Risk Factors for Three Phases of 12-Month Mortality in 1657 Patients from a Defined Population After Acute Aneurysmal Subarachnoid Hemorrhage

Petros N. Karamanakos[1], Mikael von und zu Fraunberg[1], Stepani Bendel[2], Terhi Huttunen[1], Mitja Kurki[1], Juha Hernesniemi[3], Antti Ronkainen[1], Jaakko Rinne[1], Juha E. Jaaskelainen[1], Timo Koivisto[1]

Key words
- Independent risk factors
- Mortality
- Multivariate analysis
- Saccular intracranial aneurysm
- Subarachnoid hemorrhage

Abbreviations and Acronyms
CI: Confidence interval
H&H: Hunt and Hess
IA: Intracranial aneurysm
ICH: Intracerebral hemorrhage
IVH: Intraventricular hemorrhage
KUH: Kuopio University Hospital
OR: Odds ratio
SAH: Subarachnoid hemorrhage (from saccular intracranial aneurysm)

From [1]Neurosurgery of NeuroCenter, and [2]Department of Intensive Care, Kuopio University Hospital, Kuopio; and [3]Department of Neurosurgery, Helsinki University Central Hospital, Helsinki, Finland

To whom correspondence should be addressed: Timo Koivisto, M.D., Ph.D. [E-mail: timo.koivisto@kuh.fi]

Citation: World Neurosurg. (2012) 78, 6:631-639.
DOI: 10.1016/j.wneu.2011.08.033

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

1878-8750/$ - see front matter

OBJECTIVE: **To analyze the impact of factors known after admission on mortality attributable to aneurysmal subarachnoid hemorrhage (SAH) resulting from saccular intracranial aneurysm (IA).**

METHODS: **Data of 1657 consecutive patients admitted alive within 24 hours after aneurysmal SAH to Kuopio Neurosurgery during the years 1980–2007 from a defined population were analyzed.**

RESULTS: **Aneurysmal SAH caused excess mortality for 12 months, after which other causes of death became dominant. The 12-month mortality curve on a logarithmic time scale indicated acute (first 3 days), subacute (4–30 days), and delayed (1–12 months) mortality, with cumulative rates of 11% at 3 days, 22% at 30 days, and 27% at 12 months. The acute mortality was predicted by Hunt & Hess (H&H) grades IV–V, ruptured aneurysm ≥ 15 mm, and acute subdural hematoma. Age, gender, intracerebral hemorrhage (ICH), and time period of admission were not independent risk factors. Advanced age, H&H grades IV–V, intraventricular hemorrhage (IVH), giant ruptured saccular IA, ruptured saccular IA on the internal carotid artery or the basilar artery bifurcation, and severe hydrocephalus in different combinations predicted subacute and delayed mortality. Patients in good condition on admission had a mortality rate of only 3.5% at 12 months, regardless of age.**

CONCLUSIONS: **Sequelae of aneurysmal SAH were the leading cause of death for 12 months. Mortality analysis of this period displayed three phases with distinct independent risk factors. These data support the creation of prognosticators for prediction on admission of the everyday individual risk of death until 12 months after aneurysmal SAH.**

INTRODUCTION

Aneurysmal subarachnoid hemorrhage (SAH) resulting from a ruptured saccular intracranial aneurysm (IA) is a devastating form of stroke that affects the working age population (2, 12, 27). Acute aneurysmal SAH is a complex and critical systemic condition. Survivors of the primary bleed require multidisciplinary neurointensive care to prevent further damage (eg, from rebleeding, hydrocephalus, increased intracranial pressure, delayed ischemic brain injury, seizures, electrolyte disturbances, cardiac and pulmonary dysfunction, and complications of the management) (2, 16). In recent multivariate analyses of large (> 500 patients) aneurysmal SAH cohorts, the subsequent outcome and mortality have mainly been reported at 2 months, 3 months, or 6 months after aneurysmal SAH (**Table 1**) (5–7, 15, 18, 21, 26, 30, 32). However, the optimal time point for the overall assessment of outcome and the significance of various risk factors at different time points after aneurysmal SAH have not been clarified.

We studied the mortality of 1657 patients admitted alive within 24 hours after aneurysmal SAH during the period 1980–2007 to Kuopio University Hospital (KUH), solely serving a defined Eastern Finnish population (12). Using the Kuopio Intracranial Aneurysm Database (www.uef.fi/ns), we analyzed the shape of the cumulative mortality curve to differentiate between early mortality and subsequent mortality and tested how factors known after admission predicted mortality at different time points after aneurysmal SAH. We also compared the mortality rates after endovascular occlusive therapy, introduced in 1993 in our center, and after microsurgical clipping. Our data support the creation of prognosticators of individual outcome after aneurysmal SAH.

