LIETUVOS SVEIKATOS MOKSLŲ UNIVERSITETAS
MEDICINOS AKADEMIJA, MEDICINOS FAKULTETAS
Neurochirurgijos klinika

Final Master’s Thesis

Literature review on:

*Early Surgery on Patients with Aneurysmal Subarachnoid Hemorrhage WFNS grades 4 and 5*

Reviewed by *Fatmahelzahraa Noureldin*

Supervised by *Egidijus Marcinkevičius MD, PhD*

Kaunas, 2020
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**SUMMARY**

_Fatmahelzahraa Noureldin_

*Early Surgery on Patients with Aneurysmal Subarachnoid Hemorrhage*  
*WFNS grades 4 and 5*

**AIM OF THE REVIEW:** This review aims to evaluate timing and approach of management of poor-grade aneurysmal subarachnoid hemorrhage, WFNS grade IV and V.

**OBJECTIVE:** Optimal management of poor-grade subarachnoid hemorrhage is controversial and is considered complicated due to the associated poor outcomes. Often these patients are managed by surveillance-only management or by less aggressive approaches. However, such treatments were linked to higher morbidity and mortality. Identification and early aggressive management of this population may lead to favorable outcomes.

**METHODS:** We used PubMed, Cochrane Library, and the reviews and reference lists of relevant articles to search for studies published from 1999 till 2018 to review 16 articles, with a total of 2032 patients, for ultra-early, early or late timing of surgery and 7 articles, with a total of 1294 patients, for surgical clipping or endovascular coiling.

**RESULTS:** Studying the outcome of timing of surgery of total population revealed, 50.6% of patients had favorable outcome: 18.4% receiving ultra-early surgery, 20.5% early and 11.8% late surgery. While 42.6% of patients had poor outcome: 20.2% undergoing ultra-early surgery, 14.3% early surgery and 8% late surgery. Analyzing the total population for modality of choice revealed, 25.6% of patients who underwent surgical clipping had favorable outcome compared to 15.8% who received endovascular coiling; while 32.1% and 20.9% of patients had unfavorable outcome. In addition to 3.9% of patients refusing the aneurysmal treatment, all suffered poor outcome.

**CONCLUSION:** All the reviewed articles agreed on the consensus that management within 24 hours from ictus is the timing of choice in managing poor grade SAH, which can reduce the increased intracranial pressure and increase cerebral perfusion to improve outcomes. Outcomes of both neurosurgical clipping and endovascular coiling were not appreciably different. However, clipping is preferred in small aneurysm with wide neck and MCA aneurysms. Coiling is preferred in larger aneurysms and aneurysms in ICA and posterior circulation.
CONFLICTS OF INTEREST

No conflicts of interest

BIOETHICAL APPROVAL

Lietuvos Sveikatos Mokslų Universitetas

Bioetikos Centras

No. BEC-MF-167
ABBREVIATIONS

ACA- anterior cerebral artery
AChA- anterior choroidal artery
AICA- anterior inferior cerebellar artery
AVM- arteriovenous malformation
EVD- external ventricular drainage
EVT- endovascular treatment
GCS- Glasgow Coma Scale
GOS- Glasgow Outcome Scale
ICA- internal carotid artery
ICH- intracerebral hemorrhage
ISAT- International Subarachnoid Aneurysm Trial
IVH- intraventricular hemorrhage
MCA- middle cerebral artery
MRS- modified Rankin scale
OphA- ophthalmic artery
PICA- posterior inferior cerebellar artery
SAH- subarachnoid hemorrhage
SCA- superior cerebellar artery
WFNS- World Federation of Neurosurgical Societies
INTRODUCTION

Subarachnoid hemorrhage is the leakage of blood into subarachnoid space, between pia and arachnoid membranes. SAH can be either traumatic or spontaneous subarachnoid hemorrhage. World Federation of Neurosurgical Societies classified SAH according to motor deficit and GCS score into 5 grades. Grade 1 and 2 are characterized by absence of motor deficit and GCS score 15 and 13-14, respectively. Present motor deficit and GCS 13-14 are described as Grade 3. Grade 4 and 5 are defined as presence or absence of motor deficit and GCS score 7-12 and 3-6, respectively. Aneurysmal subarachnoid hemorrhage (SAH) is associated with a mortality of 40-60% due to the initial bleed and further 20-25% seeking medical attention later in poor clinical condition and hence, termed as poor grade patients. [1]

Poor outcomes are usually secondary to early brain injury, associated with increased intracranial pressure which causes decreased cerebral perfusion and transient global cerebral ischemia or delayed cerebral ischemia. Poor-grade SAH management is deemed complicated as well as controversial. This is associated with the related complications SAH causes, such as intracerebral hemorrhage, hydrocephalus, intraventricular hemorrhage, and vasospasm. Clinically, poor-grade SAH are characterized by decreased GCS score and focal neurological deficit. [4, 5] Some physicians still assume a bleak course from the onset for these SAH patients, who quickly decline in level of consciousness; but clinical experience has taught us patients may improve quite dramatically if cared for acutely and aggressively. [6]

