

## Original article

## Clinical presentation and long-term outcome of 144 patients with microscopic polyangiitis in a monocentric German cohort

Jan H. Schirmer<sup>1</sup>, Marvin N. Wright<sup>2</sup>, Reinhard Vonthein<sup>2,3</sup>, Kristine Herrmann<sup>1,a</sup>, Bernhard Nölle<sup>4</sup>, Marcus Both<sup>5</sup>, Frank O. Henes<sup>6</sup>, Andreas Arlt<sup>7</sup>, Wolfgang L. Gross<sup>8</sup>, Susanne Schinke<sup>1</sup>, Eva Reinhold-Keller<sup>1</sup>, Frank Moosig<sup>1</sup> and Julia U. Holle<sup>1</sup>

## Abstract

**Objective.** To evaluate the clinical presentation and long-term outcome of a vasculitis centre cohort of patients with microscopic polyangiitis (MPA) with respect to organ manifestations, treatment, chronic damage and mortality.

**Methods.** We performed a retrospective chart review at our vasculitis referral centre. MPA patients admitted between 1991 and 2013 classified by a modified European Medicines Agency algorithm were diagnosed and treated according to a standardized interdisciplinary approach.

**Results.** Comprehensive data from standardized interdisciplinary workups was available for 144 patients (median follow-up 72 months). The overall standardized mortality ratio was 1.40 (95% CI 0.91, 2.07;  $P=0.13$ ). We observed a higher mortality [hazard ratio (HR) 4.04 (95% CI 1.21, 13.45),  $P=0.02$ ] in 17 patients with MPA-associated fibrosing interstitial lung disease (ILD) and 56 patients with peripheral nervous system involvement [HR 5.26 (95% CI 1.10, 25.14),  $P=0.04$ ] at disease onset. One hundred and fifteen patients (79.9%) responded to the initial treatment. Sixty-one (42.3%) achieved complete remission and 54 (37.5%) achieved partial remission. Twenty (13.9%) showed a refractory disease course.

**Conclusion.** MPA patients at our tertiary rheumatology referral centre seemed to have a less severe phenotype resulting in a less severe disease course and better outcome than reported in other cohorts. Fibrosing ILD was significantly associated with mortality in this cohort.

**Key words:** pulmonary fibrosis, MPA, interstitial lung disease, ANCA, vasculitis.

## Rheumatology key messages

- Long-term outcome is good in microscopic polyangiitis patients with mild chronic renal disease.
- Fibrosing interstitial lung disease is a significant mortality factor in microscopic polyangiitis.
- Sensorimotor as well as distal symmetrical sensory neuropathy are frequent in microscopic polyangiitis.

<sup>1</sup>Department of Rheumatology, University Medical Center Schleswig-Holstein and Klinikum Bad Bramstedt, Bad Bramstedt, <sup>2</sup>Department of Medical Biometry and Statistics, University of Lübeck, University Medical Center Schleswig-Holstein, Campus Lübeck, <sup>3</sup>Center for Clinical Trials Lübeck, University of Lübeck, Lübeck, <sup>4</sup>Department of Ophthalmology, <sup>5</sup>Department of Radiology and Neuroradiology, University Medical Center Schleswig-Holstein, Campus Kiel, Kiel, <sup>6</sup>Clinic and Policlinic for Diagnostic and Interventional Radiology, University Medical Center Hamburg-Eppendorf, Hamburg, <sup>7</sup>Department of Medical and Neurological Rehabilitation, Klinikum Bad Bramstedt, Bad Bramstedt and <sup>8</sup>University Medical Center Schleswig-Holstein, Campus Lübeck, Lübeck, Germany

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## Introduction

Microscopic polyangiitis (MPA) is a pauci-immune necrotizing vasculitis, predominantly affecting small and medium-sized vessels, commonly involving the kidney and lung and

Correspondence to: Jan H. Schirmer, Vasculitis Center, Klinikum Bad Bramstedt, Department of Rheumatology and Clinical Immunology, Oskar-Alexander-Strasse 26, 24576 Bad Bramstedt, Germany.  
E-mail: j.schirmer@klinikumbb.de

<sup>a</sup>Present address: Department of Rheumatology, University Medical Center Carl Gustav Carus, Dresden, Germany

presenting as necrotizing GN or pulmonary capillaritis [1]. It is strongly associated with ANCA, usually with specificity to MPO and less frequently to PR3. Compared with the other ANCA-associated vasculitides (AAVs), granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis, older age, higher mortality and lower relapse rates have been observed in MPA [2, 3].

