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Risk of tuberculosis in patients with spondyloarthritis: data from a centralized electronic database in Hong Kong

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Background/Objectives

Tuberculosis (TB) is one of the most infectious comorbidities in spondyloarthritis (SpA). Our goals were to determine the crude incidence rate of and risk factors for TB in SpA.

Methods

Clinical data of 2984 patients with SpA from 11 rheumatology centres were reviewed. This included demographics, duration of follow-up, comorbidities including diabetes, chronic kidney disease, chronic heart disease, chronic lung disease, stroke and malignancies, date of diagnosis of tuberculosis, use of non-steroidal anti- inflammatory drugs, duration of glucocorticoid therapy for more than 6 months, conventional (cDMARD) and biological (bDMARD) disease modifying anti-rheumatic drug therapies. Crude incidence rates were reported. Cox regression models were used to determine the risk factors for TB in patients with SpA.

Table 3 Crude incidence rates of TB

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	Patients with SpA		General population (11)	
Patient-years	27,308.4			
Number of events	43			
Incidence per 1000 patient-years	0.64		0.54	
	on DMARD	not on DMARD		
Patient-years	18,204.2	9104.2		
Number of events	29	14		
Incidence per 1000 patient-years	0.62	0.65	0.54	
	Male	Female	Male (age adjusted)	Female (age adjusted)
Patient-years	18,693.8	8614.5		
Average age	49	52		
Number of events	36	7		
Incidence per 1000 patient-years	0.52	1.23	0.48	0.41

TB Tuberculosis; *SpA* Spondyloarthritis; *DMARD* Disease modifying antirheumatic drug

Table 4 Univariate and multivariate cox regression models of tuberculosis in SpA

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	Univariate regression		Multivariate logistic regression	
Characteristic	**Hazard Ratio (95% CI)**	***P* value**	**Hazard Ratio (95% CI)**	***P* value**
Age (years)	0.93 (0.91–0.95)	< 0.001	0.94 (0.91–0.96)	< 0.001
Male sex	2.29 (1.02–5.15)	0.05	1.88 (0.79–4.50)	0.16
Smoking	1.74 (0.95–3.19)	0.07	1.19 (0.60–2.35)	0.62
Alcohol use	2.29 (1.06–4.94)	0.04	2.44 (1.03–5.80)	0.04
History of psoriasis	0.51 (0.21–1.20)	0.12		
History of IBD	1.43 (0.20–10.37)	0.73		
DM	0.72 (0.26–2.03)	0.54		
Past history of TB	6.88 (3.28–14.41)	< 0.001	5.92 (2.52–13.94)	< 0.001
CKD	0.89 (0.32–2.51)	0.83		
CLD	4.48 (2.07–9.72)	< 0.001	3.81 (1.60–9.06)	0.002
Malignancy	2.07 (0.74–5.80)	0.17		
CHD	0.88 (0.31–2.47)	0.81		
Other immunosuppressive states	0.95 (0.13–6.89)	0.96		
History of CVA	1.46 (0.52–4.09)	0.48		
Glucocorticoid therapy > 6 months	2.21 (0.93–5.25)	0.03	2.60 (1.01–6.70)	0.05
Sulfasalazine	0.63 (0.34–1.16)	0.14		
Methotrexate	0.57 (0.27–1.19)	0.13		
Lefluonomide	0.05 (0.00–13.72)	0.29		
Infliximab	5.08 (2.49–10.34)	< 0.001	3.94 (1.82–8.53)	< 0.001
Etanercept	0.57 (0.14–2.36)	0.44		
Adalimumab	1.83 (0.72–4.67)	0.21		
Certolizumab	0.05 (0.00–32,169)	0.66		
Golimumab	0.05 (0.00–13.94)	0.29		
Secukinumab	0.05 (0.00–282.43)	0.49		
Ustekinumab	0.05 (0.00–657,547)	0.72		

SpA Spondyloarthritis; *CI* Confidence interval; *IBD* Inflammatory bowel disease; *DM* Diabetes mellitus; *TB* Tuberculosis; *CKD* Chronic kidney disease; *CLD* Chronic lung disease; *CHD* Chronic heart disease; *CVA* Cerebrovascular accident

