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ORIGINAL RESEARCH

Ankylosing spondylitis and mortality following hospitalised pneumonia: a population-based cohort study

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ABSTRACT

Objective Little is known about the prognosis of infections in patients with ankylosing spondylitis (AS) compared with patients without AS. The purpose of this study was to examine whether AS is associated with poorer outcomes in patients who are hospitalised with pneumonia.

Methods In a population-based cohort study including patients with hospitalised pneumonia with and without AS, we compared 90-day rates of mortality, all-cause readmission (90 days post-discharge) and pulmonary complications including pulmonary embolism, empyema and pulmonary abscess. We used Cox regression analyses to compute crude and adjusted HRs while adjusting for sex, age and level of comorbidity.

Results A total of 387 796 patients (median age 71 years) were hospitalised for pneumonia in Denmark between 1997 and 2017. Among these, 842 (0.2%) had AS (median age 65 years). The 90-day mortality was 12.5% in patients with AS and 15.5% in patients with non-AS pneumonia, with crude and adjusted 90-day HRs of 0.79 (95% CI 0.66 to 0.96) and 0.95 (95% CI 0.79 to 1.16), respectively. The 90-day post-discharge readmission rate was 27.3% in patients with AS and 25.4% in patients without AS, with a corresponding adjusted readmission HR of 1.12 (95% CI 0.98 to 1.27). Relative risk of pulmonary complications among patients with AS compared with patients without AS decreased over the study period, with adjusted HRs of 1.63 (95% CI 0.82 to 3.27) in 1997–2006 falling to 0.62 (95% CI 0.31 to 1.23) in 2007–2017.

Conclusions AS is not associated with increased mortality following hospitalisation for pneumonia. Furthermore, no increased risk of readmission or pulmonary complications in patients with AS was detected in recent study years.

Key messages

What is already known about this subject?

- Ankylosing spondylitis is associated with increased mortality compared with general population members of similar age.
- A highly increased risk of respiratory infections among patients with ankylosing spondylitis has been reported, and this may add to an increased risk of death.

What does this study add?

- Patients with ankylosing spondylitis did not exhibit an increased mortality or increased risk of readmission following hospitalisation with pneumonia.
- Furthermore, an initially elevated risk for pulmonary complications in patients with ankylosing spondylitis decreased over time.

How might this impact on clinical practice?

- Reassuringly, current management of pneumonia in patients with ankylosing spondylitis appears appropriate.

INTRODUCTION AND AIMS

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease often diagnosed in young age and with average age at disease onset of 24.8 years.[1] AS is associated with increased mortality compared with general population members of similar age.[2 3] Previous studies have found this fact to be related to an increased cardiovascular and cerebrovascular mortality, but also to an increased risk of death from infections including respiratory tract infections.[4 5]

A highly increased risk of respiratory infections among patients with AS was reported (OR 5.83, 95% CI 3.38 to 10.1) in a German study comparing the cumulative prevalence of self-reported infections in the previous 12 months among 1080 patients with AS and 102 patients with disc herniation.[6] In contrast, little is known about the *prognosis* of infections in patients with AS compared with members of the general population without AS. It therefore remains unclear if the increased risk of dying from respiratory and other infections in AS can be explained solely by an increased risk of acquiring infections, or if patients with AS have worse infection outcomes as well.

Pneumonia remains a common cause of morbidity and mortality worldwide. A study from 2013 showed that pneumonia hospitalisations in Denmark increased from 4.96/1000 population in 1997 to 8.09 in 2011. The mortality following hospitalised

Table 1 Characteristics of patients with and without ankylosing spondylitis (AS) who were hospitalised for pneumonia from 1997 to 2016 in Denmark

