Canadian Best Practice Recommendations for Stroke Care

3.6 Acute Subarachnoid Hemorrhage
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**Search Strategy**

**Identification**
- Cochrane, Medline, and CINAHL and National Guideline Clearing House were searched

**Screening**
- Titles and Abstracts of each study were reviewed. Bibliographies of major reviews or meta-analyses were searched for additional relevant articles.

**Eligibility**
- Excluded articles: Non-English, Commentaries, Case-Studies, Narratives, Book Chapters, Editorials, Non-systematic Reviews (scoping reviews), and conference abstracts.
- Included Articles: English language articles, RCTs, observational studies and systematic reviews/meta-analysis. Relevant guidelines addressing the topic were also included.

**Included**
- A total of 17 Articles and 2 Guidelines

Cochrane, Medline, CINAHL, and National Guideline Clearing House were search using the medical subject headings (*Aneurysm, Ruptured/ or *Subarachnoid Hemorrhage AND *Emergency Service, Hospital/ OR Assessment or Acute). Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 17 articles and 2 guidelines were included and were separated into separate categories designed to answer specific questions.

May 21st, 2013
Guidelines

What existing clinical practice guidelines include Acute Subarachnoid Hemorrhage?

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<th>Guideline</th>
<th>Recommendations</th>
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| American Association of Neuroscience Nurses. Care of the patient with aneurysmal subarachnoid hemorrhage. Glenview (IL): American Association of Neuroscience Nurses; 2009 Dec. 30 p. | Patient Care Preaneurysm Securement Assessment Upon admission of the patient to the intensive care unit (ICU), hourly neurologic exam checks (including a complete neurologic exam, National Institutes of Health Stroke Scale, Glasgow Coma Scale, and hemodynamic monitoring) are performed and compared to baseline to detect early deterioration because of aneurysmal rebleed, acute hydrocephalus, ischemia related to inadequate cerebral perfusion (from early cerebral vasospasm or other causes), or other medical complications. Airway and Oxygenation Intubation and mechanical ventilation may be indicated for patients with decreased mental status, compromised airways, or acute lung injuries from subarachnoid hemorrhage (SAH; e.g., neurogenic pulmonary edema), aspiration, or a Glasgow Coma Scale motor score of withdrawal. Modes of ventilation vary, especially in patients who have pulmonary complications following SAH. The goal is to maintain adequate oxygenation and ventilation without compromising both intracranial and cerebral perfusion pressures. Positive end expiratory pressure of 5 cm H2O may be used cautiously in the aSAH patient; however, it does decrease blood pressure (BP) and may lead to cerebral ischemia (Level 2; Muench et al., 2005). Pressure-controlled ventilation should be considered if the patient has significant aspiration or early acute respiratory distress syndrome. Patients recovering from aSAH are critically ill patients at risk for many common secondary injuries such as atelectasis and pneumonia. Hourly monitoring of breath sounds and frequent deep breathing should be encouraged. Coughing is discouraged in the SAH patient before aneurysm securement because of the increased risk of aneurysm rupture with the increased intracranial pressure (ICP) and BP that occurs during coughing. BP Management The exact relationship between aneurysmal rebleed and BP remains to be identified; however, most clinicians agree that to prevent rebleed, BP control is achieved before aneurysm securement. Systolic BP is kept between 90 and 140 mm Hg before...
Aneurysm securement (Level 3; Suarez, Tarr, & Selman, 2006). There are a variety of vasoactive agents used to maintain BP within an acceptable range. Choice of vasoactive agent and BP target range varies depending upon institutional policy (i.e., policy and procedures) and managing clinician preference. Some institutions require clinicians to follow systolic BP, and other institutions follow mean arterial pressure. Typically, BP is maintained within the target range using an initial bolus followed by commencement of an intravenous (IV) drip that is titrated to maintain BP within the target range (Level 2; Kraus, Metzler, & Coplin, 2002). Use of sublingual agents that may cause a rapid drop in BP is not recommended. BP should be lowered in a controlled manner as a sudden drop in BP increases the risk of cerebral ischemia.

Hypotension occurring before aneurysm securement places the patient recovering from aSAH at risk for ischemia. Hypotension should be treated with rapid IV fluid replacement beginning with isotonic saline (0.9%) and colloids as necessary. For persistent hypotension, IV vasopressors should be instituted.

