

## PAPER

# Subarachnoid haemorrhage in patients $\geq 75$ years: clinical course, treatment and outcome

D J Nieuwkamp, G J E Rinkel, R Silva, P Greebe, D A Schokking, J M Ferro



See Editorial Commentary, p 900

*J Neurol Neurosurg Psychiatry* 2006;77:933–937. doi: 10.1136/jnnp.2005.084350

See end of article for authors' affiliations

Correspondence to:  
D J Nieuwkamp,  
Department of Neurology,  
University Medical Centre  
Utrecht, C03.236, PO Box  
85500, 3584 CX Utrecht,  
The Netherlands; d.  
nieuwkamp@umcutrecht.nl

Received  
16 November 2005  
Revised version received  
5 April 2006  
Accepted 6 April 2006  
Published Online First  
25 April 2006

**Background:** The number of elderly patients being admitted with aneurysmal subarachnoid haemorrhage (SAH) has been increasing. Treatment of the aneurysm may be offset by the higher rate of surgical or endovascular complications.

**Aim:** To study the clinical condition at onset, complications during clinical course, treatment and outcome in a consecutive series of elderly patients.

**Methods:** Patients who were  $\geq 75$  years at the onset of SAH were selected from the databases of two hospitals. Data on clinical condition at onset (poor condition defined as World Federation of Neurological Surgeons (WFNS) Scale IV and V), clinical course, treatment and outcome were extracted. Univariate and multivariate regression analyses were carried out to identify predictors for in-hospital death and poor outcome, defined as death or dependency.

**Results:** The data of 170 patients were retrieved, of whom 25 (15%) patients were independent at discharge; none of these patients had been admitted in a poor condition. Poor clinical condition on admission (odds ratio (OR) 7.9; 95% confidence interval (CI) 3.7 to 17) and recurrent haemorrhage (OR 7.5; 95% CI 2.5 to 23) were the strongest predictors for in-hospital death. Recurrent haemorrhage was the strongest predictor for poor outcome in the subset of patients who were admitted in good clinical condition. In all, 10 of 47 (21%) patients were independent at discharge after neurosurgical clipping (n = 34) or endovascular coiling (n = 13).

**Conclusion:** Elderly patients with SAH have a poor prognosis. The effect of the initial haemorrhage is the most common reason for poor outcome. For patients who are admitted in good clinical condition, the most important complication leading to poor outcome is recurrent haemorrhage. Treatment of the aneurysm in patients  $\geq 75$  years is feasible, may improve the outcome and should be strongly considered in patients who are admitted in a good condition.

The incidence of subarachnoid haemorrhage (SAH) does not decrease, and probably even increases after the seventh decade of life.<sup>1,2</sup> The death rate in patients increases with age.<sup>2</sup> With the ageing of the population, the number of patients with SAH increases. In our institutions, the proportion of patients with SAH who are  $\geq 75$  years has risen to about 10%.

Rebleeding is an important complication after SAH; in 80% of instances, it results in death or dependence.<sup>3</sup> If the aneurysm is left untreated, the risk of rebleeding within the first month after the haemorrhage is 40%.<sup>4</sup> Treatment of the aneurysm in itself is not without risks either, and increasing age is an important risk factor for complications from operative or endovascular occlusion of aneurysms.<sup>5–7</sup> Even for unruptured aneurysms, the risk of poor outcome in patients  $\geq 50$  years varies from 10% to 30%, depending on the size and site of the aneurysm and the method of treatment.<sup>7</sup> In patients with SAH, the risks of treatment of the aneurysm are probably even higher—for example, owing to the increased risk of secondary ischaemia.<sup>4</sup> Thus, for elderly patients with SAH, treatment of the aneurysm may be less beneficial than in younger patients or not beneficial at all. Most previous studies on elderly patients with SAH were based on small samples, were not restricted to old people, or described only those patients in whom the aneurysm was treated. We studied the clinical condition at onset, complications during clinical course, treatment of the aneurysm and outcome in a consecutive series of patients who were  $\geq 75$  years of age at the onset of SAH. In addition, we assessed the risk factors for

poor outcome and occurrence of complications in these patients.