High frequencies of chronic renal disease (CRD) and end-stage renal disease (ESRD) are the most important complications of MPA with significant impact on survival [4]. Compared with the well-studied renal involvement affecting the majority of MPA patients, other organ manifestations have been studied in less detail. A significant proportion of MPA patients suffer from pulmonary involvement, especially diffuse alveolar haemorrhage (AH) and fibrosing interstitial lung disease (ILD). Fulminant AH and the pulmorenal syndrome (fulminant AH and renal failure) are important mortality factors in AAV [5]. The effect of fibrosing ILD on survival is controversial [6, 7].

Standardized monocentric long-term observations of large MPA cohorts are rare. In our tertiary referral centre, AAV patients have been diagnosed and treated for >20 years by an interdisciplinary team specializing in vasculitis by using standardized clinical workups for AAV [8]. The aim of this study was to describe the demographic data, clinical manifestations, treatment strategies and outcomes in a single centre.

## Methods

### Patients

Charts of MPA patients attending our department (Vasculitis Centre, Department of Rheumatology and Clinical Immunology, Bad Bramstedt, Germany) from February 1991 to December 2013 were reviewed. They were included in this study if they were classified as MPA using the European Medicines Agency (EMA) algorithm ( $n = 138$ ; 87 of these were biopsy proven according to the Chapel Hill Consensus Conference criteria) [1, 9]. We also included patients with positive PR3-C- or MPO-P-ANCA but without biopsy-proven vasculitis or renal involvement if they had a clinical vasculitis correlate ( $n = 3$  with pulmonary haemorrhage and  $n = 3$  with rapid progressive mononeuritis multiplex) and no evidence of granulomatous disease, other causes or other EMA algorithm exclusion criteria. AAV patients were not included if they were either double-positive for PR3 and MPO-ANCA or had biopsy-proven extrarenal small vessel vasculitis but a negative ANCA status and no signs of renal disease (unclassified small vessel vasculitis). To complete data until the end of 2013 for patients without follow-up visits and for mortality analysis, additional evidence such as reports from co-treating physicians were used and standardized phone interviews were carried out. This study was conducted retrospectively with the approval of the ethics committee of the University of Lübeck, Germany. Data were analysed anonymously.

### ANCA analysis

ANCA analysis was done by IIF and confirmed by ELISA as described earlier [8, 10].

### Definitions, disease assessment and outcome measures

Definitions of disease stages, activity and response to therapy were applied according to the EULAR recommendations for clinical studies in systemic vasculitis [11]. The BVAS was calculated routinely (in different versions) [12]. Remission was defined as BVAS=0 and a glucocorticoid dose  $\leq 10$  mg prednisolone equivalent and partial remission/response was defined as  $\geq 50\%$  reduction in BVAS. For calculation of disease extent and chronic damage, the Disease Extent Index and Vasculitis Damage Index were retrospectively applied to the patients [13, 14]. Fibrosing ILD was defined as evidence of pulmonary fibrosis with or without infiltrates or ground-glass opacities in radiographic reports. CT scans of 18 patients with fibrosing ILD were available and reviewed for plausibility.

### Treatment

Treatment was carried out according to EULAR recommendations for the management of primary small and medium vessel vasculitis [15]. Until CYC-sparing protocols were established [16], higher continuous oral CYC doses and higher cumulative CYC doses were used.

Generalized or severe renal disease was treated with high-dose prednisolone (1 mg/kg body weight, oral or i.v.) and CYC (pulsed or continuous oral) or rituximab (RTX). Cystitis prophylaxis with mesna and trimethoprim-sulfamethoxazole prophylaxis against *Pneumocystis jirovecii* pneumonia were routinely used in patients receiving CYC or RTX.

In cases of severe or progressive renal disease, plasmapheresis was performed at the treating physician's discretion. Refractory disease was treated using oral CYC or RTX. Single refractory cases were treated with anti-TNF agents.

