondylitis, DISH diffuse idiopathic skeletal hyperostosis.

length of stay (LOS) in hospital and intensive care unit (ICU), and MC were retrospectively evaluated.

All patients with AS and a traumatic fracture of the spine between January 1, 2003 and December 31, 2019 were included. Patients younger than 18 years; with spine fractures and unknown preexisting AS, DISH or Forestier's disease; conservative management of spine fractures in AS; and patients referred for rehabilitation of SCI after surgical treatment of spine fractures in AS in other hospitals were excluded. Therefore, of 220 patients with the diagnoses of spine fracture in AS, 54 were excluded, resulting in 166 patients who met the criteria and were included in the analysis (Figure 1).

Data Collection

In addition to standard parameters, such as number of patients, referral, age, sex, body mass index (BMI), admission to the ICU, need for tracheostomy, LOS in hospital and ICU, the following relevant comorbidities were analyzed in the study: chronic heart failure (CHF), classified as New York Heart Association grade II or higher,¹⁷ chronic obstructive pulmonary disease (COPD) with preexisting medication, diabetes mellitus with preexisting medication and chronic renal failure (CRF), classified as Kidney Disease Outcome Quality Initiative grade 2 or higher.¹⁸ Preoperative hypoalbuminemia was classified as a serum albumin less than 3.5 g/dL before surgical treatment.¹⁹ The CCI as a measure of patient comorbidity burden was also calculated for each patient.²⁰

Delayed diagnosis was defined as lack of documentation of an existing spinal fracture within 24 hours of the patient's initial assessment. Minor trauma was classified as simple ground-level falls or falls from sitting position.

Spinal fractures were classified as single or multiple fractures of one region of the spine (cervical, thoracic and lumbar) or as multiregion fractures (cervical and thoracic, cervical and

lumbar, thoracic and lumbar, and as fractures of all regions of the spine). SCI were divided into incomplete or complete paraplegia or tetraplegia of the cervical, thoracic and lumbar spinal cord and classified according to the American Spinal Injury Association (ASIA) impairment scale (AIS) A to D.²¹ Neurological improvement of SCI during hospitalization was classified as improvement of one grade or more on the AIS.

Surgical treatment was defined as any operative procedure by an anterior and/or posterior approach of the spine, e.g. decompression and screw or plate fixation with or without graft implantation from the iliac crest or cage implantation because of unstable fractures of the spine with or without SCI. Surgical stabilization of the spine was performed via fusion surgery of one region of the spine (cervical, thoracic and lumbar) or as multiregion spondylodesis of the spine (cervical and thoracic, cervical and lumbar, thoracic and lumbar, lumbar and sacral, and as spondylodesis of all regions of the spine). A definitive stabilization of the spine fractures within one surgery was defined as single-stage surgery.

Major Complications

MC during hospitalization were divided into SSI, IF, NP and death or in-hospital mortality. These complications were chosen based on the available literature, stating that wound infections, IF, pneumonia or respiratory insufficiency, and death are the most common complications in patients with fractures of the ankylosed spine.³ SSI was defined based on the Centers for Disease Control and Prevention definition for deep SSI.^{22,23} In brief, this definition includes signs of infection, such as temperature $> 38^{\circ}\text{C}$, localized edema, erythema, deep wound dehiscence, and / or purulent drainage with the presence of organisms cultured from the wound or the presence of a deep abscess. Persistent unstable fractures after initial surgical treatment or failed osteosynthesis was considered as IF and led to surgical revision. NP was classified as new infiltrate on chest radiograph plus 2 of the following symptoms: abnormal white blood cell count ($< 4000 \mu\text{l}$ or $> 12000 \mu\text{l}$), presence of fever or hypothermia ($< 36^{\circ}\text{C}$ or $> 38^{\circ}\text{C}$), purulent sputum and deterioration in gas exchange.²⁴ Death or in-hospital mortality was defined as death of patients with spine fractures in AS after surgical treatment during hospitalization.