Intracranial Pressure Monitoring

When a patient shows symptoms of increasing ICP, or is at increased risk of increased ICP because of large blood load, an external ventricular catheter or subarachnoid bolt is inserted. This can be done in the operating room (during surgical clipping or as a separate surgical procedure) or emergently at the bedside to decrease ICP. Poor clinical grade on admission, acute neurologic deterioration, or progressive enlargement of ventricles on CT scan are clear indications for the use of an external ventricular device (Level 2; Mayberg et al., 1994; Rordorf et al., 1997; Suzuki et al., 2000). Newer data suggest that external ventricular drainage does not include likelihood of aneurysm rehemorrhage when drainage is performed at moderate pressures (<10 cm H2O) (Level 2; Fountas et al., 2006). Aseptic technique is essential during external ventricular drain or subarachnoid bolt insertion because an infection can occur, especially if the drain is left in for an extended period of time. Cultures are to be routinely performed, and antibiotics are initiated if any signs of infection are present. Some clinicians and institutions use prophylactic antibiotics for aSAH patients with an external ventricular drain, although there is no literature supporting this practice.

Although all of these catheters allow monitoring of ICP, the external ventricular catheter permits cerebral spinal fluid (CSF) drainage to control ICP and clear blood from the CSF. The external ventricular catheter is associated with a higher infection rate than other catheters (Level 2; Lozier et al., 2002). Care related to CSF management varies by institution and clinician preference. Continuous drainage of CSF from an external ventricular drain (EVD) at a specified level (above the external auditory meatus or foramen of Monroe as per institutional policy) prevents ICP from rising above that level and allows for continuous clearance of bloody CSF from the ventricles and subarachnoid space (see Guide to the Care of the Patient with Intracranial Pressure Monitoring: AANN Reference Series for Clinical Practice).

In febrile patients (temperature ≥38.3°C or as per institutional policy), fever reduction should be achieved with administration of acetaminophen every 4–6 hours to achieve normothermia (Level 3; Suarez, Tarr, & Selman, 2006). Surface or intravascular cooling is instituted to maintain temperature <38.3°C if medications are not effective (Level 3; Suarez, Tarr, & Selman, 2006). It is important to control fever in this population as it is associated with poorer recovery from aSAH (Level 2; Commichau, Scarmeas, & Mayer, 2003; Fernandez et al., 2007). Surveillance cultures may be obtained daily in patients.
3.6 Acute Subarachnoid Hemorrhage

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<tr>
<td>Manifestations and Diagnosis of SAH: Summary and Recommendations</td>
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<tr>
<td>1. SAH is a medical emergency that is frequently misdiagnosed. A high level of suspicion for SAH should exist in patients with acute onset of severe headache (Class I, Level of Evidence B).</td>
</tr>
<tr>
<td>2. Computed tomography (CT) scanning for suspected SAH should be performed (Class I, Level of Evidence B), and lumbar puncture for analysis of cerebrospinal fluid (CSF) is strongly recommended when the computed tomography scan is negative (Class I, Level of Evidence B).</td>
</tr>
<tr>
<td>3. Selective cerebral angiography should be performed in patients with SAH to document the presence and anatomic features of aneurysms (Class I, Level of Evidence B).</td>
</tr>
<tr>
<td>4. Magnetic resonance angiography (MRA) and CT angiography (CTA) may be considered when conventional angiography cannot be performed in a timely fashion (Class IIb, Level of Evidence B).</td>
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Emergency Evaluation and Preoperative Care: Summary and Recommendations

| 1. The degree of neurological impairment using an accepted SAH grading system can be useful for prognosis and triage (Class IIa, Level of Evidence B). |
| 2. A standardized emergency department (ED) management protocol for the evaluation of patients with headaches and other symptoms of potential SAH currently does not exist and should probably be developed (Class IIa, Level of Evidence C). |

Hospital Characteristics and Systems of Care: Summary and Recommendations

| 1. Early referral to high-volume centers that have both experienced cerebrovascular surgeons and endovascular specialists is reasonable (Class IIa, Level of Evidence B). |