	AS N (%)	Non-AS N (%)
N	842 (0.2)	386.954 (99.8)
Age, median (IQR)	65 (52–74)	71 (57–81)
16–29 years	22 (2.6)	15.965 (4.1)
30–44 years	102 (12.1)	35.690 (9.2)
45–59 years	195 (23.2)	58.375 (15.1)
60–74 years	316 (37.5)	111.667 (28.9)
75 years and above	207 (24.6)	165.247 (42.7)
Sex		
Female	218 (25.9)	190.532 (49.2)
Male	624 (74.1)	196.422 (50.8)
Pneumonia 1997–2006	274 (0.2)	161.597 (99.8)
Pneumonia 2006–2017	568 (0.3)	224.500 (99.7)
Comorbidity within 10 years before pneumonia		
Congestive heart failure	97 (11.5)	30.946 (8.0)
Peripheral vascular disease	66 (7.8)	26.598 (6.9)
Previous myocardial infarction	48 (5.7)	20.386 (5.3)
Chronic pulmonary disease	152 (18.1)	60.981 (15.8)
Cerebrovascular disease	91 (10.8)	48.986 (12.7)
Hemiplegia	19 (2.7)	1.917 (0.5)
Dementia	7 (0.8)	13.304 (3.4)
Connective tissue disease	79 (9.4)	9.834 (2.5)
Peptic ulcer disease	54 (6.4)	17.479 (4.5)
Diabetes type I and II	77 (9.1)	30.399 (7.8)
Diabetes with end organ damage	46 (5.5)	17.004 (4.4)
Moderate to severe renal disease	45 (5.3)	13.961 (3.6)
Any tumour	98 (11.6)	52.629 (13.6)
Leukaemia	5 (0.6)	3.484 (0.9)
Lymphoma	13 (1.5)	6.205 (1.6)
Metastatic solid tumour	18 (2.1)	9.365 (2.4)
Mild liver disease	16 (1.9)	5.636 (1.5)
Moderate-to-severe liver disease	2 (0.2)	1.72 (0.45)
AIDS	0	545 (0.1)
Comorbidity index (level of Charlson Index Score)		
Low (0)	350 (41.6)	180.629 (46.8)
Medium (1–2)	316 (37.5)	137.850 (35.7)
High (≥3)	176 (20.1)	67.934 (17.6)
Duration of hospital stay in days, median (IQR)	6 (3–11.5)	7 (4–12)

pneumonia is high and seems largely unchanged over decades.[7] To date, no population-based pneumonia cohort outcome study has focused on patients with AS.

Pre-existing lung disease is associated with poorer outcomes after pneumonia.[8 9] Studies have reported that lung disease including apical fibrosis, interstitial lung disease and chest wall abnormalities are associated with AS, and that chronic obstructive pulmonary disease (COPD) is more frequent among patients with AS than controls.[10 11] Moreover, inflammatory disease activity and AS-related therapy might influence pneumonia outcomes.

We hypothesised that AS is associated with increased mortality, risk of complications and readmission in patients who are hospitalised with pneumonia. In addition, we wanted to explore if relative risks of these outcomes decreased over time in patients with AS versus patients without AS, and if AS disease activity and AS therapy influence the pneumonia prognosis.

PATIENTS AND METHODS

Setting and study population

We conducted a population-based cohort study in Denmark with approximately 5.8 million inhabitants. All Danish citizens are assigned a unique personal identification number (CPR) at birth or immigration which we used to cross-link data from different medical registries at the individual level.[12] We used the Danish National Patient Register (DNPR) to identify patients with pneumonia. Since 1977, the DNPR has recorded all inpatient hospitalisations in the entire Danish population and since 1995 all instances of contact with hospital outpatient clinics. The DNPR records admission and discharge dates and up to 20 discharge diagnoses per contact coded according to the International Classification of Diseases, edition 10 (ICD-10) during the period of this study and ICD-8 during earlier periods.[13] The records also include CPR numbers, patients' municipalities, identification of the hospital wards, and dates and times of activities performed, including information on the type of examinations, surgeries and treatments. We included all adult patients (≥16 years) with a first-time *primary* hospital discharge diagnosis of pneumonia (for ICD-10 codes, please see online additional file 1) between January 1997 and 31 July 2017; thus, patients with a prior discharge diagnosis of pneumonia were excluded. A previous evaluation of the validity of the pneumonia diagnosis in DNPR found a positive predictive value (PPV) of 90% (95% CI 82% to 95%).[14]

