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Concise Report

The epidemiology of Takayasu arteritis in the UK

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Objectives. Takayasu arteritis (TAK) is a large-vessel vasculitis of unknown aetiology. The annual incidence in hospital-based studies is 1–2/million. The UK General Practice Research Database (UKGPRD) contains complete primary care records on 3.6 million people. There are no data on the incidence of TAK in the UK or from primary care anywhere in the world. The aim of this study was to determine the annual incidence of TAK in the UK using the UKGPRD and in a well-defined hospital population [Norfolk Vasculitis Register (NORVASC)].
Methods. We identified all patients in the UKGPRD with a first diagnosis of TAK during 2000–05, using the Read code (G757); and in the NORVASC population. The annual incidence was calculated as the number of incident cases divided by total person-years.
Results. A total of 14 (13 females) subjects were identified with a first diagnosis of TAK during 2000–05 in the UKGPRD. The median age was 51.0 years (interquartile range 28–66). The overall annual incidence of TAK was 0.8/million (95% CI 0.4, 1.3). The incidence was stable throughout the study period. The mean prevalence of TAK was 4.7/million. There were six patients (five females) aged <40 years presenting in 2000–05 with TAK. The annual incidence in those aged <40 years was 0.3/million. In the NORVASC population, one case was identified (0.4/million/year) with three prevalent cases (7.1/million).
Conclusion. This is the first population-based study of the epidemiology of TAK. The annual incidence and prevalence are consistent with previous studies.

Key words: Takayasu arteritis, Epidemiology, Vasculitis.

Introduction

Takayasu arteritis (TAK) is a large-vessel vasculitis of unknown aetiology. It occurs predominately in those aged <40 years and presents with a vasculitis confined to the aorta and its branches. TAK has been described worldwide with an incidence of up to 3.3/million, but is usually considered to be most common in Asia [1]. In most series, there appears to be an excess of patients of Asian descent. The available data on incidence and prevalence are limited and derived from hospital data.

The UK General Practice Research Database (UKGPRD) provides the opportunity of studying the epidemiology of chronic and rare disease in a primary care population, via access to a large population of patients with comprehensive computerized records. The UKGPRD has been successfully used to investigate the incidence of other chronic relapsing–remitting conditions, such as SLE and GCA [2–4]. The recording of diagnosis leading to hospital attendance varies between 73% for venous thromboembolic disease and 93% for IBD, suggesting that recording is better for chronic disease [5, 6]. The epidemiology of TAK has not previously been studied in a primary care setting or within the UK.

The Norfolk Vasculitis Register (NORVASC) prospectively identifies all patients with a diagnosis of systemic vasculitis attending the Norfolk and Norwich University Hospital, UK, and has been maintained since 1988.

The existence of the primary care UKGPRD and the secondary care-based Norfolk Register NORVASC, gives the opportunity of investigating the incidence of TAK in primary and secondary care settings in the UK.

The aim of this study was to estimate the incidence and prevalence of TAK in the UK in two distinct settings, the UKGPRD and the NORVASC register.

Methods

Study populations

UKGPRD. The UKGPRD provides complete anonymized electronic data collected from routine general practice case records. It contains details of primary medical care, prescribing and prevention. At present, ~3.6 million patients are included from 433 general practices. The geographical distribution of the GPRD population is similar to that of the general UK population and comparison of the age and sex distribution has shown that it is similar to that recorded in the UK National Census [7, 8]. The data are collected routinely and the quality is monitored on a regular basis. The population of practices participating changes with time, as practices join and leave the database. Patient's records are included from when either the patient registers with a participating practice or the practice joins the scheme. Similarly, data collection stops when the patient leaves the practice by transferring to a different practice or death, or the practice leaves the scheme.

The study population comprised all adults and children whose general practices had contributed research quality data for ⩾3 years to the UKGPRD during the study period. These practices are considered by the UKGPRD to be 'up to standard'.