For maintenance of remission and remission induction in early systemic disease, MTX (0.3 mg/kg body weight/week initially and folic acid substitution) or AZA (2 mg/kg body weight initially) were usually used (less frequently MMF, LEF or prednisolone monotherapy).

### Statistical analysis

Standardized mortality ratios (SMRs) were estimated using data from the Human Mortality Database for Germany from 1991 to 2011 [17]. For 2012 and 2013, no population and death counts were available and the data from 2011 were used. The SMRs were adjusted for the year of death, age and gender. CIs were computed assuming a Poisson distribution for the observed number of deaths. Survival rates for 1, 5, 10 and 20 years after first diagnosis were computed using the Kaplan-Meier estimator.

The effects of organ involvement and therapy on survival and relapse-free survival were explored by Kaplan-Meier plots. For both endpoints a proportional hazards model

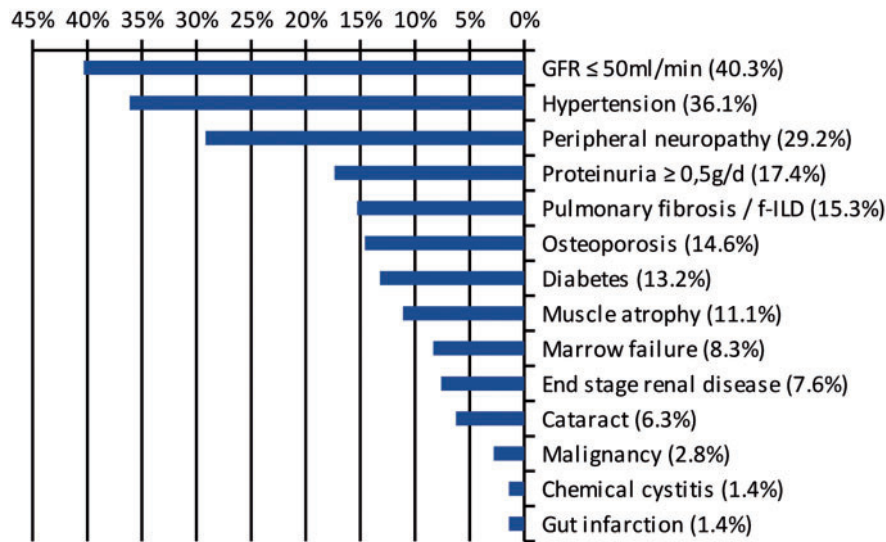
TABLE 1 Demography and organ involvement

Demography		
Age at diagnosis, mean (s.d.) [range], years		59.3 (14.4) [18–86]
Male:female, <i>n</i>		65:79
Follow-up		
Mortality from diagnosis, median (IQR) [range], months <sup>a</sup>		72.0 (74.5) [0–265]
Relapse from diagnosis, median (IQR) [range], months <sup>b</sup>		33.5 (58.8) [0–198]
Follow-up within centre, median (IQR) [range], months		18.5 (49.8) [0–197]
ANCA status, <i>n</i> (%)		
MPO-P-ANCA		138 (95.8)
PR3-C-ANCA		6 (4.2)
No ANCA		0 (0.0)
Disease severity and extent	Disease onset	Whole follow-up
Localized disease, <i>n</i> (%)	0 (0.0)	0 (0.0)
Early systemic disease, <i>n</i> (%)	9 (6.3)	7 (4.9)
Generalized disease, <i>n</i> (%)	118 (81.9)	120 (83.3)
Severe renal disease, <i>n</i> (%)	17 (11.8)	17 (11.8)
DEI, mean (s.d.) [range]	6.7 (2.3) [2–15]	7.1 (2.4) [2–15]
Organ involvement, <i>n</i> (%)	Disease onset	Whole follow-up
Lung	72 (50.0)	76 (52.8)
Alveolar haemorrhage	32 (22.2)	37 (25.7)
Fibrosing interstitial lung disease	17 (11.8)	22 (15.3)
Infiltrates, X-ray/CT	47 (32.6)	52 (36.1)
Pleural effusion	12 (8.3)	13 (9.0)
Kidney	114 (79.2)	117 (81.3)
Renal limited disease, K only	2 (1.4)	2 (1.4)
Chronic renal disease, GFR ≤ 50 ml/min	—	58 (40.3)
Chronic proteinuria, ≥ 0.5 g/day	—	25 (17.4)
Dialysis ever	—	19 (13.2)
End-stage renal disease	—	11 (7.6)
General symptoms	132 (91.7)	132 (91.7)
Musculoskeletal	116 (80.6)	120 (83.3)
Myositis, biopsy-proven muscular vasculitis	—	6 (4.2)
Skin	24 (16.7)	26 (18.1)
Peripheral nervous system <sup>c</sup>	56 (38.9)	61 (42.4)
Pure sensory neuropathy	—	30 (20.8)
Motor/sensorimotor/mononeuritis multiplex	—	27 (18.8)
CNS	3 (2.1)	5 (3.5)
Gastrointestinal	5 (3.5)	7 (4.9)
Eye	15 (10.4)	20 (13.9)
Heart	9 (6.3)	11 (7.6)
Ear, nose and throat/ upper airways	3 (2.1)	3 (2.1)
Auricular chondritis	1 (0.7)	1 (0.7)
No renal and lung involvement	13 (9.0)	10 (6.9)