Data on AS

Data on AS were obtained from the DNPR and DANBIO (for ICD codes, please see online additional file 1). While DANBIO contains information on subcohorts of patients with AS, all patients with AS seen in hospital clinics are registered in the DNPR. DANBIO is a nationwide, Danish register where clinical data on patients with rheumatic diseases are recorded. DANBIO was initiated in 2000 as a nationwide voluntary register, and in 2006 DANBIO was approved by the Danish National Board of Health as a national quality of care registry.[15] Since then, it has been mandatory to register all patients with AS on biologics and

Table 2 90-day all-cause mortality following hospitalisation with pneumonia in patients with or without ankylosing spondylitis (AS)

	All-cause mortality at 90 days N (%)		HRs 90-day mortality	
			Crude	Adjusted*
	AS	Non-AS	AS	AS
All patients hospitalised for pneumonia 1997–2017†	105 (12.5)	59.767 (15.5)	0.79 (0.66 to 0.96)	0.95 (0.79 to 1.16)
1997–2006	38 (13.9)	25.208 (15.6)	0.88 (0.64 to 1.21)	1.03 (0.75 to 1.41)
2007–2017†	67 (11.8)	34.559 (15.4)	0.76 (0.59 to 0.96)	0.94 (0.74 to 1.20)

HRs, including 95% CIs, calculated using Cox proportional-hazards regression analysis. Patients without AS used as reference group.
*Adjusted for sex, age and level of comorbidity before admission.
†Until 31 July 2017.

since 2015 all newly diagnosed patients with AS. Patients are registered in DANBIO, when they are seen by a rheumatologist in hospital or private outpatient clinics. The recorded information includes the current treatment, disease activity (see below), C reactive protein, functional status and visual analogue scale scores of pain, fatigue, and of the patient and physician's global assessment.

Data on disease activity and functional status

We obtained information on the latest registration of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) from DANBIO. BASDAI combines information on morning stiffness, localised tenderness, fatigue and joint pain (reference), and in Denmark a score above 4 usually indicates that the patient is a candidate for treatment with biologics. The BASDAI has a good test–retest (r=0.93; p<0.001) reliability, reflects the entire spectrum of disease and is sensitive to change.[16]

We used the Bath AS Functional Index (BASFI) as a measure of the patient's functional limitation and the Bath AS Metrology Index (BASMI) as a measure of the patient's axial status. BASMI has been found reproducible for both intraobserver (r=0.99, p<0.001) and interobserver variability (r=0.97, p<0.001) and sensitive to change.[17] BASFI has been shown as a reliable tool in assessing function in patients with AS and is able to capture changes across the whole spectrum of disease.[18]

Data on medication

Data on AS treatment were assessed from both DNPR and DANBIO.[15] In the DNPR, treatment with disease-modifying antirheumatic drugs (DMARDs) and biologics are coded in relation to visits at hospital outpatient clinics. For AS outpatient visits, the use and types of DMARDs and/or biologics are recorded. We retrieved DNPR information on all treatments registered within 12 months prior to pneumonia hospitalisation. For the subgroup of patients with pneumonia who were registered in the DANBIO database, we also retrieved information from the last visit within 12 months before the pneumonia hospitalisation. If the patient had more than one registration in DANBIO within that year, the latest visit data were used.

We categorised all patients with AS according to the type of preadmission AS medication into the following groups: treatment with DMARD (either as monotherapy or as DMARD combination therapy), anti-TNF alfa treatment as monotherapy, anti-TNF alfa treatment in combination with one or more DMARDs, and no recorded AS therapy. The patients were categorised according to the last registered treatment type before the pneumonia hospitalisation.