The study period was from 1 January 2000 to 31 December 2005. UKGPRD records for patients with a diagnosis of TAK were identified using the Read codes for TAK (G757) [8]. Incident cases were defined as those with a first diagnosis of TAK during 2000–05. Entry date was considered as the date at which a diagnosis of TAK was first given. In addition, we searched for patients with aortic arch syndrome, an inflammatory occlusive vasculopathy of the major branches of the thoracic aorta, which may be used as a synonym for TAK), using Read code (G575.11).

Details of the denominator population were provided by the UKGPRD by age and gender for each year of the study.

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NORVASC. The study population comprised all adults and children registered on the NORVASC database during 2000–05. We have previously described the NORVASC database [9]. In brief, all patients attending the Norfolk and Norwich Hospital with a diagnosis of systemic vasculitis have been prospectively recorded since 1 January 1988. The denominator population is patients registered with general practitioners in the former Norwich Health Authority. The population covered by the database in 2002 was 445 000 (215 000 males). The population is 98.5% Caucasian of UK descent, which is higher than the average for England (90.9%) and ~9.6% of the population is aged >75 years (England, average 7.5%) [10]. The study period was from 1 January 2000 to 31 December 2005. Cases were classified using the ACR (1990) criteria for TAK [11].

Case definition and verification. The anonymized medical records of all incident cases were requested from the UKGPRD to verify the diagnosis of TAK. Data were extracted from the records and the ACR (1990) classification criteria for TAK were applied; at least three out of the six criteria are required for a diagnosis of TAK (Table 1) [11]. Although the aggregated data from UKGPRD contained details of age and gender, the individual anonymized records did not. On review of the aggregated data, 50% of the patients were aged >40 years. One of the criteria for TAK is age at symptom onset <40 years, and therefore a secondary analysis was conducted on patients aged <40 years. In the NORVASC population, we had access to the medical records for a comprehensive retrospective case note review.

Statistics

The annual incidence of TAK was calculated as the number of incident cases divided by the total person-time. The prevalence was calculated as the number of prevalent cases divided by the number of people registered with the database in each calendar year. Ninety-five percent confidence intervals (95% CIs) were calculated using the Poisson distribution for the UKGPRD population. Only one incident patient was identified in the NORVASC population and therefore CIs were not calculated.

Ethical approval

Ethical approval for this study was given by the Independent Scientific Advisory Committee (ISAC) of the UKGPRD under the terms of general approval for observational studies from the UK multicentre Research Ethics Committee. The NORVASC database has ethical approval from the Norwich Research Ethics Committee.

Results

UKGPRD

A total of 16 (1 male and 15 females) subjects were identified with a first diagnosis of TAK during 2000–05. Following case verification, two cases transpired to have been originally diagnosed before 2000 and were therefore excluded from the incidence analysis. The median age at first diagnosis of TAK in the remaining 14 cases (13 females) was 51.0 years (interquartile range 28–66), with eight patients being aged >40 years. The annual incidence of TAK was 0.8/million (95% CI 0.4, 1.3). The incidence was stable throughout the study period (Fig. 1). Symptom onset before the age of 40 years is one of the ACR (1990) classification criteria for TAK; we analysed the population aged <40 years separately. There were six patients (one male) aged <40 years diagnosed in 2000–05 with TAK. The annual incidence in those aged <40 years was 0.3/million.

The annual prevalence of TAK in this period was 4.7/million (95% CI 3.1, 8.5). Figure 2 shows the point prevalence at the end of each year. There was a gradual increase in the prevalence during the course of the study from 3.6 to 6.3/million.

Two cases of aortic arch syndrome were also identified, but both were aged >80 years at the time of entry onto the UKGPRD, suggesting that the likely diagnosis was large-vessel involvement due to GCA. They were therefore not included in the analysis.

Verification

We requested photocopies of the anonymized medical records of the 16 patients with newly diagnosed TAK; however, only eight were available for review from UKGPRD. The medical records had the age of the patient removed during the anonymization

TABLE 1. ACR classification criteria for TAK

(i)	Age <40 years old: development of symptoms or signs related to TAK at age <40 years.
(ii)	Claudication of extremities: development and worsening of fatigue and discomfort in muscles of one or more extremity while in use, especially the upper extremities.
(iii)	Decreased brachial arterial pulse: decreased pulsation of one or both brachial arteries.
(iv)	Blood pressure difference >10 mmHg: difference of >10 mmHG in systolic blood pressure between arms.
(v)	Bruit over subclavian: bruit audible on auscultation over one or both arteries or aorta subclavian arteries or abdominal aorta.
(vi)	Arteriogram abnormality: arteriographic narrowing or occlusion of the entire aorta, its proximal branches or large arteries in the proximal upper or lower extremities, not due to atherosclerosis, fibromuscular dysplasia or similar causes; changes usually focal or segmental.