The incidence of patients with poor grade SAH varies from 24-45% in various series. [2] Although mortality from aneurysmal SAH has decreased significantly over the past several decades, current estimates of case mortality in the United States and Western Europe remain as high as 40% for all patients. Improvements in microsurgical and endovascular techniques, coupled with the development of neurocritical care as a distinct discipline, have contributed to the steady decline in overall morbidity and mortality from aneurysmal SAH. [3] However, timing of aggressive treatment of poor-grade SAH is still controversial and a topic of debate. This review aims to evaluate the best timing and modality to treat poor-grade SAH.
AIMS AND OBJECTIVES

**AIM OF THE REVIEW:** This review aims to evaluate timing and approach of management of poor-grade aneurysmal subarachnoid hemorrhage, WFNS grade IV and V.

**OBJECTIVE:**

1. To evaluate optimal timing of management: ultra-early (within 24h), early (24-72h) and delayed (>72h).
2. To assess post-operative complications related to timing of management.
3. To evaluate optimal modality of approaches: surgical clipping and/or endovascular coiling.
4. To assess post-operative complications related to modality of approaches.
MATERIAL AND METHODS

Our concern is to review relevant articles regarding timing and modality of poor-grades WFNS (grade IV and V) SAH.

Selection Methods:
PubMed, Cochrane Library, and reviews and reference lists of relevant articles were searched for studies published from 1999 till 2018. Search words included: “timing of poor-grade subarachnoid hemorrhage surgery”, “early surgery for poor-grade subarachnoid hemorrhage”, “early surgery for ruptured aneurysmal subarachnoid hemorrhage” and “delayed surgery of poor-grade subarachnoid hemorrhage”.

Selection Criteria of Articles:
1. WFNS grade 4 and 5
2. Confirmation of aneurysmal SAH
3. Meeting definition of timing
4. Outcomes are defined according to Modified Rankin scale score or Glasgow Outcome Scale score
5. Outcomes measured not less than 3 months

Definitions:

• Definition of surgery timing: Surgery performed within 24 hours of onset of SAH is defined as ultra-early surgery; surgery performed from 24 to 72 hours of onset as early surgery; and surgery performed after 72 hours of onset as late surgery.

• Definition of outcome: Favorable outcome is defined as either MRS (0-2) or GOS (4-5); while poor outcome is defined as either MRS (3-6) or GOS (1-3).

The MRS (Table 1) has shown moderate inter-rater reliability that improves with structured interviews. GOS (Table 2) was designed to rate outcomes among patients with head injuries but now it is used to rate outcomes among patients with stroke, in particular hemorrhages. The utility of the GOS seems to be best suited for patients with SAH because of the link of GCS with the WFNS scale. The spectrum of grades on the GOS may reflect serious diffuse or multi-focal brain injury, which may occur with SAH. The GOS does not differentiate between some of the more mildly affected patients.[36]
Fisher grade scale (Table 3) is used to visualize the amount of subarachnoid hemorrhage on CT scans and classify them into grades 1-4. Fisher scale can be also used to predict the incidence and severity of cerebral vasospasm. 
Rosen and Macdonald’s review concluded that Fisher scale does not consider the clot density and clearance rate factors which are as important.

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>No significant disability despite symptoms; able to carry out all usual duties and activities</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability; requiring some help, but able to walk without assistance</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability; bedridden, incontinent and requiring constant nursing care and attention</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>

Table 1 - Modified Rankin Scale score
<table>
<thead>
<tr>
<th>Level</th>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Death</td>
<td>Dead</td>
</tr>
<tr>
<td>2</td>
<td>Persistent vegetative state</td>
<td>Minimal responsiveness</td>
</tr>
<tr>
<td>3</td>
<td>Severe disability</td>
<td>Conscious but disabled; dependent on others for daily support</td>
</tr>
<tr>
<td>4</td>
<td>Moderate disability</td>
<td>Disabled but independent; can work in sheltered setting</td>
</tr>
<tr>
<td>5</td>
<td>Good recovery</td>
<td>Resumption of normal life despite minor neurologic and/or psychological deficits</td>
</tr>
</tbody>
</table>

*Table 2- Glasgow Outcome Scale score*

<table>
<thead>
<tr>
<th>Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No SAH or IVH detected</td>
</tr>
<tr>
<td>2</td>
<td>Diffuse thin (&lt;1mm) SAH</td>
</tr>
<tr>
<td></td>
<td>No clots</td>
</tr>
<tr>
<td>3</td>
<td>Localized clots and/or layers of blood &gt;1 mm in thickness</td>
</tr>
<tr>
<td></td>
<td>No IVH</td>
</tr>
<tr>
<td>4</td>
<td>Diffuse or no SAH</td>
</tr>
<tr>
<td></td>
<td>ICH or IVH present</td>
</tr>
</tbody>
</table>

*Table 3- Fisher Grading Scale*
RESULTS

A total of 43 articles were identified during initial search. Additional 24 articles extracted from the reference list. 3 articles were removed due to being duplicates, leaving 64 articles. 32 articles were found to be ineligible based on irrelevant titles and abstracts. After detailed evaluation of the remaining 32 articles, 12 full-text articles were excluded for not meeting the selection criteria. Of the studies included in meta-analysis, 16 articles were regarding surgery timing and 4 articles concerning modality of choice.

