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Incidence and survival rates in Wegener's granulomatosis, microscopic polyangiitis, Churg–Strauss syndrome and polyarteritis nodosa

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Objective. To estimate the incidence of and survival rates for WG, microscopic polyangiitis (MPA), Churg–Strauss syndrome (CSS) and PAN within a defined population in southern Sweden.

Methods. Cases were retrieved using hospital records and a serology database. All new cases of WG, MPA, CSS and PAN between 1997 and 2006 were included, provided they met pre-defined criteria, and were followed until 30 June 2008. The study area comprised two health care districts with a total population of 641 000. The standardized mortality ratio (SMR) was estimated using Swedish population data as a reference.

Results. A total of 140 (WG, 63; MPA 65; CSS 6; and PAN 6) cases (52% women) with a median age of 67.6 (range 20–96) years fulfilled the inclusion criteria. The annual incidence per million of the population (95% CI) was estimated to be 9.8 (7.4–12.2) for WG, 10.1 (7.7–12.6) for MPA and 0.9 (0–1.7) for both CSS and PAN. The highest incidence was found in patients aged $\geqslant$75 years (79.1/million). The 1- and 5-year survival rates were 87.8 and 71.6% for all patients, but lower for MPA (80 and 55%) compared with WG (95 and 83%; $P = 0.001$), although the difference was not significant in the multivariate analysis. The SMR was 2.77 (95% CI 2.02, 3.71) for all patients.

Conclusions. The incidence of WG and MPA was equal in our district, but there was a difference in survival rates related to age and renal function. A progressive increase in age-specific incidence rates was observed.

Key words: Incidence, Vasculitis, ANCA, Arteritis, Wegener's granulomatosis.

Introduction

Primary systemic vasculitides [PSV: WG, microscopic polyangiitis (MPA), Churg–Strauss syndrome (CSS) and PAN] are rare systemic diseases characterized by inflammation of blood vessels resulting in different degrees of organ dysfunction; if untreated, they are associated with high morbidity and mortality rates [1]. ANCAs are common in WG, MPA and CSS, and the diseases are collectively referred to as ANCA-associated systemic vasculitis (AASV). PAN is a disease in which vasculitis is limited to medium-sized and small arteries, without evidence of glomerulonephritis, and is not associated with ANCA.

The aetiology of PSV is unknown, although a significant association has been found with farming and exposure to silica, indicating that environmental factors play a role [2]. Long-term population-based incidence estimates are important for comparing incidence rates between different regions of the world with varying exposure to presumed aetiological factors. Over the last decade, a number of studies have been published on the subject of the epidemiology of PSV in Europe, New Zealand and Australia [3–13]. Compared with older studies, nearly all of them exhibit increased incidence and prevalence rates of PSV, findings explained by many authors as due to greater awareness of PSV as well as wider availability of ANCA analysis [14, 15]. Furthermore, the European studies have demonstrated a geographical variation along a north–south axis, with a higher frequency of WG in the north and more MPA in the south [16]. However, discrepancies between studies can also be the result of the different methodologies used to identify patients with PSV, ensure case completeness, diagnose systemic vasculitis or assign individual patients to separate disease categories. Many of the studies refer to either the ACR classification criteria 1990 [17] or the Chapel Hill Consensus Conference (CHCC) on disease definitions [18]. However, neither of these documents contain diagnostic criteria suitable for epidemiological studies, forcing researchers to develop their own adaptations. An algorithm for the classification of PSV in epidemiological studies has recently been published, developed with the support of the European Medicine Agency (EMEA) [19]. We applied the EMEA algorithm in a point prevalence study [10] and found it to be robust and predictable.

Most studies of survival among patients with PSV are based on either cohort studies from large tertiary referral centres or clinical multicentre studies [20–24]. Both types of study are associated with a substantial risk of sampling bias. Clinical studies always contain exclusion criteria that frequently limit access to elderly persons and other patients with poor prognosis, and such patients are less likely to be sent to referral clinics.

In the prevalence study mentioned above [10], we used a variety of retrieval sources, and capture–recapture analysis revealed that we achieved a case completeness of 96%. We also demonstrated that if we had used the three best retrieval sources, we would have identified 93% of the prevalent cases, missing very few with a recent diagnosis. Using this simplified retrieval method and the EMEA classification algorithm, we performed a 10-year incidence study of WG, MPA, CSS and PAN in a well-defined stable population in southern Sweden. The aims of the present study were to estimate the annual incidence rates of WG, MPA, CSS and PAN, and to investigate survival rates of these diseases within a defined geographical area.

Patients and methods

Study area and population

The study area consists of two health care districts in South Sweden (central and south-west Skåne) containing

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14 municipalities with a total area of 3294 km^2 (~0.8% of the total area of Sweden). The population of the area at the beginning of the study period in 1997 was 616 287, which increased to 667 240 by 31 December 2006 [25]. The population density in the study area was 202/km^2 compared with 22 for the country as a whole. The denominator population used in the incidence estimates was the mean of the population during the study period (641 759), which represented ~7% of the total population of Sweden. Women made up 50.4% of the study population, and the age distribution was as follows: 0–14 years, 18.8%; 15–54 years, 54.6%; and >55 years, 26.6% [25].

