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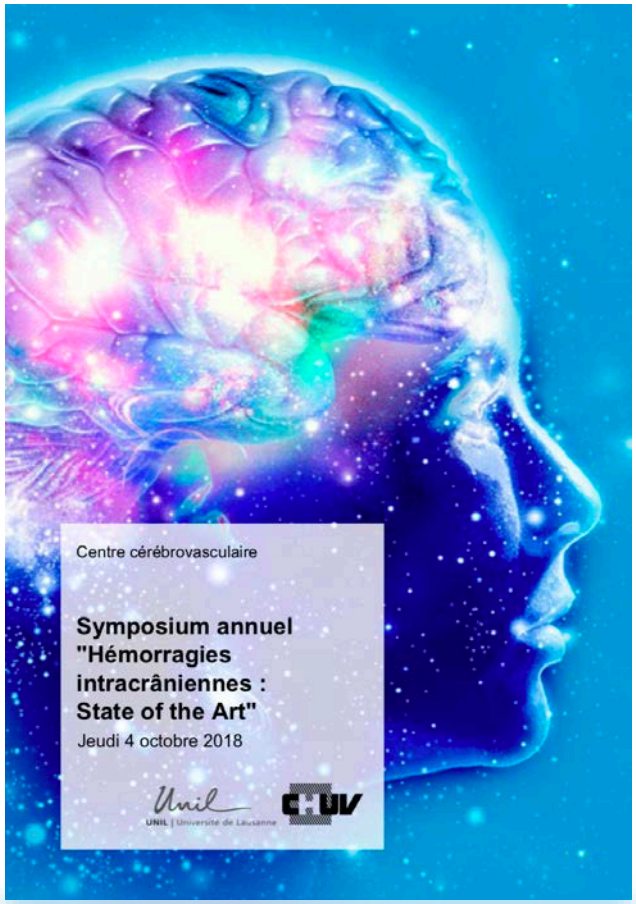

Clinical manifestations, diagnosis and medical management of aneurysmal SAH

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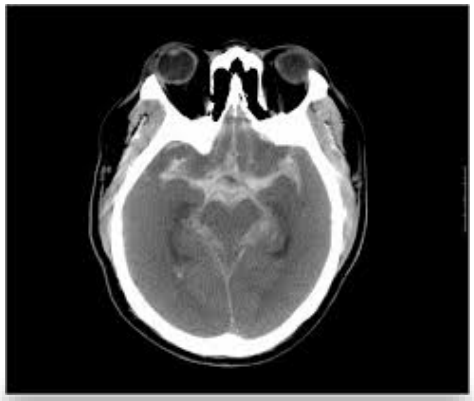

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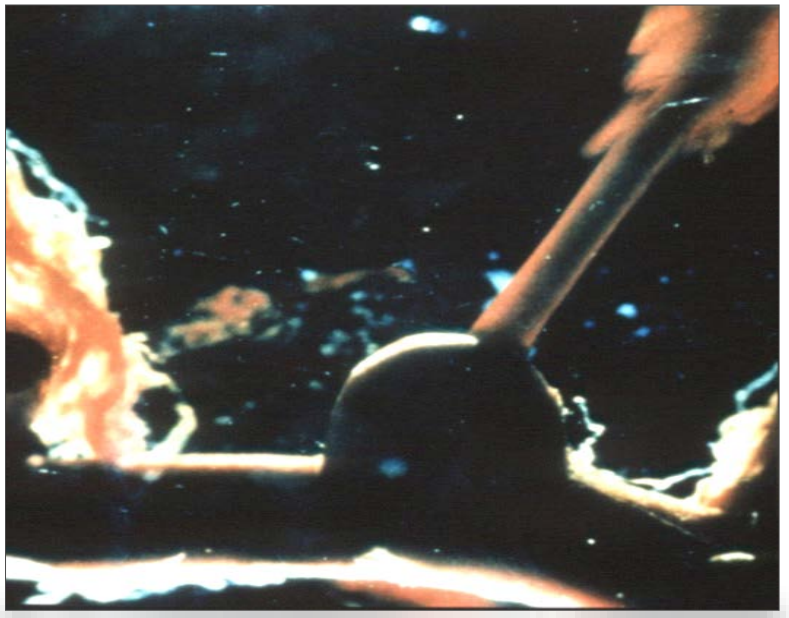
Aneurysmal SAH



- Incidence: ≈ 10/100‘000/y (3-25/100‘000/y)
- Age: ≈ 40-65 Jahre

Labovitz DL et al. Neuroepidemiology 2006

Shea AM et al. Neurosurgery 2007

Clinical manifestations

- Sudden and severe headache (97%)
- Lateralized in 30%
- May be associated with:
  - (brief) loss of consciousness
  - nausea or vomiting
  - meningismus

Gorelick et al. Neurol 1986

Schieving WI. J Engl J Med 1997

- Seizure < 10%
- Sudden death 10-15%

Butzkueven et al. Neurology 2000

Clinical manifestations

THE LANCET
Volume 344, Issue 8922, 27 August 1994, Pages 590-593

Clinical practice

Prospective study of sentinel headache in aneurysmal subarachnoid haemorrhage

F.H.H. Linn MD [a], E.F.M. Wijdicks MD [a], J. van Gijn FRCPE [a], F.A.C. Weerdesteyn-van Vliet RN [a], Y. van der Graaf MD [b], A.I.M. Bartelds MD [c]

Prospective
n = 148
25% SAH

Ann Emerg Med. 1998 Sep;32(3 Pt 1):297-304.

Worst headache and subarachnoid hemorrhage: prospective, modern computed tomography and spinal fluid analysis.

Morgenstern LB[1], Luna-Gonzales H, Huber JC Jr, Wong SS, Uthman MO, Gurian JH, Castillo PR, Shaw SG, Frankowski RF, Grotta JC.

Retrospective
n = 107
19% SAH

Clinical manifestations

Table 2 Studies that describe patients with aneurysmal SAH and the number with a history of sentinel headaches that were sudden and severe

Study and country	Number with aneurysmal SAH	Number with a sentinel headache (% and 95% CI)	Number who reported sentinel headache to a physician
History by direct questioning of patient or relative			
Verweij 1988 (18) Holland	30	13 (43%) (25, 63)	7/13
Bassi 1991 (22) Italy	364	74 (20%) (16, 25)	57/74
Hauerberg 1991 (23) Denmark	1076	139 (13%) (11, 15)	99/122
Sorensen 1992 (19) Denmark	99	36 (36%) (27, 47)	20/36
Linn 1994 (9)* Holland	21	2 (10%) (1, 30)	N/A since all were referred by their GPs
Jakobsson 1996 (24) Sweden	422	84 (20%) (16, 24)	34/84
Linn 1998 (15)* Holland	42	8 (19%) (9, 34)	N/A since all were referred by their GPs
Fridriksson (5) 2001† Sweden	152	50 (33%) (25, 41)	14/50 (excludes patients whose GPs had received an educational intervention)
History from the medical records			
Leblanc 1987 (25) Canada	87	25 (29%) (20, 39)	10/25

Test for heterogeneity: $\chi^2 = 83.72$, d.f. = 8, $P < 0.0001$.
*Patients were all those referred by their GPs with sudden severe headache and found to have aneurysmal SAH.
†Information obtained by questionnaire.

Polmear et al. Cephalalgia 2003

Diagnosis

Misdiagnosis of SAH is not infrequent, and usually results from three common errors:

- Failure to appreciate the spectrum of clinical presentation associated with SAH
- Failure to obtain a head CT scan or to understand its limitations in diagnosing SAH
- Failure to perform a lumbar puncture and correctly interpret the results

Edlow JA et al. N Engl J Med. 2000

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Diagnosis

Original Investigation

Clinical Decision Rules to Rule Out Subarachnoid Hemorrhage for Acute Headache

Jeffrey J. Perry, MD, MSc; Ian G. Stiell, MD, MSc; Marco L. A. Sivilotti, MD, MSc; Michael J. Bullard, MD; Corinne M. Hohl, MD, MHSc; Jane Sutherland, MEd; Marcel Émond, MD, MSc; Andrew Worster, MD; Jacques S. Lee, MD, MSc; Duncan Mackey, MD; Merril Pauls, MD; Howard Lesiuk, MD; Cheryl Symington, RN, ENCC; George A. Wells, PhD

JAMA 2013

Box 2. The Ottawa SAH Rule

For alert patients older than 15 y with new severe nontraumatic headache reaching maximum intensity within 1 h

Not for patients with new neurologic deficits, previous aneurysms, SAH, brain tumors, or history of recurrent headaches (≥3 episodes over the course of ≥6 mo)

Investigate if ≥1 high-risk variables present:

1. Age ≥40 y
2. Neck pain or stiffness
3. Witnessed loss of consciousness
4. Onset during exertion
5. Thunderclap headache (instantly peaking pain)
6. Limited neck flexion on examination

SAH indicates subarachnoid hemorrhage.

Sensitivity

100%

(95% CI, 97.2%-100.0%)

Specificity

15%

(95% CI, 13.8%-16.9%)

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Diagnosis

Initial Misdiagnosis and Outcome After Subarachnoid Hemorrhage

Robert C. Kowalski, BS
Jan Claassen, MD
Kurt T. Kreiter, PhD
Joseph E. Bates, MA
Noeleen D. Ostapkovich, MS
E. Sander Connolly, MD
Stephan A. Mayer, MD

Context Mortality and morbidity can be reduced if aneurysmal subarachnoid hemorrhage (SAH) is treated urgently.

Objective To determine the association of initial misdiagnosis and outcome after SAH.

Design, Setting, and Participants Inception cohort of 482 SAH patients admitted to a tertiary care urban hospital between August 1996 and August 2001.

Main Outcome Measures Misdiagnosis was defined as failure to correctly diagnose SAH at a patient's initial contact with a medical professional. Functional outcome was assessed at 3 and 12 months with the modified Rankin Scale; quality of life (QOL), with the Sickness Impact Profile.

Results Fifty-six patients (12%) were initially misdiagnosed, including 42 of 221 (19%) of those with normal mental status at first contact. Migraine or tension headache (36%) was the most common incorrect diagnosis, and failure to obtain a computed tomography (CT) scan was the most common diagnostic error (73%). Neurologic complications occurred in 22 patients (39%) before they were correctly diagnosed, including 12 patients (21%) who experienced rebleeding. Normal mental status, small SAH volume, and right-sided aneurysm location were independently associated with misdiagnosis. Among patients with normal mental status at first contact, misdiagnosis was associated with worse QOL at 3 months and an increased risk of death or severe disability at 12 months.

Conclusions In this study, misdiagnosis of SAH occurred in 12% of patients and was associated with a smaller hemorrhage and normal mental status. Among individuals who initially present in good condition, misdiagnosis is associated with increased mortality and morbidity. A low threshold for CT scanning of patients with mild symptoms that are suggestive of SAH may reduce the frequency of misdiagnosis.