Table 1 Baseline characteristics of SpA patients with and without TB

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	SpA with TB	SpA without TB	*P* value	Total
Chinese ethnicity	43/43 (100%)	2896/2926 (99.0%)	0.51	2939/2969 (99.0%)
Male sex	36/43 (83.7%)	1993/2926 (68.1%)	0.03	2029/2969 (69.3%)
Age (years)	43.5 ± 16.2	49.9 ± 14.6	0.01	49.8 ± 14.6
Duration of follow up (years)	12.6 ± 5.5	9.2 ± 5.9	< 0.001	9.2 ± 1.2
Radiographic sacroiliitis	34/42 (81.0%)	1906/2784 (68.5%)	0.08	1305/1707 (76.4%)
HLA-B27 status	13/16 (81.3%)	1292/1691 (76.4%)	0.65	1940/2826 (68.6%)
Smoking	19/43 (44.2%)	856/2875 (29.8%)	0.04	875/2918 (30.0%)
Alcohol use	8/43 (18.6%)	232/2875 (8.1%)	0.01	240/2918 (8.1%)
Past history of TB	9/43 (20.9%)	69/2926 (2.4%)	< 0.001	78/2969 (2.6%)
psoriasis	6/43 (14.0%)	636/2926 (21.7%)	0.22	642/2969 (21.6%)
IBD	1/43 (2.3%)	46/2926 (1.6%)	0.69	47 (2969) (1.6%)
ReA	0/43 (0.0%)	6/2926 (0.2%)	0.77	6/2969 (0.2%)
Diabetes Mellitus	4/43 (9.3%)	265/2926 (9.1%)	0.96	269/2969 (9.1%)
Chronic kidney disease	4/43 (9.3%)	183/2926 (6.3%)	0.41	187/2969 (6.3%)
Malignancy	4/43 (9.3%)	111/2926 (3.8%)	0.06	115/2969 (3.9%)
Chronic lung disease	8/43 (18.6%)	90/2926 (3.1%)	< 0.001	98/2969 (3.3%)
Chronic heart disease	4/43 (9.3%)	190/2926 (6.5%)	0.46	194/2969 (6.5%)
Cerebrovascular accident	4/43 (9.3%)	99/2926 (3.4%)	0.04	103/2969 (3.5%)
Other immunosuppressive states	1/43 (2.3%)	56/2926 (1.9%)	0.85	57/2969 (1.9%)

SpA Spondyloarthritis; *TB* Tuberculosis; *IBD* Inflammatory bowel disease; *ReA* Reactive arthritis