The study area is located in the middle and south-west of Scania (Swedish: Skåne) the southernmost county of Sweden. Over 90% of the population lives in cities. In Scania, agricultural land constitutes ~49.4% of the area compared with only 7.9% for the whole of Sweden. About 57.2% of employees work within the trade, health care, mining, manufacturing and energy supply sectors. Only 2.5% of labour force is employed in the areas of agriculture, forestry, hunting and fishing.

Case retrieval

Searches were made in clinical databases at the Departments of Nephrology and Rheumatology at the University Hospitals of Lund and Malmö and the Department of Internal Medicine at the Hospitals of Landskrona and Trelleborg using the International Classification of Diseases (ICD-10), codes M300–M320. In addition, the database of the Wieslab AB private laboratory in Lund was searched for positive analysis of PR3 and MPO ANCA. The patients included in the study were all newly diagnosed cases, who fulfilled the study criteria of WG, MPA, CSS and PAN, and were resident in the area at the time of diagnosis between 1 January 1997 and 31 December 2006.

Classification

All available medical records of retrieved patients living in the study area at the time of diagnosis were thoroughly reviewed in order to establish a diagnosis of vasculitis and subsequently for classification into the four disease categories studied. The EMEA algorithm described by Watts *et al*. [19] was applied stepwise to all patients. The algorithm is based on the ACR classification criteria for CSS, WG and PAN [26–28], as well as the CHCC on the nomenclature of vasculitis [18]. The case identification, review of case records and data collection were carried out by the first author (A.J.M.). In borderline cases and when classification difficulties arose, consensus was reached between two of us (A.J.M. and M.S.).

Data collection

Data from case records were collected from the time of diagnosis, including demographics, diagnosis delay (time in months from the first symptoms of vasculitis to diagnosis), blood pressure, relevant laboratory and serology data as well as the results of histopathology and radiology investigations. Patients were followed up from the time of diagnosis until 30 June 2008 or death using the Swedish census data (www.skatteverket.se). Both the date of diagnosis and first symptom attributed to vasculitis were registered in order to take account of seasonal variation. The seasons were defined as follows: winter (December–February), spring (March–May), summer (June–August) and autumn (September–November). The study was divided into two 5-year periods (1997–2001 and 2002–06), in order to identify possible changes in incidence rates. Population density was calculated for each municipality in order to study possible differences in incidence rates.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences, SPSS 12.0.1 for Windows (SPSS, Chicago, IL, USA). The differences between groups were compared by means of the non-parametric Mann–Whitney U-test and chi-square (χ^2) test where appropriate. The P-value of <0.05 is considered to be statistically significant. The Kaplan–Meier method was employed to estimate survival rates. The expected number of deaths was calculated by multiplying sex-, age- and calendar period-specific person-years of follow-up with corresponding rates for the entire Swedish population. The standardized mortality ratio (SMR) was obtained by dividing the observed number of deaths by the expected number. Assuming a Poisson distribution of the observed cases, 95% CIs were calculated. The following factors were investigated in a univariate analysis as potential predictors of reduced survival: age, gender, serum creatinine (s-crea), ear–nose–throat (ENT) involvement, blood pressure, diagnosis WG and ANCA specificities. Cox regression was used in the analysis and all potential predictors were adjusted for age. A multivariate analysis was performed on variables with a statistically significant P-value in the univariate analysis. Data are presented as median and range if not otherwise stated. The study was approved by the local Ethics Committee at the Faculty of Medicine, Lund University (LU 283-02).

Results

One hundred and forty patients (women 73; 52%) in our study area were diagnosed with PSV between 1 January 1997 and 31 December 2006. The median age at diagnosis was 67.6 (20–92) years for all patients (Table 1). The patients were classified as follows: WG, 63; MPA, 65; CSS, 6; and PAN, 6. The classification of PSV in this study and the effect of EMEA algorithm on our results are shown in Table 2. No case was left unclassified by the algorithm. The diagnosis of PSV was made within 2 months of the first symptoms in 82 (59%) patients and after >6 months in 24 (17%) patients. The median time of diagnosis delay was 2 (range 0–96) months. A diagnosis of vasculitis was supported by histopathology in 109 (78%) cases and by angiography in 3 (2%) cases. In the remaining 28 (20%) cases, the diagnosis was made on the basis of typical clinical symptoms of vasculitis in conjunction with a positive ANCA test and/or surrogate markers for granulomatous disease or renal vasculitis. In patients with AASV ($n=134$), 123 (92%) tested positive for ANCA at time of diagnosis, 67 (55%) tested positive for either PR3 or cytoplasmic ANCA (c-ANCA) and 56 (45%) tested positive for either MPO or perinuclear ANCA (p-ANCA).