JAMA. 2004;291:866-869 www.jama.com

SUBARACHNOID HEMORRHAGE (SAH) affects nearly 30 000 individuals annually in North America and results in serious impairment or death in 40% to 60% of cases.[1] Outcome is highly dependent on early diagnosis and aggressive intervention.[1,2] Immediate aneurysm repair is particularly crucial because rebleeding occurs in 26% to 73% of patients within days or weeks after the initial rupture if the aneurysm is untreated.[1,2]

The reported frequency of misdiagnosis of SAH ranges from 12% to 51%.[3-11] Correct diagnosis can be confounded be-

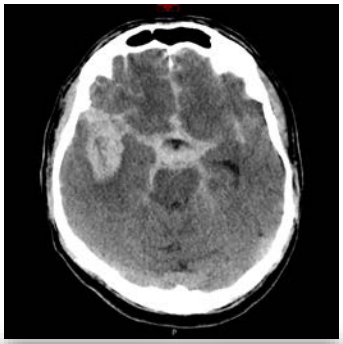
N = 482

SAH misdiagnosis 12%

Table 1. Clinical Features of 56 Misdiagnosed Patients

	No. (%)
Type of medical contact	
Emergency department	24 (43)
Physician's office	17 (32)
Hospital admission*	7 (12)
Clinic	5 (9)
Other†	3 (4)
Diagnostic error	
No CT performed	41 (73)
CT or LP results misinterpreted	9 (16)
CT done, but no LP performed	4 (7)
Other‡	2 (4)
Preliminary misdiagnosis	
Migraine/tension headache	20 (36)
Viral syndrome	6 (11)
No diagnosis	7 (12)
Musculoskeletal pain§	4 (7)
Sinusitis	3 (5)
Hypertension	3 (5)
Meningitis	3 (5)
Arteriovenous malformation	2 (4)
Unknown	2 (4)
Other‖	6 (11)
Complications of delay in diagnosis¶	
Decreased level of consciousness	14 (25)
Aneurysm rebleeding	12 (21)
Symptomatic hydrocephalus	7 (12)
Symptomatic vasospasm	4 (7)
None	28 (50)
Unknown	6 (11)

Diagnosis



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CT

- <6h: SAH sensitivity ≈ 100%
- <24h: SAH sensitivity 92%
- 5d: SAH sensitivity 58%
- 3 w: SAH sensitivity <10%
- ICH 20-40%
- IVH 15-35%
- SDH 5%
- Distribution of blood poor predictor of the site of an aneurysm (excepted ACA or ICH)

Sensitivity of Early Brain Computed Tomography to Exclude Aneurysmal Subarachnoid Hemorrhage
A Systematic Review and Meta-Analysis

Nicole M. Dubosh, MD; M. Fernanda Bellolio, MD; Alejandro A. Rabinstein, MD; Jonathan A. Edlow, MD

MRI

- FLAIR AND SWI SAH sensitivity ≈ 100%

Dubosh N et al. Stroke 2016

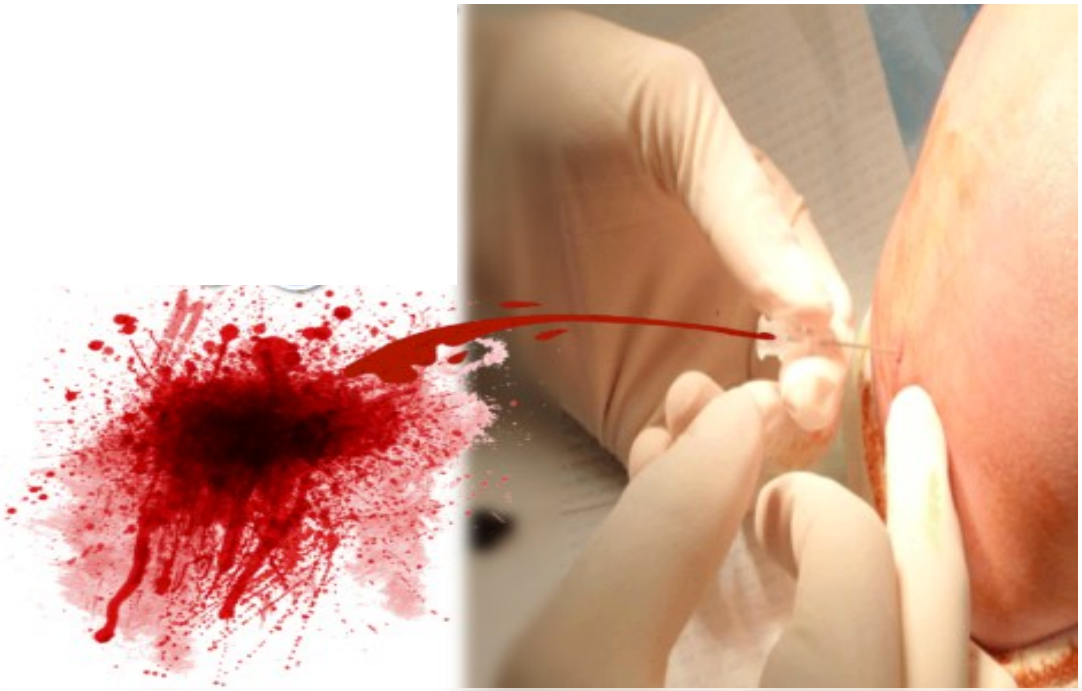
Connolly ES Jrr et al. Stroke 2012

Backes D et al. Stroke 2012

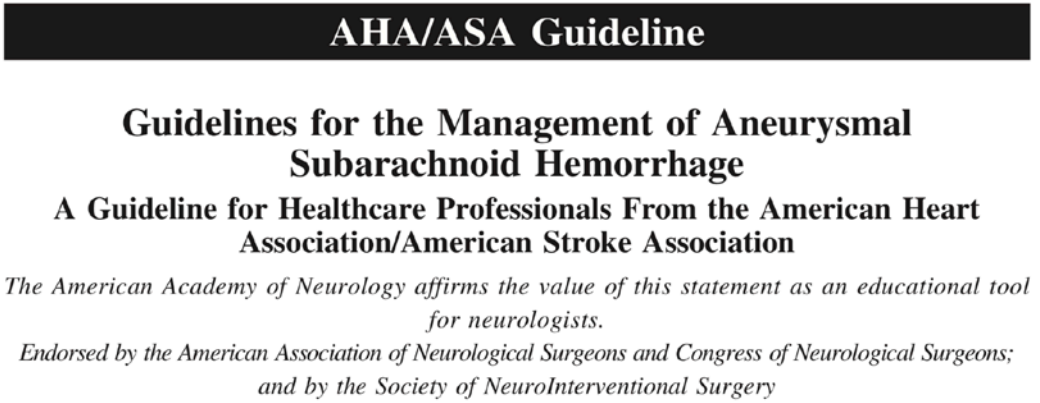
Edlow JA et al. Stroke 2012

Mitchell P et al. J Neurol Neurosurg Psychiatry 2001

Diagnosis



Diagnosis



AHA/ASA Guideline

Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons; and by the Society of NeuroInterventional Surgery

LP

- Lumbar puncture is mandatory if there is a strong suspicion of SAH despite a normal head CT
- There is a lack of evidence to support the use of CT alone, even if performed within 6h of headache onset

Vermeulen M, et al. J Neurol Neurosurg Psychiatry 1990

Connolly ES Jr et al. Stroke 2012

Diagnosis

Table 1. Methods for Distinguishing Traumatic LP from True SAH

CSF Finding	Traumatic LP	True SAH
Opening pressure	Normal	Elevated in 60% of cases
"3-tube test"	Initially bloody with gradual clearing	Persistently bloody
Visual inspection for xanthochromia	Clear	Xanthochromia
Spectrophotometry for xanthochromia	No hemoglobin breakdown products	Presence of hemoglobin breakdown products
RBC count	Diminishing in progressive tubes	Persistent (NB: there is no specific threshold number)
WBC count	Proportional to peripheral blood	Proportional to peripheral blood initially, then relatively increased later
Clot formation	Occurs rarely	Absent
D-dimer level	Absent	Present
Crenated RBCs	Absent	Present
Erythrophages	Absent	Present
Repeat LP at higher interspace	Usually clear	Findings similar to those of the first tap

Shah et al, J Emerg Med 2002

Table 2
Sensitivity of CSF findings for the diagnosis of aSAH

	Sensitivity	95% CI
CSF RBC count >2000 × 10^6/L	96.9%	89.3-99.1
CSF xanthochromia*	84.5%	73.1-91.6
Either CSF RBC count >2000 × 10^6/L or xanthochromia	100%	94.3-100

* Xanthochromia is defined as a noted visible presence of yellow, orange, or pink discoloration of CSF supernatant.

Mark et al. Am J Emerg Med 2015

Diagnosis

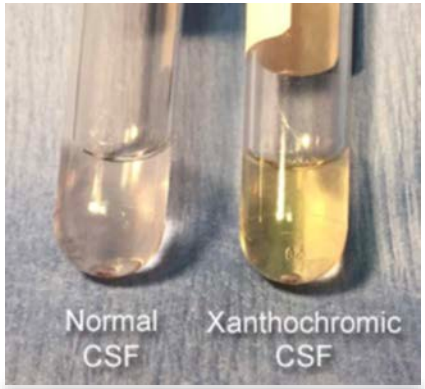
RBC lyse	→	hemoglobin	→ *In vivo or in vitro*	oxyhemoglobin (pink/pink-orange) 4-10h	→ *in vivo only*	bilirubin (yellow) >24h-4w

Xanthochromia

- Hemoglobin degradation products
- Blood has been in the CSF for > 2h

➢ LP performed within 2h after SAH: no xanthochromia

- Can last >2 weeks (70% 3 weeks, 40% 4 weeks)



Diagnosis

LP Spectrophotometry

RBC lyse	→	hemoglobin	→	oxyhemoglobin (pink/pink-orange)	→	bilirubin (yellow)
			In vivo or in vitro	4-10h	*in vivo only*	>24h-4w

- highly sensitive for bilirubin (>95%) when lumbar puncture is done >12 hours after SAH
- low to moderate specificity for the diagnosis of SAH