Bivariable Analysis

The following variables were used to test the associated factors of MC in patients with AS undergoing surgical management for a spine fracture: referral, male gender, age > 70 years, BMI > 30 , CHF, COPD, diabetes mellitus, CRF, alcohol use, nicotine use, preoperative hypoalbuminemia, CCI of zero points, CCI of one to 2 points, CCI of 3 to 4 points, CCI > 5 points, delayed diagnosis > 24 hours, minor trauma, single and multiple fractures of one region and multiregion fractures of the spine (cervical, cervical and thoracic, cervical and lumbar, thoracic, thoracic and lumbar, lumbar, and fractures of all regions of the spine), SCI, cervical SCI, thoracic SCI, lumbar SCI, AIS A,

AIS B, AIS C, AIS D, AIS E, surgery > 24 hours after diagnosis, 2-stage surgery, surgery > 8 p.m., surgery time > 3 hours, blood transfusion during surgery, loss of blood cells > 750 ml during surgery, anterior approach, posterior approach and combined approach, spondylodesis of one region and multiregion spondylodesis of the spine (cervical, cervical and thoracic, cervical and lumbar, thoracic, thoracic and lumbar, lumbar, lumbar and sacral, and spondylodesis of all regions of the spine), ICU stay > 48 hours after surgery, the need for tracheostomy, SSI, IF, NP, and death.

Statistical Analysis

Statistical analysis was performed using Microsoft[®] Office Excel[®] for Mac 2019 (Microsoft Corporation, Redmond, WA, USA) and IBM[®] SPSS[®] Statistics Version 26 2019 (IBM Corporation, Armonk, NY, USA). For categorical variables, frequency counts were computed and presented along with their percentages. For continuous variables, means were computed along with their standard deviations. Bivariable analysis was performed to compare statistical differences of MC (SSI, IF, NP, and death). Chi-square tests or Fisher's exact tests were used to compare these categorical variables. In the multivariable logistic regression models for MC (including death), MC (excluding death), and death, only variables significant at the $p \leq 0.05$ level were included. Significance for final results was set at $p \leq 0.05$ a priori.

Results

Clinical Data on Admission

We identified 174 traumatic fracture incidents in 166 patients with AS undergoing surgical management. The mean age of the 32 women and 134 men was 70.7 ± 13.1 years, with a mean BMI of $28 \pm 4.9 \text{ kg/m}^2$. Two women and 6 men received surgical treatment of different regions of the spine because of simple ground-level falls with new spine fractures at different times during the observation period. Most of the included patients ($n = 139 / 79.8\%$) fractured their spine after minor trauma; delayed diagnosis was described in 79 patients (45.4%), with a mean of 11.4 ± 11.6 days (range 2–73 days) from trauma to diagnosis.

Comorbidities were common in the study population, with a description of CRF in 50 patients (28.7%), COPD in 53 patients (30.5%), and diabetes mellitus in 75 patients (43.7%). Pre-existing CHF was documented in 119 patients (68.4%). Further patient characteristics are summarized in Table 1.

A single fractured vertebra in one spinal region was observed in 79 patients (45.4%). Over half of patients ($n = 95 / 54.6\%$) showed more than one fracture of the spine after trauma, with multiple fractures of one region in 70 patients (40.2%) and multiregion fractures in 25 patients (14.4%). The cervical spine was the region most commonly fractured, with fractures in 88 patients (50.5%). Fractures in the thoracic spine were present in 84 patients (48.2%) and fractures in the lumbar

Table 1. Clinical Data of All Patients Before Surgical Management (n = 174).

	Total
Baseline characteristics	
Patients	166
Male	134 (77)
Age (years)	70.7 ± 13.1
BMI (kg/m ²)	28 ± 4.9
Referral	133 (76.4)
Minor trauma	139 (79.9)
Delayed diagnosis	79 (45.4)
Comorbidities	
Chronic heart failure	119 (68.4)
COPD	53 (30.5)
Diabetes mellitus	76 (43.7)
Chronic renal failure	50 (28.7)
Hypalbuminemia	21 (12.1)
CCI (points)	1.9 ± 1.8
Region of fracture	
Cervical spine	68 (39.1)
Thoracic spine	65 (37.4)
Lumbar spine	16 (9.2)
Multiregion	25 (14.3)
Cervical and thoracic spine	13 (7.5)
Cervical and lumbar spine	6 (3.4)
Thoracic and lumbar spine	5 (2.9)
Cervical, thoracic and lumbar spine	1 (0.6)
Vertebrae involved in fracture	
One	79 (45.4)
Two or more	95 (54.6)
SCI	
Cervical	31 (17.8)
Thoracic	27 (15.5)
Lumbar	6 (3.4)

Data presented as absolute numbers (percentage) or mean ± standard deviation.