TABLE 1. Annual incidence rates of WG, MPA, CSS and PAN in a defined population[a] in Southern Sweden

Disease	No. of patients	Age at diagnosis, median (range), years	Incidence/million (95% CI)
WG	63	67.6 (20–84)	9.8 (7.4, 12.2)
Men	33	64.7 (22–83.5)	10.4 (6.8, 13.9)
Women	30	68.8 (20–84)	9.3 (6.0, 12.6)
MPA	65	70 (29–92)	10.1 (7.7, 12.6)
Men	30	74 (29–88.7)	9.4 (6.1, 12.8)
Women	35	60 (37–92)	10.8 (7.2, 14.4)
CSS	6	61 (26–66.6)	0.9 (0.2, 1.7)
Men	2	62 (60.7–63.4)	0.6 (0, 1.5)
Women	4	54 (26–66.6)	1.2 (0, 2.4)
PAN	6	66 (41–79)	0.9 (0.2, 1.7)
Men	2	70.7 (62–79)	0.6 (0, 1.5)
Women	4	62 (41–77.7)	1.2 (0, 2.4)
Total	140	67.6 (20–92)	21.8 (18.2, 25.4)
Men	67	69.5 (22–88.7)	21.0 (16.0, 26.1)
Women	73	66.6 (20–92)	22.6 (17.4, 27.7)

[a]Total population 641 763.

TABLE 2. Classification of 140 patients with PSV[a] according to EMEA algorithm[b]

Disease and classification	No. of patients (incidence according to ACR/CHCC); 95% CI	No. of patients (incidence according to EMEA[b]); 95% CI
CSS		6 (0.9); 0.2, 1.7
ACR CSS	6 (0.9); 0.2, 1.7	
WG		63 (9.8); 7.4, 12.2
ACR WG	51 (7.9); 5.8, 10.1	
CHCC WG[c]	1	
CHCC MPA and surrogate markers for WG[c]	5	
Surrogate markers for WG + positive PR3 or MPO ANCA[c]	6	
MPA		65 (10.1); 7.7, 12.6
CHCC MPA with no surrogate markers for WG	53 (8.3); 6, 10.5	
Surrogate markers for renal vasculitis + positive PR3 or MPO ANCA[d]	12	
PAN		6 (0.9); 0.2, 1.7
CHCC PAN	3 (0.5); 0, 1.0	
Visceral or renal angiography showing multiple microaneurysms		

[a]PSV includes WG, MPA, CSS and PAN. [b][19], ACR CSS [26]; ACR WG [28]; CHCC WG, CHCC MPA and CHCC PAN [18]. [c]Without fulfilling ACR criteria for WG. [d]Without fulfilling histological proof for CHCC definition for MPA.

Incidence rates

The annual incidence rates per million of the population were estimated to be 9.8 (95% CI 7.4, 12.2) for WG, 10.1 (95% CI 7.7, 12.6) for MPA and 0.9 (95% CI 0.2, 1.7) for each of CSS and PAN (Table 1). The annual incidence rate was 21.8/million (95% CI 18.2, 25.4) for all patients and 20.9 (95% CI 17.3, 24.4) for AASV. Age-specific incidence rates revealed a clear increase with age (Fig. 1). The highest incidence rate was in the $\geqslant$75-year age group, 79.1/million (95% CI 55.2, 103.0). Overall, there was no difference in the sex-specific incidence rates, although the incidence in the 35- to 54-year age group was higher in women (23.5 *vs* 6.9 for men; $P = 0.005$), and the reverse was true for $\geqslant$75-year age group (117.4/million *vs* 56.7 for women; $P = 0.016$). We could not find any statistically significant differences in incidence rates between the various municipalities in terms of population densities (data not shown).

Temporal variations

The annual incidence rate during the first 5 years of the study was 24 (95% CI 18.5, 29.4) compared with 19.9 (95% CI 15, 24.7) for the second 5-year period, although this difference is not statistically significant. Data regarding the season during which the first symptom of vasculitis occurred were available for 139 of the 140 patients. The onset of symptoms took place during the winter months for 39 (28%) patients, spring in 25 (18%) patients, summer in 42 (30%) patients and autumn in 33 (24%) patients, none of which are statistically significant. Similarly, we could not detect any statistical seasonal difference for the date of diagnosis.

Survival

Forty-five patients (25 men) died during the follow-up period, which lasted until 30 June 2008 (no patient was lost to follow-up). The median time of follow-up was 59 (range 1–133) months; the median time to death was 19 (range 1–110) months. Nine patients (20% of deaths) died within 3 months of diagnosis. For all patients, absolute survival rates were 87.8% at 1 year, 71.6% at 5 years and 55% at 10 years (Fig. 2A). Survival was worse for patients with MPA compared with those with WG ($P = 0.001$) (Fig. 2B). There was no difference in survival rates of patients with different ANCA specificities ($P = 0.232$) (Fig. 2C).