## METHODS

From the SAH prospective databases of two hospitals, we retrieved the data of patients who were admitted from January 1990 to December 2004 and were  $\geq 75$  years at the onset of SAH. The diagnosis of SAH was based on the clinical history and the presence of SAH on CT. For patients included in this study, we collected data on anticoagulant treatment before SAH, loss of consciousness at the onset of haemorrhage and clinical condition on admission. Clinical condition was assessed by means of the World Federation of Neurological Surgeons (WFNS) Grading Scale for SAH.<sup>8</sup> We dichotomised clinical condition on admission into good (WFNS I–III) and poor (WFNS IV and V). We recorded the presence of cisternal blood, intracerebral extension of haemorrhage, intraventricular extension of haemorrhage, presence of subdural haematoma and enlargement of ventricles by CT. We also extracted the results of conventional angiography, CT angiography or MR angiography, if performed. In view of the purpose of the study, we recorded whether neurosurgical clipping or endovascular treatment was given. Regarding the clinical course, we collected data on the following complications: recurrent intracranial haemorrhages, secondary cerebral ischaemia, hydrocephalus, other intracranial complications such as infections, and medical

**Abbreviations:** GOS, Glasgow Outcome Scale; SAH, subarachnoid haemorrhage; WFNS, World Federation of Neurological Surgeons

**Table 1** Baseline characteristics

	All (n = 170)	Age (years)		
		75–79 (n = 107)	80–84 (n = 40)	≥85 (n = 23)
Women	139 (82)	88 (82)	32 (80)	19 (83)
Anticoagulant treatment				
Yes	13 (8)	9 (8)	4 (10)	—
Unknown	14 (8)	11 (10)	2 (5)	1 (4)
Loss of consciousness*				
No	68 (40)	39 (36)	17 (43)	12 (52)
<1 h	22 (13)	14 (13)	4 (10)	4 (17)
>1 h	37 (22)	23 (22)	11 (28)	3 (13)
Duration unknown	33 (19)	23 (22)	6 (15)	4 (17)
WFNS Scale				
I	56 (33)	38 (36)	13 (33)	5 (22)
II and III	54 (32)	33 (31)	10 (25)	11 (48)
IV and V	60 (35)	36 (34)	17 (43)	7 (32)
CT*				
ICH	34 (20)	22 (21)	10 (25)	2 (9)
IVH	83 (49)	50 (47)	18 (45)	15 (65)
SDH	7 (4)	6 (6)	1 (3)	—
Ventricles enlarged	58 (34)	38 (36)	13 (33)	7 (30)
Angiography				
Aneurysm proved	97 (57)	61 (57)	23 (58)	13 (57)
Aneurysm absent	28 (16)	18 (17)	6 (15)	4 (17)
Not performed	45 (26)	28 (26)	11 (28)	6 (26)
Site of aneurysm				
Carotid	36 (21)	23 (22)	8 (20)	5 (22)
MCA	16 (9)	14 (13)	2 (5)	—
Ant com art	42 (25)	26 (24)	10 (25)	6 (26)
Posterior circulation	14 (8)	8 (8)	3 (8)	3 (13)
Patients with >1 aneurysm	13 (12)†	8 (11)	4 (17)	1 (7)
Intervention				
Clip	34 (20)	29 (27)	4 (10)	1 (4)
Coil	13 (8)	7 (7)	6 (15)	—
Wrapping	2 (1)	2 (2)	—	—
No intervention	121 (71)	69 (65)	30 (75)	22 (96)
Complications				
Recurrent haemorrhage	27 (16)	21 (20)	3 (8)	3 (13)
Secondary ischaemia	37 (22)	24 (22)	8 (20)	5 (22)
Hydrocephalus	70 (41)	47 (44)	15 (38)	8 (35)
Medical complications	79 (47)	43 (40)	25 (63)	11 (48)
Outcome at discharge				
In-hospital death	85 (50)	53 (50)	20 (50)	12 (52)
Dependent (GOS 3)	60 (35)	37 (35)	15 (38)	8 (35)
Independent (GOS 4)	11 (7)	8 (8)	2 (5)	1 (4)
Good recovery (GOS 5)	14 (8)	9 (8)	3 (8)	2 (9)
Cause of death				
Initial haemorrhage	28 (32)	17 (29)	7 (37)	4 (36)
Recurrent haemorrhage	24 (27)	18 (31)	4 (21)	2 (18)
Secondary ischaemia	8 (9)	7 (12)	—	1 (9)
Other intracranial complications	8 (9)	6 (10)	1 (5)	1 (9)
Medical complications	13 (15)	6 (10)	5 (26)	2 (18)