Abbreviations: BMI body mass index, COPD chronic obstructive pulmonary disease, CCI Charlson comorbidity index, SCI spinal cord injury.

spine in 28 patients (16.1%). Spine fractures with SCI were present in 64 patients (36.7%) and mainly affected the cervical spine (n = 31 / 17.8%) and thoracic spine (n = 27 / 15.5%). These details are also listed in Table 1.

Surgical Treatment and Postoperative Care

Surgical treatment within 24 hours after diagnosis of a spine fracture was obtained in 108 patients with AS (62.1%). Surgery time within 3 hours was observed in 101 patients (58%), and spondylodesis of a spine fracture in the daytime was performed in 129 patients (74.1%). In total, 65 patients (37.3%) needed blood transfusions during surgery, and loss of blood greater than 750 ml was documented in 38 patients (21.8%) (Table 2).

A dorsal approach for spondylodesis was used in 117 patients (67.2%), followed by a combined approach in 32 patients (18.4%) and an anterior approach in 25 patients (14.3%). Spondylodesis of one region of the spine was obtained

Table 2. Clinical Data of All Patients After Surgical Management (n = 174).

	Total
Surgical management	
Surgery < 24 hours after diagnosis	108 (62.1)
Surgery time < 3 hours	101 (58)
Surgery > 8 p.m.	45 (25.8)
Two-stage surgery	13 (7.4)
Blood transfusion	65 (37.3)
Loss of blood > 750 ml	38 (21.8)
Approach	
Anterior	25 (14.3)
Posterior	117 (67.2)
Combined	32 (18.4)
Region of spondylodesis	
Cervical	40 (23)
Thoracic	36 (20.7)
Lumbar	1 (0.6)
Multiregion	97 (55.7)
Cervical and thoracic	40 (23)
Thoracic and lumbar	46 (26.4)
Lumbar and sacral	3 (1.7)
Cervical, thoracic and lumbar	8 (4.6)
Major complications	
Surgical site infection	30 (17.2)
Implant failure	16 (9.2)
Nosocomial pneumonia	54 (31)
Death	26 (14.9)
LOS	
ICU (days)	13.7 ± 21.8
Hospital (days)	55.7 ± 60.9

Data presented as absolute numbers (percentage) or mean ± standard deviation.

Abbreviations: LOS length of stay, ICU intensive care unit.

in 77 patients (44.3%), and instrumentation of 2 or more regions of the spine was necessary in 97 patients (55.7%).

Overall, 158 patients (92%) were admitted to the ICU postoperatively, and 91 of them (52.3%) had an ICU stay > 48 hours. Mean LOS in the ICU of all patients was 13.7 ± 21.8 days (range 1–116 days) (Table 2). Tracheostomy during the ICU stay was needed in 43 patients (24.7%).

Major Complications During Hospitalization

MC in patients with AS undergoing surgical management for a spine fracture were found in 87 patients (50%). The reported incidences of MC were as follows: SSI, 17.2%; IF, 9.2%; and NP, 31% (Table 2). In-hospital mortality was 14.9%. Reasons for death during hospitalization were NP 21 (80.7%), followed by 4 cardiac arrests (15.4%) and one intracerebral hemorrhage (3.8%). The time from trauma to death after surgical management was 32 ± 23 days (range 3–77 days).

CRF and ICU stay > 48 hours were significantly different in at least 3 tested bivariable analyses of MC. Significant differences in age > 70 years, COPD, hypalbuminemia, CCI > 5 points, cervical SCI, AIS A and the need for tracheotomy were found in at least 2 MC (Tables 3–6).

Table 3. Bivariable Analysis of Surgical Site Infection After Surgical Management (n = 174).

	Yes (n = 30)	No (n = 144)	p value*
Diabetes mellitus	18 (60)	58 (40.2)	0.048
Chronic renal failure	13 (43.3)	37 (25.7)	0.045
Thoracic spine fracture	17 (56.6)	48 (33.3)	0.016
Posterior approach	27 (90)	90 (62.5)	0.004
Thoracic spondylodesis	12 (40)	24 (16.6)	0.004
Red blood cell loss > 750 ml	11 (36.6)	27 (18.7)	0.031

Data presented as absolute numbers (percentage).

*p ≤ 0.05, Chi square test or Fisher's exact test.