Vermeulen Met al. J Neurol Neurosurg Psychiatry 1989

Cruickshank A et al. BMJ 2005

Beetham R et al. J Neurol Neurosurg Psychiatry 2004

Petzold A et al. Stroke 2005

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Diagnosis

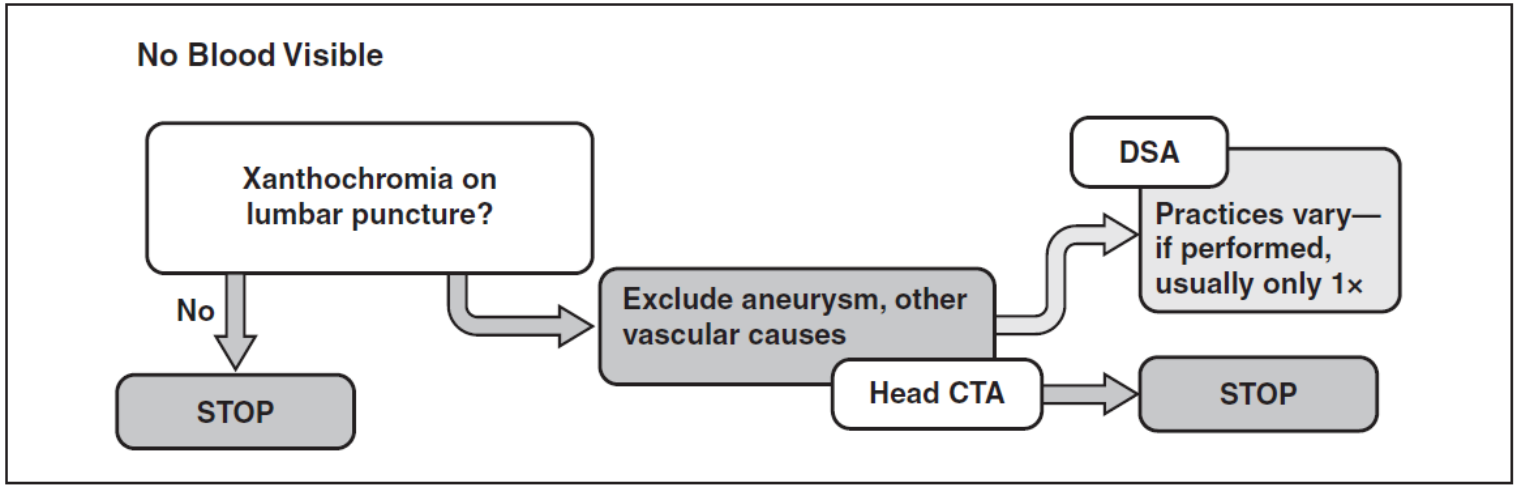
Why to tap?

- **4.7 - 8.6%** positive LPs after negative CT

Sayer et al, Acad Emerg Med 2015
Martin et al, Br J Neurosurg 2015
Blok et al. Neurology 2015
Gangloff et al. Clincal Biochemistry 2015
Migdal, et al. Am J Emerg Med 2015

- Aneurysma detection after positive LP: **8.1 - 45%**

Chalouhi et al, Neurosurgery 2013
Horstman et al. J Neurol 2012
Bakker et al. J Neurol Neurosurg Psychiatry 2004
Wallace et al. Stroke 2013
Sayer et al. Acad Emerg Med 2015
Martin et al. Br J Neurosurg 2015
Gangloff et al. Clincal Biochemistry 2015



Marder et al. AJR 2014

Sensitivity for aneurysms: 92-98%

Menke et al. Ann Neurol 2011
Chenet al. Neurosurgery 2008
Uysal et al. Emerg Radiol 2008
Peker et al. Diagn Interv Radiol 2009
El Khaldi et al. Radiol Med 2007
Tipper et al. Clin Radiol 2005
Agid et al. Neuroradiology 2006
Wang et al. Acta Neurochir 2010
van Gelder et al. Neurosurgery 2003
Kokkinis etl al. Br J Neurosurg 2008
Chappell et al. Neurosurgery 2003
MacKinnon et al. Clin Radiol 2013
Westerlaan et al. Radiology 2011

Diagnosis

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CT < 6h

LP > (6)-12h

Identifying the etiology

- Aneurysm 85%
- Perimesencephalic 10%
- Dissection
- AVM/AVF
- Spinal AVM
- Mycotic
- Pituitary apoplexy
- other

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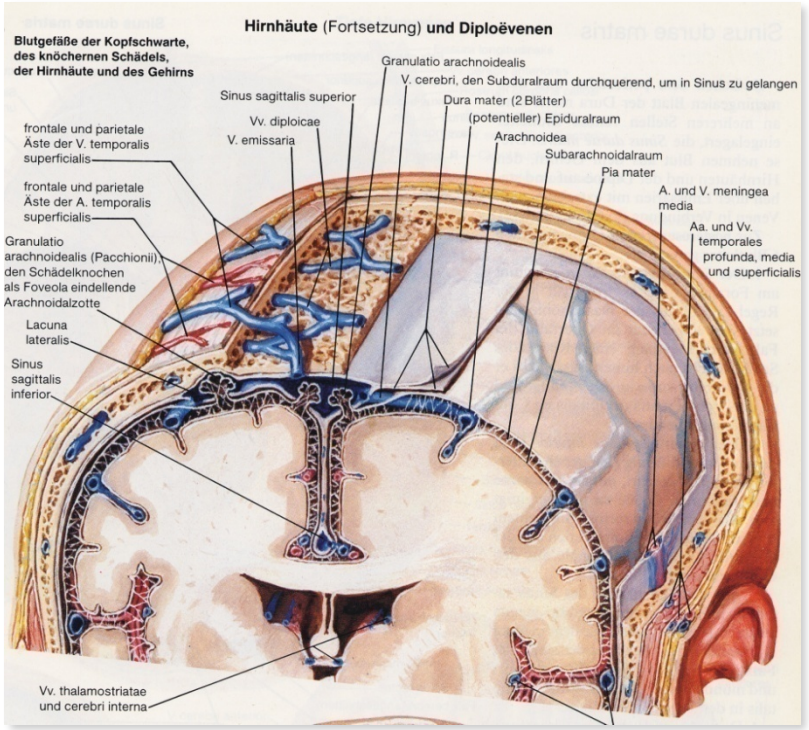
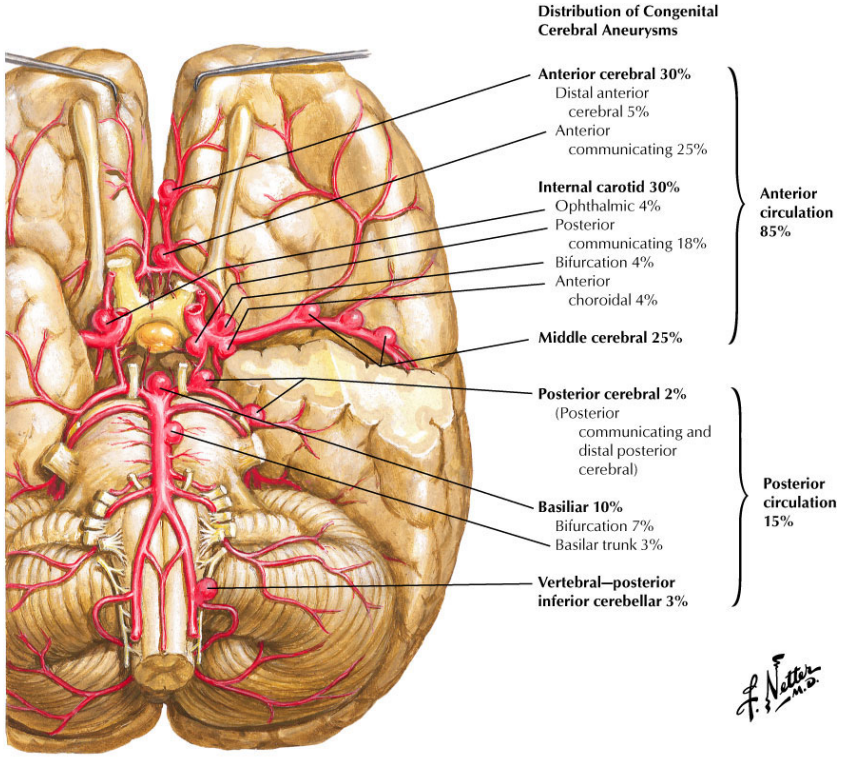
Identifying the etiology





Identifying the etiology: CTA

ORIGINAL RESEARCH ■ EVIDENCE-BASED PRACTICE

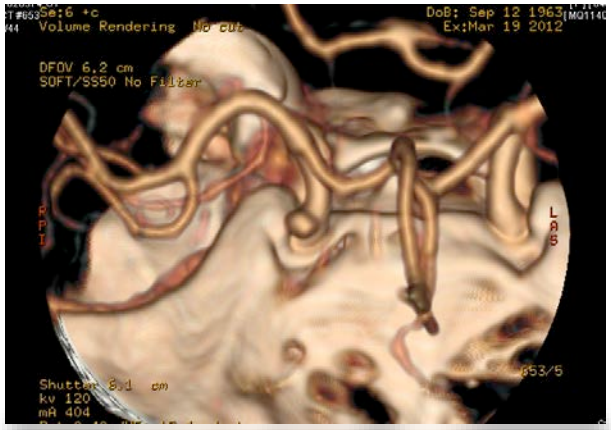
Intracranial Aneurysms in Patients with Subarachnoid Hemorrhage: CT Angiography as a Primary Examination Tool for Diagnosis—Systematic Review and Meta-Analysis[1]

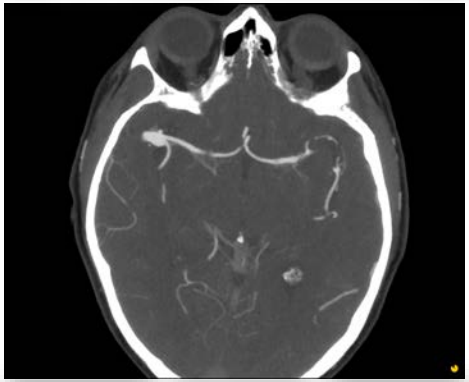
Henriëtte E. Westerlaan, MD

Radiology

quality. Pooled sensitivity was 98% (95% CI: 97%, 99%), and pooled specificity was 100% (95% CI: 97%, 100%).