Values are given as n (%).

Ant com art, anterior communicating artery; GOS, Glasgow Outcome Scale; GOS 3, dependent; GOS 4, independent; GOS 5, good recovery; ICH, intracerebral haemorrhage; IVH, intraventricular haemorrhage; MCA, middle cerebral artery; SDH, subdural haematoma; WFNS, World Federation of Neurological Surgeons.

\*Total <170 because of unknown data.

†Percentage of all patients with at least one proved aneurysm.

complications. Secondary cerebral ischaemia was defined as the occurrence of a new hypodense lesion on CT, compatible with the clinical features of secondary cerebral ischaemia. Medical complications were included only if they had led to clinical deterioration of the patient. For outcome, we used data on the Glasgow Outcome Scale (GOS) at discharge and at 2–4 months after the onset of SAH.<sup>9</sup>

### Data analysis

We compared the baseline characteristics of patients in both hospitals. The proportion of patients who were in poor clinical condition on admission differed between the two centres: 15% (95% confidence interval (CI) 7% to 28%) of patients in Lisbon and 44% (95% CI 35% to 53%) of patients in Utrecht. Otherwise, the baseline characteristics of the patients were similar. General management of SAH was

similar; all patients were treated with nimodipine and kept normovolaemic. For the patients who were in good clinical condition the proportions of patients who underwent angiography and treatment of the aneurysm were similar as were the proportion of patients with complications and the proportion of patients that died during admission. We therefore decided to combine both groups of patients in subsequent analyses.

Because follow-up data were not available for all patients and we assessed outcome at discharge, whereas the proportion of independent patients increased after discharge, we used two different outcome measurements for outcome at discharge: death (GOS 1) and poor outcome defined as death or dependence (GOS 1–3). We calculated odds ratios (ORs) with corresponding 95% CIs of baseline characteristics and the occurrence of medical complications for in-hospital death

and for poor outcome, and carried out stepwise forward multivariate logistic regression analyses for those factors that were independent predictors in the univariate analyses ( $p < 0.05$ ). Similar analyses were carried out for the subgroup of patients who were admitted in good clinical condition.

## RESULTS

From the databases, we retrieved the data of 178 patients who were  $\geq 75$  years at the onset of SAH: 124 from Utrecht and 54 from Lisbon. Of these patients, 6 (3%) had a perimesencephalic pattern of haemorrhage on CT, one had a plexus papilloma and one had a dissection of the vertebral artery as the cause of SAH. These eight patients were excluded. Further analyses were carried out on the remaining 170 patients with a probable or definite aneurysmal cause of SAH. Table 1 shows the baseline characteristics of these 170 patients. The median length of admission was 22 days.

All 27 patients with a recurrent haemorrhage after admission died or remained dependent as a result of the haemorrhage. Of the 27 patients, 18 (67%) with recurrent haemorrhage were admitted in good clinical condition. Data on the timing of rebleeding were available for 22 of the 27 patients. The median day on which the recurrent haemorrhage occurred was day 3 (range 0–29). Secondary ischaemia occurred in 37 (22%) patients and symptomatic hydrocephalus in 70 (41%).