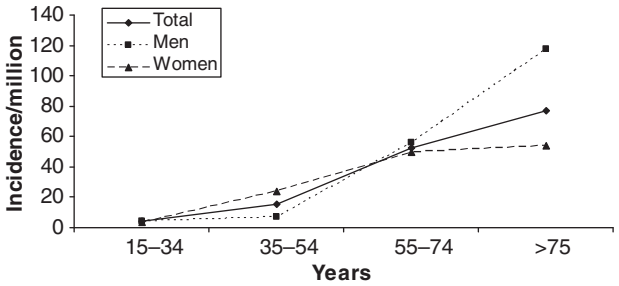

FIG. 1. Age- and gender-specific incidence in 140 patients with PSV (WG, 63; MPA, 65; CSS, 6; and PAN, 6).

The survival rate for all PSV patients deteriorated with increasing age ($P < 0.001$) (Fig. 2D). Higher mortality was also significantly associated with increased s-crea level (Table 3). ENT involvement and a diagnosis of WG were associated with increased survival, but when a multivariate analysis was applied, this effect was no longer significant. When studying patients with WG, no significant benefit of ENT involvement was observed. There was no statistically significant difference in the survival rate between male and female patients (Table 3). The survival of patients with PSV was reduced compared with the Swedish population [SMR 2.77 (95% CI 2.02, 3.71); 2.48 (95% CI 1.60, 3.65) for men and 3.27 (95% CI 1.99, 5.04) for women]. Older female patients had a 4.29-fold increase in the risk of death compared with the general population. Similarly, patients with a diagnosis of MPA, renal involvement and no ENT involvement had an increased risk of death (Table 4).

WG

A total of 63 patients (30 women) were classified as WG, which represents an annual incidence rate of 9.8/million inhabitants (95% CI 7.4, 12.2). When using only the ACR WG 1990 criteria for classification, the incidence of WG (51 patients) was 7.9/million (95% CI 5.8, 10.1) (Table 2). The major reason for failure to fulfil the ACR criteria was that the disease was limited to the airways. Overall, 30 (48%) patients had systemic disease with renal involvement at diagnosis. The median diagnosis delay was 2 (0.5–96) months. The diagnosis was supported by biopsy-proven vasculitis in 47 patients, where histological evidence of granulomatous inflammation was found in 45% of the biopsies (21 patients). Results from ANCA analysis were available for all patients, 78% of which were positive for PR3/c-ANCA and 16% for MPO/p-ANCA. The corresponding figures for the 30 patients with renal involvement were 90% and 6.6%. A total of 14 patients died during follow-up. The median time from diagnosis to death was 20.5 (2–110) months, and the median follow-up period was 75 (2–133) months. The 1-, 5- and 10-year survival for patients with WG was estimated to be 95, 83 and 65%, respectively (Fig. 2B). In univariate analysis, patients with WG had significantly better chances of survival compared with those with MPA, but the difference was no longer statistically significant applying a multivariate analysis due to stronger effect of other factors for the prediction of survival (e.g. renal function and age).

MPA

Sixty-five patients (35 women) were classified as MPA, representing an annual incidence rate of 10.1/million inhabitants (95% CI 7.7, 12.6) (Table 1). If using the CHCC definition of MPA (53 patients; no WG surrogate markers), the incidence of MPA would have been 8.3/million (95% CI 6, 10.5). Of a total of 65 MPA patients, 64 exhibited renal involvement. Of these, 5 (8%) had renal limited disease without manifestation in any other organ