American neuro-critical care GL; July 2011

Diringer in Neurocritical care
# Evidence Summary

## Imaging

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<tr>
<th>Study/Type</th>
<th>Quality Rating</th>
<th>Sample Description</th>
<th>Method</th>
<th>Outcomes</th>
<th>Key Findings and Recommendations</th>
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<tr>
<td>Perry et al. 2011 Canada Prospective cohort</td>
<td>NA</td>
<td>3,132 consecutive alert (GCS=15) patients &gt;15 years, admitted to 11 institutions (2000-2009), presenting with non-traumatic acute headache or with syncope associated with headache who underwent emergency head CT, using third generation scanners as part of their diagnostic investigation. Patients were excluded if onset of headache was &gt;14 days, history of recurrent headaches, focal neurological deficits; papilloedema or history aneurysm, ventricular shunt, or brain neoplasm</td>
<td>Radiologists who were blinded to the study and data forms but who had routine clinical information, interpreted all CT scans. The reference standard was presence of subarachnoid blood identified on unenhanced CT, visible xanthochromia in the cerebrospinal fluid; or red blood cells (&gt;5×10⁶/L) in the final tube of cerebrospinal fluid collected and an aneurysm identified on cerebral angiography.</td>
<td>The sensitivity (SN), specificity (SP), + predictive value (PPV), - predictive value (NPP), + likelihood ratio (+LR) and – likelihood ratio (-LR) of CT to identify SAH were calculated. Results were stratified by time to CT (≤6 or &gt;6 hours).</td>
<td>Most patient in the entire cohort were young (mean age &lt;45 years), 60.3% were women, mean pain score (0-10 scale) was 8.7. 30.4% of patients had a CT scan within 6 hours of symptom onset, 49% underwent lumbar puncture after negative CT results. 240 patients (7.7%) were diagnosed with SAH. Overall: SN=93%, SN=100%, PPV=100%, NPP=99.4%, +LR=∞, -LR=0.07. (all 95% CIs were tight) For 953 patients who were scanned within 6 hours, SN, SP, PPV, and NPV were all 100% For 2,179 patients who were scanned &gt; 6 hours: SN=85.7%, SP=100%, PPV=100%, NPV=99.2%, +LR=∞, -LR=0.14.</td>
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<td>Cortnum et al. 2010 Denmark</td>
<td>NA</td>
<td>499 patients admitted to a single institution from 2000-2005 with suspected/verified SAH</td>
<td>The medical records were reviewed together with CT scan, angiography, and results from cerebral spinal fluid analysis by 2 members of</td>
<td>Sensitivity and specificity of CT to identify SAH. (Lumbar puncture was the referenced standard)</td>
<td>SAH was excluded in 203 patients based on the results of CT and lumbar puncture. 296 patients had confirmed SAH. Of these 295 were based on positive CT results. In a single patient, diagnosis was based on lumbar puncture</td>
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### 3.6 Acute Subarachnoid Hemorrhage

#### Study/Type
- **Retrospective**

#### Quality Rating
- NA

#### Sample Description
- Clinical history, examination findings, and time from onset of symptoms until CT scan (days) were also recorded.
- All patients received a CT scan. If the scan was positive, an angiography was performed. If the scan was negative, a lumbar puncture was performed.

#### Method
- Performed on day 6.

#### Outcomes
- Overall CT scanning had a sensitivity of 99.7% (95% CI 98.1–99.9%) and a specificity of 100% (98.2–100%).

#### Key Findings and Recommendations

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### Surgical Considerations

#### Study/Type
- Li et al. 2013
- China
- Systematic review and meta-analysis

#### Quality Rating
- NA

#### Sample Description
- 27 studies (11,568 patients) including 4 RCTs and 23 prospective/retrospective studies which included patients undergoing treatment for SAH.
- Sample sizes of included studies ranged from 18 to 2,174. The mean ages of included patients were between 45 and 58 years.

#### Method
- The outcomes of patients who had clipping and coiling procedures following SAH were compared.

#### Outcomes
- Primary outcomes: Poor outcome (mMR 3-6 or Glasgow Outcome Scale 1-3), mortality and rebleeding at end of follow-up

#### Key Findings and Recommendations
- Overall, treatment with coil was associated with an increased change of better outcome: OR=1.25, 95% CI 1.12-1.40, p<0.0001.

