Descriptive Epidemiology in Relation to Gender Differences and Treatment Modalities 10 Years After Intracranial Aneurysm Rupture in the Stockholm Cohort 1996–1999

Ann-Christin von Vogelsang[1,2], Yvonne Wengström[1], Mikael Svensson[3,4], Christina Forsberg[1]

Key words
- Epidemiology
- Gender
- Intracranial aneurysm
- Subarachnoid hemorrhage

Abbreviations and Acronyms
ACA: Anterior cerebral artery
ACoA: Anterior communicating artery
CI: Confidence interval
ICA: Internal carotid artery
ICD: International Classification of Diseases
ICH: Intracerebral hemorrhage
ISAT: International Subarachnoid Aneurysm Trial
MCA: Middle cerebral artery
SAH: Subarachnoid hemorrhage

From the [1]Department of Neurobiology, Care Sciences and Society, Karolinska Institutet; [2]Red Cross University College; [3]Department of Clinical Neuroscience, Karolinska Institutet; and [4]Department of Neurosurgery, Karolinska University Hospital, Stockholm, Sweden

To whom correspondence should be addressed: Ann-Christin von Vogelsang, M.S.N., Ph.D. [E-mail: ann-christin.von-vogelsang@ki.se]

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OBJECTIVE: **To describe epidemiology in relation to gender differences and treatment modalities 10 years after intracranial aneurysm rupture in the Stockholm cohort 1996–1999.**

METHODS: **A total of 468 consecutive patients with aneurysmal subarachnoid hemorrhage were followed-up in a retrospective cohort design 10 years after rupture. Information on medical history, clinical variables, and treatments were obtained from patient records. Causes of death were obtained from patient records and The Swedish Cause of Death Register. Incidence of ruptured aneurysms per 100,000 people were calculated from male, female, and overall population data per year from 1996–1999.**

RESULTS: **Ten years after aneurysm rupture 63.9% ($n = 296$) of patients were still alive. The overall 28-day case fatality was 19.4%; most often deaths were due to the initial hemorrhage. There were no significant differences in survival time between patients treated with clipping (8.4 years, 95% confidence interval 8.1–8.8), compared with endovascularly treated patients (8.2 years, 95% confidence interval 7.4–9.1) (log rank $P = 0.550$). The female incidence was higher than that of men, and women were significantly older at the onset of aneurysm rupture (55.7 vs. 52.8 years, $P = 0.027$).**

CONCLUSIONS: **Ten years after rupture, most treated patients were still alive. The mortality was highest in the first month after rupture, due to the initial hemorrhage. Gender differences were apparent in incidence, but 10 years after the rupture mortality rates and survival times were equal between men and women. Survival time was equal between patients within active treatment modalities.**

INTRODUCTION

Studies have shown wide variations in subarachnoid hemorrhage (SAH) incidence between geographic regions (6). Even within countries incidence differs; in Sweden incidence rates increase by latitude from 11.4–15.2 per 100,000 person-years, from south to north, respectively, and the geographic differences in incidence is greater in women (21). However, not all SAHs are caused by ruptured aneurysms. Other conditions could also cause SAH (33), and the percentage of SAHs originating from ruptured aneurysms varies between >75% to >90% among studies (42). Previous Swedish epidemiologic SAH studies do not distinguish between aneurysmal and nonaneurysmal SAH (20, 21, 30, 39). Ronne-Engstrom et al. (34) reported a specified incidence in ruptured aneurysms of 5.5/100,000 person-years in a Swedish sample from a region north of Stockholm during 1997–2006.

Gender differences in SAH and intracranial aneurysm rupture have been described previously; higher SAH incidences have been found in women than in men (6, 21, 39). Significantly higher frequency of multiple aneurysms in women has been found in Dutch (41) and Japanese populations (18). In a meta-analysis of 58 study populations from 21 countries, the SAH incidence declined 0.6% per year between 1950 and 2005 (6). In northern Sweden a significant decreased male SAH incidence was found between 1985 and 2000, but this decrease was not evident for women (39). Commonality of aneurysm sites for men and women also differs among regions. The most common rupture site for men has been found to be in an area including the anterior cerebral artery (ACA) and the anterior communicating artery (ACoA) (1, 10, 41). For women the most common site differs between studies; the internal carotid artery (ICA) in Norwegian (1) and Japanese (10) populations, the middle cerebral artery (MCA) in a Finnish population (41), and the ACA/ACoA area in a Dutch population (41). Higher mean age among women compared with men has been reported at first-ever stroke for overall stroke types (2), and also for aneurysmal SAH (1, 10). The mean age of both men and women at onset aneurysmal SAH has increased the past decades (31).

Comparisons of survival after aneurysmal SAH in relation to treatment modalities have previously been reported in the International Subarachnoid Aneurysm Trial (ISAT), 1 and 5 years after aneurysm rupture, at both follow-ups significantly more deaths occurred among patients allocated to open surgery compared with endovascular-treated patients (27, 28).

The major causes of death after aneurysmal SAH are related to the initial hemorrhage (5). In Sweden the 28-day case fatality rate has been reported to be 31.7% (21). In studies where death causes are reported after the first year onset aneurysmal SAH, the majority of deaths are cardiac related or due to malignancies (7, 13, 28).