<sup>a</sup>Including external reports and phone interviews. <sup>b</sup>Including external reports. <sup>c</sup>No detailed records on type of involvement available for four patients. DEI: Disease Extent Index; GFR: glomerular filtration rate.

(Cox regression) was fitted for covariates with at least 10 patients and at least two events per subgroup or continuous measurement. To prevent confounding, both models were adjusted for age and gender. For sensitivity analysis, the Cox regression for survival was repeated without

adjustment. The 95% CIs were computed and  $P \leq 0.05$  was considered significant. Pairwise deletion was used to handle missing data. All reported CIs are 95% CIs. All computations were done using R version 3.0.2 (R Project for Statistical Computing, Vienna, Austria) [18].

**Fig. 1** Frequency >1% of Vasculitis Damage Index items during the whole follow-up

GFR: glomerular filtration rate.

## Results

### Demographic data and organ involvement

Demographic data, follow-up time, organ involvement, disease severity, disease extent and ANCA status are shown in Table 1. There was a slight female predominance in our cohort.

We analysed mortality data for a median of 72.0 months from diagnosis (including external reports and phone interviews). Clinical follow-up with detailed information on relapse (including external reports) was available for a median of 33.5 months. Median follow-up within our centre was 18.5 months. Thirty-six of the patients were diagnosed at our centre and 108 were referred after being diagnosed externally.

Rates of organ involvement were compared with representative published MPA cohorts (supplementary Table S1, available at *Rheumatology* Online) [3, 19–24]. The most common major organ involvements were renal [mean maximum baseline creatinine 2.47 mg/dl (s.d. 2.10), range 0.70–13.40], followed by pulmonary (mainly AH and fibrosing ILD) and peripheral nervous system involvement. Usual interstitial pneumonia was the most frequently (55.6%) observed pattern of fibrosing ILD in patients with available CT images.

About half of the patients with kidney involvement developed CRD and about a quarter had chronic proteinuria. Nineteen patients required haemodialysis at disease onset and nine of them recovered renal function during induction treatment. Eleven patients developed ESRD. In one case, ESRD manifested 10 months after diagnosis; the other 10 patients did not recover from renal failure at disease onset.

The type of peripheral nervous system involvement was differentiated by electrophysiology. Frequencies of pure

sensory neuropathy (distal symmetrical) and motor or sensorimotor neuropathy (including mononeuritis multiplex) were nearly equal (20.8% and 18.8%). In six cases, myositis with biopsy-proven small vessel vasculitis was documented.

While 17 (11.8%) patients stated that they had ENT symptoms on pointed questioning, only 3 (2.1%) had outward symptoms, with 1 suffering from auricular chondritis. In nine cases, nasal mucosa biopsies of clinically non-specific lesions were performed that showed no signs of vasculitis or granulomatous inflammation.

### Chronic damage and infection

The most frequent items scored by the Vasculitis Damage Index (Fig. 1) were CRD (glomerular filtration rate ≤ 50 ml/min), hypertension and chronic peripheral neuropathy. The most frequent potentially therapy-associated complication was hypertension, followed by infectious disease during remission induction [25 patients (17.4%)], osteoporosis, diabetes, muscle atrophy, marrow failure, cataract, malignancy and chemical cystitis. Four patients developed a malignancy: one had bronchial carcinoma, but no detailed information was available on the kind of tumour in the other three patients.