Figure 1- PRISMA 2009 Flow Diagram of included studies
Timing of Surgery

- Patient characteristics

On reviewing 16\textsuperscript{5, 7-25} articles with 2032 cases, 823 of cases (40.5\%) underwent ultra-early surgery, 720 cases (35.4\%) early surgery, and 489 cases (24.1\%) late surgery. The studied population age ranged from 15 to 93 years old, with median age of 54 years in ultra-early and early, and 55 years in late surgery. The number of cases of male and female patients is 677 males (33.3\%) and 1140 females (56.1\%) and 215 patients were unclassified (10.5\%). The male patients were 175 (8.6\%) operated on ultra-early surgery, 193 (9.5\%) early surgery, 157 (7.7\%) late surgery and 152 (7.5\%) unidentified. The female patients were 302 (14.9\%) in ultra-early surgery set, 335 (16.5\%) in early surgery, 296 (14.6\%) in late surgery and 207 (10.2\%) unidentified. Detailed patient history including hypertension, diabetes mellitus and smoking were not discussed in most of the articles. According to timing of surgery, the location of the ruptured aneurysms was 1563 (76.9\%) in anterior circulation (557 (27.4\%) in ultra-early surgery, 634 (31.2\%) in early surgery, 170 (8.4\%) in late surgery and 202 (9.9\%) unidentified), 464 (22.8\%) in posterior circulation (118 (5.8\%) in ultra-early surgery, 139 (6.8\%) in early surgery, 82 (4\%) in late surgery and 125 (6.2\%) unidentified), and 80 (3.9\%) in other locations including vertebrobasilar/ SCA/ PICA/ AICA/ AChA/ OphA (49 (2.4\%) in ultra-early surgery and 31 (1.5\%) unidentified). Eighty patients (3.9\%) had multiple aneurysms. Three articles did not discuss the location of ruptured aneurysms. Aneurysm size was discussed in some articles\textsuperscript{[8, 10, 11, 13, 14, 15, 21]} and ranged from 2-33mm. The mean size would not accurate due to insufficient data. Fisher scale on CT\textsuperscript{[5,7,8,10,11,13,14,15,16,21]} was performed on 1071 (52.6\%) patients. Grades I-II were found in 49 patients (2.4\%) receiving ultra-early surgery, 85 (4.2\%) in early surgery, 30 (1.5\%) in late surgery and 68 (3.3\%) in unidentified patients. While grades III-IV were noticed in 173 patients (8.5\%) from the ultra-early surgery group, 261 (12.8\%) from early surgery, 257 (12.6\%) from late surgery and 148 (7.3\%) unidentified patients.
Brain herniation was analyzed only in 3 articles\textsuperscript{[8,14,15]} in a total of 99 patients (5%), 23 patients (1.3%) in ultra-early surgery group, 31 (1.5%) in early surgery, 14 (0.7%) in late surgery and 31 (1.5%) unidentified.

Five articles\textsuperscript{[7,8,13,14,21]} evaluated intracerebral hematoma in 238 patients (11.7%), 54 (2.7%) underwent ultra-early surgery, 98 (4.8%) early surgery, 40 (2%) in late surgery and 46 patients (2.3%) were unidentified.

Six articles\textsuperscript{[5,13,14,20,21]} described intraventricular hemorrhage in 271 patients (13.4%), 34 (1.7%) receiving ultra-early surgery, 91 (4.5%) receiving early surgery, 61 (3%) receiving late surgery and 85 patients (4.2%) were unidentified.

Seven articles\textsuperscript{[5,8,12,13,14,17,21]} performed external ventricular drainage before surgery in 456 patients (22.5%), 89 (4.4%) from ultra-early surgery group, 153 (7.5%) from early surgery group, 170 (8.4%) from late surgery group and 44 patients (2.2%) were unidentified.