- Using results from RCTs:
  - A lower percentage of patients in the coil group had a poor outcome (23.4% vs. 31.1%) and the odds for a better outcome associated with the coil group were higher: OR=1.48, 95% CI 1.24-1.76, p=0.0001.

- There was no difference in the odds of better outcome when the results from observation studies were included (OR=1.11, 95% CI 0.96-1.28,
## 3.6 Acute Subarachnoid Hemorrhage

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<td><strong>McDougall et al. 2012</strong>&lt;br&gt;USA (BRAT)&lt;br&gt;Quasi-RCT</td>
<td>CA: ☒&lt;br&gt;Blinding: Patient ☒ Assessor ☒&lt;br&gt;ITT: ☒</td>
<td>472 patients 18-80 years who were admitted to the ICU with acute nontraumatic SAH were included. Patients with traumatic SAH and those presenting to the hospital more than 14 days after hemorrhage were excluded.</td>
<td>Patients were randomly assigned to receive aneurysm clipping (n=238) or coil embolization (n=233) and treated within 24 hours, when possible.</td>
<td>Primary outcome: Proportion of patients with poor outcome (mRS 3-6) at 1 year.&lt;br&gt;Secondary outcomes: Rebleeding, death</td>
<td>Overall, there was no difference in 1-year mortality between groups (OR=1.07, 95% CI 0.88-1.30, p=0.51). Results from 8 studies included.&lt;br&gt;Overall, rebleeding rate was lower in patients who had received clipping. (OR=0.43, 95% CI 0.28-0.67, p=0.001).</td>
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<td><strong>Taki et al. 2011</strong>&lt;br&gt;Japan (PRESAT)&lt;br&gt;Observational</td>
<td>NA</td>
<td>588 patients ≥20 years with confirmed SAH from 29 institutions. Patients were excluded if they had ruptured fusiform, dissecting.</td>
<td>Patients were treated using either endovascular treatments or surgical clipping at the discretion of the site investigators.</td>
<td>Primary outcome: Factors associated with a poor outcome at 1 year (mRS 3-6).</td>
<td>26 patients were lost to follow-up.&lt;br&gt;150 patients (28.1%) had poor outcomes and mortality at 1 year was 9.4%.&lt;br&gt;54% of patients who had surgical clipped had a p=0.17.</td>
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<td>(Prospective cohort)</td>
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<td>traumatic, mycotic, or arteriovenous malformation–related aneurysms or SAH of unknown etiology.</td>
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<td>poor outcome at 1 year compared with 46% of patients who had a coiling procedure (p=0.05).</td>
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<td>Type of treatment (coil vs. surgery) and size and location of the aneurysm were not significant predictors on outcome on univariate or multivariable analyses.</td>
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<td>Significant independent predictors of poor outcome were increasing age, admission WFNS grade IV–V, preadmission aneurysmal rupture, vasospasm-induced cerebral infarct, pneumonia, sepsis, shunt-dependent hydrocephalus and seizure, post clipping hemorrhagic complications and post coiling ischemic complications.</td>
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<td>Molyneux et al. 2002</td>
<td>CA: ☑</td>
<td>2,143 patients from 42 institutions with definitive SAH occurring within the previous 28 days or intracranial aneurysm, considered to be the cause. Exclusion criteria: SAH occurred &gt; 28 days, the patient was regarded as unsuitable for one or both treatments.</td>
<td>Patients were randomly assigned to receive neurosurgical clipping (n=1070) or endovascular treatment by detachable platinum coils (n=1073)</td>
<td>Primary outcome: Proportion of patients with poor outcome (mRS 3-6) at 2 months and 1 year. Secondary outcomes: One-year case fatality and non-procedural occurrences of rebleeding.</td>
<td>Recruitment was stopped following planned interim analysis (follow-up continues). At one-year, data from 801 patients randomized to the endovascular treatment group and 793 randomized to the neurosurgical group, were analyzed. At two months, fewer patients in the endovascular treatment group were dead or dependent (25.4%, vs. 36.4%, RR=0.698, 95% CI 0.609-0.801, p&lt;0.0001). Patients in the surgery group were 72% more likely to have a poor outcome after adjusting for age (&gt;50 years) and Hunt &amp; Hess scores &gt;II (RR=1.72, 95% CI 1.09-2.76, p=0.02). At one-year, fewer patients in the endovascular treatment group were dead or dependent (23.7%, vs. 30.6%, RR= 0.774, 95% CI 0.658-0.911, p=0.0019). The relative and absolute risk reductions in dependency or death associated with endovascular</td>
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<td>Molyneux et al. 2005</td>
<td>UK (ISAT Additional reporting)</td>
<td>RCT</td>
<td>Data from 1,063 patients in the endovascular treatment group and 1,055 for patients in the neurosurgery group were analyzed.</td>
<td>Mortality, occurrences of rebleeding and seizure.</td>
<td>Median follow-up period was 4 years. There were more deaths within the first 7 years of patients in the neurosurgery group (147 vs. 116, log rank= p=0.03). After the first year, there were 7 cases of rebleeding in the endovascular group and 2 in the neurosurgery group (p=0.22). There was a significant reduction in seizure risk after the first procedure associated with endovascular treatment (RR=0.52, 95% CI 0.37-0.74)</td>
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<tr>
<td>Molyneux et al. 2009</td>
<td>UK (ISAT-long-term follow-up)</td>
<td>RCT</td>
<td>813 patients in the endovascular treatment group and 769 patients in the neurosurgery group were eligible for long-term follow-up</td>
<td>5-year clinical outcomes, rebleeding</td>
<td>Total loss to follow-up was 2.7% at a mean of 9 years. There were 24 rebleeds that occurred &gt;1 year following treatment, 17 in the endovascular treatment group and 7 in the neurosurgery group. The difference between groups was non-significant based on intention-to-treat analysis (log rank p=0.06), but was significant based on per protocol analysis (log rank p=0.02)</td>
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### 3.6 Acute Subarachnoid Hemorrhage