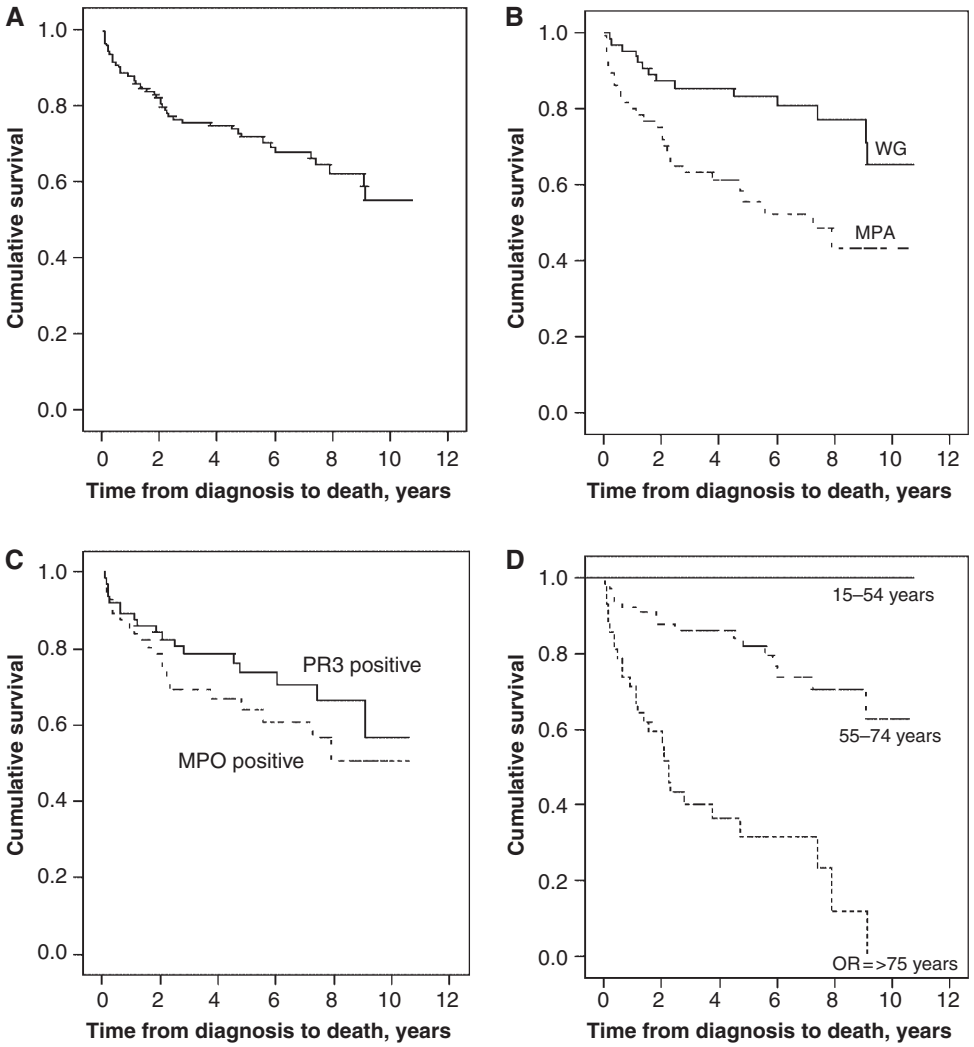

FIG. 2. Survival curves in PSV according to Kaplan–Meier analysis. (**A**) Overall survival in 140 patients with PSV (WG, 63; MPA, 65; CSS, 6; and PAN, 6). (**B**) Survival in WG *vs* MPA. (**C**) Survival according to ANCA specificity (PR3 64 and MPO 56 patients). (**D**) Survival according to different age groups (15–54 years, 33 patients; 55–74 years, 65 patients; and ≥75 years, 42 patients).

TABLE 3. Predictors of survival in PSV[a]

	Univariate analysis		Multivariate analysis	
Predictors	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age, increased by 10 years	1.11 (1.07, 1.15)	<0.001	3.05 (1.78, 5.2)	0.001
Sex (men)	1.4 (0.79, 2.05)	0.238		
SBP, increased by 10 mmHg	1.14 (0.98, 1.32)	0.086		
S crea, increased by 100 μmol/l	1.17 (1.09, 1.27)	<0.001	1.14 (1.01, 1.20)	0.023
Diagnosis WG[b] (only WG and MPA)	0.40 (0.20, 0.80)	0.010		
ENT involvement	0.29 (0.14, 0.61)	0.001		
ENT (only WG[c])	0.47 (0.15, 1.47)	0.197		
PR3 positivity	0.64 (0.34, 1.23)	0.187		
MPO positivity	1.37 (0.71, 2.61)	0.340		

All variables in the table are adjusted for age (see 'Patients and methods' section). [a]PSV includes WG, MPA, CSS and PAN. [b]Analysis including only patients with WG and MPA. [c]Analysis including only patients with WG. SBP: systolic blood pressure at presentation; HR: hazard ratio; CI: confidence interval; ENT: ear-nose-throat.

system, 29 had manifestation in two, 25 in three and 5 in four or more organ systems. The median diagnosis delay was 1.5 (0–18) months. Fifty-three (82%) patients with MPA had histopathology confirmation of vasculitis (renal: 52 patients; skin: one patient). Results from ANCA analysis were available for all patients, 68% had positive MPO/p-ANCA and 29% had tested positive for PR3/c-ANCA. During follow-up, 29 patients died, the median time from diagnosis to death being 16 (1–95) months. The median follow-up period was 45 (1–131) months. The 1-, 5- and 10-year survival for patients with MPA was estimated to be 80, 55 and 43%, respectively (Fig. 2B).

CSS and PAN

Six patients were classified as CSS and the same number as PAN. The annual incidence rates for both diseases were 0.9/million

TABLE 4. Standardized mortality ration (SMR) in patients with PSV compared with the Swedish population as a whole

	Person-year	Observed deaths	Expected deaths	SMR (95% CI)
Men				
55–74 years	188	10	4.12	2.43 (0.92, 3.93)
≥75 years	63	15	5.8	2.59 (1.28, 3.89)
Women				
55–74 years	172	6	2.59	2.32 (0.46, 4.17)
≥75 years	44	14	3.26	4.29 (2.04, 6.54)
Diagnosis				
WG	365	14	7.89	1.77 (0.84, 2.70)
MPA	250	29	7.35	3.95 (2.51, 5.38)
Renal involvement				
Present	420	39	12.11	3.22 (2.21, 4.23)
Absent	257	6	4.12	1.46 (0.29, 2.62)
ENT involvement				
Present	323	9	5.52	1.63 (0.57, 2.70)
Absent	354	36	10.7	3.36 (2.27, 4.46)

(95% CI 0.2, 1.7). All CSS patients fulfilled the ACR criteria for that diagnosis, whereas the diagnosis of PAN was based on biopsy-proven fibrinoid necrosis involving medium-sized vessels in three patients and angiography findings in further three. The median diagnosis delay was 2.5 (0–12) months for CSS and 4 (0–13) months for PAN. MPO–ANCA was positive in two CSS patients, whereas, by definition, all PAN patients were ANCA negative. One patient in each disease category died during follow-up. Median follow-up time was 61.5 (25–98) months for CSS patients and 83.5 (4–115) months for PAN patients.