- **Outcomes of timing of surgery**

  Studying the outcome of timing of surgery of total population revealed, 1029 patients (50.7%) had favorable outcome: 373 (18.4%) receiving ultra-early surgery, 416 (20.5%) early and 240 patients (11.8%) late surgery.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
 & Ultra-early (<24h) & Early (24-72h) & Late (>72h) & Unidentified \\
\hline
Population & 823 (40.5\%) & 720 (35.5\%) & 489 (24.1\%) & 0 \\
\hline
Sex & & & & \\
* Males & 175 (8.6\%) & 193 (9.5\%) & 157 (7.7\%) & 152 (7.5\%) \\
* Females & 302 (14.9\%) & 335 (16.5\%) & 296 (14.6\%) & 207 (10.2\%) \\
\hline
Age (median) & 54 & 54 & 55 & 0 \\
\hline
Location of aneurysm & & & & \\
* Anterior circulation & 557 (27.4\%) & 634 (31.2\%) & 170 (8.4\%) & 202 (9.9\%) \\
* Posterior circulation & 118 (5.8\%) & 139 (6.8\%) & 82 (4\%) & 125 (6.2\%) \\
* Other & 49 (2.4\%) & 0 & 0 & 31 (1.5\%) \\
\hline
Fisher scale & & & & \\
* Grade I-II & 49 (2.4\%) & 85 (4.2\%) & 30 (1.5\%) & 68 (3.3\%) \\
* Grade III-IV & 173 (8.5\%) & 261 (12.8\%) & 257 (12.6\%) & 148 (7.3\%) \\
Brain herniation & 23 (1.3\%) & 31 (1.5\%) & 14 (0.7\%) & 31 (1.5\%) \\
ICH & 54 (2.7\%) & 98 (4.8\%) & 40 (2\%) & 46 (2.3\%) \\
IVH & 34 (1.7\%) & 91 (4.5\%) & 61 (3\%) & 85 (4.2\%) \\
EVD & 89 (4.4\%) & 153 (7.5\%) & 170 (8.4\%) & 44 (2.2\%) \\
\hline
\end{tabular}
\caption{Timing of surgery: Patients’ characteristics}
\end{table}
Eight hundred-sixty-five patients (42.5%) had poor outcome: 410 (20.2%) undergoing ultra-early surgery, 290 (14.3%) surgery and 165 (8%) late surgery. Missing data, either due to lost follow up or missed data, accounts for 6.8% of patients.

<table>
<thead>
<tr>
<th></th>
<th>Ultra-early (&lt;24h)</th>
<th>Early (24-72h)</th>
<th>Late (&gt;72h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable outcome</td>
<td>373 (18.4%)</td>
<td>416 (20.5%)</td>
<td>240 (11.8%)</td>
</tr>
<tr>
<td>Poor outcome</td>
<td>410 (20.2%)</td>
<td>290 (14.3%)</td>
<td>165 (8%)</td>
</tr>
</tbody>
</table>

Table 5 - Outcomes of timing of surgery

- **Post-operative complications**

Although not all articles addressed post-operative complications, 13 articles discussed vasospasm, hydrocephalus, delayed cerebral ischemia, cerebral infarction, post-operative rebleeding and pneumonia. Vasospasm [8, 13, 14, 15, 18, 19] was found in 80 patients (3.9%), 22 (1.1%) are from ultra-early set, 7 (0.3%) from early surgery set, 29 (1.4%) from late surgery and 22 patients (1.1%) were unidentified. Hydrocephalus [5, 8, 12, 13, 14, 15, 16, 18] presented in 287 patients (14.1%), 85 (4.2%) from ultra-early surgery group, 7 (0.3%) from early surgery group, 168 (8.3%) from late surgery group and 27 patients (1.3%) were unidentified. Delayed cerebral ischemia [12, 21] was noticed in 71 patients (3.5%), 20 (1%) ultra-early surgery patients and 51 (2.5%) from early surgery patients. Cerebral infarction [5, 8, 11, 13, 14, 15, 17, 18] was observed in 223 patients (11%), 14 (0.7%) from the ultra-early surgery group, 36 (1.8%) from early surgery group, 141 (6.9%) from late surgery group and 32 patients (1.6%) were unidentified. Post-operative rebleeding [8, 11, 12, 13, 14, 15, 16, 17, 20] was occurred in 93 patients (4.6%), 49 ultra-early surgery patients (2.4%), 22 early surgery patients (1.1%), 14 late surgery patients (0.7%) and 8 (0.4%) patients were not grouped. Pneumonia [8, 13, 14, 15] was noticed in 166 patients (8.2%), 22 (1.1%) ultra-early surgery patients, 34 (1.7%) early surgery patients, 44 (2.2%) late surgery patients and 66 (3.2%) of patients were unidentified.
Table 6 - Post-operative complications of timing of surgery

