Incidence and outcome of subarachnoid haemorrhage: a retrospective population based study

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Abstract

***Objectives*—The purpose was to define the incidence and case fatality rates of subarachnoid haemorrhage in the population of Devon and Cornwall.**

***Methods*—A retrospective population based design was employed with multiple overlapping methods of case ascertainment. A strict definition of subarachnoid haemorrhage was used. Age and sex specific incidence rates and relative risks for death at different time intervals are calculated.**

***Results*—Eight hundred cases of first ever subarachnoid haemorrhage were identified; 77% of cases were verified by CT, 22% by necropsy, and 1% by lumbar puncture. The incidence rates are higher than those previously reported in the United Kingdom. The age standardised incidence rate (/100 000 person-years) for females was 11.9 (95% confidence interval (95% CI) 9.5–15.0), for males 7.4 (5.4–10.0), and the total rate was 9.7 (7.5–12.6). The case fatality rates at 24 hours, 1 week, and 30 days were 21 (18–24)%, 37 (33–41)%, and 44 (40–49)% respectively. The relative risk for death at 30 days for those over 60 years:under 60 years was 2.95 (2.18–3.97).**

***Conclusion*—The incidence of subarachnoid haemorrhage in the United Kingdom is higher than previously reported. Three quarters of the mortality occurs within 3 days.**

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Keywords: incidence; subarachnoid haemorrhage; mortality

Over the past half century roughly 60 papers have been published exploring the incidence of subarachnoid haemorrhage, almost exclusively in the developed world. Unfortunately there are significant methodological problems with much of this work.[1] For incidence rates in the United Kingdom there are three studies, two of which were completed before the advent of CT.[2 3] The results of these early studies may be unreliable due to diagnostic inaccuracy. There is evidence that incidence rates of subarachnoid haemorrhage decline as the proportion of cases verified by CT increases.[4] The most recent United Kingdom study reported 33 cases of subarachnoid haemorrhage as part of a larger stroke registry.[5] Although population based, the findings on subarachnoid haemorrhage need to be interpreted with caution in view of the few cases.

The present study was initiated to provide incidence and outcome data for subarachnoid haemorrhage using a retrospective population based design.

Methods

ETHICS

Ethical approval was obtained from the South and West Devon Health Authority ethics committee.

STUDY AREA

The two counties of Devon and Cornwall have an area of 10 347.4 km^2. The population in 1991 (1991 United Kingdom census) was 1 475 643 and in 1996 (midcensus estimate, Office of National Statistics (ONS)) it was 1 504 847, an increase of less than 2%. The population is overwhelmingly white (99.27%) (1991 United Kingdom census).

The study area is isolated on a peninsula and is served by five district general hospitals and one tertiary referral centre for neurosurgery. During the study period there was a CT unit at each of the hospitals in the two counties. A modern ambulance service, as well as two helicopters, operated in the study area.

Patients with a sudden neurological catastrophe were first taken to the nearest hospital where they were stabilised and scanned. All tertiary care was provided at the neurosurgery department at Plymouth. Cerebral angiography was only performed at Plymouth and all patients considered fit enough underwent three vessel angiography. Care of patients with subarachnoid haemorrhage during the study period was the responsibility of three consultant neurosurgeons but in general a policy of early surgery was followed in patients with a demonstrated aneurysm. Nimodipine[6] was given routinely and hypertensive hypervolaemic treatment[7] used to combat vasospasm as needed.

CASE ASCERTAINMENT

Multiple overlapping methods of case ascertainment were employed. (1) The patient administration systems of all five district general hospitals in the two counties were searched for all patients coded as having a discharge diagnosis consistent with subarachnoid haemorrhage (appendix) between 1 January 1992 to 31 December 1996. (2) The ONS provided a list of all people with Devon and Cornwall post codes who died during the

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study period whose cause of death was classified as subarachnoid haemorrhage (codes as appendix). (3) The imaging database at Plymouth was searched for all patients undergoing cerebral angiography during the study period. (4) The operative database at Plymouth was searched for all patients undergoing aneurysm surgery during the study period (Office of Population Sensuses and Surveys (OPCS) codes L30-L309, L33-L339).

All medical records were reviewed by myself. General practitioner records were obtained for people not admitted to hospital. A diagnosis of subarachnoid haemorrhage was accepted if there was a history of abrupt onset of severe headache or unconsciousness with signs of meningeal irritation with or without focal neurological signs supported by CT or necropsy evidence of subarachnoid haemorrhage. In a few cases no CT or necropsy was performed and these cases were only included if there were no focal signs at onset and a typical history was verified by a uniformly bloody and xanthochromic CSF demonstrated by a non-traumatic lumbar puncture.