Neurosurgical clipping was carried out in 34 (20%) patients, endovascular coiling in 13 (8%) and wrapping of the aneurysm in 2 (1%). The median age of the patients in whom the aneurysm was treated (78; range 75–86 years) was lower than that of the patients in whom the aneurysm was not treated (80; range 75–92 years). In all, 94% of patients in whom the aneurysm was clipped, 92% of those in whom the aneurysm was coiled and 53% of those in whom the aneurysm was not treated, were admitted in good clinical condition (WFNS I–III). The death rate for patients who were admitted in good neurological condition in whom the aneurysm was treated by means of clipping or coiling was 14%, compared with 48% for patients not treated for aneurysm. At discharge, 10 of 47 (21%, 95% CI 11% to 36%) patients in whom the aneurysm was treated were independent, in contrast with 14 of 121 (12%, 95% CI 6% to 17%) patients who were not treated. The prognosis according to location of the aneurysm was not statistically significantly different between patients with aneurysms of the anterior communicating artery and those with aneurysms at other locations; 6 of 42 (14%) patients with aneurysms of the anterior communicating artery showed a good outcome at

discharge, compared with 7 of 66 (11%) patients with aneurysms at other locations. Outcome at 2–4 months after SAH was available for a subgroup of patients (table 2).

Within the group of 133 patients with follow-up data available, 48 patients were alive at the time of discharge, 34 (71%) were dependent and 14 (29%) independent. At follow-up, 8 of the 48 (17%) patients had died, 16 (33%) were dependent and 24 (50%) independent. In 37 patients, no follow-up data were available; at discharge, 26 (70%) patients were dependent and 11 (30%) independent.

Table 3 lists the risk factors for the two outcome categories (in-hospital death and death plus dependence).

In-hospital death was related to loss of consciousness, poor condition on admission, intraventricular extension of the haemorrhage and recurrent haemorrhage. With multivariate logistic regression analyses, only poor condition on admission (OR 11; 95% CI 4.7 to 24) and recurrent haemorrhage (OR 10; 95% CI 3.0 to 34) remained independent predictors.

None of the 60 patients who were admitted in poor condition (0%; 95% CI 0% to 6%) or any of the seven patients with subdural haematoma (0%; 95% CI 0% to 41%) on admission was independent at discharge. In the subset of 110 patients who were admitted in good clinical condition, the only statistically significant predictor for poor outcome was recurrent haemorrhage (all the 18 patients with rebleeding died or were dependent at the time of discharge).

## DISCUSSION

We found that, on average, the overall outcome was poor in patients who were admitted with SAH and who were  $\geq 75$  years. Half the patients died and only one of six patients regained independence at the time of discharge. In this subset of patients  $\geq 75$  years, the death rate did not increase with increasing age. The most important risk factor for poor outcome was the effect of the initial haemorrhage, indicated by poor clinical condition on admission. The most important risk factor for poor outcome in patients who were admitted in good neurological condition was rebleeding. Treatment of the aneurysm should therefore be strongly considered in patients with good clinical condition on admission to prevent poor outcome from rebleeding. Treatment of the aneurysm in patients who are in poor condition should, on the contrary, be considered with caution because of the high a priori chance of poor outcome in this group of patients.

About 70% of patients who developed recurrent haemorrhage were admitted in good clinical condition. As rebleeding occurred within 4 days after the haemorrhage in half of the patients, the aneurysm should probably be treated as soon as