<table>
<thead>
<tr>
<th></th>
<th>Ultra-early (&lt;24h)</th>
<th>Early (24-72h)</th>
<th>Late (&gt;72h)</th>
<th>Unidentified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasospasm</td>
<td>22 (1.1%)</td>
<td>7 (0.3%)</td>
<td>29 (1.4%)</td>
<td>22 (1.1%)</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>85 (4.2%)</td>
<td>7 (0.3%)</td>
<td>168 (8.3%)</td>
<td>27 (1.3%)</td>
</tr>
<tr>
<td>Delayed Cerebral Ischemia</td>
<td>20 (1%)</td>
<td>51 (2.5%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cerebral Infarction</td>
<td>14 (0.7%)</td>
<td>36 (1.8%)</td>
<td>141 (6.9%)</td>
<td>32 (1.6%)</td>
</tr>
<tr>
<td>Post-operative Rebleeding</td>
<td>49 (2.4%)</td>
<td>22 (1.1%)</td>
<td>14 (0.7%)</td>
<td>8 (0.4%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>22 (1.1%)</td>
<td>34 (1.7%)</td>
<td>44 (2.2%)</td>
<td>66 (3.2%)</td>
</tr>
</tbody>
</table>

Surgical Clipping versus Endovascular Coiling

- **Patient characteristics**

Analyzing 7 [7,9,11,22,23,24,25] articles (1294 patients) about modality of choice for treating poor-grade aneurysmal SAH, 759 patients (58.7%) underwent surgical clipping, 484 patients (37.4%) received endovascular coiling, and 51 patients (12) (3.9%) did not accept aneurysmal treatment. The studied population age ranged from 15 to 93 years old.

The number of male and female population is 422 (32.6%) and 872 (67.4%), respectively. The male patients account for 171 patients (13.2%) who underwent clipping, 126 patients (9.7%) who received EVT and 125 patients (9.7%) were unidentified; while 455 female patients (35.2%) who underwent clipping, 148 (11.4%) who received EVT and 269 patients (20.8%) were unidentified.

Nine hundred patients (69.5%) had ruptured aneurysms in anterior circulation compared to 337 patients (26.1%) in posterior circulation, 44 patients (3.4%) in other locations, including vertebrobasilar/ SCA/ PICA/ AICA/ AChA/ OphA, and 13 patients (1%) were not known. Of the anterior circulation aneurysms, 434 patients (33.5%) underwent clipping, 188 (14.5%) received EVT and 278 (21.5%) were unidentified. While from the posterior circulation, 163 patients (12.6%) underwent clipping, 71 (5.5%) received EVT and 103 (8%) were unidentified.

From the other locations, 30 patients (2.3%) underwent clipping and 14 (1.1%) coiling.
Aneurysm size was discussed in some articles and ranged from 2-33mm. The mean size would not accurate due to insufficient data. Fisher CT was done for 495 patients (38.2%). One hundred-thirty-nine patients (10.7%) were found to have grade I-II opposed to 356 (27.5%) having grade III-IV. In patients who underwent clipping, 108 (8.3%) showed grade I-II compared to 299 (23.1%) grade III-IV. While 31 patients (2.4%) receiving endovascular coiling presented with grade I-II and 57 (4.4%) with grade III-IV.

Three articles [22, 23, 24] noticed brain herniation in findings of 169 patients (13.1%). Clipping patients were 58 (4.5%) compared to 22 EVT patients (1.7%) and 89 unidentified patients (6.9%).

Three articles [7, 22, 23] discussed the findings of hematoma. ICH patients accounted for 150 (11.6%) of total population, 26 (2%) of which underwent clipping, 6 (0.5%) received EVT and 118 (9.1%) were unidentified.

One hundred-three patients (8%) had IVH, 51 (3.9%) underwent clipping opposite to 52 (4%) receiving endovascular coiling.

One article [12] described 76 patients (5.9%) with hydrocephalus but were not grouped under approach groups.

<table>
<thead>
<tr>
<th></th>
<th>Clipping</th>
<th>Coiling</th>
<th>Unidentified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>759 (58.7%)</td>
<td>484 (37.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Males</td>
<td>171 (13.2%)</td>
<td>126 (9.7%)</td>
<td>125 (9.7%)</td>
</tr>
<tr>
<td>* Females</td>
<td>455 (35.2%)</td>
<td>148 (11.4%)</td>
<td>269 (20.8%)</td>
</tr>
<tr>
<td>Location of aneurysm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Anterior circulation</td>
<td>434 (33.5%)</td>
<td>188 (14.5%)</td>
<td>278 (21.5%)</td>
</tr>
<tr>
<td>* Posterior circulation</td>
<td>163 (12.6%)</td>
<td>71 (5.5%)</td>
<td>103 (8%)</td>
</tr>
<tr>
<td>* Other</td>
<td>30 (2.3%)</td>
<td>14 (1.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Fisher scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Grades I-II</td>
<td>108 (8.3%)</td>
<td>31 (2.4%)</td>
<td>0</td>
</tr>
<tr>
<td>* Grades III-IV</td>
<td>299 (23.1%)</td>
<td>57 (4.4%)</td>
<td>0</td>
</tr>
<tr>
<td>Brain herniation</td>
<td>58 (4.5%)</td>
<td>22 (1.7%)</td>
<td>89 (6.9%)</td>
</tr>
<tr>
<td>ICH</td>
<td>26 (2%)</td>
<td>6 (0.5%)</td>
<td>118 (9.1%)</td>
</tr>
<tr>
<td>IVH</td>
<td>51 (3.9%)</td>
<td>52 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>0</td>
<td>0</td>
<td>76 (5.9%)</td>
</tr>
</tbody>
</table>