Careful elimination of all duplicate entries based on surname and date of birth was performed. To eliminate possible duplication of women who had married and changed surname during the study period a check was made for any woman with the same first name and date of birth. People normally resident outside Devon and Cornwall and patients with a primary history of head trauma were excluded. Patients were only included if they presented with their first ever subarachnoid haemorrhage. Patients found on angiography to have arteriovenous malformations were excluded as were patients whose CT demonstrated primary intracerebral haemorrhage. In questionable cases scans were reviewed to ensure exclusion of primary intracerebral haemorrhage with secondary subarachnoid haemorrhage. Outcome data were obtained from the medical records and death within 30 days was recorded.

ANALYSIS

Age and sex specific incidence rates are calculated. The denominator used was the population of Devon and Cornwall taken as the average of the mid-year estimates for the study period in mid-decade age bands. Confidence intervals were generated by assuming the counts followed a Poisson distribution. For comparison purposes summary rates were standardised by the direct method to the population of England and Wales (ONS 1991 census). Groups were compared with Student's t test and the χ^2 test for continuous variables and proportions respectively. The null hypothesis was rejected when $p<0.05$. The influence of age and sex on death at 1, 7, and 30 days were compared by calculating relative risks. Multivariate logistic regression analysis was used to control for confounding.

Data handling was performed using Microsoft Access V 7.0 and analysis carried out with Microsoft Excel V 7.0 and SPSS V 8.0 on a personal computer.

Results

CASE ASCERTAINMENT

A total of 901 medical records were reviewed. Cases were excluded for the following reasons: arteriovenous malformation (24), primary head injury (18), previous subarachnoid haemorrhage (13), primary intracerebral haemorrhage (10), and lack of verification by CT, lumbar puncture, or necropsy (five). The medical records of 31 patients could not be found. Eight hundred cases of first ever subarachnoid haemorrhage were identified during the 5 year study period. Subarachnoid haemorrhage was verified by CT in 609 (77%) patients, necropsy in 181 (22%), and a typical history and lumbar puncture in 10 (1%).

Of the 671 patients admitted to hospital, all but six appeared in the patient administration databases. These six were all miscoded as 436.9 (acute but ill defined cerebrovascular disease). Excluding those with arteriovenous malfunction there were 21 false positives, all of whom had been coded with a primary diagnosis of subarachnoid haemorrhage. Each admission database included five diagnosis fields. The other excluded patients had subarachnoid haemorrhage coded in one of the secondary fields. Six hundred and thirty seven of the admitted patients were correctly coded with a primary diagnosis of subarachnoid haemorrhage. If only the primary diagnosis field had been searched there would have been 34 false negatives in the admission databases. Nineteen of these had a primary diagnosis of intracerebral haemorrhage, nine had been coded as non-ruptured aneurysms, five as sequelae of subarachnoid haemorrhage, and one as other aneurysm of specified artery.

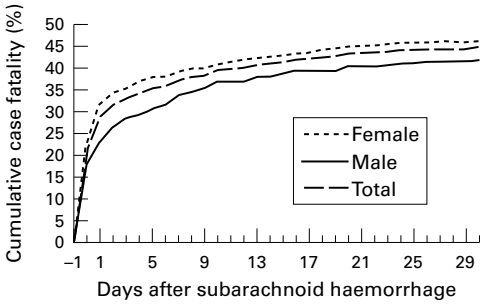
AGE STRUCTURE

There were 516 (64%) women and 284 men. The mean age at diagnosis of the cohort was 61 (SD 15) years. Women were significantly older than men ($p<0.0005$). The mean age for

Table 1 Age and sex specific incidence rates for subarachnoid haemorrhage/100 000 person-years

	Age (y)							
	0–14	*15–24*	*25–34*	*35–44*	*45–54*	*55–64*	*65–74*	*>75*
n	1	4	12	40	93	100	136	130
Female*	0.2 (0.0–0.8)	0.9 (0.2–2.2)	2.5 (1.2–4.3)	7.8 (5.5–10.0)	20.9 (16.0–25.0)	23.6 (19.0–28.0)	30.9 (26.0–36.0)	29.2 (24.0–34.0)
n	0	3	16	34	61	69	64	37
Male*	0.0 (0–0.5)	0.6 (0.1–1.8)	3.4 (1.9–5.4)	7.0 (4.8–9.7)	14.0 (10.0–17.0)	17.6 (13.0–22.0)	18.0 (13.0–23.0)	15.2 (10.0–20.0)
n	1	7	28	74	154	169	200	167
Total*	0.1 (0.0–0.7)	0.7 (0.1–2.0)	2.9 (1.6–4.8)	7.4 (5.2–10.0)	17.5 (13.0–21.8)	20.7 (16.0–25.6)	25.2 (20.0–30.5)	24.2 (19.0–29.8)

n=Number of cases.
*Numbers are rates/100 000 person-years (95%CI).