**Table 2** Outcome at discharge according to neurological condition on admission and aneurysm treatment

	Outcome at discharge (GOS)				Outcome at follow up (GOS)				
	Number of patients	In-hospital death	Dependent	Independent	Number of patients	Death n (%)	Dependent n (%)	Independent n (%)	
All patients	170	85 (50)	60 (35)	25 (15)	All patients*	133	93 (70)	16 (12)	24 (18)
Clipping	34	4 (12)	22 (65)	8 (24)	Clipping	28	7 (25)	7 (25)	14 (50)
Coiling	13	3 (23)	8 (62)	2 (15)	Coiling	8	4 (50)	2 (25)	2 (25)
No occlusion	121	78 (65)	29 (24)	14 (12)	No occlusion	95	82 (86)	7 (7)	6 (6)
WFNS I–III	110	37 (34)	48 (44)	25 (23)	WFNS I–III	79	43 (54)	12 (15)	24 (31)
Conservative	64	31 (48)	19 (30)	14 (22)	Conservative	44	33 (75)	5 (11)	6 (14)
Clipping	32	4 (13)	20 (63)	8 (25)	Clipping	26	7 (27)	5 (19)	14 (54)
Coiling	12	2 (17)	8 (67)	2 (17)	Coiling	7	3 (43)	2 (29)	2 (29)
WFNS IV–V	60	48 (80)	12 (20)	—	WFNS IV–V	54	51 (93)	4 (7)	—
Conservative	57	47 (83)	10 (18)	—	Conservative	51	49 (96)	2 (4)	—
Clipping	2	—	2 (100)	—	Clipping	2	—	2 (100)	—
Coiling	1	1 (100)	—	—	Coiling	1	1 (100)	—	—

Values are n (%).

GOS, Glasgow Outcome Scale; GOS 3, dependent; GOS 4, independent; GOS 5, good recovery; WFNS, World Federation of Neurological Surgeons.

\*Total <170 because of unknown data.

**Table 3** Risk factors for in-hospital death and for death or dependency at discharge

	In-hospital death		Death or dependency at discharge	
	OR	95% CI	OR	95% CI
Women	0.7	0.3 to 1.5	1.1	0.4 to 3.3
Age $\geq 80$	1.1	0.6 to 2.0	1.3	0.5 to 3.2
Oral anticoagulants	1.7	0.5 to 5.5	0.8	0.2 to 4.1
Loss of consciousness	3.0	1.6 to 5.9	1.4	0.6 to 3.4
Poor condition on admission (WFNS IV–V) Scale*	7.9	3.7 to 17	$\infty$	0.0 to $\infty$
Intracerebral extension of haemorrhage	1.6	0.8 to 3.5	2.1	0.6 to 7.3
Intraventricular extension of haemorrhage	2.4	1.3 to 4.4	1.9	0.8 to 4.6
Subdural extension of haemorrhage*	6.6	0.8 to 56	$\infty$	0.0 to $\infty$
Secondary ischaemia	0.8	0.4 to 1.7	1.6	0.5 to 4.8
Hydrocephalus	1.2	0.7 to 2.2	2.5	0.9 to 6.6
Rebleeding*	7.5	2.5 to 23	$\infty$	0.0 to $\infty$
Medical complications	0.9	0.5 to 1.6	0.9	0.4 to 2.2

WFNS, World Federation of Neurological Surgeons.

\*These patients had a poor outcome (death or dependence) at discharge.

possible. The cumulative risk of recurrent haemorrhage is highest on the first day after the haemorrhage and decreases steadily afterwards.<sup>4</sup> Treatment of the aneurysm carries a considerable risk of complications. Even for unruptured aneurysms in patients  $\geq 70$  years, treatment of the aneurysm is associated with poor outcome rates of up to 30%,<sup>4, 7, 10</sup> and these rates are probably higher in patients with ruptured aneurysms. Therefore, probably only early treatment has a beneficial effect. If treatment is postponed, the risks of treatment may be higher than the risk of rebleeding.

Patients who were admitted in good neurological condition, and in whom the aneurysm was treated, had a much lower death rate than those without treatment of the aneurysm. At discharge, the proportions of independent patients in the treatment and conservative groups were similar. Thus, the reduced death rate after treatment of the aneurysm resulted in a larger proportion of dependent patients at discharge. However, recovery after SAH extends over a long period of time, between 4 and 18 months after SAH, outcome still improved markedly.<sup>11</sup> Outcome at follow-up, 2–4 months after SAH, although not available for all patients, showed an increase in the proportion of independent patients. An additional increase in this proportion of independent patients is consequently possible.<sup>11</sup>