*Table 7- Intervention approach: Patients’ characteristics*
• **Outcomes of intervention approach**

Analyzing the total population for modality of choice revealed, 331 patients (25.6%) who underwent surgical clipping had favorable outcome compared to 205 patients (15.8%) who received endovascular coiling; while 416 clipping patients (32.1%) and 271 coiling patients (20.9%) had unfavorable outcome. Twenty patients[^9] (1.5%) were missing data from one article due to inadequate follow-up. The 51 patients[^12] (3.9%) refusing the aneurysmal treatment all died.

<table>
<thead>
<tr>
<th></th>
<th>Clipping</th>
<th>Coiling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favorable outcome</td>
<td>331 (25.6%)</td>
<td>205 (15.8%)</td>
</tr>
<tr>
<td>Poor outcome</td>
<td>416 (32.1%)</td>
<td>271 (20.9%)</td>
</tr>
</tbody>
</table>

**Table 8- Outcomes of clipping and coiling**

<table>
<thead>
<tr>
<th></th>
<th>Clipping</th>
<th>Coiling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiological Hydrocephalus</td>
<td>7 (3.4%)</td>
<td>19 (9.4%)</td>
</tr>
<tr>
<td>Clinical Hydrocephalus</td>
<td>2 (1%)</td>
<td>14 (6.9%)</td>
</tr>
<tr>
<td>Symptomatic Vasospasm</td>
<td>13 (6.4%)</td>
<td>14 (6.9%)</td>
</tr>
<tr>
<td>Cerebral Infarction</td>
<td>23 (11.3%)</td>
<td>15 (7.4%)</td>
</tr>
<tr>
<td>Aneurysm rebleeding</td>
<td>2 (1%)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>39 (19.2%)</td>
<td>31 (15.3%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>6 (3%)</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>5 (2.5%)</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

**Table 9- Post-operative complications of clipping and coiling**

• **Post-operative complications**

Only one[^23] article addressed post-operative complications accounting for 203 patients (15.7%). Eight patients (3.9%) suffered from aneurysm rebleeding, 2 patients (1%) undergoing clipping and 6 patients (3%) receiving EVT. Cerebral infarction was found in 38 patients (18.7%), 23 clipping patients (11.3%) and 15 EVT patients (7.4%). Symptomatic vasospasm was noticed in 27 patients (13.3%),
13 clipping patients (6.4%) and 14 coiling patients (6.9%). Radiological hydrocephalus was observed in 26 patients (12.8%), 7 clipping patients (3.4%) and 19 coiling patients (9.4%). Clinical hydrocephalus presented in 16 patients (7.9%), 2 clipping patients (1%) and 14 coiling patients (6.9%). Seizures were observed in 11 patients (5.4%), 6 clipping patients (3%) and 5 coiling patients (2.5%). Pneumonia was found in 70 patients (34.5%), 39 clipping patients (19.2%) and 31 coiling patients (15.3%). Renal failure was found in 7 patients (3.4%), 5 clipping patients (2.5%) and 2 coiling patients (1%).
DISCUSSION