### Therapy

One hundred and fifteen patients (79.9%) responded (completely or partially) to the initial remission induction treatment. Sixty-one (42.3%) achieved complete remission and 54 (37.5%) achieved partial remission (response). Twenty (13.9%) were refractory to the initial treatment (no detailed data on response were available for nine patients). Sixty (41.7%) patients received oral CYC, 63 (43.8%) received i.v. pulse CYC [mean cumulative dose for first induction 13.7 g (s.d. 13.6), range 0–81] and 21

**TABLE 2** Proportional hazards model (survival/relapse-free survival)

Demography	Hazard ratio (95% CI), <i>P</i> -value	
	Survival	Relapse-free survival
Age at diagnosis	<b>1.05 (1.01, 1.10), 0.01</b>	1.00 (0.98, 1.02), 0.88
Gender, female	0.57 (0.23, 1.45), 0.24	0.89 (0.50, 1.57), 0.69
DEI	0.72 (0.44, 1.16), 0.18	0.97 (0.76, 1.24), 0.82
Organ involvement at disease onset		
Lung, alveolar haemorrhage	2.65 (0.58, 12.04), 0.21	1.12 (0.48, 2.63), 0.79
Lung, fibrosing interstitial lung disease	<b>4.04 (1.21, 13.45), 0.02</b>	1.94 (0.93, 4.06), 0.08
Lung, other	1.15 (0.17, 7.68), 0.88	1.10 (0.40, 2.99), 0.85
Kidney	3.30 (0.65, 16.69), 0.15	1.09 (0.47, 2.54), 0.84
Kidney, chronic renal disease, GFR ≤50 ml/min	2.51 (0.95, 6.66), 0.06	0.97 (0.55, 1.73), 0.93
Musculoskeletal	4.29 (0.70, 26.29), 0.12	1.41 (0.53, 3.75), 0.49
Skin	3.11 (0.60, 16.16), 0.18	0.98 (0.38, 2.48), 0.96
Peripheral nervous system	<b>5.26 (1.10, 25.14), 0.04</b>	1.59 (0.66, 3.82), 0.30
Therapy and disease course		
Cumulative CYC dose first induction	1.00 (0.95, 1.05), 0.95	<b>0.97 (0.94, 0.99), 0.01</b>
Cumulative CYC dose whole follow-up	0.97 (0.93, 1.01), 0.18	<b>1.02 (1.00, 1.04), 0.03</b>
Refractory after first induction	2.65 (0.77, 9.05), 0.12	1.62 (0.79, 3.33), 0.19

Statistically significant results shown in bold. DEI: Disease Extent Index; GFR: glomerular filtration rate.

(14.6%) received other immunosuppressants such as MTX or steroid monotherapy for initial induction.

#### Mortality and relapse analysis

Twenty-five (17.4%) patients died during follow-up. The SMR was 1.40 (95% CI 0.91, 2.07; *P*=0.13) for the whole cohort. It was slightly higher in females [1.60 (95% CI 0.80, 2.87) *P*=0.18] compared with males [1.24 (95% CI 0.68, 2.09), *P*=0.48]. The 1 year mortality rate was 1.4% (two patients). In both cases no information on the cause of death was available. After 1, 5, 10 and 20 years the estimated survival rates were 98.6% (95% CI 96.6, 100.0), 89.6% (95% CI 84.1, 95.4), 75.1% (95% CI 65.7, 85.8) and 60.4% (95% CI 46.5, 78.6).

Relapses were observed in 49 (34.0%) patients (59 relapses: 12 minor, 47 major) within the clinical follow-up time. Time from diagnosis to first relapse was a mean 38.9 months (s.d. 33.1, range 4–154; median 33). Estimated relapse-free survival rate was 91.3% (95% CI 86.5, 96.4) and 43.3% (95% CI 33.8, 55.5) for 1 and 5 years, respectively. The results of the proportional hazards model are shown in Table 2; Kaplan–Meier plots are shown in Fig. 2A for survival and Fig. 2B for relapse-free survival. Higher mortality was found in patients with fibrosing ILD (Fig. 2C), peripheral nervous system involvement (P, Fig. 2D) and for higher age at diagnosis.