Note that for the purposes of classification a patient shall be said to have TAK if at least three of these six criteria are present. The presence of any three or more criteria yields a sensitivity of 90.5% and specificity of 97.8%. Reproduced from [11].

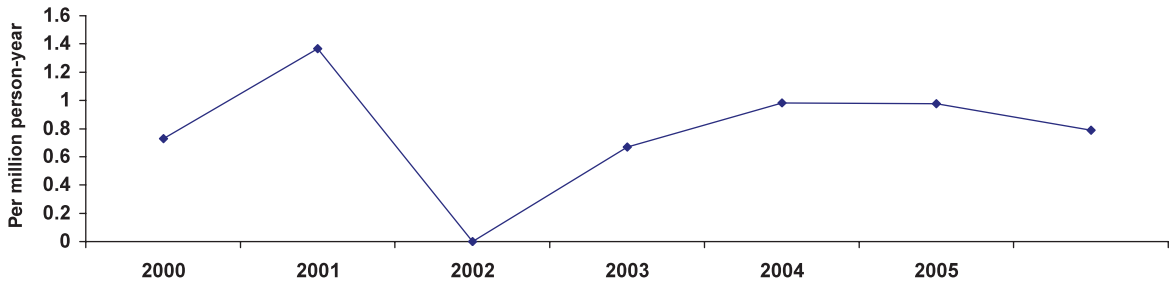

FIG. 1. Incidence of TAK in the UKGPRD.

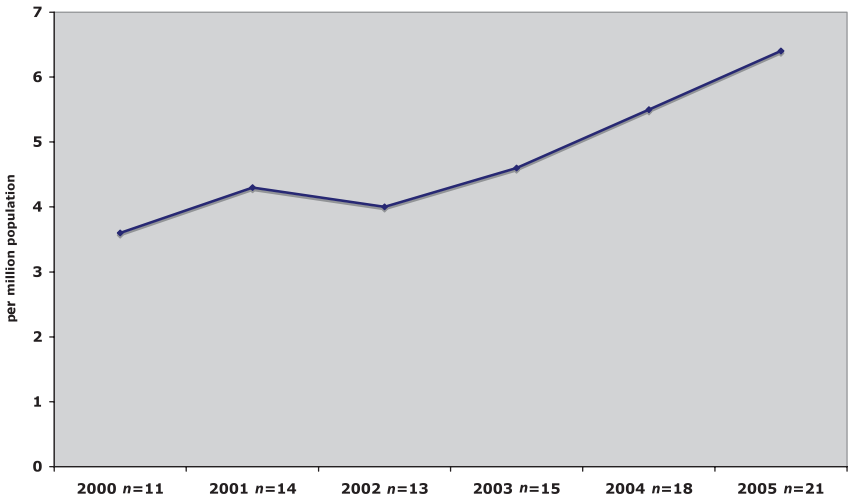

FIG. 2. Prevalence of TAK in the UKGPRD.

TABLE 2. Epidemiology of TAK

Year	Place	Incidence/million	Prevalence/million	Reference
1982–84	Japan[a]	1–2	NR	Koide [12]
1994	Japan[a]	NR	40	Toshihiko [13]
1989–94	Kuwait[b]	2.2 (overall)	7.8	El-Reshaid *et al.* [14]
		3.3 (age <40 years)	9.5	
1971–83	Olmsted County, USA	2.6	NR	Hall *et al.* [15]
1969–75	Sweden	0.8	6.4	Waern *et al.* [16]
1998–02	Schleswig-Holstein, Germany	0.5	NR	Reinhold-Keller *et al.* [17]
1990–99	Vilnius, Lithuania	1.3	NR	Dadoniene *et al.* [18]
2000–05	UKGPRD, UK	0.8 (overall)	4.7	This study
		0.3 (age <40 years)		
2000–05	Norwich, UK	0.4	7.1	This study

