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# Risk of re-bleed in cases of aneurysmal subarachnoid hemorrhage upon external ventricular drain placement: Systematic review

## Abstract

**Background:** Aneurysmal Subarachnoid Hemorrhage (aSAH) requires immediate treatment which can lead to better patient outcomes. If acute hydrocephalus is present, a drain should be placed before securing the ruptured aneurysm due to the rapid and devastating outcomes of hydrocephalus. There is still no consensus on whether ventriculostomy should be done before or after securing the ruptured aneurysm and whether ventriculostomy can lead to the re-rupture of an unsecured aneurysm. However, many studies showed that drain placement before aneurysmal treatment is associated with increased risk of rebleeding. The aim of this systematic review is to be able to assess the re-bleeding risk caused by drain placement in cases of aneurysmal subarachnoid hemorrhage before securing the aneurysm.

**Methods:** We searched a total of four online databases (PUBMED, EMBASE, SCIENCE DIRECT and COCHRANE LIBRARY) for papers published between March 1992 and April 2022 based on pre-defined search criteria. Main outcomes were measurement of rebleeding rate after external ventricular drain placement before securing the aneurysm, associated factors, control group comparison, mortality rate and EVD-related hemorrhage in patients on dual antiplatelet therapy.

**Results:** A total of 22 studies are included in this systematic review with a total number of 5492 aSAH patients. We found that the highest rebleeding rate with pre-operative CSF- drainage via EVD was 53.47% while 27.8% via ELD compared to the 14.57% in the control group without pre-operative drainage. Only a few studies reported the number of mortalities among patients with pre-operative drainage and the highest mortality rate was 22%. Finally, prolongation of drainage, amount of CSF drained, and the time between drainage and securing the aneurysm were the most associated risk factors.

**Conclusion:** The risk of aneurysmal re-rupture in patients with CSF drainage before securing the aneurysm is higher than in patients without drainage. However, this review shows the need for further research to be able to assess the optimal timing and duration of drain placement following acute hydrocephalus in patients with aSAH, in addition to the safety of CSF drainage in such patients before securing the aneurysm.

**Keywords:** Aneurysmal subarachnoid hemorrhage; External ventricular drain; Re-bleed risks; Acute hydrocephalus.

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## Introduction

Intracranial saccular aneurysms, also known as berry aneurysms, are out-pouching vascular lesions that most commonly occur at the bifurcation of arteries in the anterior or posterior circulation of the Circle of Willis [1]. There are several risk factors associated with the formation of saccular aneurysms reported in literature and include: family history of a first degree relative, smoking, hypertension, female sex, and medical history of connective tissue disorders (e.g., Marfan syndrome, Ehlers-Danlos syndrome type IV) [1-3]. Patients with cerebral aneurysms can be asymptomatic or can present with headache or neurologic deficits depending on the location and size of the aneurysm. Aneurysms are weak spots in the walls of an artery, hence, they pose a risk of rupture being 0.05% every year for aneurysms less than 1 cm, whereas aneurysms larger than 1 cm or located in the posterior circulation have a higher risk [2]. Ruptured aneurysms lead to Subarachnoid Hemorrhage (SAH) referred to as aneurysmal subarachnoid hemorrhage (aSAH) with an incidence rate estimated to be 1 per 10,000 cases of ruptured aneurysms in the United States [3]. 20-30% of the time, SAH can lead to Hydrocephalus (HCP) due to the disruption of the arachnoid granulation impending proper Cerebrospinal Fluid (CSF) resorption, which in turn can lead to neurologic deterioration and necessitates the need for either a permanent ventricular shunt or an External Ventricular Drainage (EVD) for CSF diversion to decrease Intracranial Pressure (ICP) [4].

Hydrocephalus is well known to be a serious complication of SAH that can occur within the first few days [4]. The neurologic dysfunction and clinical deterioration of a patient following HCP requires urgent intervention [5,6]. Although ventriculostomy remains the mainstream treatment of hydrocephalus in the cases of aSAH, there is still no consensus on whether ventriculostomy should be done before or after securing the ruptured aneurysm and whether ventriculostomy can lead to the re-rupture of an unsecured aneurysm [6,7]. A study by Voldby and Enevoldsen showed that active drainage contributed to a re-rupture [8]. Pare, et al concluded that the risk of rebleeding with active drainage increased to 30% compared to an 8% rebleed risk in patients without drainage [8]. These results could not be confirmed by another study by Hellingman et. al. as their data showed 7 out of 34 patients with HCP had rebleeding after EVD insertion compared to 7 out of 34 patients with HCP without EVD insertion [6,9-11]. Therefore, this systematic review aims at reviewing the published data to assess the re-bleeding risk associated with CSF drainage in patients with aSAH.