**Timing of Surgery**

The timing of intervention of poor WFNS grades subarachnoid hemorrhage due to ruptured aneurysms has been a topic of debate for years. Rapid, prompt diagnosis with different types of accurate and updated investigations together with timing and method of choice of management will affect the results that may range up to death. Out of total study population, the outcome was favorable in 18.4% of patients who underwent ultra-early management (clipping or coiling), 20.5% of patients in early management and 11.8% of patients in late management. Although results from the reviewed articles show that early surgery has more percentage of favorable outcome, all articles agreed on the consensus that management within 24 hours from ictus is the timing of choice in managing poor grade SAH. The explanation is not clear in the study and needs more workup. Majority of articles’ study population was older age patients. Few articles discussed poor-grade SAH in younger patients directing our attention that not only advanced age suffer from poor-grade SAH. From the general population, the number of female and male patients was 56.1% and 33.3%, respectively. Although female sex is a known risk factor of SAH\(^{[35]}\), some literature found that the outcome of SAH is the same in both sexes\(^{[26]}\). In the reviewed articles, there has been no focus on the effect of sexes on the outcome of patients. Three quarters of cases were in anterior circulation and near a quarter of cases were in posterior circulation and 3.9% in other locations. Although location of aneurysm doesn’t predict the outcome of the surgery, it plays a role in method of choice of management, either neurosurgical clipping or endovascular coiling. Aneurysms located in posterior circulation are more prone to have poor outcome\(^{[7]}\). This may be because this cohort of patients are understated in publications as they have high mortality rate related to rupture before receiving medical treatment as well as the requirements of a skilled surgeon to operate on those difficult locations. The proximity of posterior circulation aneurysms to the brainstem and the common occurrence of intraventricular hemorrhage with expansion of the fourth ventricle may explain the devastating effects of the initial aneurysm rupture in the posterior fossa\(^{[30]}\). Not all articles discussed the aneurysm size and the presence of ICH and IVH. In the articles mentioning size of aneurysm, the size ranged from 2-33 mm. Larger aneurysms have higher risk of rebleeding before aneurysm treatment\(^{[22]}\). ICH was found in 11.6% of the study population. ICH is often associated with poor outcome that may be due to the effect of the intracranial mass. Clipping and early evacuation can reduce the intracranial pressure and improve outcome.
IVH were found in 13.3% of patients. IVH is considered a strong predictive factor due to the implied risk of vasospasm-associated ischemia occurrence. The location of the ruptured aneurysm had a contradictory effect on the occurrence and severity of IVH—the highest incidence of IVH was observed among patients with aneurysms of the posterior circulation, while more severe IVH were associated with rupture of aneurysms of the anterior circulation, particularly at the distal ACA. The severity of IVH in SAH and its effect on functional outcome and clinical complications have been poorly investigated. IVH severity is an established independent predictor of poor outcome; however, there has been no link between the development of delayed neurological deficits and cerebral infarction with IVH severity. Zheng et al. stated that vasospasm was related with higher Fisher grades on CT as a result of stimulation of vasoconstrictors leading to delayed vasospasm. Van Der Jagt et al. studied patients who underwent EVD before early surgery (<72h) and concluded that EVD did not reduce the incidence of rebleeding in those patients, which may be explained by the fact that EVD is a precipitating factor of rebleeding.
**Surgical Clipping versus Endovascular Coiling**

With modern technologies and advanced techniques in neurosurgical clipping and endovascular coiling, a question of whether to clip or to coil poor-grade aneurysmal SAH arises. As both surgical clipping and endovascular coiling have advantages and disadvantages, they coexist rather than replace each other. Clipping is attributed for its long-term durability which is controversial in coiling. ISAT established that coiling has higher risk of rebleeding after procedure. However, on the long term follow up, after 1 year, coiling was shown a notable survival without disabilities. Tykocki et al [7] concluded that mortality rate was higher in coiling, but not significantly higher than in clipping. On the other hand, Lindgren et al [34] determined that at a 5- and 10-year follow up, outcomes of both neurosurgical clipping and endovascular coiling were not appreciably different. Of the 7 reviewed articles, 32.1% of clipping patients had poor outcome compared to 20.9% of coiling patients. The advantages of endovascular coiling are less invasiveness, easy access to vertebrobasilar system and multiple aneurysms in distant areas. The disadvantage of surgical clipping is the fact that it requires open surgery which is accompanied with more morbidity in elderly patients. Although coiling is less invasive than clipping surgery and a study on vasospasm after operation showed a significantly higher risk in clipping group, but the ischemic infarct end point showed no statistical difference [38]. Coiling is not valuable in all aneurysms as it does not remove the intracerebral hemorrhage or mass effect of giant aneurysms [27]. Majority of cases (69.6%) from reviewed articles suffered from aneurysmal SAH in anterior circulation, 33.5% of them underwent clipping and 14.5% coiling, compared to 26% in posterior circulation, where 12.6% underwent clipping and 5.5% coiling. The incidence of SAH in posterior circulation is believed to be low varying between 5-10% of all intracranial aneurysms. The underrepresentation of posterior circulation in most of the series of SAH patients is believed to be partly due to the high mortality rate associated with the rupture prior to receiving medical treatment [30]. Posterior circulation aneurysms are difficult to expose and operate, and thus coiling is more often used to treat [32]. In Zhao et al [23] study population, almost all patients with posterior circulation aneurysms received endovascular treatment in their study population. Horiuchi et Hongo [25] stated “In the elderly, internal carotid and posterior communicating artery aneurysms or MCA aneurysms were reported to be predictors of good outcome. Our data indicated that poor pre-operative grade and ACA aneurysm were independent risk factors of unfavorable outcome of clipping surgery.” Lusseveld et al [33] concluded that EVT is the preferred treatment for patients with ruptured basilar bifurcation but if it was not possible surgical treatment may be considered.
Zheng et al\textsuperscript{[38]} deduced that clipping is preferred for small aneurysms with wide neck and MCA aneurysms and coiling for larger aneurysms and ICA and posterior circulation aneurysms. The study population ranged from 15 to 93 years. While advanced age is an established risk factor of SAH and considered an important prognostic factor, some authors diagnosed poor-grade SAH in patients as young as 15 years. Shirao et al\textsuperscript{[37]} found that patients \( \geq 65 \) years undergoing endovascular coiling showed more favorable outcomes than those undergoing surgical clipping. However, Horiuchi et Hongo\textsuperscript{[25]} proposed that advanced age was not a risk factor for poor outcome in patient undergoing clipping. From the study population, 40.5\% of clipping patients and 29.9\% of coiling patients were males and 52.2\% of clipping patients and 17\% of coiling patients were females. In the reviewed articles, the effect of treatment modalities on sexes was not addressed. Aneurysm size could not be evaluated appropriately due to insufficient data from articles. Schuss et al\textsuperscript{[22]} deduced that patients with large aneurysms (> 10 mm) have a higher risk for rebleeding before aneurysm treatment. However, Zheng et al\textsuperscript{[38]} established that aneurysm size is not associated with poor outcome proposing that “larger aneurysms more often have a poor clinical condition on admission but the risk of clinical and surgical complications is essentially the same as in patient with small aneurysms” and owing this inconsistency to treatment selection bias. Oppong et al\textsuperscript{[39]} noticed that IVH severity is associated with hydrocephalus that results from CSF pathway obstruction. Kang et al\textsuperscript{[40]} concluded that “early weaning of EVD and placement of ventriculoperitoneal shunt would effectively treat SAH-induced hydrocephalus in severe SAH”. In Hoogmoed et al\textsuperscript{[12]} population, the reason for not treating the aneurysm was poor neurologic condition alone in 22 patients and a combination of poor neurologic condition and complications or comorbidities in 29; neurologic condition after cardiopulmonary resuscitation, advanced age, medical complications (e.g., pneumonia, sepsis) or carcinoma.
Post-operative complications