Discussion

This population-based study estimated the incidence and survival rates of WG, MPA, CSS and PAN in a well-defined stable population in South Sweden over a 10-year period, utilizing validated epidemiological tools for case retrieval [10]. In our previous prevalence study, capture–recapture analysis indicated that this method yields case completeness of well over 90%. The diagnosis of vasculitis was made in accordance with pre-defined criteria using clinical, serological, pathological and radiological data as described elsewhere [19]. In the present study, we found that the overall annual incidence rate of PSV was 21.8/million inhabitants. Our results are slightly higher than those reported from the UK and Spain, and almost twice as high as those from Germany [4, 6, 29]. A major part of this difference can be found in elderly patients. We found the highest incidence rate among patients ⩾75 years of age, whereas other researchers have reported a decline after a peak at around the age of 60 years [4, 6]. Our figure of 117.4/million for men aged >75 years is substantially higher than, for instance, the 70/million reported by Watts *et al.* [4]. The reason for this discrepancy is not clear, but a possible explanation is that there is a high awareness about vasculitic diseases in our area, combined with good access to secondary and tertiary care for elderly people in Sweden. At our departments, ANCA has been part of the routine diagnostic work-up for progressive renal insufficiency in all age groups for more than two decades, and most elderly patients in this study were found to have renal involvement. Organ biopsy was performed in 35 out of 42 patients aged >75 years at diagnosis.

Overall, the gender-specific incidence did not differ, although it was significantly higher in women in the 35- to 54-year age group and higher in men aged ⩾75 years. In our study, the WG incidence rate of 9.8/million is somewhat lower than that of 12 recently reported in another Swedish study [9], which may be due to methodological differences. Knight *et al.* [9] identified all patients with a discharge diagnosis of WG in the inpatients registry, and based on their previous studies, assumed a diagnosis validity of 89%. We found that only 60% of the patients who were assigned ICD codes for PSV in clinical registries had sufficient clinical and/or histopathology evidence to enable a valid diagnosis of vasculitic disease in accordance with the EMEA algorithm. In line with our results, a recently published study on the incidence of WG in Finland used the ICD codes for case identification and found that only ~62% of identified cases fulfilled the ACR criteria and were eligible for inclusion in the study [11]. The incidence we find for WG is in the same range as the figure of 8/million found in Norway [5] and considerably higher than the 4.9/million in Spain [30]. This finding is in line with the north–south hypothesis put forward by Watts *et al.* [16]. In contrast, however, the incidence of MPA in our district is similar to that reported from Spain, a finding that clearly challenges this hypothesis.

Naturally, the high MPA incidence might be due to an environmental factor. However, our study does not shed light on the role of any specific factors. Differences between geographical areas in the incidence of MPA have recently been demonstrated in a study from Australia, where a higher incidence was found in rural compared with urban areas [13], which contrasts with previous findings from Germany and Spain [6, 31]. The geography of our area does not allow us to conduct a similar analysis to that reported in the Australian study. However, we were unable to find any differences in incidence rates between areas of high and low population density. We are convinced that the high incidence of MPA was not an effect of the EMEA algorithm, since the latter tends to classify borderline cases as WG rather than MPA. We are inclined to believe that differences in the diagnostic work-up of elderly patients with renal insufficiency are a major factor behind differences in incidence rates between different areas, making it difficult to identify other factors of importance. We did not find any tendency towards an increased incidence of PSV over time. Instead, the annual rate appeared to be constant, a finding that is supported by an earlier report from Germany [8]. These results are consistent with the notion that the higher incidence rates reported during the 1990s were a consequence of increased ANCA testing rather than changes in environmental factors related to aetiology.

We could not find any significant seasonal variation in the onset of vasculitis and previous studies on this subject have revealed divergent results. Mahr *et al.* [32] found that the incidence of WG seemed to be highest during the summer. Carruthers *et al.* [33] presented evidence for a higher incidence during the winter and a similar finding was revealed by Raynauld *et al.* [34]. In a hospital-based study from central Sweden, Tidman *et al.* [3] found that the onset of symptoms was only higher in winter for patients with positive cANCA, and when looking at diagnosis categories there was no seasonal variation. We believe that the data sources in our study are fairly reliable, since all information was registered in case records at the time of diagnosis, and in many patients the diagnostic delay was relatively short.