Sex specific cumulative case fatality rates for the first 30 days after subarachnoid haemorrhage.

women (range) was 63 (11–96) years and for men it was 57 (19–91) years. Eighty five per cent of the patients were over 45 years of age.

INCIDENCE

Age and sex specific incidence rates are shown in table 1. Male and female rates begin to diverge above the age of 45 years. Above the age of 65 the female rates are significantly higher. Summary rates (/100 000 person years) standardised to the population of England and Wales (1991 census) were for women 11.9 (9.5–15.0), for men 7.4 (5.4–10.0), and the total rate was 9.7 (7.5–12.6).

CASE FATALITY RATES

One hundred and twenty nine patients (16%) died without receiving medical attention and a further 44 patients reached hospital but died within 24 hours, making the case fatality rate for the day of subarachnoid haemorrhage 21 (18–24)%. The case fatality rates at 1 week and 30 days were 37 (33–41)% and 44 (40–49)% respectively. The cumulative case fatality rates by sex for the first 30 days are shown in the figure. Rates rose steeply for the first 3 days and then levelled off suggesting that the initial damage done by the bleed was responsible for the greatest proportion of the 30 day case fatality.

Table 2 presents the relative risks of death at 1, 7, and 30 days after subarachnoid haemorrhage. Women were more likely to die from their subarachnoid haemorrhage but the confidence intervals contained 1. Age was strongly related to mortality. When age and sex were controlled age remained a significant predictor of mortality.

PATIENTS ADMITTED TO HOSPITAL

Six hundred and seventy one patients survived to be admitted to hospital but a further 44 died within 24 hours, leaving 627 (78% of the whole cohort) patients alive in hospital after 24 hours.

Table 2 Relative risk of death at 1, 7, and 30 days after subarachnoid haemorrhage

	24 Hours *Relative risk (95% CI)*	*7 Days* *Relative risk (95% CI)*	*30 Days* *Relative risk (95% CI)*
Under 60 y	1.00	1.00	1.00
Over 60 y*	3.47 (2.35–5.12)	2.36 (1.74–3.20)	2.95 (2.18–3.97)
Male	1.00	1.00	1.00
Female†	1.25 (0.85–1.84)	1.23 (0.89–1.69)	1.15 (0.84–1.57)
Under 60 y	1.00	1.00	1.00
Over 60 y†	3.44 (2.32–5.11)	2.33 (1.70–3.15)	2.91 (2.15–3.93)

*Unadjusted.
†Derived from logistic regression controlling for age and sex.

Of these, 490 were either transferred or admitted to Plymouth (61% of the original cohort). The mean age of patients not sent for neurosurgical evaluation, 67.9 years, was significantly higher than the age of those that were, 57.1 years ($p<0.0005$). The 7 and 30 day case fatality rates for those not transferred were 59% and 73% compared with 9% and 18% for those who were transferred.

Of the 490 patients admitted to Plymouth, 409 underwent cerebral angiography; 17% of angiograms showed no cause for the haemorrhage. Of the 339 patients with positive angiograms, 293 (86%) underwent clipping of their aneurysms. This represents 38% of the whole cohort. A further 27 patients underwent external ventricular drainage or shunting.

Discussion

This investigation provides incidence and outcome data on the largest cohort of patients with first ever subarachnoid haemorrhage yet reported in a population based study. The counties of Devon and Cornwall are relatively geographically isolated making them an ideal setting for this type of enquiry. Multiple overlapping methods were used to ensure maximum case ascertainment and the strictest definition of subarachnoid haemorrhage was employed. Ninety nine per cent of cases were verified by either necropsy or CT. Systematic review of all medical records and scans ensured exclusion of primary intracranial haemorrhage and subarachnoid haemorrhage secondary to other causes.