Radiology 2011





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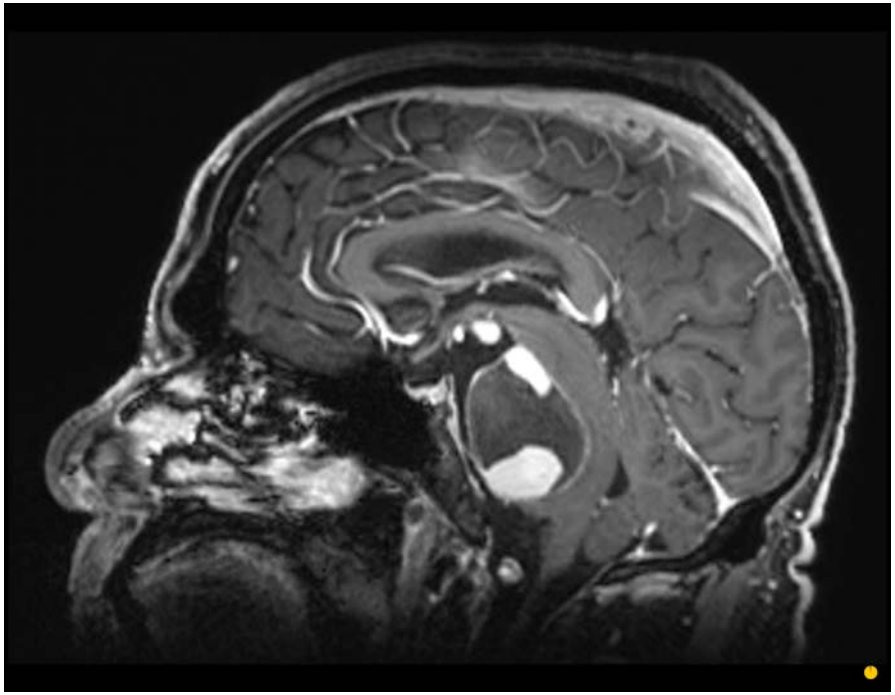
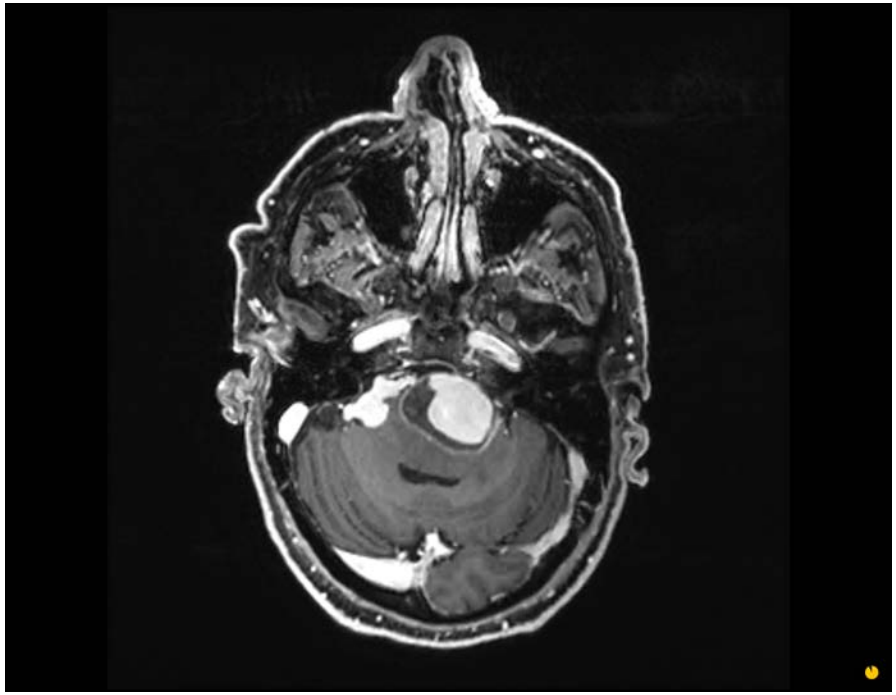
Identifying the etiology: MRI





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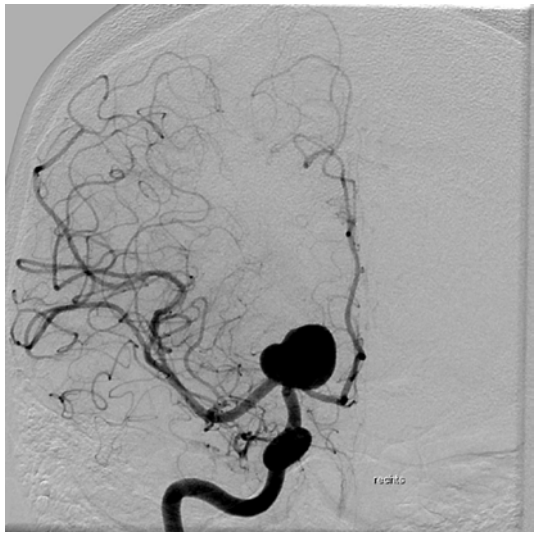
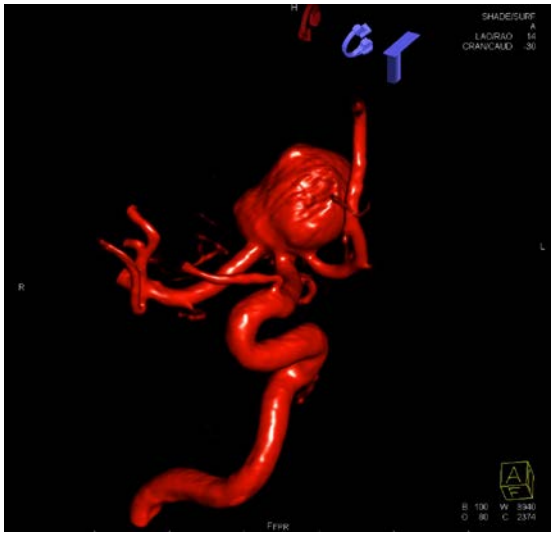
Identifying the etiology: DSA





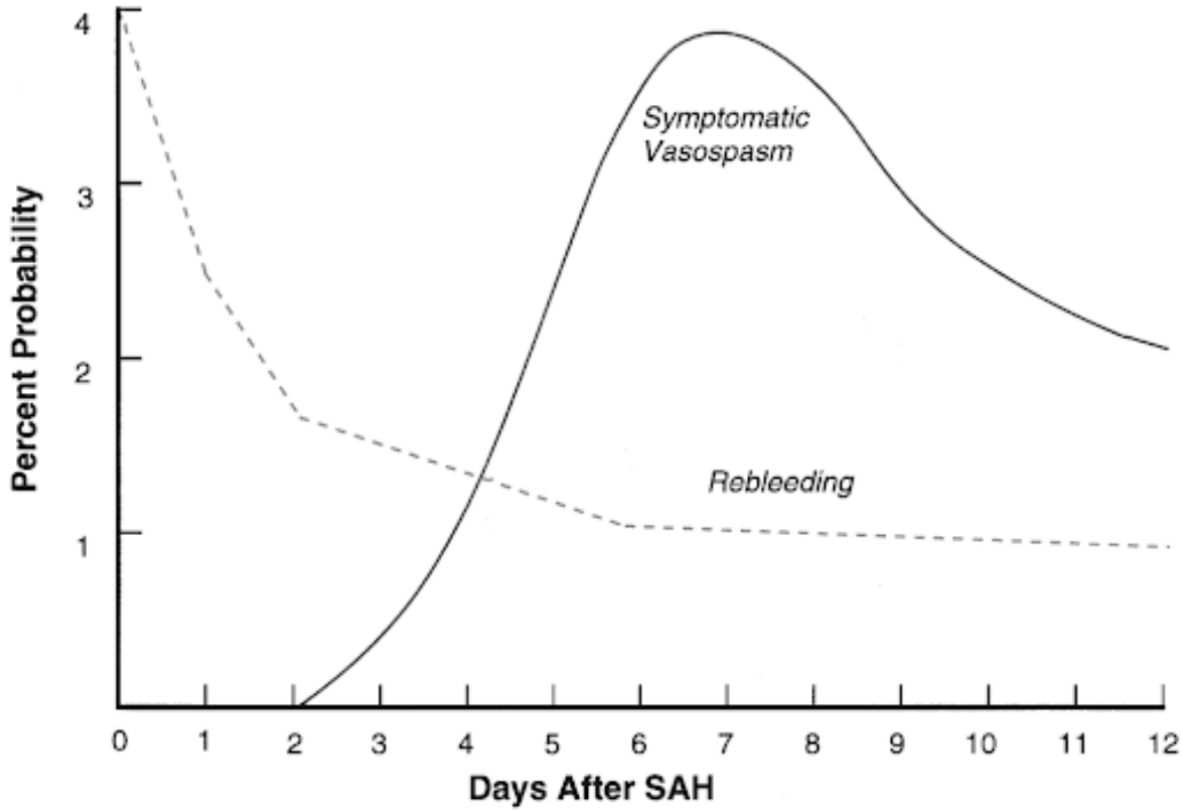
WFNS SAH grading system

Grade	Glasgow coma scale score	Motor deficit
I	15	Absent
II	14-13	Absent
III	14-13	Present
IV	12-7	Present or absent
V	6-3	Present or absent

WFNS = World Federation of Neurological Surgeons'

Hunt & Hess SAH grading system

Grade	Criteria	Index of Perioperative Mortality (%)
0	Aneurysm is not ruptured	0-5
I	Asymptomatic or with minimal headache and slight nuchal rigidity	0-5
II	Moderate to severe headache, nuchal rigidity, but no neurologic deficit other than cranial nerve palsy	2-10
III	Somnolence, confusion, medium focal deficits	10-15
IV	Stupor, hemiparesis medium or severe, possible early decerebrate rigidity, vegetative disturbances	60-70
V	Deep coma, decerebrate rigidity, moribund appearance	70-100



Bracard et al. Interv Neuroradiol. 2008

Stroke
Journal of the American Heart Association

American Heart Association | American Stroke Association

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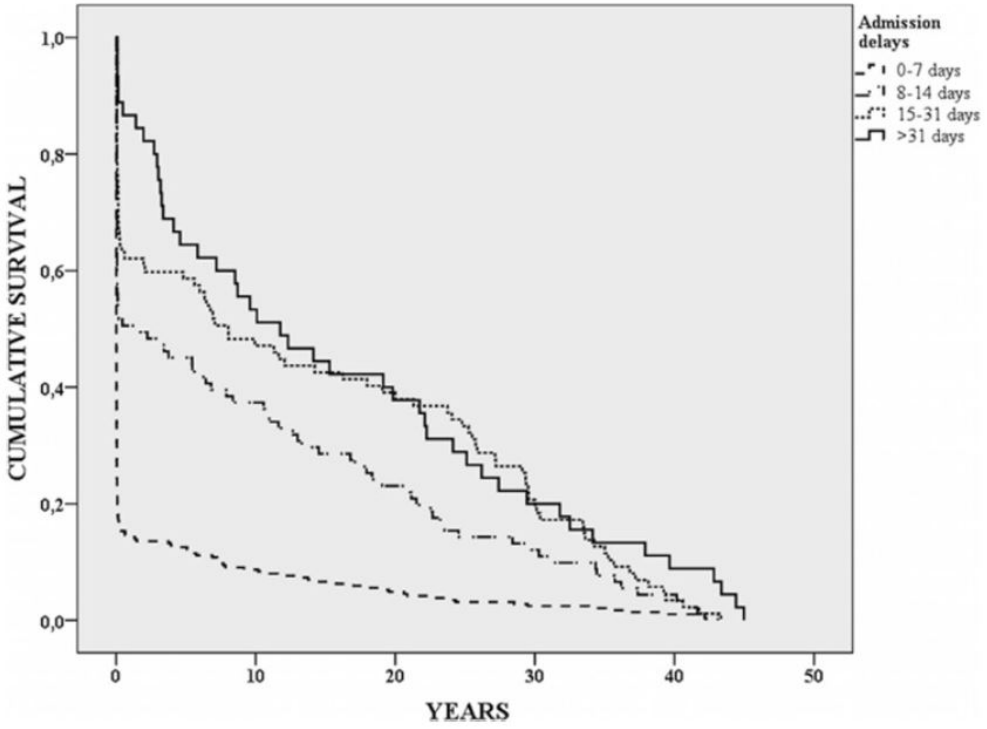
Natural History of Ruptured but Untreated Intracranial Aneurysms