Table 4. Bivariable Analysis of Implant Failure After Surgical Management (n = 174).

	Yes (n = 16)	No (n = 158)	p value*
Surgery time > 3 hours	12 (75)	61 (38.6)	0.007
ICU stay > 48 hours	12 (75)	79 (50)	0.048

Data presented as absolute numbers (percentage).

Abbreviations: ICU intensive care unit.

*p ≤ 0.05, Chi square test or Fisher's exact test.

Table 5. Bivariable Analysis of Nosocomial Pneumonia After Surgical Management (n = 174).

	Yes (n = 54)	No (n = 120)	p value*
Age > 70 years	40 (74)	63 (52.5)	0.007
COPD	24 (44.4)	29 (24.1)	0.007
Chronic renal failure	21 (38.8)	29 (24.1)	0.024
Hypoalbuminemia	11 (20.3)	10 (8.3)	0.041
CCI 3 to 4 points	17 (31.4)	20 (16.6)	0.027
CCI > 5 points	9 (16.6)	8 (6.6)	0.041
Delayed diagnosis	38 (70.3)	41 (34.1)	0.001
Multiregion fractures	12 (22.2)	13 (10.8)	0.048
SCI	34 (62.9)	30 (25)	0.000
Cervical SCI	24 (44.4)	7 (5.8)	0.000
AIS A	19 (35.1)	7 (5.8)	0.000
Combined approach	17 (31.4)	15 (12.5)	0.005
Surgery > 8 p.m.	21 (38.8)	24 (20)	0.008
Blood transfusion	26 (48.1)	39 (32.5)	0.048
ICU stay > 48 hours	50 (92.6)	41 (34.1)	0.000
Tracheostomy	36 (66.6)	7 (5.8)	0.000

Data presented as absolute numbers (percentage).

Abbreviations: COPD chronic obstructive pulmonary disease, CCI Charlson comorbidity index, SCI spinal cord injury, AIS American Spinal Injury Association impairment scale, ICU intensive care unit.

*p ≤ 0.05, Chi square test or Fisher's exact test.

As listed in Table 7, multivariable regression analyses demonstrated that ICU stay > 48 hours (odds ratio (OR) 4.12, 95% confidence interval (CI) 2.19–14.19, p = 0.025) was significantly associated with MC (including death). A posterior approach for spondylodesis (OR 4.86, 95% CI 1.17–20.25, p = 0.030), ICU stay > 48 hours (OR 4.97, 95% CI 1.94–12.74, p = 0.001) and cervical SCI (OR 5.65, 95% CI 1.03–31.03, p = 0.046) were significantly related to MC (excluding

Table 6. Bivariable Analysis of In-Hospital Mortality After Surgical Management (n = 174).

	Yes (n = 26)	No (n = 148)	p value*
Age > 70 years	23 (88.4)	80 (54)	0.001
BMI > 30 kg/m ²	11 (42.3)	35 (23.6)	0.047
Chronic heart failure	23 (88.4)	96 (64.8)	0.017
COPD	14 (53.8)	39 (26.3)	0.005
Chronic renal failure	16 (61.5)	34 (22.9)	0.000
Hypoalbuminemia	8 (30.7)	13 (8.7)	0.002
CCI > 5 points	11 (42.3)	6 (4)	0.000
Cervical SCI	10 (38.4)	21 (14.1)	0.003
AIS A	10 (38.4)	16 (10.8)	0.000
Blood transfusion	17 (65.3)	48 (32.4)	0.001
ICU LOS > 48 hours	23 (88.4)	68 (45.9)	0.000
Tracheostomy	16 (61.5)	27 (18.2)	0.000
NP	21 (80.7)	33 (22.3)	0.000

Data presented as absolute numbers (percentage).

Abbreviations: BMI body mass index, COPD chronic obstructive pulmonary disease, CCI Charlson comorbidity index, SCI spinal cord injury, AIS American Spinal Injury Association impairment scale, ICU intensive care unit, NP nosocomial pneumonia.

*p ≤ 0.05, Chi square test or Fisher's exact test.

Table 7. Associated Factors of Major Complications (n = 174).