The group of patients with SAH  $\geq 75$  years differed in several aspects from the series of patients with SAH in general. Firstly, the proportion of women (82%) in this series was much higher than that in our database of all patients with SAH (62%; unpublished data) and in other studies from western European populations (60%).<sup>12</sup> This is probably, at least to some extent, due to the higher percentage of older women than older men in the general population. Secondly, in the entire series of 178 patients, only 3% had perimesencephalic haemorrhage, whereas, in general, the proportion of patients with perimesencephalic haemorrhage is about 10%.<sup>13, 14</sup> Thirdly, the proportion of medical complications and hydrocephalus was higher in patients with SAH  $\geq 75$  years than in patients with SAH in general.<sup>15</sup>

The retrospective design of the study has introduced some limitations. One limitation is that treatment was not according to a prespecified protocol, but was left to the discretion of the doctor or surgeon treating the patient in either of the two centres. A second limitation is that patients were recruited over a prolonged period. During this period, the proportion of patients with no confirmation of the aneurysm decreased from 58% for patients who were admitted between 1990 and 1994, to 23% for those who were admitted between 1995 and 1999, and to 20% for

patients who were admitted between 2000 and 2004. Moreover, treatment for aneurysm had changed in this period with the introduction of coiling. The data on clinical condition on admission, clinical course, treatment, complications and outcome, however, were prospectively collected for the databases and are therefore not subject to bias. In the Santa Maria Hospital, Lisbon, Portugal, serial transcranial Doppler analysis was routinely carried out; however, it was not carried out in the University Medical Centre Utrecht, Utrecht, The Netherlands, because the positive and negative predictive values of transcranial Doppler analysis are moderate.<sup>16</sup> For all patients, we had data on secondary ischaemia, defined as the occurrence of a new hypodense lesion on CT, which was compatible with the clinical features of secondary cerebral ischaemia.

Our study differs from most other studies in the large proportion of patients  $>80$  years, the detailed information on the clinical course and complications, and the risk factor analyses for poor outcome. Parts of the results of our study are supported by data from previous studies. Many studies found a poor outcome for elderly patients with SAH, although the age limit for the elderly was often considered to be 70 years,<sup>17–21</sup> and sometimes even 65 years.<sup>22–25</sup> In our study, death rate did not increase with increasing age. In contrast, in a Japanese study, an increased death rate was found for patients  $\geq 79$  years compared with those aged 70–79 years.<sup>26</sup>

Others have also reported that patients can have a good outcome after surgical treatment, but the number of patients  $\geq 80$  years in those studies was very small or unspecified.<sup>17, 18, 27</sup> We did not observe independent outcome at discharge in patients who were admitted in a poor condition, but in studies assessing outcome at 3–16 months after the haemorrhage the proportion of independent patients ranged from 12% to 38%.<sup>17–19, 21, 27</sup> Thus, at longer periods of follow-up, some patients who were admitted in poor condition recovered to an independent state. Whether this related to treatment for aneurysm or to withholding treatment for aneurysm is unclear.

Endovascular treatment is less invasive than operation and therefore enables more rapid recovery, which is advantageous in older patients. The disadvantage is that higher age increases the risk of complications from angiography and therefore most likely also from endovascular procedures.<sup>28</sup> The number of patients who were treated by endovascular coiling was too small for a formal comparison. A few other studies have dealt with endovascular treatment in elderly patients with SAH, where favourable outcomes up to 48%

were reported.<sup>25–29,33</sup> Endovascular treatment may therefore be a good alternative for elderly patients with SAH. Data from the International Subarachnoid Aneurysm Trial, in which neurosurgical clipping was compared with endovascular coiling, were not conclusive for patients  $\geq 70$  years. In this trial, a relatively small number of patients  $\geq 70$  years was included, because individual investigators often expected that elderly patients would fare worse with surgery, which prevented their inclusion in the trial.<sup>34</sup>

Our results show that treatment of the aneurysm in patients who are admitted in good neurological condition can lead to a good outcome and suggest that patients in good clinical condition have a higher chance of good recovery if the aneurysm is treated. The conclusion, however, that patients in good clinical condition have a higher chance of good recovery if the aneurysm is treated is based on an indirect comparison. A randomised study comparing aneurysm occlusion with no treatment for aneurysm in the elderly will probably never be undertaken. In theory, a case-control study could be possible if datasets are available from large hospitals where aneurysms are never treated in patients with SAH at old age and from hospitals where aneurysms are usually treated in patients with SAH at old age. In the absence of such datasets, we have to base our treatment decisions on observational studies.