#### Study/Type

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The standardized mortality ratios were significantly higher for patients in both the endovascular treatment group and the neurosurgery group compared with the estimated expected number of deaths from a UK cohort (SMR=1.37 and 1.77, respectively).

At 5 years, fewer patients in the endovascular therapy group were dead (11% vs. 14%, RR=0.75, 95% CI 0.58-0.97, p=0.03).

At 5 years, conditional upon survival, the percentage of patients who were independent (mRS≤2) was similar (83% endovascular group vs. 82% neurosurgery group, RR=0.99, 95% CI 0.94-1.03, p=0.61).

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### Prophylactic Seizure Treatment

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<tr>
<td>Rosengart et al. 2007 USA Retrospective</td>
<td>NA</td>
<td>3,552 patients from 162 institutions in 21 countries with aneurysmal SAH who had been recruited into four RCTS (evaluating tirilazad) from 1991-1997.</td>
<td>Comparisons of outcomes of patients treated with antiepileptic drugs (AED) and those who were not treated with AEDs.</td>
<td>Predictors of AED use, the effect of AEDs on in-hospital complications including neurological worsening (decrease in GCS 2 or more points or increase in NIHSS scores of ≥8 points), vasospasm, cerebral infarction, edema and hydrocephalus Unfavourable outcome (death, vegetative state, or severe disability) at 3</td>
<td>The mean age of patients was 52 years, 83% were female and 90% underwent surgery to clip ruptured aneurysm a median of 29 hours after symptom onset. AEDs were used in 65.1% of cases. Independent predictors of AED usage were: younger age, lower systolic blood pressure on admission and worse WFNS grade. Patients treated with AEDs were more likely to have a poor outcome at 3 months (33% vs. 26%, adjusted OR=1.56, 95% CI, 1.16-2.10, p=0.003)</td>
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May 21st, 2013
Patients treated with AEDs were at increased risk of vasospasms (adjusted OR=1.87, 95% CI 1.43-2.44, p=0.001), neurological worsening (adjusted OR=1.61, 95% CI 1.25-2.06, p=0.001) and cerebral infarction (adjusted OR=1.33, 95% CI 1.01-1.74, p=0.04).
3.6 Acute Subarachnoid Hemorrhage

References