The present study indicates that the survival rate for PSV was reduced compared with that of the general Swedish population, with a 2.77-fold increase in mortality. Matteson *et al.* [35] and Westman *et al.* [36] presented similar results in studies on patients with WG and renal vasculitis. In absolute terms, our results of 1- and 5-year survival were similar to a recently published study from our area that included AASV with renal involvement [37]; slightly better for MPA and WG than the results reported by Lane *et al.* [20] but worse than the 5-year survival of MPA reported by Guillevin *et al.* [38]. High age at diagnosis and high entry s-crea were the predictors of reduced survival in our patients. Similar results have been found in other studies [20, 24, 39, 40]. Previous reports indicated that the presence of ENT involvement was associated with better WG survival [24, 41]. When our analysis was confined to WG patients, the presence of ENT involvement had no significant impact on survival. In the present study, the mortality rate was twice as high for MPA as for WG. The better survival for WG patients explains why the

prevalence of WG was twice that of MPA despite similar incidence rates [10]. However, logistic regression analysis indicates that the difference in survival rate can be largely explained by the variation in age and renal function.

In conclusion, the overall incidence of and increased mortality due to PSV in our study is comparable with that reported from other European countries, with the exception of the relatively high incidence rate for MPA. We found no seasonal variation in onset of PSV. WG and MPA have the same incidence, but lower MPA survival leads to huge differences in their respective prevalence. The difference in survival rates can be explained by age and disease severity.

Rheumatology key messages

- In Southern Sweden, the incidence of MPA is almost equal to that of WG.
- Age-specific incidence showed a clear increase with age (peak incidence in $\geqslant$75-year age group).
- Survival was significantly higher for WG compared with MPA.