Comorbidity data

We obtained information on the 19 conditions included in the Charlson Comorbidity Index recorded within 10 years before the pneumonia hospitalisation from the DNPR. A previous study found the coding in the DNPR for the 19 Charlson conditions to have an overall PPV of 98%.[19] In addition, the index has previously been validated as a predictor of 1-year mortality following hospitalisation.[20 21] We did not include the AS diagnosis when we computed the Charlson Comorbidity Index score, and we categorised the scores into three levels: score of 0, low; score of 1–2, medium; score of 3+, high.

Pneumonia outcomes

Death from any cause within 90 days from the pneumonia hospitalisation was a main study outcome. We ascertained the exact date of eventual death from the Danish Civil Registration System.[12] Other outcomes were all-cause readmission rate within 90 days after initial pneumonia hospitalisation discharge, and hospital diagnoses of pulmonary complications associated with the initial hospitalisation or up to 90 days after the admission date. We defined complications as pulmonary embolism, empyema or pulmonary abscess (please see online supplementary appendix for ICD-10 codes). Information on both readmission and pulmonary complications were obtained from the DNPR.

Statistical analysis

Pneumonia prognosis in patients with AS versus patients without AS

We followed all patients with pneumonia from the date of pneumonia admission until death, migration or 90 days after the discharge date, whichever came first. We

Table 3 90-day all-cause readmission and complications following hospitalisation with pneumonia in patients with and without ankylosing spondylitis (AS)

	1997–2017*		1997–2006		2007–2017*	
	AS	Non-AS	AS	Non-AS	AS	Non-AS
90-day readmission, n (%)	230 (27.3)	98.445 (25.4)	78 (28.5)	39.106 (24.2)	152 (26.8)	59.238 (26.4)
Crude 90-day HR	1.08 (0.95 to 1.22)	1.00 (ref)	1.14 (0.91 to 1.43)	1.00 (ref)	0.96 (0.82 to 1.12)	1.00 (ref)
Adjusted 90-day HR†	1.12 (0.98 to 1.27)	1.00 (ref)	1.15 (0.92 to 1.44)	1.00 (ref)	1.05 (0.89 to 1.23)	1.00 (ref)
Pulmonary complication, n (%)	16 (1.9)	7.610 (2.0)	8 (2.9)	2.650 (1.6)	8 (1.4)	4.941 (2.2)
Crude HR complication	0.99 (0.61 to 1.62)	1.00 (ref)	1.74 (0.87 to 3.48)	1.00 (ref)	0.60 (0.30 to 1.21)	1.00 (ref)
Adjusted HR complication	0.97 (0.59 to 1.58)	1.00 (ref)	1.63 (0.82 to 3.27)	1.00 (ref)	0.62 (0.31 to 1.23)	1.00 (ref)

HRs with 95% CIs were calculated using a Cox proportional-hazards model.
*Until 31 July 2017.
†Adjusted for sex, age and level of comorbidity (Charlson Index).

estimated mortality, rates for readmission and pulmonary complications after 90 days for patients with AS and patients without AS. Cox regression was used to compute crude and adjusted HRs for death, readmission and pulmonary complications within 90 days following admission for pneumonia while comparing patients with AS and those without AS, controlling for age, sex and level of comorbidities. In order to evaluate if the prognostic impact of AS on pneumonia changed over time, we stratified the analysis by calendar time for pneumonia diagnosis (1997–2006 and 2007–2017).

Prognostic effect of AS disease activity and therapy among patients with AS

Internally among patients with pneumonia with AS, we compared 90-day mortality between high and low levels of preadmission BASDAI (reference: BASDAI <4), BASFI (reference: BASFI <4) and BASMI (reference BASMI <4). We also compared 90-day mortality associated with the different treatment categories, using 'no treatment' as reference. We used Cox regression while adjusting for sex, age and level of comorbidities.

Statistical analyses were performed using the Stata V.12.1 statistical software package (StataCorp, College Station, TX, USA). We presented HRs as point estimates with 95% CIs.