Miikka Korja, Riku Kivisaari, Behnam Rezai Jahromi and Hanna Lehto

Stroke. 2017;48:1081-1084; originally published online March 1, 2017;
doi: 10.1161/STROKEAHA.116.015933
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628



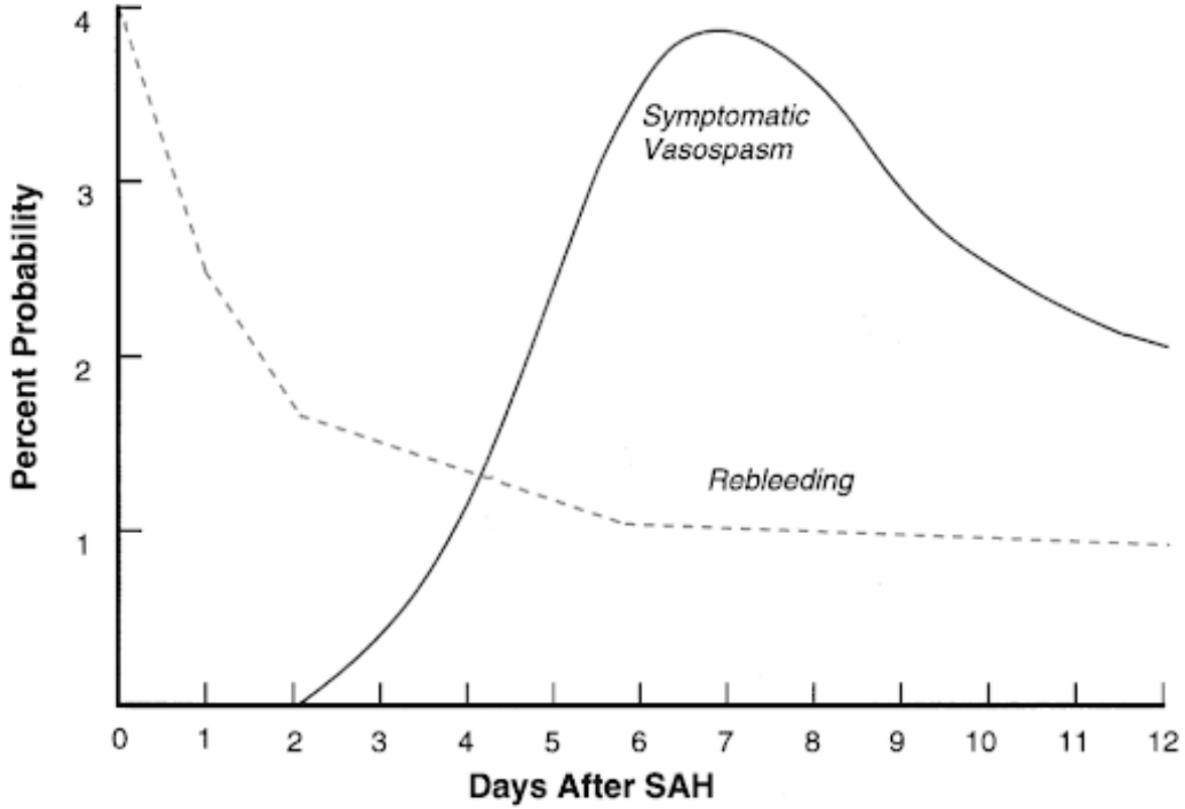
N = 510
Medium survival time: 20d

1-year mortality
90% for poor-grade pts
75% for good-grade pts

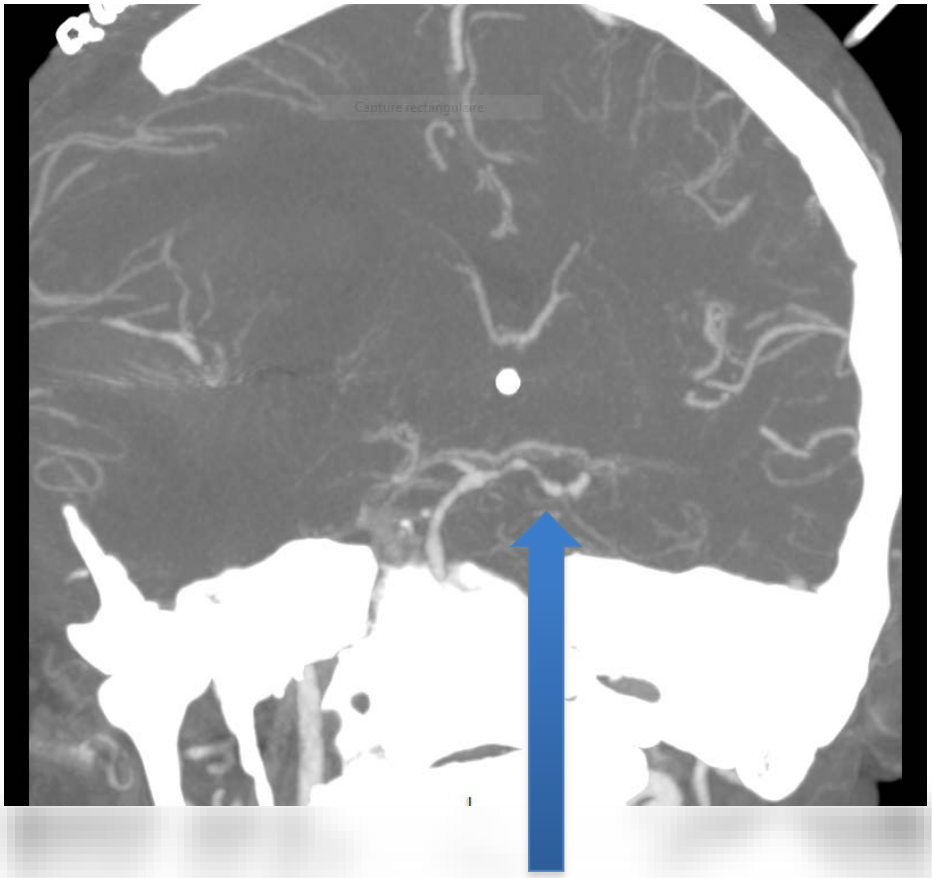
Vasospasms

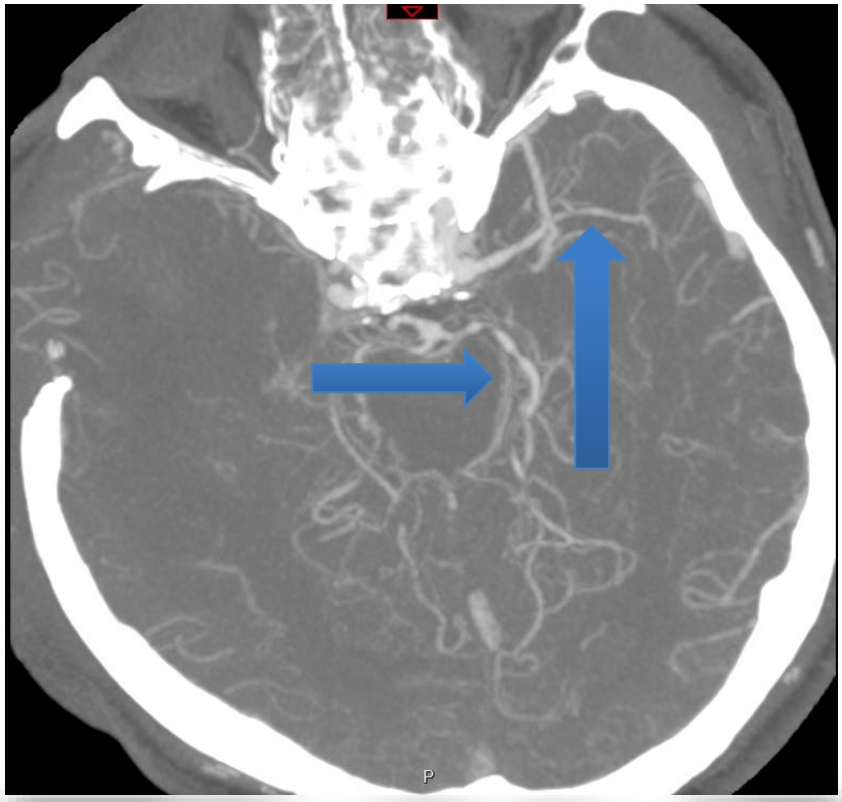
- More frequent complication after SAH
- 40-70%, symptomatic in 17-40%