Major complications including death	OR	95% CI	p value*
ICU > 48 hours	4.12	2.19–14.19	0.025
Major complications excluding death	OR	95% CI	p value*
Posterior approach	4.86	1.17–20.25	0.030
ICU > 48 hours	4.97	1.94–12.74	0.001
Cervical SCI	5.65	1.03–31.03	0.046
Death	OR	95% CI	p value*
Age > 70 years	8.63	1.11–62.50	0.039
NP	16.06	2.56–100.48	0.003
CCI > 5 points	39.93	4.46–357.58	0.001

Data presented as odds ratio with 95 % confidence interval.

Abbreviations: ICU intensive care unit, SCI spinal cord injury, NP nosocomial pneumonia, CCI Charlson comorbidity index, OR odds ratio, CI confidence interval.

*p ≤ 0.05.

death). Age > 70 years (OR 8.63, 95% CI 1.11–62.50, p = 0.039), NP (OR 16.06, 95% CI 2.56–100.48, p = 0.003) and CCI > 5 points (OR 39.93, 95% CI 4.46–357.58, p = 0.001) were significantly associated with in-hospital mortality.

Clinical Data on Discharge

Mean LOS in the hospital was 55.7 ± 60.9 days (Table 2), including all patients with SCI and postoperative rehabilitation at the department of SCI at the authors' institute. Neurological improvement during hospitalization was noted in 20 patients (11.5%). Two patients improved from AIS A to C (1.1%), 4 from AIS B to C (2.3%), 3 from AIS B to D (1.7%), one from AIS B to E (0.6%), 8 from AIS C to D (4.6%), and 2 from AIS D to E (1.1%) (Table 8).

Table 8. Neurological Status on Admission and on Discharge (n = 174).

AIS on admission		AIS on discharge					Death
		AIS A	AIS B	AIS C	AIS D	AIS E	
AIS A	26 (14.9)	14 (8)	-	2 (1.1)	-	-	10 (5.7)
AIS B	9 (5.2)	-	1 (0.6)	4 (2.3)	3 (1.7)	1 (0.6)	-
AIS C	13 (7.5)	-	-	2 (1.1)	8 (4.6)	-	3 (1.7)
AIS D	16 (9.2)	-	-	-	13 (7.4)	2 (1.1)	1 (0.6)
AIS E	110 (63.2)	-	-	-	2 (1.1)	96 (55.1)	12 (6.9)
Total	174 (100)	14 (8)	1 (0.6)	8 (4.6)	26 (14.9)	99 (56.9)	26 (14.9)

Data presented as absolute numbers (percentage).

Abbreviations: AIS American Spinal Injury Association impairment scale.

Neurological deterioration was observed in 2 patients (1.1%) after surgical treatment of unstable fractures (from AIS E to AIS D). Of the 148 patients (85.1%) who survived the in-hospital stay, 89 patients (51.1%) were discharged home, 36 patients (20.6%) were referred to acute (geriatric) rehabilitation and 23 patients (13.2%) were discharged to a nursing home.

Follow Up

Follow up (FU) data after discharge from the hospital were collected from 84 patients (48.3%) after 12 weeks. No re-admission to the hospital because of SSI or IF during was documented the observation period at the authors' institute.

Discussion

We were able to perform a monocentric analysis in a large patient population with AS undergoing surgical management for a spine fracture over an observation period of 17 years. The main findings of this study were that: (1) patients with AS have high incidences of SSI (17.2%), IF (9.2%), NP (31%), and death (14.9%); and (2) several factors are significantly associated with MC. ICU stay > 48 hours was related to MC (including death). A posterior approach for spondylosis, ICU stay > 48 hours and cervical SCI were associated with MC (excluding death). AS patients aged > 70 years and CCI > 5 points on admission and NP during hospitalization had increased odds of death. We believe that determining the factors associated with MC will help the treating physicians in their discussions with patients and the patients' legal representatives about outcome expectations.