High cumulative CYC doses during the first induction treatment were associated with longer relapse-free survival but not with reduced mortality. In contrast, a high cumulative CYC dose during whole follow-up was associated with shorter relapse-free survival. (It should be noted that the CYC dose was measured on a continuous scale. Consequently the hazard ratios (HRs) correspond to a dose increase of 1 g in this case.)

No statistically significant association with death or relapse was found for other organ involvements (including CRD; Fig. 2E), refractory disease or Disease Extent Index.

In the sensitivity analysis without adjustment for age and gender, the effects of fibrosing ILD, CRD and peripheral nervous system involvement were overestimated.

#### Discussion

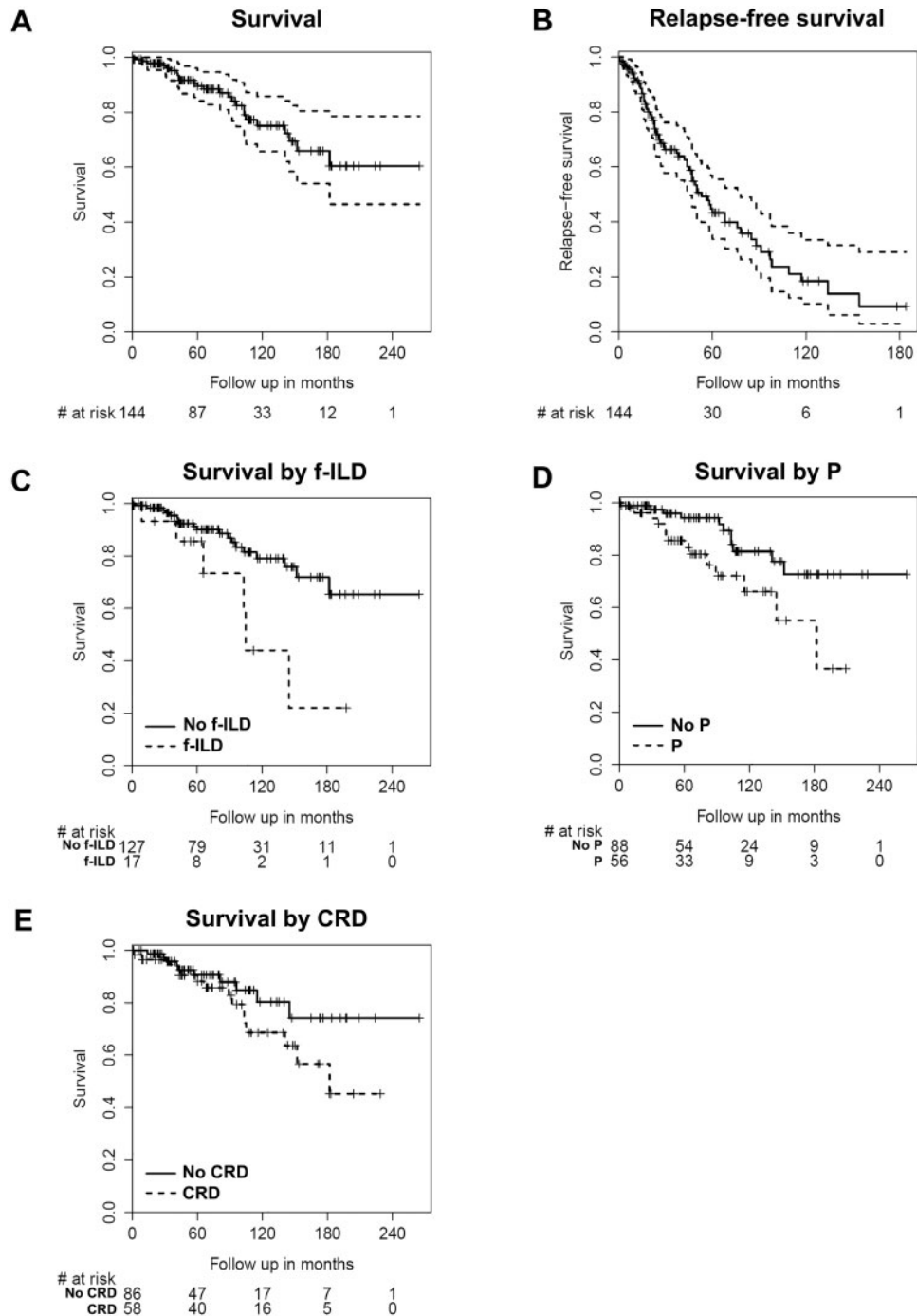
SMRs of 3.95 (95% CI 2.51, 5.38) [25] as well as 1, 5 and 10 year survival rates of 71.1–100%, 45.1–80% and 43–80%, respectively, have been reported for MPA [4, 25, 26]. We observed a lower SMR [1.40 (95% CI 0.91, 2.07)] and higher survival rates compared with the data from the literature. Mortality was not significantly higher than in the German population after adjusting for age and sex.