The aim of this study was to describe epidemiology in relation to gender differences and treatment modalities 10 years after intracranial aneurysm rupture in a Stockholm case series 1996–1999.

METHODS

All patients with aneurysmal SAH admitted for intracranial aneurysm rupture at a neurosurgery clinic in Stockholm, Sweden, between January 1, 1996, and December 31, 1999 were included. In Sweden neurosurgical clinics serve well-defined geographic referral areas. This clinic is the only neurosurgical clinic in the Stockholm County Council, and during 1996–1999 the number of inhabitants in the clinic's uptake area increased from 1.74–1.8 million (35). Patients were identified through clinical registers and the inclusion criteria were Swedish citizenship and living in Sweden, for the ability to retrieve Swedish registers' data on survival and death cause. The majority of the included patients came from the Stockholm County referral area. Eleven patients came from other neurosurgical clinics due to shortage of intensive care beds, or temporary inability to perform surgical or endovascular treatment; these patients were excluded from the incidence analysis. Likewise, a small number of patients from our referral area were initially treated with aneurysm occlusion at another neurosurgical clinic, and were thereafter referred to our intensive care unit; these patients were included in all analyses.

Each individual was followed from onset SAH until death, or 10 years after intracranial aneurysm rupture. The diagnosis and aneurysm site was based on angiogram, surgery, or autopsy, and, in 44 patients, computerized tomography. Information about medical history, clinical variables, and treatments were retrospectively obtained from the patients' digital and paper records. The clinic has, since the early 1990s, adopted a management protocol for ruptured intracranial aneurysms involving early referral, earliest possible aneurysm repair, and aggressive antivasospasm treatment (36). The scale for clinical assessment at admission was the grading system of Hunt and Hess (12). Neurological outcome status was evaluated with the Glasgow outcome scale (15), assessed by clinicians and documented at hospital discharge.

The incidence of ruptured aneurysms per 100,000 people was calculated from male, female, and overall population data in Stockholm County per year from 1996–1999 (35). Causes of death were obtained from patient records, death certificates, and International Classification of Diseases codes (ICD-9 and ICD-10) from the Swedish Cause of Death Register. The Swedish Cause of Death Register registers the main cause of death, and up to 20 underlying and contributing causes of death for all deaths among Swedish citizens (37).

The following clinical background parameters were used in this study: Multiple SAH: description of two or more onset SAH reported in the patient records; Multiple aneurysms: no distinction was made between intradural and extradural aneurysm; Additional treatment: if more than one aneurysm treatment procedure was performed to obliterate ruptured aneurysm during initial hospital stay; and Complementary treatment: additional treatment of earlier ruptured aneurysm, not at initial hospital stay. When comparing treatment modalities, patients were divided into three categories: clipping, coiling, and conservative. In the clipping category four patients were treated with clipping and trapping. In the category of conservatively treated patients two cases treated with wrapping are included. Five patients (3 women and 2 men) emigrated between 1998 and 2005 and were excluded from analyses of case fatality, mortality, and survival time. The aneurysm locations were divided into four categories, previously defined by Koivisto et al. (22): ACA: anterior cerebral artery, anterior communicating artery, pericallosal artery; MCA: middle cerebral artery; ICA: internal carotid artery, ophthalmic artery, posterior communicating artery, and anterior choroidal artery; and vertebrobasilar arteries. The Stockholm regional board for ethics of research involving humans approved the study (2006/1431-31/1).

Data Analysis

SPSS for Windows 16.0 (SPSS Inc.; Chicago, Illinois, USA) was used for statistical analy-

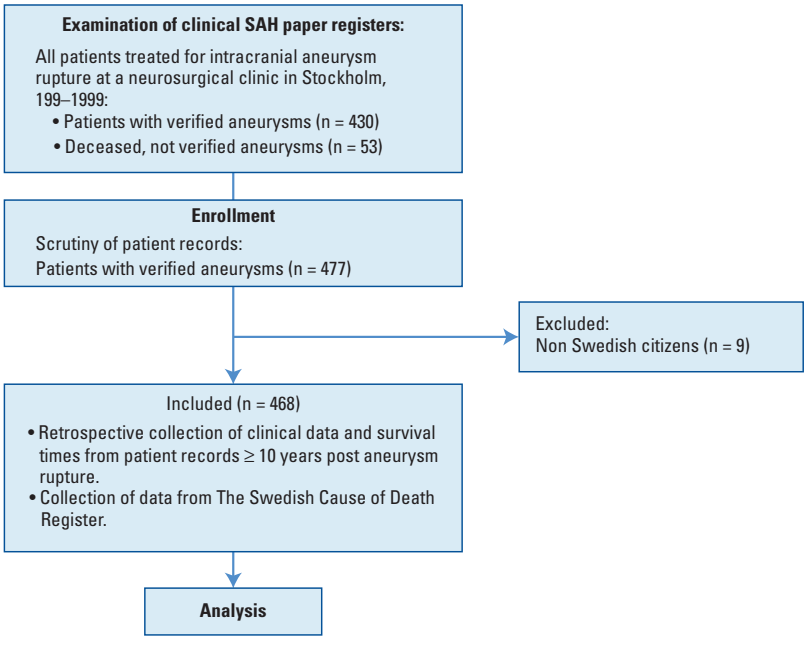

Figure 1. Flow diagram of participants and data collection.