Kassel NF et al. Stroke 1985
Kreiter KT e tal. Stroke 2009



Bracard et al.,Interv. Neuroradiol. 2008

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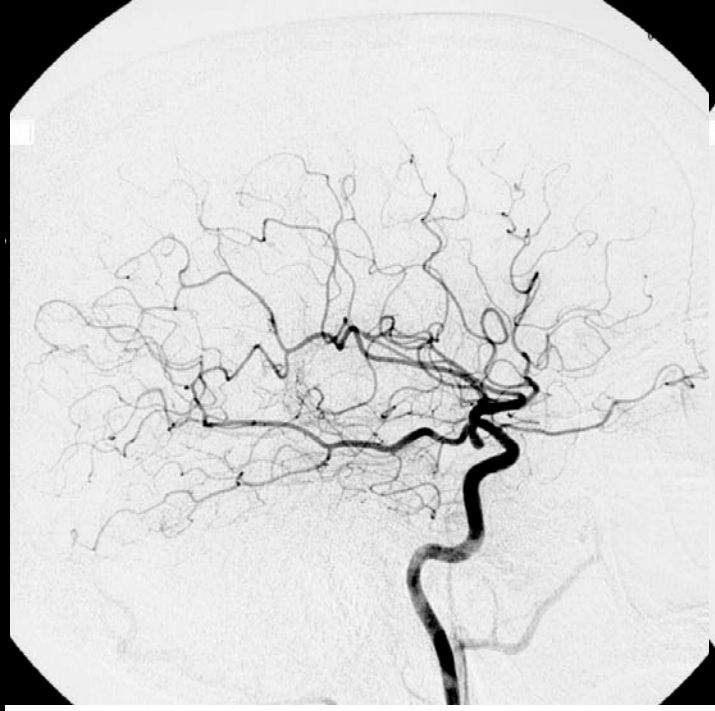
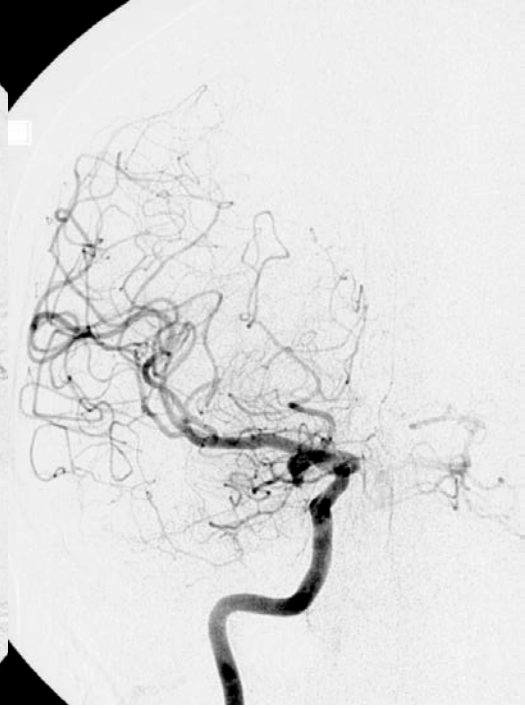
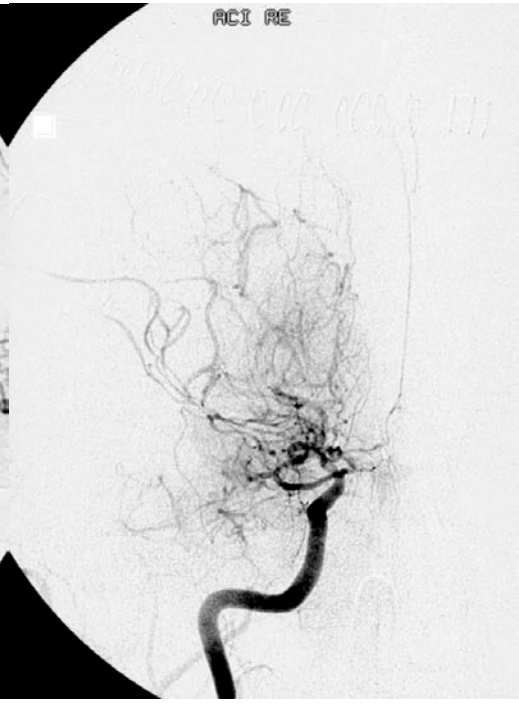
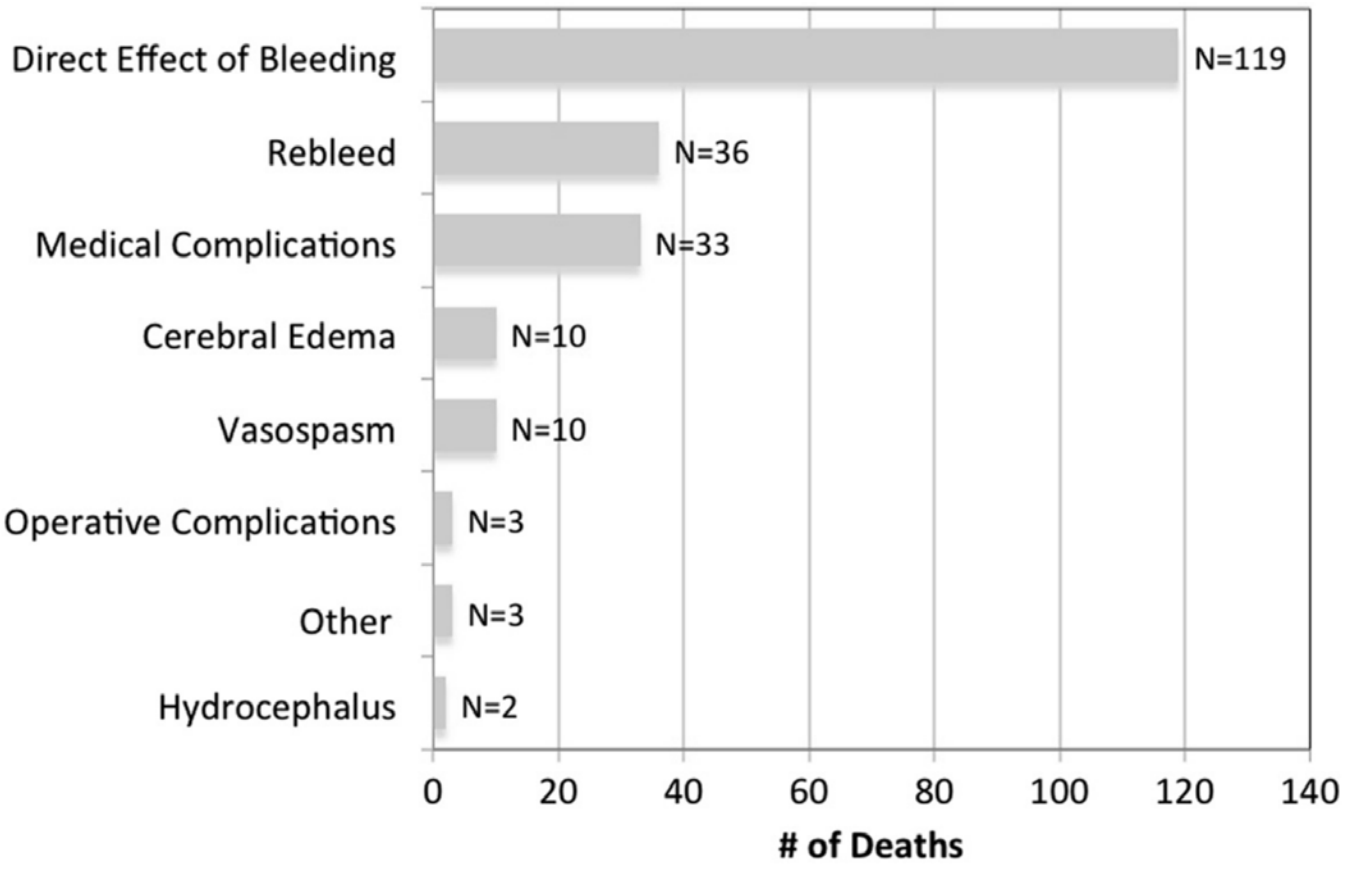





ACI RE


ACI RE



Lantigua et al. Critical Care 2015

Fisher CT grading scale

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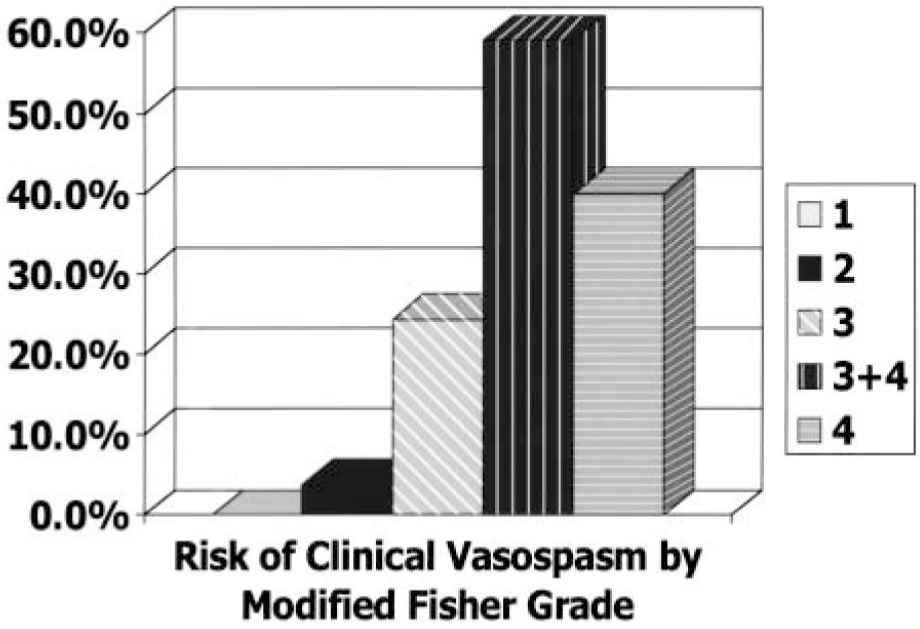
Grade	CT finding(s)
1	No blood detected
2	Diffuse thin layer of subarachnoid blood (vertical layers <1 mm thick)
3	Localized clot or thick layer of subarachnoid blood (vertical layers ≥1 mm thick)
4	Intracerebral or intraventricular blood with diffuse or no subarachnoid blood