While there is increasing interest in better understanding the MC of patients with AS undergoing surgical management for a spine fracture, there remains limited research in the literature. Westerveld et al published data of 345 surgically and conservatively treated patients with spine fractures in AS in their systematic review.³ In total, 187 patients (59.2%) received surgical treatment. The rates of MC in the surgical group were 4.8% for SSI, 17.6% for IF, and 6.4% for NP. Overall mortality within 3 months after injury was 17.7%. We found different incidences of MC in our series, except for mortality. However, the authors used 76 articles to publish data of 345 patients with spine fracture in AS and reported a mean age of 59.1 years in the

AS cohort, which is significantly lower than our cohort (70.7 years), possibly explaining the decreased rates of SSI and NP. However, the authors did not discuss the high incidence of IF. Analyses of the National Inpatient Sample (NIS) database or the PearlDiver Patient Records database with the inclusion of more than 900 patients with AS each showed lower rates of SSI, IF, NP and in-hospital mortality compared to our results.^{4,6,7,16} However, the use of national databases may have led to under-reported or inaccurate data of MC, with the bias of misinterpretation of the available data because of the accuracy of billing codes and miscoding or noncoding by physicians as potential sources of error. We were unable to find any other explanation for the different incidences. Several monocentric studies have also examined clinical outcomes of patients with ASD undergoing conservative or surgical management for a spine fracture, often grouping AS with DISH, which significantly limits the ability to compare our AS-specific results.^{5,9-11,14,15}

Overall, the incidences of SSI, IF, NP, and in-hospital mortality were in line with our results and showed on one hand that patients with AS or DISH undergoing surgical management have high risks of complications and, on the other hand, that NP, IF, NP and death are the main complications during hospitalization.^{5,9-11,14,15} Despite the above mentioned limitations for comparison, the authors would like to comment that all studies reported useful information of MC in patients with ASD undergoing surgical management for a spine fracture.^{3-6,9-16}

We were able to describe several factors that increased the odds of postoperative MC in patients with AS. In our study, all associated factors of MC during hospitalization were non-modifiable factors in AS patients with acute, unstable spine fracture and the need of spinal fusion without delay. We therefore believe our findings might be important to give physicians better insight into the incidence and sequelae of MC in patients with traumatic fractures of the ankylosing spine, provide prognostic information, and improve the patient and family expectations before surgical treatment. Patients and the patients' legal representatives need to know about the potentially high risk of adverse events during hospitalization.

To the best of our best knowledge, associated factors of MC, such as ICU stay, cervical SCI or posterior approach of spondylosis, have not been described in the literature in patients with AS or DISH undergoing surgical treatment for a spine

fracture.^{3-6,9-16} Vazan et al listed a mean ICU stay of 11.6 days in their monocentric study of 41 ASD patients, with surgical management and the need of tracheostomy in 5 patients (12.2%) because of prolonged weaning.¹⁴ Another monocentric study with 112 ASD patients by Caron et al reported about the need for tracheostomy in 11 patients (10%).¹⁰ However, the authors described no further information about the ICU stay or possible adverse effects.^{10,14} Correlations between the ICU stay, age, comorbidity, tracheostomy, NP and mortality are well known in the literature, causing important worldwide health problems and being associated with substantial morbidity and mortality.²⁵⁻²⁷ Despite the paucity of comparable studies, we believe these findings can also be applied to patients with AS.

SCI rates after traumatic spine fractures in patients with ASD range between 27.5% and 58%.^{9,10,16} However, only 2 studies have described an association of SCI after traumatic spine fractures with MC.^{9,16} No data of cervical SCI were listed in their analyses. Previous reports of SCI patients older than 65 years even without ASD showed an increased risk of complications and worse functional outcomes.^{28,29} Overall, we believe that older patients with AS and (cervical) SCI, especially AIS A, are at high risk of suffering from MC after traumatic spine fracture. A posterior approach for spondylodesis was also associated with MC (excluding death) in our study. However, surgical stabilization via a posterior approach was only significantly different in our bivariable analysis of SSI. These findings were also published as risk factors for SSI in general spine surgery and were likely also the main reasons in our study.^{30,31} The general trend in the literature is for a combined anterior-posterior approach to have the highest risk of SSI, followed by posterior approach, with the anterior approach often reducing the risk of SSI.³²

Associated factors of mortality in patients with an ankylosed spine are well described in the current literature.^{2,5,7,11,16} It should be noted that all studies used data of conservatively and surgically treated patients with AS or DISH for their analyses. Similar to our findings, data from the NIS between 2005 and 2011 have shown that increased age, increased rates of comorbidities, and NP along with other factors, such as cervical spine fractures and SCI, are associated with in-patient mortality in hospitalized patients with AS.^{7,16} This was also described by Robinson et al by using extracted data from 1987 to 2011 in the Swedish patient registry and Swedish mortality registry.² AS patients with older age and higher rates in the CCI next to SCI and male gender had increased odds of death during hospitalization. In addition, older age was also related to mortality in monocenter studies with ASD patients.^{5,11} Based on the included data, we indicate that older male AS patients with several comorbidities and the diagnosis of a cervical spine fracture with concomitant SCI on admission and the occurrence of NP during hospitalization are at especially high risk of death after surgical treatment.^{2,5,7,11,16} We therefore believe that our findings will be important to provide prognostic information about clinical outcomes for the treating physicians, patients and their families.