Table 2 NSAID, glucocorticoid, and DMARD therapy in SpA with and without TB

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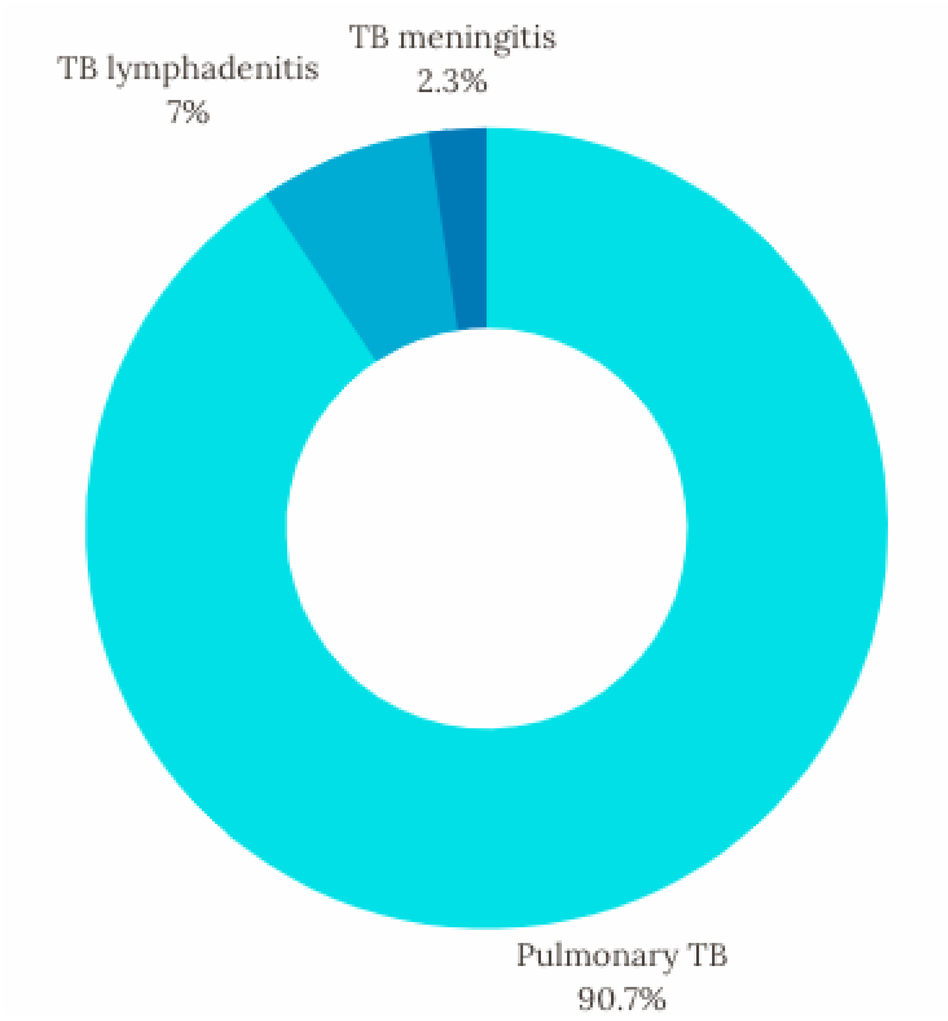
	SpA with TB	SpA without TB	*P* value
NSAIDs	43/43 (100.0%)	2783/2926 (95.1%)	0.14
glucocorticoid therapy > 6 months	6/43 (14.0%)	148/2926 (5.1%)	0.01
DMARDs	29/43 (67.4%)	1831/2926 (62.6%)	0.51
cDMARDs	21/43 (48.8%)	1609/2926 (55.0%)	0.42
sulfasalazine	16/43 (37.2%)	1253/2926 (42.8%)	0.46
methotrexate	9/43 (20.9%)	763/2926 (26.1%)	0.45
leflunomide	0/43 (0.0%)	156/2926 (5.3%)	0.12
bDMARDs	17/43 (39.5%)	709/2926 (24.2%)	0.02
TNFi	17/43 (39.5%)	666/2926 (22.8%)	0.001
infliximab	10/43 (23.3%)	98/2926 (3.3%)	< 0.001
etanercept	2/43 (4.7%)	268/2926 (9.2%)	0.31
adalimumab	5/43 (11.6%)	235/2926 (8.0%)	0.39
golimumab	0/43 (0.0%)	196/2926 (6.7%)	0.08
certolizumab	0/43 (0.0%)	39/2926 (1.3%)	0.45
secukinumab	0/43 (0.0%)	69/2926 (2.4%)	0.31
ustekinumab	0/43 (0.0%)	19/2926 (0.6%)	0.60

NSAID Non-steroidal anti-inflammatory drug; *SpA* Spondyloarthritis; *TB* Tuberculosis; *DMARDs* Disease modifying anti-rheumatic drugs; *cDMARDs* Conventional disease modifying antirheumatic drugs; *bDMARDs* Biologic disease modifying antirheumatic drugs; *TNFi* Tumour necrosis factor inhibitor

Fig.1 Sites of TB infection



Conclusion

Incidence of TB was higher in patients with SpA. Glucocorticoid therapy beyond 6 months and infliximab therapy increased the risk of TB. Rheumatologists should avoid prolonged use of glucocorticoids and consider DMAR Ds other than infliximab in the treatment of at-risk patients.