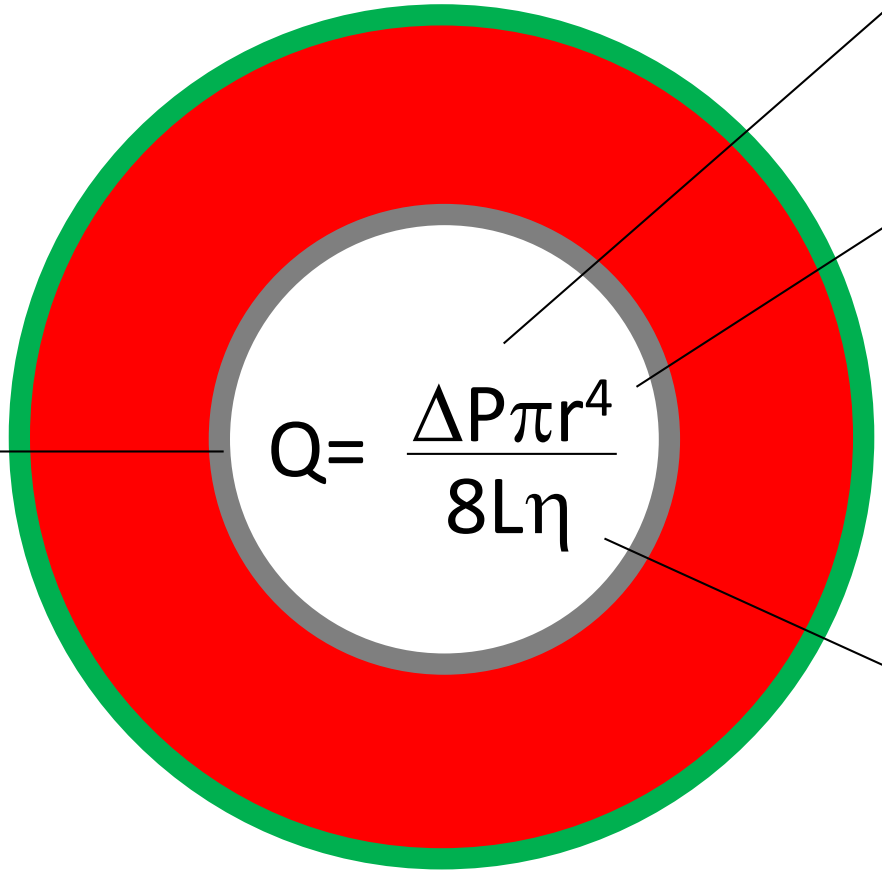
CT = Computed tomography

Fisher et al, Neurosurg, 1980



Klimo P et al. JNS 2004

Flow



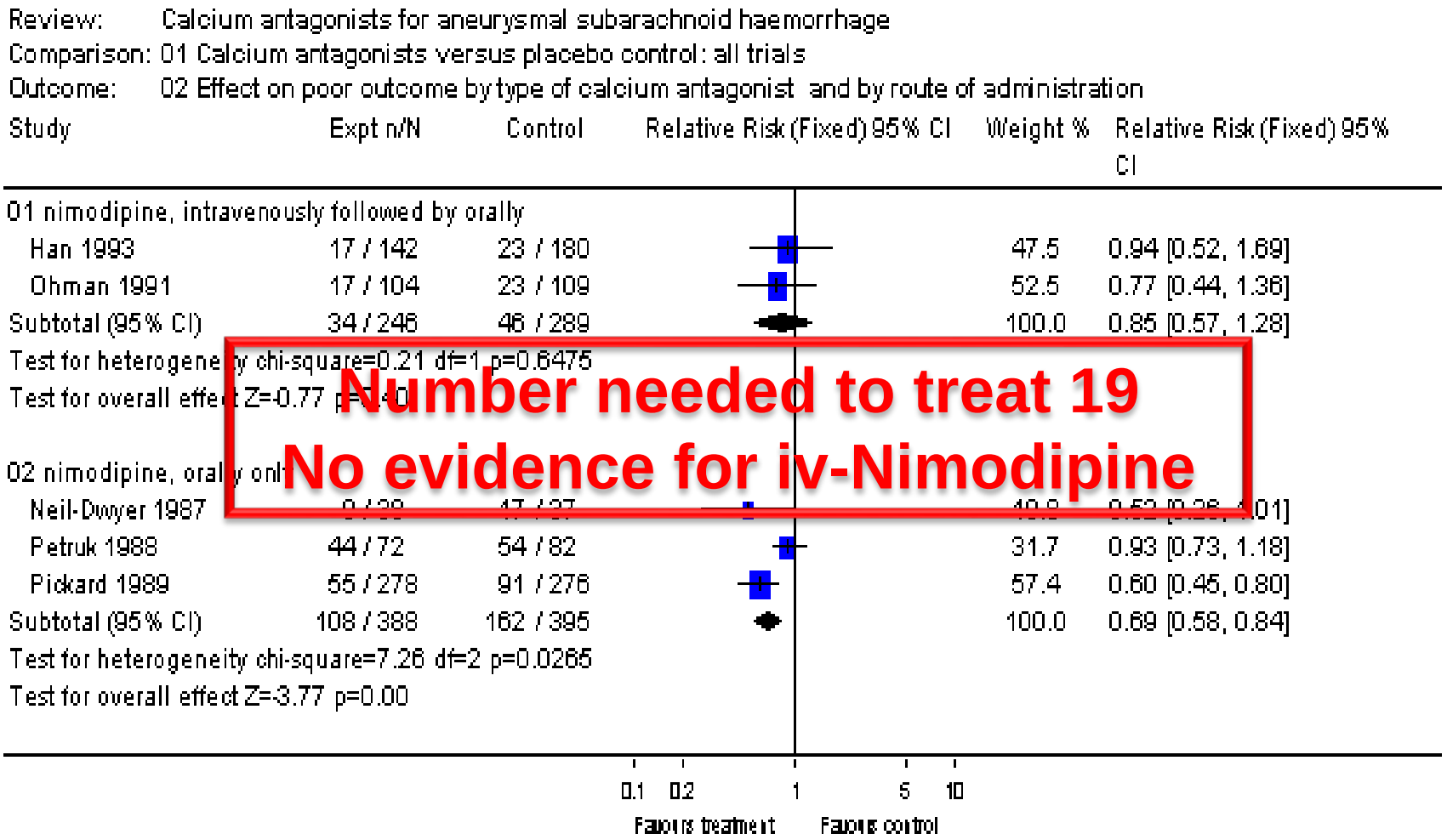
Presure:
Hypertension

Radius:
Nimodipine (Nimotop)
21 days 6 x 60 mg po
(or 1-2 mg iv)

Viscosity:
Haemodilution
Cave: O_2-Transport

(Hagen-Poiseuille-Law for laminar flow)

Calcium antagonists



Number needed to treat 19

No evidence for iv-Nimodipine

Cochrane Data Syst Rev, 2007

Calcium antagonists

Nimodipine 60mg po, 6h, 21 days or till vasospasm

	Risk Ratio	95% CI of Risk Ratio
Poor Outcome (death or dependence)	0.67	0.55 – 0.81
Case fatality	0.8	0.63 – 1.03
Clinical signs of secondary ischemia	0.64	0.49 – 0.83
Cerebral infarction on CT/MRI	0.71	0.57 – 0.89
Rebleeding during clinical course	0.75	0.53 – 1.04

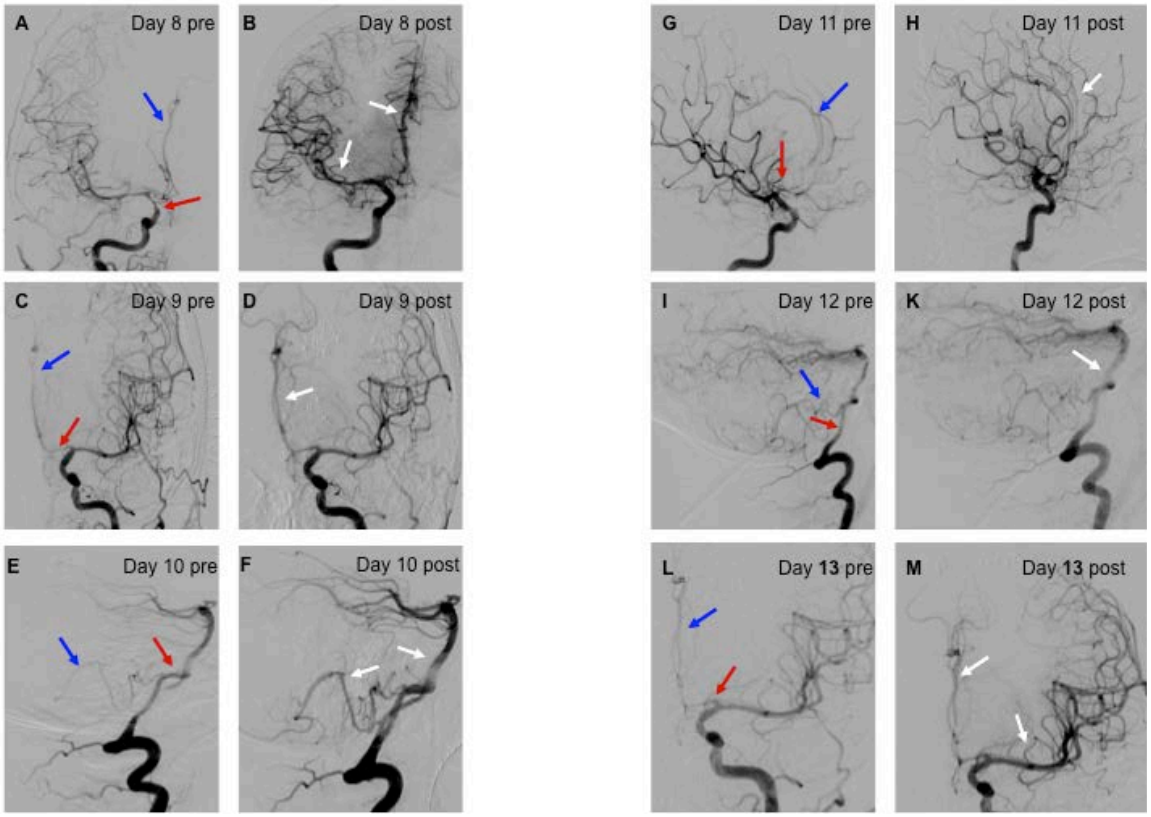
Dorhout Mees et al. Cochrane Database Syst. Rev. (2007)

Triple-H therapy

- Hypertension
- Haematocrit 28-33%
- Hyper-, Normovolemia (Hb > 8-10 g/dl (> 11g/dl if DCI?))

Endovascular treatment (angioplasty)

Nimodipine i.a., Papaverin i.a., mechanic angioplasty



Andereggen L et al. AJNR 2017

Other complications

- Acute/chronic hydrocephalus (25%)
- Seizure (6-18%)

Connolly ED Jr et al. Stroke 2012

- Other (pulmonary, cardiac, electrolytic, infectious, thromboembolic, GI,…)
- CAVE: hyperglycemia, fever, anemia, troponin, hypothalamic/pituitary dysfunction,…