There are several limitations associated with the present study that should be considered. A retrospective study design

may often lead to underreporting of comorbidities and mortality. The lack of a control group did not allow any specific recommendations regarding independent predictors associated with MC. The purpose of this study was to analyze factors associated with MC exclusively during the hospitalization of patients with AS. Therefore, we did not intend to analyze any follow-up data beyond 12 weeks. Furthermore, the institutional review board approval did not include a recall for FU. Nevertheless, patients suffering a MC might have been treated in a different hospital, and some bias is possible and likely to cause an attenuation in the reported incidences. Therefore, conclusions based on our results should be drawn carefully. However, we present a large patient population with AS undergoing surgical treatment for a spine fracture in a university, tertiary health care center over a long observation period and were able to find several factors significantly associated with MC.

Conclusion

Patients with AS and surgical treatment of spinal fractures are at high risk of MC during hospitalization. From the authors point of view, it is of high clinical significance to characterize factors associated with postoperative MC in this population. Overall, we quantified clinical outcomes, showing that the incidences of SSI, IF, NP, and mortality during hospitalization were high. ICU stay > 48 hours was related to MC (including death). A posterior approach for spondylodesis, ICU stay > 48 hours and cervical SCI were associated with MC (excluding death). AS patients aged > 70 years and CCI > 5 points on admission and NP during hospitalization had increased odds of death. We believe our results will give physicians better insight into the incidence and sequelae of major complications in patients with fractures of the ankylosing spine, provide prognostic information and improve patient and family expectations. However, future research with large matched control cohorts is needed to find independent predictors of MC in patients with AS undergoing surgical management for a spine fracture.

Authors' Note

CU, EY and CK had full access to all data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. CU and EY are responsible for the study design. EY, MH, CR, MA, TAS and CK contributed substantially to the study design, data analysis and interpretation and the writing of the paper.