We could not assess possible post-operative complications on a larger scale as only one article evaluated the issue. Zhao et al [23] found that hydrocephalus (radiological hydrocephalus 3.4% in clipping patients and 9.4% in coiling patients and clinical hydrocephalus 1% in clipping and 6.9% in coiling patients) incidence was higher in coiling than in clipping. This may be due to the fact that during open surgery clot is removed and cistern is opened which reduces hydrocephalus occurrence. Pneumonia percentage was high in both clipping (19.2%) and coiling (15.3%) with a slight difference between methods. The results may be explained by the prolonged hospital stay, increased risk of infection in patients over 60 years due to low immunity, poor physiological status, higher incidence of comorbid illness and depressed level of consciousness causes loss of protective pharyngeal reflexes, with poor tussive capacity leading to aspiration and inability to breathe deeply[28]. Vasospasm occurrence did not differ between the two modalities, 6.4% of clipping patients and 6.9% of coiling patients. Van Loon et al [11] described that the incidence of vasospasm in poor-grade patients after coiling may be accounted to the hypervolemic hemodilution therapy after the procedure due to compaction of coils. Another reason may be the prolonged use (24 hour) of heparin after EVT. However, several studies comparing surgical and endovascular treatments of aneurysmal SAH have failed to demonstrate a significant difference between the modalities with regards to incidence of clinically symptomatic vasospasm. Zheng et al [24] found that elders suffer higher risk of rebleeding, hydrocephalus and vasospasm.
CONCLUSION

In conclusion, all the reviewed articles agreed on the consensus that management within 24 hours from ictus is the timing of choice in managing poor grade SAH patients which can reduce the increased intracranial pressure and increased cerebral perfusion to improve outcomes.

Outcomes of both neurosurgical clipping and endovascular coiling were not appreciably different. However, clipping is preferred in small aneurysms with wide neck and MCA aneurysms. Coiling is preferred in larger aneurysms and aneurysms in ICA and posterior circulation.

Although location of aneurysm doesn’t reveal the outcome of surgery it plays a role in method of choice of management.

Aneurysm size doesn’t reflect on the outcome of SAH; however, is more likely to be associated with complications. Larger aneurysms have higher risk of pre-operative rebleeding.

Intracerebral hemorrhage is often associated with poor outcome that may be due to the effect of the intracranial mass. Clipping and early evacuation can reduce the intracranial pressure and improve outcome.

Intraventricular hemorrhage severity has been reported as independent predictor of poor outcome but there is no association between the development of delayed neurological deficits and cerebral infarction with IVH severity demonstrated.

Hydrocephalus as a post-SAH complication is found more in coiling compared to clipping due to the fact that during open surgery clot is removed and the cisterns are opened which reduces hydrocephalus development.

Females predominate the study population and is a known risk factor of SAH, yet some literature found that the outcome of SAH is the same in both males and females.

Advanced age is an independent predictive factor of poor outcome that has highly associated with the presence of IVH. Vasospasm was found to be related to higher Fisher grades.
REFERENCES


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