It is generally recognised that studies of the incidence of cerebrovascular disease should be done prospectively, because many stroke episodes are mild and medical attention is not always sought.[8] This reasoning is less cogent in the study of subarachnoid haemorrhage, which is virtually always a dramatic event. Nevertheless, it is possible that some patients, especially in the older age groups dying before they could be admitted to hospital, may have been missed. The omission of these "false negatives" would be to reduce both the incidence and case fatality rates reported here. It is likely, therefore, that the rates found in this study are underestimates. Hopefully, the risk of missing patients who die before reaching medical attention is minimal because in the United Kingdom any sudden unexpected death, the hallmark of fatal subarachnoid haemorrhage, should be notified to the coroner and in such cases a necropsy, with examination of the brain, is routine.

Incidence rates for subarachnoid haemorrhage have recently been reviewed and the rates found in this study are only slightly higher than the European average.[9] The only other modern study reporting incidence rates for subarachnoid haemorrhage in the United Kingdom was conducted between 1981 and 1986 in Oxfordshire as part of a population based stroke registry.[5] Table 3 compares the age standardised incidence rates. The confidence intervals for the Oxford study are wide due to the few cases (33). The strictest possible definition of subarachnoid haemorrhage was used in the

Table 3 Age standardised incidence rates (direct method) of subarachnoid haemorrhage in Oxford and Devon and Cornwall

	Male	*Female*	*Total*
Oxford	3.8 (0.5–19.0)	10.8 (3.3–29.6)	7.3 (1.9–24.3)
Devon and Cornwall	7.4 (5.4–10.0)	11.9 (9.5–15.0)	9.7 (7.5–12.5)

present study and it is, therefore, very unlikely that the rates reported here are exaggerated. As discussed above, it is more likely that these rates are an underestimate. Case ascertainment in the Oxford study was exhaustive, but the study area was not as geographically isolated as Devon and Cornwall and this may have allowed for some loss of cases. The Oxford study has been criticised for not having a geographically discrete population and for using the age/sex registers of local general practices as its denominator.[9] The use of such lists can lead to inclusion of "ghosts", patients who have died but who have not been removed from the register. This will cause an overestimation of the "at risk" population, thereby lowering incidence rates.

The case fatality rates reported here are not unusual for modern population based studies.[10] Although it is well recognised that incidence rates are higher in women there is no evidence that sex is a predictor of death.[11 12] Many studies have confirmed the positive correlation between age and death rates and in this study controlling for sex makes very little difference in this age disadvantage.

Analysis of the patients undergoing neurosurgical investigation emphasises the highly selective nature of this group. The outcomes in these patients are very unrepresentative of the disease as a whole.

This study reinforces the previous impression that subarachnoid haemorrhage is a devastating event. A third of the patients in this cohort were dead within 3 days. Only 38% of this cohort underwent treatment for the cause of their haemorrhage. It would seem as if strategies will be required to prevent subarachnoid haemorrhage before inroads will be made into the mortality of this disastrous disease.

Appendix

ICD 10 used to search for subarachnoid haemorrhage*

I60	Subarachnoid haemorrhage
I60.0	Subarachnoid haemorrhage from carotid siphon and bifurcation
I60.1	Subarachnoid haemorrhage from middle cerebral artery
I60.2	Subarachnoid haemorrhage from anterior communicating artery
I60.3	Subarachnoid haemorrhage from posterior communicating artery
I60.4	Subarachnoid haemorrhage from basilar artery
I60.5	Subarachnoid haemorrhage from vertebral artery
I60.6	Subarachnoid haemorrhage from other intracranial artery
I60.7	Subarachnoid haemorrhage from intracranial artery, unspecified
I60.8	Other subarachnoid haemorrhage
I60.9	Subarachnoid haemorrhage, unspecified
I61.5	Intracerebral haemorrhage, intraventricular
I61.9	Intracerebral haemorrhage, unspecified
I62	Other nontraumatic intracranial haemorrhage
I62.0	Subdural haemorrhage (acute) (nontraumatic)
I62.1	Nontraumatic extradural haemorrhage
I62.9	Intracranial haemorrhage (nontraumatic), unspecified
I67.1	Cerebral aneurysm, nonruptured
I69.0	Sequelae of subarachnoid haemorrhage
I69.1	Sequelae of intracerebral haemorrhage
I69.2	Sequelae of other nontraumatic intracranial haemorrhage
I72.0	Aneurysm of carotid artery
I72.9	Aneurysm of unspecified site

*Corresponding ICD-9 codes used before April 1994.

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