RESULTS

A total of 387 796 patients were hospitalised for pneumonia between 1997 and 2017. Among these 842 (0.2%) had AS. As expected, the proportion of men was higher among patients with AS (74.1%) than among patients without AS (50.8%) (table 1). Patients with AS were younger (median age 65 vs 71 years) and had higher comorbidity including higher prevalence of chronic lung disease. Among patients with AS, 57.6% had one or more comorbidities compared with 53.3% among patients without AS. The median duration of hospital stay for patients with AS was 6(3-15) days compared with 7(4-12) days for patients without AS.

Mortality in patients with AS versus patients without AS

We found a 90-day mortality in patients with pneumonia with AS of 12.5% compared with 15.5% in patients with non-AS pneumonia. Corresponding crude 90-day HR was 0.79 (95% CI 0.66 to 0.96). After adjustment for differences in age the HR increased to 1.07 (95% CI 0.88 to 1.29), and with further adjustment for sex and comorbidity, the HR was 0.95 (95% CI 0.79 to 1.16) (table 2).

Among patients without AS, the 90-day pneumonia mortality remained steady across the two calendar periods with rates of 15.6% and 15.4%, while the 90-day mortality in patients with AS tended to be highest in the first period with a rate of 13.9% compared with 11.8% in the second period. When comparing the 90-day mortality between patients with AS and patients without AS, we found adjusted HRs of 1.03 (95% CI 0.75 to 1.41) in the

first period 1997–2006 and 0.94 (95% CI 0.74 to 1.20) in the second period 2007–2017.

Readmission and pulmonary complications in patients with AS versus patients without AS

Among the patients with AS, 27.3% were readmitted within 90 days after discharge compared with 25.4% of the patients without AS. The corresponding crude 90-day post-discharge HR for readmission was 1.08 (95% CI 0.95 to 1.22), and the adjusted HR was 1.12 (95% CI 0.98 to 1.27). The readmission rate among patients with AS patients was slightly lower in the second period (26.8%) than in the first (28.5%) (table 3), resulting in adjusted HRs of readmission associated with AS of 1.15 (95% CI 0.92 to 1.44) in the first period and 1.05 (95% CI 0.89 to 1.23) in the second period. The risk of pulmonary complications among patients with AS compared with patients without AS decreased more clearly over time, with adjusted HRs of complications for the first and second periods of 1.63 (95% CI 0.82 to 3.27) and 0.62 (95% CI 0.31 to 1.23), respectively.

Prognostic effect of AS functional status, disease activity and therapy

Prior to admission, 185 (22%) of the patients with AS had at least one registration in DANBIO. In 133 patients, the last registration was within 1 year prior to admission (table 4). The proportion of men was 70.8%, similar to the entire cohort, while the patients in DANBIO were slightly younger than in the entire cohort of patients with AS with a median age of 55 (43–65).

BASDAI measurements within 1 year prior to admission were available for 110 patients. Compared with the group with low BASDAI (<4), we found crude and adjusted 90-day HR for mortality with BASDAI >4 of 1.00 (95% CI 0.95 to 1.05) and 0.99 (95% CI 0.94 to 1.05), respectively. BASFI measurements were available for 109 patients. Compared with the group with low BASFI (<4), crude and adjusted 90-day HR for mortality with BASFI >4 were 1.03 (95% CI 0.97 to 1.08) and 1.02 (95% CI 0.96 to 1.09), respectively. BASMI measurements were available for 70 patients. Compared with the group with low BASMI (<4), we found crude and adjusted 90-day HR for mortality with BASMI >4 of 1.01 (95% CI 0.96 to 1.06) and 0.99 (95% CI 0.94 to 1.05), respectively.

Among the patients with AS, 18 (2%) were treated with one or more DMARDS, 87 (10.3%) were treated with anti-TNF alfa monotherapy and 44 (5.2%) received a combination of anti-TNF alfa and DMARDs. Among non-treated patients, 68% were 60 years or older compared with patients treated with either anti-TNF alfa monotherapy or in combination with DMARDs, of which 33% and 27% were 60 years or older, respectively. Among patients treated with DMARDs, 55% were 60 years or older and in this group 50% were women—while in all other groups approximately 70% were men. The 90-day mortality was higher among non-treated (13.6%) than patients treated with DMARD (5.6%), anti-TNF (5.8%) or anti-TNF alfa and DMARD in combination (6.8%), respectively. The low number of exposed hampered our ability to adjust for potential confounding factors. Neither anti-TNF alfa monotherapy, treatment with DMARDs nor anti-TNF alfa therapy in combination with one or more DMARDS were associated with increased mortality (table 5).