METHODS

Catchment Population of Kuopio University Hospital

During the study period from 1980–2007, the Department of Neurosurgery of KUH solely provided full-time (24 hours a day, 7 days a week) neurosurgical services for the KUH catchment area in Eastern Finland (12). From 1980–2007, the geographic area remained the same, but the population de-

Table 1. Independent Risk Factors for Poor Outcome After Aneurysmal Subarachnoid Hemorrhage in Large Series (> 500 Patients) Since 2000

Series	Number of Patients	Occlusive Therapy		Measure and Time Point for Poor Outcome	Independent Risk Factors for Poor Outcome
		Microsurgical	Endovascular		
Molyneux et al., 2005, ISAT Study (18)	2128	1055	1063	mRS 3–6 at 12 months	Age, WFNS, aneurysm location
Wartenberg et al., 2006 (30)	513	310	95	mRS 4–6 at 3 months	Fever, anemia, hyperglycemia (after adjustment for age, aneurysm size > 10 mm, H&H grade, rebleeding, infarct owing to vasospasm)
Rosengart et al., 2007, Tirilazad Trial (26)	3567	3567	0	GOS 1–3 at 3 months	Age, WFNS grade, SAH thickness on initial CT, posterior circulation saccular IA, large saccular IA size, IVH, ICH, high systolic blood pressure on admission, history of hypertension, prior SAH, myocardial infarction and liver disease, temperature on day 8 ≥ 38°C, anticonvulsant use, no therapeutic hypervolemia or induced hypertension, symptomatic vasospasm, cerebral infarction
Frontera et al., 2008 (6)	573	NA	NA	Mortality at 3 months	Bloodstream infection (after control for age, H&H grade, and aneurysm size)
Güresir et al., 2008 (7)	585	NA	NA	mRS 3–6 at 6 months	Age, ICH > 50 cm^3, early hydrocephalus, aneurysm obliteration within 6 hours after aneurysmal SAH
Zacharia et al., 2009 (32)	787	NA	NA	mRS 4–6 at 3 months	Age, total scans, poor admission H&H, premorbid mRS ≤ 1, risk of renal failure, new infarct secondary to vasospasm, diabetes
Coghlan et al., 2009, IHAST Study (5)	1000	1000	0	Mortality at 3 months	Age, WFNS II and III vs. I, NSSTTWA, QTc per 1-msec increase, HR ≤ 60 or 81–138 vs 61–70
Langham et al., 2009 (15)	2397	1269	905	Extended GOS 5–8 at 6 months	Age, WFNS grade, amount of blood on CT, aneurysm size > 10 mm, concurrent medical conditions, deterioration before aneurysm occlusion
O'Kelly et al., 2010 (21)	3120	2342	778	Hemorrhage-free survival (time to death or readmission for SAH)	Coiling, male sex, age, Charlson index, ICH, aneurysm size > 2.5 cm, ventilated, hydrocephalus

CT, computed tomography; GOS, Glasgow Outcome Scale; H&H, Hunt and Hess; HR, heart rate; IA, intracranial aneurysm; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; mRS, modified Rankin Scale; NA, not available; NSTTWA, nonspecific ST/T-wave changes in ECG; QTc, QT interval corrected in ECG; SAH, subarachnoid hemorrhage (from saccular intracranial aneurysm); WFNS, World Federation of Neurological Surgeons.

creased from 863,726 to 851,066 (12). The median age increased, from 31 to 42 years in men and from 34 to 45 years in women, but the proportion of men remained unchanged at 49% (12). The KUH area contains four central hospitals with neurologic units of their own.

Kuopio Intracranial Aneurysm Database

Patients with aneurysmal SAH have been routinely admitted to KUH for acute angiography and treatment, if not moribund or very aged. Exact numbers of rejection are unavailable. KUH Neurosurgery maintains a database on all cases of aneurysmal SAH admitted to KUH since 1977. The data are prospective since 1990, and earlier cases have been entered from the hospital records. The database is run by a dedicated full-time nurse, who interviews all new patients with aneurysmal SAH and collects and codes into variables detailed information, including family history. The criterion for a saccular IA family is at least two affected first-degree relatives. Clinical data from the hospital periods and follow-up visits are entered. Clinical data from the national registries such as the causes of death, cancer, hospital diagnoses, and use of prescribed drugs are entered. Several studies on saccular IA have been published from the database (3, 8, 9, 11, 17, 23–25, 28, 31).