A 1 year mortality rate (early death) of 11% was reported for AAV. Half of those deaths were due to infectious adverse events, 14% of those 11% due to active vasculitis [27]. Only two (1.4%) cases of early death were observed in our cohort.

The observed lower mortality may be influenced by less severe renal involvement in our cohort. CRD (40.3%) and ESRD (7.6%) were observed less frequently compared with other studies (CRD 60% and ESRD 34%) [19, 21, 26, 28]. Other frequent chronic damage (Vasculitis Damage Index) items in our study were in accordance with the most frequent items of MPA patients in the long-term data of the European Vasculitis Study Group (EUVAS) clinical trials [28].

We consider our results of only slightly higher mortality, comparatively high survival rates and low rates of CRD and ESRD to be influenced by referral bias. Most severely diseased patients are probably initially treated in nephrology



**Fig. 2** Kaplan–Meier curves

(A) Survival of the whole cohort of 144 (solid curve) with 95% CI (dotted curves). (B) Relapse-free survival of the whole cohort of 144 (solid curve) with 95% CI (dotted curves). (C) Survival by fibrosing interstitial lung disease (f-ILD) at diagnosis ( $P = 0.02$ ). (D) Survival by peripheral nervous system (P) involvement at diagnosis ( $P = 0.04$ ). (E) Survival by chronic renal disease (CRD,  $\text{GFR} \leq 50 \text{ ml/min}$ ) ( $P = 0.06$ ). CRD: chronic renal disease; GFR: glomerular filtration rate.

and intensive care units and may remain in long-term care in these hospitals. Therefore severe disease and early death may be underrepresented in this cohort, leading to reduced SMRs. Low mortality and ESRD rates may also

result from standardized interdisciplinary workups, therapy and patient education at our centre [8]. This cohort suggests that there is a phenotype of MPA with a less severe course and good long-term outcome.

Fibrosing ILD was associated with poor prognosis in our study. It has been described in 7.2–45% of MPA patients [6, 7, 23, 29]; it is mostly observed in MPA, but on rare occasions in other types of AAV [30, 31]. ANCA-associated fibrosing ILD (with or without evidence of vasculitis) seems to be associated with MPO-ANCA but only rarely with other ANCA subtypes [32, 33]. It can initially manifest like idiopathic pulmonary fibrosis and precede the full-blown clinical manifestation and diagnosis of MPA by years [6, 29, 32, 34].

There are controversial reports dealing with the question of whether fibrosing ILD has a significant impact on mortality in MPA [6, 7, 35]. It stands to reason that fibrosing ILD is associated with mortality because fibrosing ILD frequently results in reduced lung function and chronic hypoxia. Chronic and end-stage respiratory failure have been reported to be relevant causes of death in MPA-associated fibrosing ILD [30, 36]. There are no evidence-based therapy indications for MPA-associated fibrosing ILD, but in a recent retrospective analysis, survival was better in patients with fibrosing ILD in AAV if CYC- or RTX-based treatment regimens were used compared with steroids alone [36]. AH was not associated with mortality in this cohort. This can be explained by low rates of fulminant AH. Outcomes are good in mild and subclinical AH [5, 37].

We also observed higher mortality in patients with peripheral nervous system involvement. In contrast, an analysis of the EUVAS long-term data showed that this disease manifestation is neither an independent risk factor of poor prognosis nor associated with life-threatening organ involvement, but occurs more frequently in cases with high baseline disease activity [38]. Reasons for these divergent results remain unclear. One possible explanation may be that in our cohort critical illness polyneuropathy was picked up, which cannot easily be differentiated from polyneuropathy due to MPA in more severely diseased patients.