#### Authors' affiliations

**D J Nieuwkamp, G J E Rinkel, P Greebe**, Department of Neurology, University Medical Centre Utrecht, Utrecht, The Netherlands  
**R Silva, D A Schokking, J M Ferro**, The Hospital Santa Maria, Universidade de Lisboa, Lisbon, Portugal

Funding: This study was in part funded by an established clinical investigator grant from the Netherlands Heart Foundation to GJER (Grant D98.014), a grant from Fundação para a Ciência e Tecnologia (Grant PRAXIS 2/2.1/SAU/1414/95) to JMF and a grant from the Netherlands Organisation for Scientific Research/ZonMw (Grant 920-03-299) to DJN.

Competing interests: None.

#### REFERENCES

- The ACROSS Group.** Epidemiology of aneurysmal subarachnoid hemorrhage in Australia and New Zealand: incidence and case fatality from the Australasian Cooperative Research on Subarachnoid Hemorrhage Study (ACROSS). *Stroke* 2000;**31**:1843–50.
- Pobereskin LH.** Incidence and outcome of subarachnoid haemorrhage: a retrospective population based study. *J Neural Neurosurg Psychiatry* 2001;**70**:340–3.
- Roos YBWE, de Haan RJ, Beenen LFM, et al.** Complications and outcome in patients with aneurysmal subarachnoid haemorrhage: a prospective hospital based cohort study in The Netherlands. *J Neural Neurosurg Psychiatry* 2000;**68**:337–41.
- Bristra EH, Rinkel GJ, Algra A, et al.** Rebleeding, secondary ischemia, and timing of operation in patients with subarachnoid hemorrhage. *Neurology* 2000;**55**:1656–60.
- Raaymakers TWM, Rinkel GJE, Limburg M, et al.** Mortality and morbidity of surgery for unruptured intracranial aneurysms: a meta-analysis. *Stroke* 1998;**29**:1531–8.
- The International Study of Unruptured Intracranial Aneurysms Investigators.** Unruptured intracranial aneurysms—risk of rupture and risks of surgical intervention. *N Engl J Med* 1998;**339**:1725–33.
- Wiebers DO.** Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet* 2003;**362**:103–10.

