Reply to the comment on: Microscopic polyangiitis: clinical characteristics and long-term outcomes of 378 patients from the French Vasculitis Study Group Registry

by Nguyen *et al*.

Sirs,

We thank Bilgin and Karadag for their interest in our series of 378 microscopic polyangiitis (MPA) patients from the French Vasculitis Study Group (1).

Several series have reported that MPA-associated interstitial lung disease (ILD) was associated with poor prognosis (2). In a German MPA cohort, mortality was four times higher in MPA-ILD patients (hazard ratio [HR] 4.04; 95% confident interval [95% CI] 1.21–13.45); p=0.02) (3), although it has not been confirmed by others (4). In our series, interstitial lung disease (ILD) failed to reach statistical significance (hazard ratio [HR] 1.64; 95% CI 0.93–2.90; p=0.09), probably due to a lack of power, as only 14.6% of our MPA patients had ILD. However, our group recently published a dedicated case-control study, comparing 62 ILD patients with antineutrophil cytoplasmic antibody (ANCA)-associated small-vessel necrotising vasculitis (AAV) with 124 AAV controls without ILD (5). In this series, 3- and 5-year overall survival rates were lower in AAV-ILD patients (80% and 66% for cases *vs*. 89.6% and 83.8% for control, respectively, p=0.008). Interestingly, only the usual interstitial pattern (UIP) (HR 2.73; p=0.002) was associated with shorter survival, but not the non-specific interstitial pneumonia (NSIP) pattern. Thus, even though AAV-ILD is not an item from the 2009-five factors score (FFS), patients with UIP are at higher risk of poor outcome.

The revised 2009-FFS has been validated on 1,108 consecutive patients with systemic necrotising vasculitis including 218 MPA, 349 periateritis nodosa, 230 eosinophilic granulomatosis with polyangiitis, and 311 granulomatosis with polyangiitis (6). This score includes 4 factors associated with poorer prognosis (including age >65 years, cardiac symptoms, gastrointestinal involvement, and renal insufficiency) and 1 with better outcome (ear, nose, and throat [ENT] symptoms). In this cohort, ENT symptoms were associated with a reduced mortality (HR 0.64; 95% CI 0.44-0.9; p=0.01). Although not statistically significant, when considering only MPA patients, the strength of the association was of the same magnitude (HR 0.46; 95% CI 0.2–1.6; p=0.28). Thus, we believe that considering ENT symptoms in MPA patients in the FFS calculation is also of interest, even if those symptoms are less frequent in MPA patients than in other AAV patients. In addition, excluding ENT symptoms from the 2009-FFS in our series did not affect our results (HR 2.57; 95% CI 1.29–5.14; p=0.008 and HR 7.67; 95% CI 3.81–15.43; p<0.001 for modified FFS=1 and ≥2, respectively, compared with a modified FFS=0).

Baseline characteristics of the 347 patients with available ANCA-status are presented in Table I, according to their ANCA-status. ANCA-positive MPA patients were older at diagnosis, had more frequently renal, cutaneous and/or severe gastrointestinal manifestations, and less frequently mononeuritis multiplex. Their 2009 FFS was significantly higher, and thus they were more frequently treated with immunosuppressant in the induction regimen. However, those findings have to be interpreted with caution, as patients were treated in different time periods, and because only three patients were ELISA and IF ANCA-negative, but 46 were IF ANCA-negative without available high-quality ELISA results.

Neurological involvement occurred in 191 (50.5%) patients; 119 had mononeuritis multiplex, 10 had CNS involvement (including stroke), 23 had confusion or psychosis and 39 had polyneuropathies.

Regarding treatment options, induction therapy consisted of glucocorticoids alone for 90 patients (23.8%) and combined with immunosuppressants for 278 (73.5%). The remaining 10 (2.6%) patients underwent plasmapheresis with glucocorticoids but without immunosuppressant. Forty-six (12.2%) patients underwent plasma exchanges for severe renal involvement (n=28), alveolar haemorrhage (n=3), both (n=5) or severe mononeuritis multiplex (n=6). Of the remaining four patients, indications were

Table I. Main clinical characteristics of 347 microscopic polyangiitis patients at diagnosis according to their ANCA status.

Clinical characteristic	ANCA- n=49	ANCA+ n=298	p-value
Sex, male/female	16 (32.7)	169 (56.7)	0.003
Age at diagnosis, median [IQR]	56.0 (15.6)	62.4 (14.3)	0.004
Year of diagnosis			
<1990	7 (14.3)	6 (2.0)	<0.001
1990–2000	26 (53.1)	69 (23.2)	
2000–2010	13 (26.5)	131 (44.0)	
>2010	3 (6.1)	92 (30.9)	
Fever >38.5°C	24 (49.0)	128 (43.0)	0.53
Weight loss >2 kg within 3 months	32 (65.3)	163 (54.7)	0.22
Arthralgias	28 (57.1)	131 (44.0)	0.118
Myalgias	25 (51.0)	115 (38.6)	0.137
Lung manifestations	15 (30.6)	132 (44.3)	0.10
Alveolar haemorrhage	3 (6.1)	53 (17.8)	0.065
Interstitial lung disease	4 (8.2)	49 (16.4)	0.202
Pleural effusion	3 (6.1)	16 (5.4)	1.00
Renal manifestations	28 (57.1)	228 (76.5)	0.007
Serum creatinine >150 μmol/L	7 (14.3)	137 (46.0)	<0.001
Anuria	2 (4.1)	9 (3.0)	1.00
Need for dialysis	3 (6.1)	32 (10.7)	0.46
Cutaneous manifestations	33 (67.3)	109 (36.6)	<0.001
Purpura	15 (30.6)	52 (17.4)	0.049
Ear, nose & throat manifestations	4 (8.2)	44 (14.8)	0.309
Eye involvement	2 (4.1)	15 (5.0)	1.00
Cardiovascular manifestations	10 (20.4)	60 (20.1)	1.00
Pericarditis	3 (6.1)	18 (6.0)	1.00
Congestive heart failure (2009 FFS item)	2 (4.1)	13 (4.4)	1.00
Gastrointestinal involvement	12 (24.5)	41 (13.8)	0.085
Abdominal pain	11 (22.4)	31 (10.4)	0.031
Severe gastrointestinal manifestations	6 (12.2)	7 (2.3)	0.003
Neurological involvement	33 (67.3)	131 (44.0)	0.018
Central nervous system involvement	0 (0)	8 (2.7)	0.518
Mononeuritis multiplex	23 (46.9)	83 (27.9)	0.012
Immunosuppressant in the induction regimen	22 (44.9)	242 (81.2)	<0.001
2009 FFS at diagnosis			
0	22 (44.9)	59 (19.8)	0.002
1	18 (36.7)	141 (47.3)	
≥2	13 (26.5)	131 (44.0)	

Results are expressed as n (%) or median [interquartile range, IQR]. Comparisons were made using t-tests and Chi-^{2} tests as appropriate.
MPA: microscopic polyangiitis; FFS: Five-Factor Score.

severe bedridden state (n=1), severe skin involvement (n=1) or unknown (n=2). Finally, the retrospective nature of our study and the differences in the management of the patients within the large time scale of our study make us difficult to evaluate the treatments' efficacy in our analyses.

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