CRD (especially later stage) is a major risk factor of mortality in AAV [39]. We observed no significantly increased mortality for overall CRD, but HRs and Kaplan-Meier plots showed a tendency towards increased mortality. This difference can be attributed to less chronic and severe renal involvement in this cohort.

Remission rates cannot be easily compared because different definitions were used [4]. Relapses were observed in 34% of patients (median time to relapse 33 months) compared with 19–39% (median time to relapse 15–43 months) in a systematic review of MPA studies [4]. Initial induction treatment with high cumulative doses of CYC was associated with a lower relapse rate. It has previously been observed that higher doses of CYC for induction therapy in MPA lead to more effective long-term disease control [4]. The positive correlation of high cumulative CYC doses during follow-up with the occurrence of relapse can be explained by the fact that major relapses were usually treated with CYC. Relapses mainly affected organs already involved at the first manifestation of the disease, in accordance with earlier reports [21].

Overall rates of organ manifestations in the present data resembled those in other MPA cohorts (supplementary Table S1, available at *Rheumatology* Online) [3, 19–24]. The mean observed age at disease onset was 59.3 years (s.d. 14.4, range 18–86), which is in the lower range of the reported data in other cohorts (56.8–71 years) [3, 19–24]. Compared with most cohorts mainly consisting of Caucasian patients, we observed slightly higher rates of females, a high percentage of MPO-P-ANCA-positive patients, a low percentage of PR3-C-ANCA-positive patients, no ANCA-negative patients, high rates for pulmonary and peripheral nervous system involvement and, rarely, specific ENT disease (except one case of auricular chondritis) [3, 19–23].

Reported rates of polyneuropathy in MPA show a wide range, from 7% to 58% [3, 19–24, 38, 40]. We observed involvement of the peripheral nervous system relatively frequently (42.4%). Similar rates have been found in single cohorts, especially in the prospective cohort by Cattaneo *et al.* [41], where all of the MPA patients underwent frequent neurologic and electrophysiological examinations (45.8–57.6%) [22–24]. Motor or sensorimotor neuropathy is considered the most typical among the neurologic AAV manifestations [38]. According to some authors, motor neuropathy is common in MPA while pure sensory neuropathy is usually not apparent [38]. In contrast, we found a high rate of distal symmetric neuropathy (20.8%), in accordance with other authors who described acrodistal symmetric sensory polyneuropathy and overlap neuropathies in MPA [41–43]. There are several possible reasons for different reported rates and types of polyneuropathy in MPA [38]. To distinguish polyneuropathy caused by uraemia, diabetes and vitamin B12 deficiency, among others, from vasculitis-related neuropathy can be challenging. Different diagnostic standard procedures, such as the periodic interdisciplinary work-ups performed in our clinic [8], might lead to high sensitivity and even identify low-grade polyneuropathy in some cases.

There are limitations to our study because of its retrospective design and limited number of patients. Furthermore, this is not an inception cohort, and many patients were included after being diagnosed externally. For these patients, external reports have been used to analyse long-term follow-up. Our clinic is a tertiary referral centre specializing in vasculitis. Consequently a referral bias may have occurred and severe courses may be underrepresented in this study. Different algorithms for classification limit the comparability of studies performed on MPA and may result in different ANCA rates, ages and organ manifestations.

A major strength of this study are comprehensive long-term follow-up data on standardized diagnostic and therapeutic procedures and long-term care performed by a single-centre interdisciplinary team specializing in vasculitis. Since the period analysed is >20 years, the study does not reflect the outcome for the actual therapeutic protocols (less CYC and more frequent use of RTX).

## Conclusion

To summarize, we demonstrated a better prognosis in a German rheumatology referral centre MPA cohort compared with the reported data from the literature. Reasons for this are less severe renal involvement and AH and a standardized monocentric therapeutic approach. Our data suggest that there is an MPA phenotype with less severe disease and good long-term outcome.

We observed significantly increased mortality in MPA-associated fibrosing ILD, which is not a well-characterized risk factor of poor prognosis in MPA. There is a need for further studies to confirm our findings.

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## Supplementary data

Supplementary data are available at *Rheumatology* Online.

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