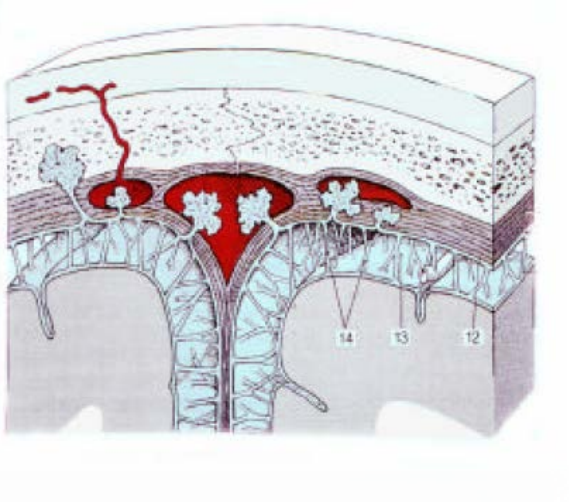
Chronic hydrocephalus

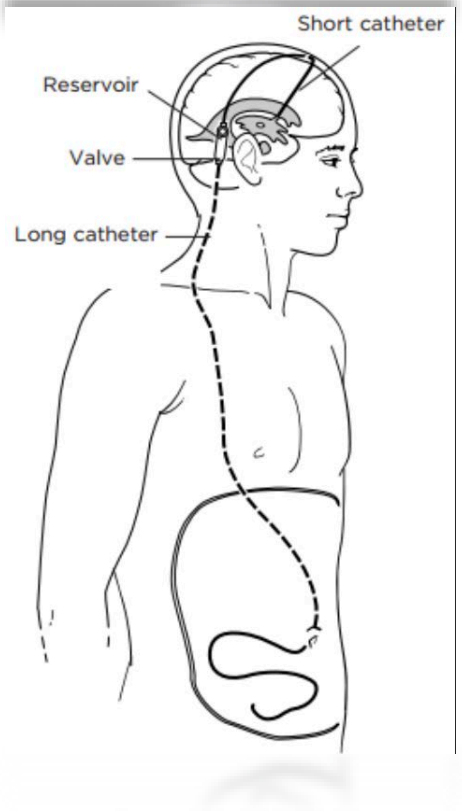
- 7% - 25%

Connolly ED Jr et al. Stroke 2012

- days - weeks after SAH

  → CT 12 weeks or before if no further clinical improvement

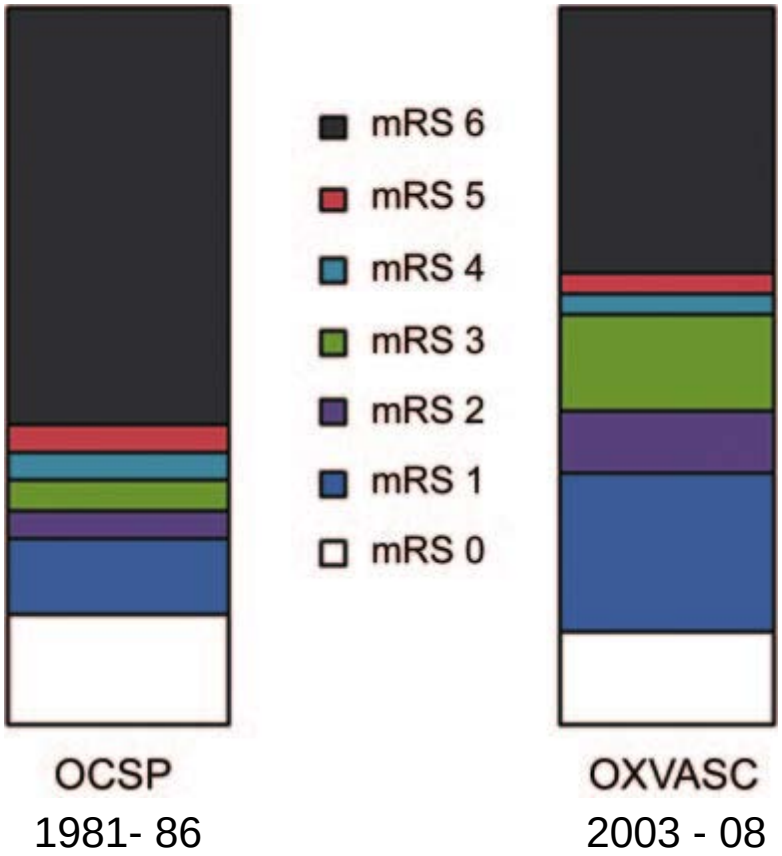




Time trends in outcome of subarachnoid hemorrhage : Population-based study and systematic review

C.E. Lovelock, G.J.E. Rinkel and P.M. Rothwell

Neurology 2010



Twelve-month modified Rankin Scale scores (mRS) in patients surviving to reach hospital in Oxford Community Stroke Project (OCSP) and Oxford Vascular Study (OXVASC)

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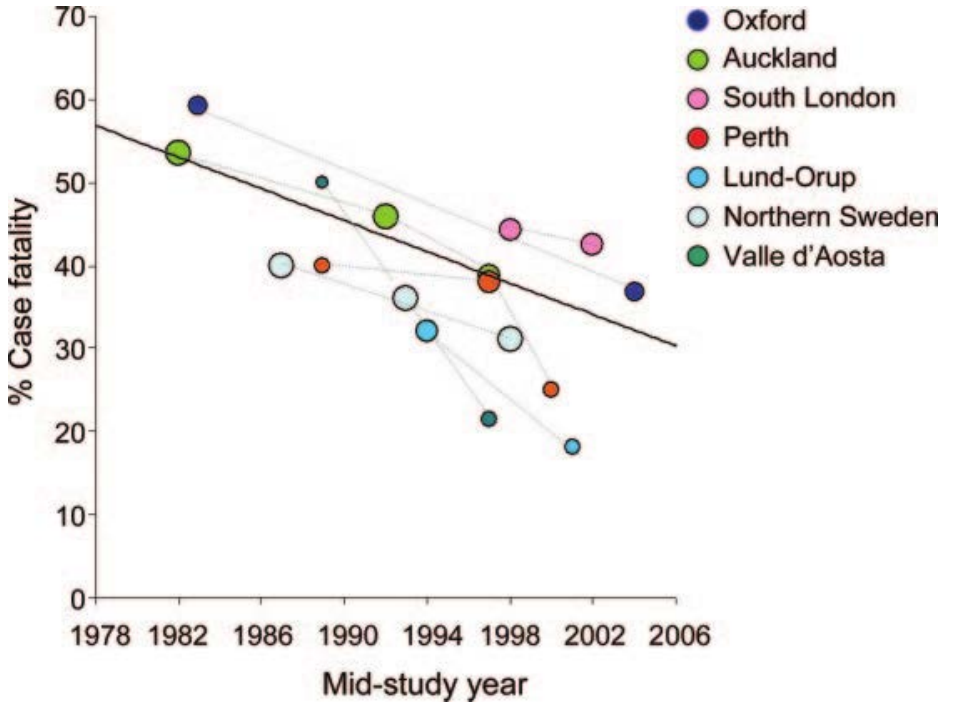

Size of each circle proportional to the log of the number of cases in each study.

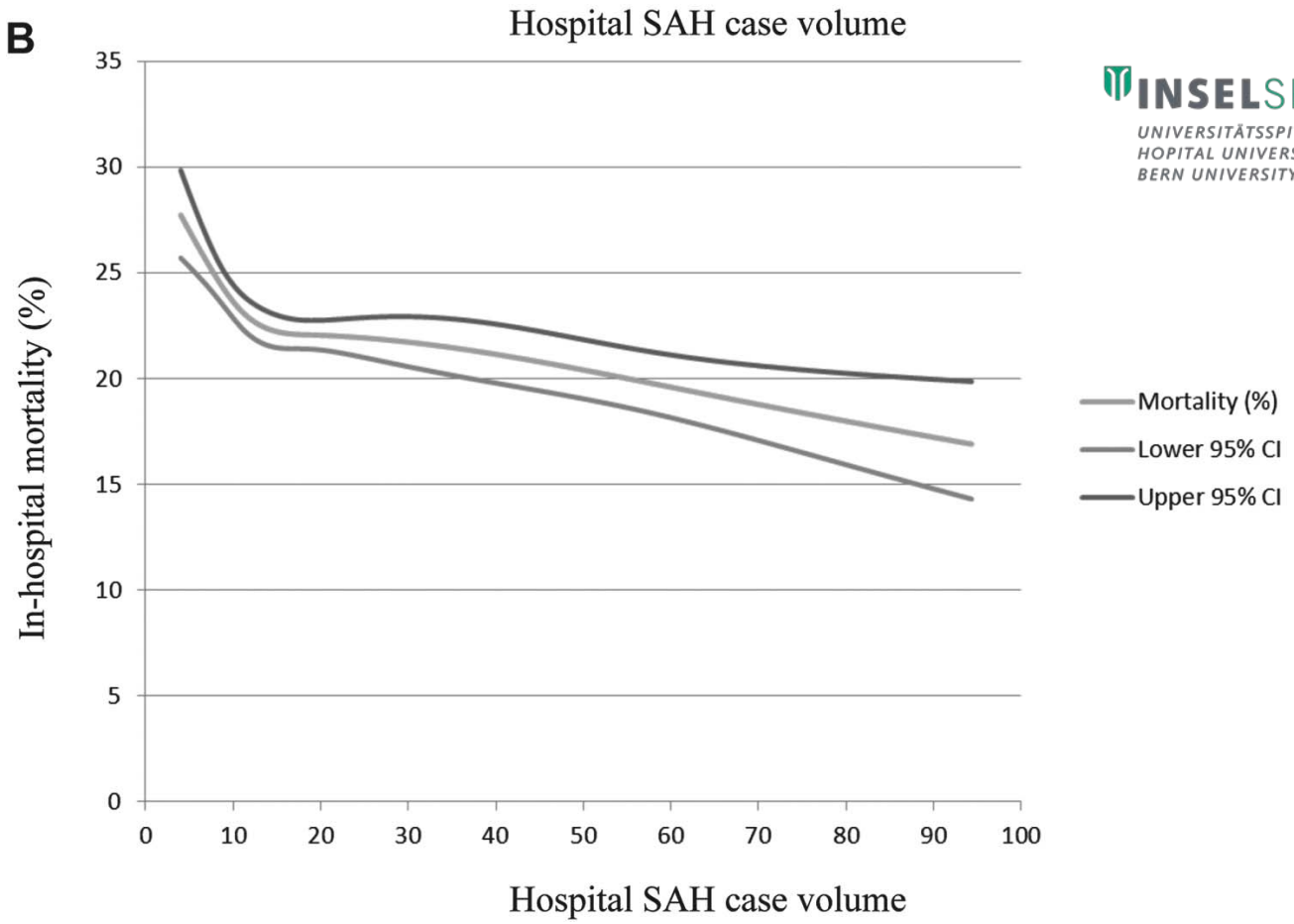

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TABLE 3. Unadjusted and Adjusted OR and 95% CI for In-hospital Mortality by Annual Hospital SAH Case Volume[a]

	Unadjusted		Adjusted for Patient Factors[b]		Adjusted for Patient and Hospitals Factors[c]	
In-hospital Mortality	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**	**OR (95% CI)**	***P* Value**
Highest vs lowest quartile	0.69 (0.61-0.77)	<.001	0.85 (0.75-0.97)	.018	0.79 (0.67-0.92)	.003
Medium high vs lowest quartile	0.76 (0.67-0.87)	<.001	0.88 (0.77-1.02)	.087	0.87 (0.75-1.01)	.078
Medium low vs lowest	0.90 (0.78-1.04)	.161	0.95 (0.82-1.11)	.539	0.95 (0.82-1.11)	.507
SAH volume (per 5 units/y)	0.95 (0.93-0.97)	<.001	0.98 (0.96-0.99)	.007	0.97 (0.95-0.99)	<.001

Prabhakaran et al. Neurosurgery 2014

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Merci

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