[a]Estimated from data in [12] and [13]. [b]Kuwait nationals only. NR: not reported.

process, and therefore it was impossible to determine whether they were aged <40 years at symptom onset as required by the ACR (1990) criteria. In four cases, three of the remaining ACR criteria were fulfilled. In two cases, two criteria were fulfilled, and in one case there was a brief reference to angiography, together with immunosuppressive therapy. In seven cases, there was angiographic evidence of TAK. We felt, therefore, that there was adequate evidence that these cases had TAK. In the eighth case, there were insufficient data to confirm the diagnosis. Two of the eight cases transpired to have had the diagnosis originally made in 1983 and 1997, and had had a very long period free of disease activity and were presenting with a relapse. These cases were excluded from the incidence study.

NORVASC

One incident patient (female aged 35 years) was identified during the study period. Three patients (all females) with TAK were alive on 31 December 2005. All cases fulfilled the ACR (1990) criteria for TAK. The annual incidence in the NORVASC population was 0.4/million with a point prevalence on 31 December 2005 of 7.1/million.

Discussion

This is the first study of the incidence of TAK from a primary care population and also the first data from the UK. Previous studies from Europe, the USA and Japan have been reported from secondary or tertiary care. Our data are consistent with these other studies, confirming the rarity of the condition (Table 2). Overall, the incidence and prevalence seem fairly uniform across the globe. The variation between these studies may be due to different methodological approaches or imprecise estimates due to the fact that most incidence rates are based on small number of cases. TAK is more common in women; in the largest study from Japan, the female to male ratio was eight to one [12]. In our study, only 1 out of 14 patients was male. We identified only three prevalent and one incident case in the NORVASC population and the calculated incidence figures is in keeping with the data from the UKGPRD (Table 2).

There are very little data on the prevalence of TAK, with other studies focusing on incidence (Table 2). The prevalence reported in our study is significantly lower than that reported from Japan, where the estimated prevalence is 40/million [13].

The low prevalence of TA makes it difficult to estimate incidence and prevalence accurately, even with access to a large database such as the UKGPRD. Case capture was probably quite high in our study, as TAK is a rare disease and unlikely to be diagnosed or managed solely in primary care. Thus, in most cases, the recorded diagnosis will reflect a secondary/tertiary care diagnosis. Studies of other chronic conditions in the UKGPRD, such as IBD, have shown that hospital contact is recorded at a high frequency for major medical events [6].

Case definition has also been difficult, with the level of detail recorded in the UKGPRD in several cases being insufficient for formal application of the validated ACR (1990) criteria. The clinical data that were available suggested that seven out of eight cases did have TAK. In four of these cases, the ACR criteria were fulfilled with three out of six criteria being positive. TAK is generally considered to be a disease of younger people and the ACR (1990) criteria have an age criterion for symptom onset placed at <40 years; this is to enable distinction from

large-vessel involvement in GCA, a condition typically occurring in those aged >50 years. This criterion is not mandatory. In our study, 50% of the cases apparently were first diagnosed at age >40 years. It is also noteworthy that 25% of the patients in Japan were diagnosed at age >40 years, suggesting that diagnosis >40 years of age is not that uncommon and that the ACR (1990) criteria may be too restrictive [11].

TAK is also characterized by long periods of quiescent disease and thus it is possible to record a relapse after many years of disease quiescence as a new presentation. This would appear to be the case in two of our cases. Our estimated incidence of 0.8/million is probably therefore an overestimate, but in the absence of a prospective register with complete clinical data collection it is difficult to see how more accurate data could be obtained in the UK. A nationwide prospective study is required.

In conclusion, we have confirmed the rarity of TAK in the UK using data from two sources—the UKGPRD and the NORVASC database. The incidence and prevalence is similar to that reported from other populations.

Rheumatology key messages

- TAK is a rare disease in the UK.
- The incidence of TAK in the UK is similar to that observed in the rest of the world.

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