- Drake CG.** Report of World Federation of Neurological Surgeons Committee on a Universal Subarachnoid Hemorrhage Grading Scale. *J Neurosurg* 1988;**68**:985–6.
- Jennett B, Bond M.** Assessment of outcome after severe brain damage. *Lancet* 1975;**1**:480–4.
- Bristra EH, Algra A, Rinkel GJ, et al.** Effectiveness of neurosurgical clip application in patients with aneurysmal subarachnoid hemorrhage. *J Neurosurg* 2002;**97**:1036–41.
- Hop JW, Rinkel GJ, Algra A, et al.** Changes in functional outcome and quality of life in patients and caregivers after aneurysmal subarachnoid hemorrhage. *J Neurosurg* 2001;**95**:957–63.
- Linn FH, Rinkel GJ, Algra A, et al.** Incidence of subarachnoid hemorrhage: role of region, year, and rate of computed tomography: a meta-analysis. *Stroke* 1996;**27**:625–9.
- Rinkel GJ, van Gijn J, Wijdicks EF.** Subarachnoid hemorrhage without detectable aneurysm. A review of the causes. *Stroke* 1993;**24**:1403–9.
- Schwartz TH, Solomon RA.** Perimesencephalic nonaneurysmal subarachnoid hemorrhage: review of the literature. *Neurosurgery* 1996;**39**:433–40.
- Roos Y.** Antifibrinolytic treatment in subarachnoid hemorrhage: a randomized placebo-controlled trial. *Neurology* 2000;**54**:77.
- Rabinstein AA, Friedman JA, Weigand SD, et al.** Predictors of cerebral infarction in aneurysmal subarachnoid hemorrhage. *Stroke* 2004;**35**:1862–6.
- Chung RY, Carter BS, Norbash A, et al.** Management outcomes for ruptured and unruptured aneurysms in the elderly. *Neurosurgery* 2000;**47**:827–32.
- Fridriksson SM, Hillman J, Saveland H, et al.** Intracranial aneurysm surgery in the 8th and 9th decades of life: impact on population-based management outcome. *Neurosurgery* 1995;**37**:627–31.
- Yamashita K, Kashiwagi S, Kato S, et al.** Cerebral aneurysms in the elderly in Yamaguchi, Japan: analysis of the Yamaguchi Data Bank of Cerebral Aneurysm from 1985 to 1995. *Stroke* 1997;**28**:1926–31.
- Ferch R, Pasqualin A, Barone G, et al.** Surgical management of ruptured aneurysms in the eighth and ninth decades. *Acta Neurochir (Wien)* 2003;**145**:439–45.
- Lanzino G, Kassell NF, Germanson TP, et al.** Age and outcome after aneurysmal subarachnoid hemorrhage: why do older patients fare worse? *J Neurosurg* 1996;**85**:410–8.
- Yoshimoto Y, Kwak S.** Age-related multifactorial causes of neurological deterioration after early surgery for aneurysmal subarachnoid hemorrhage. *J Neurosurg* 1995;**83**:984–8.
- Stachniak JB, Layton AJ, Day AL, et al.** Craniotomy for intracranial aneurysm and subarachnoid hemorrhage: is course, cost, or outcome affected by age? *Stroke* 1996;**27**:276–81.
- Johansson M, Cesarini KG, Contant CF, et al.** Changes in intervention and outcome in elderly patients with subarachnoid hemorrhage. *Stroke* 2001;**32**:2845–949.
- Braun V, Rath S, Antoniadis G, et al.** Treatment and outcome of aneurysmal subarachnoid haemorrhage in the elderly patient. *Neuroradiology* 2005;**47**:215–21.
- Inagawa T.** Trends in incidence and case fatality rates of aneurysmal subarachnoid hemorrhage in Izumo City, Japan, between 1980–1989 and 1990–1998. *Stroke* 2001;**32**:1499–507.
- Laidlaw JD, Siu KH.** Aggressive surgical treatment of elderly patients following subarachnoid haemorrhage: management outcome results. *J Clin Neurosci* 2002;**9**:404–10.
- Qureshi AI, Luft AR, Sharma M, et al.** Prevention and treatment of thromboembolic and ischemic complications associated with endovascular procedures: part II—clinical aspects and recommendations. *Neurosurgery* 2000;**46**:1360–75.
- Sugiura Y, Hiramatsu H, Miyamoto T, et al.** Endovascular treatment of ruptured intracranial aneurysms using platinum coils in patients over 80 years of age. *No Shinkei Geka* 1999;**27**:147–54.
- Rowe JG, Molyneux AJ, Byrne JV, et al.** Endovascular treatment of intracranial aneurysms: a minimally invasive approach with advantages for elderly patients. *Age Ageing* 1996;**25**:372–6.
- Johansson M, Norback O, Gal G, et al.** Clinical outcome after endovascular coil embolization in elderly patients with subarachnoid hemorrhage. *Neuroradiology* 2004;**46**:385–91.
- Sadat J, Dib M, Lonjon M, et al.** Endovascular treatment of ruptured intracranial aneurysms in patients aged 65 years and older: follow-up of 52 patients after 1 year. *Stroke* 2002;**33**:2620–5.
- Birchall D, Khangure M, McAuliffe W, et al.** Endovascular management of acute subarachnoid haemorrhage in the elderly. *Br J Neurosurg* 2001;**15**:35–8.
- Molyneux AJ, Kerr RS, Yu LM, et al.** International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet* 2005;**366**:809–17.