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References

1 Walton EW. Giant-cell granuloma of the respiratory tract (Wegener's granulomatosis). Br Med J 1958;2:265–70.
2 Lane SE, Watts RA, Bentham G, Innes NJ, Scott DG. Are environmental factors important in primary systemic vasculitis? A case-control study. Arthritis Rheum 2003;48:814–23.
3 Tidman M, Olander R, Svalander C, Danielsson D. Patients hospitalized because of small vessel vasculitides with renal involvement in the period 1975–95: organ involvement, anti-neutrophil cytoplasmic antibodies patterns, seasonal attack rates and fluctuation of annual frequencies. J Intern Med 1998;244:133–41.
4 Watts RA, Lane SE, Bentham G, Scott DG. Epidemiology of systemic vasculitis: a ten-year study in the United Kingdom. Arthritis Rheum 2000;43:414–9.
5 Koldingsnes W, Nossent H. Epidemiology of Wegener's granulomatosis in Northern Norway. Arthritis Rheum 2000;43:2481–7.
6 Gonzalez-Gay MA, Garcia-Porrua C, Guerrero J, Rodriguez-Ledo P, Llorca J. The epidemiology of the primary systemic vasculitides in northwest Spain: implications of the Chapel Hill Consensus Conference definitions. Arthritis Rheum 2003;49:388–93.
7 Mahr A, Guillevin L, Poissonnet M, Ayme S. Prevalences of polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome in a French urban multiethnic population in 2000: a capture-recapture estimate. Arthritis Rheum 2004;51:92–9.
8 Reinhold-Keller E, Herlyn K, Wagner-Bastmeyer R, Gross WL. Stable incidence of primary systemic vasculitides over five years: results from the German vasculitis register. Arthritis Rheum 2005;53:93–9.
9 Knight A, Ekbom A, Brandt L, Askling J. Increasing incidence of Wegener's granulomatosis in Sweden, 1975–2001. J Rheumatol 2006;33:2060–3.
10 Mohammad AJ, Jacobsson LT, Mahr AD, Sturfelt G, Segelmark M. Prevalence of Wegener's granulomatosis, microscopic polyangiitis, polyarteritis nodosa and Churg-Strauss syndrome within a defined population in Southern Sweden. Rheumatology 2007;46:1329–37.
11 Takala JH, Kautiainen H, Malmberg H, Leirisalo-Repo M. Incidence of Wegener's granulomatosis in Finland 1981–2000. Clin Exp Rheumatol 2008;26:S81–5.
12 Gibson A, Stamp LK, Chapman PT, O'Donnell JL. The epidemiology of Wegener's granulomatosis and microscopic polyangiitis in a southern hemisphere region. Rheumatology 2006;45:624–8.
13 Ormerod AS, Cook MC. Epidemiology of primary systemic vasculitis in the Australian Capital Territory and south-eastern New South Wales. Intern Med J 2008;38:816–23.
14 Scott DG, Bacon PA, Elliott PJ, Tribe CR, Wallington TB. Systemic vasculitis in a district general hospital 1972–1980: clinical and laboratory features, classification and prognosis of 80 cases. Q J Med 1982;51:292–311.
15 Andrews M, Edmunds M, Campbell A, Walls J, Feehally J. Systemic vasculitis in the 1980s—is there an increasing incidence of Wegener's granulomatosis and microscopic polyarteritis? J R Coll Physicians Lond 1990;24:284–8.
16 Watts RA, Gonzalez-Gay MA, Lane SE, Garcia-Porrua C, Bentham G, Scott DG. Geoepidemiology of systemic vasculitis: comparison of the incidence in two regions of Europe. Ann Rheum Dis 2001;60:170–2.
17 Hunder GG, Arend WP, Bloch DA *et al.* The American College of Rheumatology 1990 criteria for the classification of vasculitis. Introduction. Arthritis Rheum 1990;33:1065–7.
18 Jennette JC, Falk RJ, Andrassy K *et al.* Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum 1994;37:187–92.
19 Watts R, Lane S, Hanslik T *et al.* Development and validation of a consensus methodology for the classification of the ANCA-associated vasculitides and polyarteritis nodosa for epidemiological studies. Ann Rheum Dis 2007;66:222–7.
20 Lane SE, Watts RA, Shepstone L, Scott DG. Primary systemic vasculitis: clinical features and mortality. Q J Med 2005;98:97–111.
21 Jayne D, Rasmussen N, Andrassy K *et al.* A randomized trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. N Engl J Med 2003;349:36–44.
22 Mekhail TM, Hoffman GS. Longterm outcome of Wegener's granulomatosis in patients with renal disease requiring dialysis. J Rheumatol 2000;27:1237–40.
23 Hogan SL, Nachman PH, Wilkman AS, Jennette JC, Falk RJ. Prognostic markers in patients with antineutrophil cytoplasmic autoantibody-associated microscopic polyangiitis and glomerulonephritis. J Am Soc Nephrol 1996;7:23–32.
24 Mahr A, Girard T, Agher R, Guillevin L. Analysis of factors predictive of survival based on 49 patients with systemic Wegener's granulomatosis and prospective follow-up. Rheumatology 2001;40:492–8.
25 Statistics Sweden. www.scb.se.
26 Masi AT, Hunder GG, Lie JT *et al.* The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum 1990;33:1094–100.
27 Lightfoot RW Jr, Michel BA, Bloch DA *et al.* The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. Arthritis Rheum 1990;33:1088–93.
28 Leavitt RY, Fauci AS, Bloch DA *et al.* The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum 1990;33:1101–7.
29 Reinhold-Keller E, Herlyn K, Wagner-Bastmeyer R *et al.* No difference in the incidences of vasculitides between North and South Germany: first results of the German vasculitis register. Rheumatology 2002;41:540–9.
30 Gonzalez-Gay MA, Garcia-Porrua C. Systemic vasculitis in adults in northwestern Spain, 1988–1997. Clinical and epidemiologic aspects. Medicine 1999;78:292–308.
31 Reinhold-Keller E, Zeidler A, Gutfleisch J, Peter HH, Raspe HH, Gross WL. Giant cell arteritis is more prevalent in urban than in rural populations: results of an epidemiological study of primary systemic vasculitides in Germany. Rheumatology 2000;39:1396–402.
32 Mahr A, Artigues N, Coste J, Aouba A, Pagnoux C, Guillevin L. Seasonal variations in onset of Wegener's granulomatosis: increased in summer? J Rheumatol 2006;33:1615–22.
33 Carruthers DM, Watts RA, Symmons DP, Scott DG. Wegener's granulomatosis—increased incidence or increased recognition? Br J Rheumatol 1996;35:142–5.
34 Raynauld JP, Bloch DA, Fries JF. Seasonal variation in the onset of Wegener's granulomatosis, polyarteritis nodosa and giant cell arteritis. J Rheumatol 1993;20:1524–6.
35 Matteson EL, Gold KN, Bloch DA, Hunder GG. Long-term survival of patients with Wegener's granulomatosis from the American College of Rheumatology Wegener's granulomatosis classification criteria cohort. Am J Med 1996;101:129–34.
36 Westman KW, Selga D, Isberg PE, Bladstrom A, Olsson H. High proteinase 3-anti-neutrophil cytoplasmic antibody (ANCA) level measured by the capture enzyme-linked immunosorbent assay method is associated with decreased patient survival in ANCA-associated vasculitis with renal involvement. J Am Soc Nephrol 2003;14:2926–33.
37 Bakoush O, Segelmark M, Torffvit O, Ohlsson S, Tencer J. Urine IgM excretion predicts outcome in ANCA-associated renal vasculitis. Nephrol Dial Transplant 2006;21:1263–9.
38 Guillevin L, Durand-Gasselin B, Cevallos R *et al.* Microscopic polyangiitis: clinical and laboratory findings in eighty-five patients. Arthritis Rheum 1999;42:421–30.
39 Koldingsnes W, Nossent H. Predictors of survival and organ damage in Wegener's granulomatosis. Rheumatology 2002;41:572–81.
40 Booth AD, Almond MK, Burns A *et al.* Outcome of ANCA-associated renal vasculitis: a 5-year retrospective study. Am J Kidney Dis 2003;41:776–84.
41 Bligny D, Mahr A, Toumelin PL, Mouthon L, Guillevin L. Predicting mortality in systemic Wegener's granulomatosis: a survival analysis based on 93 patients. Arthritis Rheum 2004;51:83–91.