Table 4 Characteristics of patients with ankylosing spondylitis who were hospitalised for pneumonia from 1997 to 2016 in Denmark and registered in DANBIO

	Registration in DANBIO at any time prior to the hospitalisation for pneumonia	Registration in DANBIO 0–12 months prior to the hospitalisation for pneumonia
N	185	133
Age, median (IQR)	53.8 (43–65)	52.2 (42–62)
16–29 years (%)	10 (5.4)	6 (4.5)
30–44 years (%)	44 (23.8)	34 (25.6)
45–59 years (%)	60 (32.4)	52 (39.1)
60–74 years (%)	56 (30.3)	33 (24.8)
75 years and above	15 (8.1)	8 (6.0)
Sex		
Female (%)	54 (29.2)	38 (28.6)
Male (%)	131 (70.8)	95 (71.4)
Year of pneumonia hospitalisation		
1997–2006	8	8
2006–2017	177	125
Comorbidity index (Charlson Index Score)		
Low (0)	103 (55.7)	80 (60.2)
Medium (1–2)	54 (29.2)	35 (26.3)
High (≥3)	28 (15.1)	18 (13.5)
Patients with BASDAI available (%)	148 (80.0)	110 (82.7)
BASDAI <4 (% of available)	66 (44.5)	51 (46.4)
Patients with BASFI available (%)	146 (78.9)	109 (82.0)
BASFI <4 (% of available)	62 (42.5)	52 (47.7)
Patients with BASMI available (%)	95 (51.4)	70 (52.6)
BASMI <4 (% of available)	49 (51.7)	39 (55.7)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath AS Functional Index; BASMI, Bath AS Metrology Index.

DISCUSSION

In this population-based study including 842 patients with AS and more than 350 000 patients without AS hospitalised due to pneumonia, patients with AS did not have higher mortality, complications and readmission rates than patients without AS after adjustment for confounding factors.

Table 5 All-cause mortality in patients with AS following hospitalisation for pneumonia according to preadmission as therapy

	N	All-cause mortality at 90 days, N (%)	HRs 90-day mortality	
			Crude	Adjusted*
No DMARD, no anti-TNF alfa	693	96 (13.6)	1 (ref)	1 (ref)
DMARD	18	1 (5.6)	0.39 (0.05 to 2.77)	0.52 (0.07 to 3.76)
Anti-TNF alfa	87	5 (5.8)	0.64 (0.41 to 1.00)	0.95 (0.60 to 1.51)
Anti-TNF alfa and DMARD combination	44	3 (6.8)	0.78 (0.53 to 1.14)	1.01 (0.69 to 1.49)

HRs, including 95% CIs, were calculated using a Cox proportional-hazards model.
*Adjusted for sex, age and level of comorbidity before admission.
AS, ankylosing spondylitis; DMARD, disease-modifying antirheumatic drug; TNF, tumour necrosis factor.

Lung disease is associated with AS. This includes chronic apical fibrosis, interstitial lung disease and chest wall abnormalities.[10 11] A recent study from Israel including 4076 patients with AS and 20 290 age-matched and sex-frequency-matched controls found a higher proportion of COPD in patients with AS than in controls (46% vs 18%).[11] We found only a slightly higher prevalence of COPD among our patients with AS than in the patients with non-AS pneumonia (18% vs 15%), but no increased crude pneumonia mortality versus non-AS individuals. In the study from Israel, the diagnoses of COPD is based on data derived from both hospital and primary care physicians' clinical records, while our study included records from hospitals and not primary care physicians. It is likely that patients with one chronic disease like AS are more likely to see their physician on a regular basis and therefore more likely to be diagnosed with COPD even in case of very mild symptoms. This is in contrast to patients either referred to hospital with COPD or diagnosed with COPD at hospitals, who are more likely to suffer from more severe COPD.