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References

- Reinhold M, Knop C, Kneitz C, Disch A. Spine fractures in ankylosing diseases: recommendations of the spine section of the German society for Orthopaedics and Trauma (DGOU). *Global Spine J*. 2018;8(2 suppl):56S-68S.
- Robinson Y, Willander J, Olerud C. Surgical stabilization improves survival of spinal fractures related to ankylosing spondylitis. *Spine (Phila Pa 1976)*. 2015;40(21):1697-1702.
- Westerveld LA, Verlaan JJ, Oner FC. Spinal fractures in patients with ankylosing spinal disorders: a systematic review of the literature on treatment, neurological status and complications. *Eur Spine J*. 2009;18(2):145-156.
- Puvanesarajah V, Cancienne JM, Shimer AL, Shen FH, Hassan-zadeh H. Complications after fusion for thoracolumbar fractures in patients with ankylosing spondylitis. *Global Spine J*. 2017;7(1):28-32.
- Westerveld LA, van Bommel JC, Dhert WJ, Oner FC, Verlaan JJ. Clinical outcome after traumatic spinal fractures in patients with ankylosing spinal disorders compared with control patients. *Spine J*. 2014;14(5):729-740.
- Kurucan E, Bernstein DN, Mesfin A. Surgical management of spinal fractures in ankylosing spondylitis. *J Spine Surg*. 2018;4(3):501-508.
- Wysham KD, Murray SG, Hills N, Yelin E, Gensler LS. Cervical spinal fracture and other diagnoses associated with mortality in hospitalized ankylosing spondylitis patients. *Arthritis Care Res (Hoboken)*. 2017;69(2):271-277.
- Kanathur N, Lee-Chiong T. Pulmonary manifestations of ankylosing spondylitis. *Clin Chest Med*. 2010;31(3):547-554.
- Teunissen FR, Verbeek BM, Cha TD, Schwab JH. Spinal cord injury after traumatic spine fracture in patients with ankylosing spinal disorders. *J Neurosurg Spine*. 2017;27(6):709-716.
- Caron T, Bransford R, Nguyen Q, Agel J, Chapman J, Bellabarba C. Spine fractures in patients with ankylosing spinal disorders. *Spine (Phila Pa 1976)*. 2010;35(11):E458-E464.
- Bernstein DN, McCalla DJ, Molinari RW, Rubery PT, Menga EN, Mesfin A. An analysis of patient and fracture characteristics and clinical outcomes in patients with hyperostotic spine fractures. *Global Spine J*. 2020;10(8):964-972.
- Rustagi T, Drazin D, Oner C, et al. Fractures in spinal ankylosing disorders: a narrative review of disease and injury types, treatment techniques, and outcomes. *J Orthop Trauma*. 2017;31(suppl 4):S57-S74.
- Hartmann S, Tschugg A, Wipplinger C, Thomé C. Analysis of the literature on cervical spine fractures in ankylosing spinal disorders. *Global Spine J*. 2017;7(5):469-481.
- Vazan M, Ryang YM, Barz M, Török E, Gempt J, Meyer B. Ankylosing spinal disease-diagnosis and treatment of spine fractures. *World Neurosurg*. 2019;123:e162-e170.
- Schiefer TK, Milligan BD, Bracken CD, et al. In-hospital neurologic deterioration following fractures of the ankylosed spine: a single-institution experience. *World Neurosurg*. 2015;83(5):775-783.
- Lukasiewicz AM, Bohl DD, Varthi AG, et al. Spinal fracture in patients with ankylosing spondylitis: cohort definition, distribution of injuries, and hospital outcomes. *Spine (Phila Pa 1976)*. 2016;41(3):191-196.
- Crouch MA. Chronic heart failure: developments and perspectives. *Consult Pharm*. 2005;20(9):751-765.
- Patel SS, Kimmel PL, Singh A. New clinical practice guidelines for chronic kidney disease: a framework for K/DOQI. *Semin Nephrol*. 2002;22(6):449-458.
- Ryan SP, Politzer C, Green C, Wellman S, Bolognesi M, Seyler T. Albumin versus American Society of Anesthesiologists Score: which is more predictive of complications following total joint arthroplasty? *Orthopedics*. 2018;41(6):354-362.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
- Maynard FM Jr, Bracken MB, Creasey G, et al. International standards for neurological and functional classification of spinal cord injury. American Spinal Injury Association. *Spinal Cord*. 1997;35(5):266-274.
- Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg*. 2017;152(8):784-791.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol*. 1999;20(4):250-278; quiz 279-280.
- Ottosen J, Evans H. Pneumonia: challenges in the definition, diagnosis, and management of disease. *Surg Clin North Am*. 2014;94(6):1305-1317.
- Cillóniz C, Dominedò C, Torres A. An overview of guidelines for the management of hospital-acquired and ventilator-associated pneumonia caused by multidrug-resistant Gram-negative bacteria. *Curr Opin Infect Dis*. 2019;32(6):656-662.
- Klompas M. Prevention of intensive care unit-acquired pneumonia. *Semin Respir Crit Care Med*. 2019;40(4):548-557.
- Ding C, Zhang Y, Yang Z, et al. Incidence, temporal trend and factors associated with ventilator-associated pneumonia in mainland China: a systematic review and meta-analysis. *BMC Infect Dis*. 2017;17(1):468.
- Arul K, Ge L, Ikpeze T, Baldwin A, Mesfin A. Traumatic spinal cord injuries in geriatric population: etiology, management, and complications. *J Spine Surg*. 2019;5(1):38-45.
- Wilson JR, Davis AM, Kulkarni AV, et al. Defining age-related differences in outcome after traumatic spinal cord injury: analysis of a combined, multicenter dataset. *Spine J*. 2014;14(7):1192-1198.
- Gu W, Tu L, Liang Z, et al. Incidence and risk factors for infection in spine surgery: a prospective multicenter study of 1764 instrumented spinal procedures. *Am J Infect Control*. 2018;46(1):8-13.
- Olsen MA, Mayfield J, Laurysen C, et al. Risk factors for surgical site infection in spinal surgery. *J Neurosurg*. 2003;98(2 suppl):149-155.
- Yao R, Zhou H, Choma TJ, Kwon BK, Street J. Surgical site infection in spine surgery: who is at risk? *Global Spine J*. 2018;8(4 suppl):5S-30S.