The AS pneumonia mortality was slightly higher in the first half of our study period (1997–2006) than in the second period (2007–2017). This may be partly caused by the fact that predominantly patients with AS with severe AS disease were seen at hospitals in the beginning of our study period and thus registered with a diagnosis of AS in the DNPR. In the second period (2007–2017), biologics were commonly used for AS and the new treatment strategies likely resulted in patients with AS being more commonly hospital registered, but also treated more efficiently. It is also possible that prednisolone was used more frequently in the first period and that this may have affected the outcome following pneumonia. Unfortunately, we lacked information on use of prednisolone so we could not address this any further.

The strengths of this study include the accuracy and the size of the data sources used. Complete follow-up data from detailed, high-quality registries allowed for extensive control of confounders. Both selection and recall bias were limited because of the prospectively recorded population-based data independently of our research question. We were able to adjust for a broad range of comorbidities using the Charlson Index, but not for lifestyle factors, such as smoking and body mass index. Since smoking is a major contributor to the risk and severity of COPD, the patients with AS might be more likely to be smokers, but the proportion of patients with AS with COPD was only slightly increased and this could not have substantially affected our results.

The identification of patients with AS through the DNPR may have excluded patients with AS with mild disease (ie, patients who were never treated at a hospital clinic or were admitted for another illness only without concomitant registration of AS in the DNPR). There is, however, no reason to suspect that their mortality should be higher following pneumonia hospitalisation than those of the patients with AS that we captured by our data sources.

Patients with AS receiving DMARDs and/or anti-TNF alfa therapy are closely monitored in the outpatient clinic and may be hospitalised earlier and/or more frequently in case of suspected infection than patients being managed without these treatments. Accordingly, at time of pneumonia hospitalisation, patients with AS receiving DMARDs and/or anti-TNF alfa therapy may be less seriously affected by the pneumonia which may result in a lower mortality.

Neither anti-TNF alfa monotherapy, treatment with DMARDs, nor anti-TNF alfa therapy in combination with one or more DMARDS were associated with increased pneumonia mortality in this study. However, the low number of drug-exposed patients and outcome events hampered our ability to adjust for all potential confounding factors, and these results should be interpreted with caution.

Patients with AS with high disease activity, decreased functional status or poorer axial status could have a poorer outcome of pneumonia than the average patient with AS. DANBIO data allowed us to identify patients with AS who potentially had high disease activity, decreased functional status and poor axial status at time of pneumonia diagnosis. We thus find it reassuring that these patients did not have high mortality following pneumonia, even if they only represent a minor part of the AS study population.

Recent studies have indicated that non-steroidal anti-inflammatory drug (NSAID) exposure at the early stage of community-acquired pneumonia is associated with a more complicated course and worse outcomes,

probably because NSAIDs mask initial symptoms and delay therapy.[22 23] It is likely that a large proportion of patients with AS in our study received NSAIDs since NSAIDs are first-line treatment in AS. Unfortunately, we lacked information on use of NSAIDs, and we were thus unable to examine whether pneumonia prognosis varied by use of these drugs. However, we did not find an increased mortality among patients with AS compared with patients without AS, which makes it unlikely that NSAID causes significantly increased mortality among patients with AS following pneumonia.

Conclusions

Despite the well-known association between AS and lung disease, our study, to our knowledge, is the first to investigate the influence of AS on the prognosis of pneumonia. Reassuringly, we found no increased pneumonia mortality among patients with AS. In addition, no increased risk of pneumonia complications or readmission was detected in patients with AS in recent years.

Contributors All authors formulated the scientific problem, interpreted the results and finalised the manuscript. MH-F was responsible for data collection and subsequent analysis. MH-F, RWT and MN developed the methods, and planned the experiments and methodology. MH-F wrote the first draft. All authors approved the final manuscript.

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Patient consent for publication Not required.

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