### Search strategy

We searched a total of four online databases (PUBMED, EMBASE, SCIENCE DIRECT and COCHRANE LIBRARY) for papers published between March 1992 and April 2022 based on predefined search criteria. Search keywords included 'aneurysmal subarachnoid hemorrhage', 'acute hydrocephalus', 'preoperative drain placement' 'external ventricular drain' and 'risk of rebleeding'. We identified eligible publications using a (title, abstract, full-article and conclusion) screening method. At each step, two reviewers screened the published articles.

### Inclusion and exclusion criteria

We focused on studies that (1) included aSAH patients with acute hydrocephalus, (2) compared rates of rebleeding between patients who had preoperative drain placement and patients who did not have any drains placed, (3) investigated the potential risk of rebleeding in patients with drain placement before securing the aneurysm, (4) reported any measurement of association, (5) assessed the risk of EVD-related hemorrhage in patients on antiplatelets therapy.

We excluded studies that (1) included conditions other than aSAH, (2) did not evaluate rebleeding risk in patients with preoperative drain placement, (3) irrelevant publications, (4) review articles without any data.

### Data extraction

Two reviewers extracted data independently from eligible manuscripts using a pre-designated format. Reviewers met to discuss and discrepancies in data were resolved.

### Synthesis of the results

We listed findings of qualified studies, calculated rates of bleeding, stratified by whether preoperative drain was placed, and type of drain used. We also determined the mortality rate after drain placement before securing ruptured aneurysm. A meta-analysis was not possible due to the heterogeneity of the date in the studies regarding the use of different methodological approaches and sources of data. As a result, the findings are presented as a narrative systematic review.

## Results

### Study selection

Overall, 22 studies have been included in this systematic review with a total number of 5492 aSAH patients.

### Study characteristics

Findings of included studies are demonstrated in Table 1. In total, 10 studies (45.45%) [6-8,10,14,15,19,20,21,28] presented the number of patients who had rebleeding after drain placement before securing ruptured aneurysm as a primary focus of their research. Seven studies (31.81%) [6-8,14,15,20,21] compared this number to a control group who had rebleeding without any drain placement, and only 4 studies (18.18%) [14,19,20,21] reported the number of deaths after preoperative drain placement.

**Table 1:** Study characteristics in the selected papers.

| Author | Country | Total number of aSAH patients | Study design | Study period | Presenting rebleeding after PDP | Comparing to a control group | Reporting mortality after PDP |
|---|---|---|---|---|---|---|---|
| Bruder et al. [12] | Germany | 444 | Retrospective | 2007-2013 | No | No | No |
| Lenschow et al. [5] | Germany | 328 | Retrospective | 2009-2021 | No | No | No |
| Sims-Williams et al. [13] | UK | 1 | Retrospective | 2014 | No | No | No |
| Ruijs et al. [14] | Netherlands | 107 | Retrospective | 1995-1997 | Yes | Yes | Yes |
| Pare et al. [7] | Canada | 128 | Retrospective | 1983-1990 | Yes | Yes | No |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Lu et al. [15] | USA | 471 | Retrospective | 2001-2016 | Yes | Yes | No |
| Oppong et al. [16] | Germany | 939 | Retrospective | 2003-2016 | No | No | No |
| Kirmani et al. [17] | India | 55 | Prospective | 2012-2015 | No | No | No |
| Zachariah et al. [18] | USA | 241 | Retrospective | 2001-2014 | No | No | No |
| Hellingman et al. [6] | Netherlands | 546 | Retrospective | 1993-2001 | Yes | Yes | No |
| Rajshekhar et al. [19] | USA | 194 | Retrospective | 1982-1989 | Yes | No | Yes |
| Lu et al. [20] | China | 152 | Retrospective | 2006-2010 | Yes | Yes | Yes |
| van den Berg et al. [21] | Netherlands | 126 | Retrospective | 2000-2007 | Yes | Yes | Yes |
| Maas et al. [22] | USA | 211 | Prospective | 2006-2018 | No | No | No |
| Evans et al. [23] | UK | 355 | Retrospective | 2015-2018 | No | No | No |
| Leschke et al. [24] | USA | 93 | Retrospective | 2005-2014 | No | No | No |
| Scholz et al. [25] | Germany | 27 | Retrospective | 2007-2009 | No | No | No |
| Gard et al. [26] | USA | 112 | Retrospective | 2012-2014 | No | No | No |
| Lim et al. [10] | Korea | 122 | Retrospective | 2010-2017 | Yes | No | No |
| Hudson et al. [27] | USA | 443 | Retrospective | 2009-2016 | No | No | No |
| Kawai et al. [28] | Japan | 93 | Retrospective | 1990-1994 | Yes | No | No |
| Mclver et al. [8] | USA | 304 | Retrospective | 1990-1997 | Yes | Yes | No |

**Measurment of rebleeding rate after preoperative drain placement**

We calculated rebleeding rates in 10 studies [6-8,10,14,15,19,20,21,28] that documented the number of aSAH patients with acute hydrocephalus who had rebleeding after drain placement before securing ruptured aneurysm (Table 2). Studies used different types of drains, sometimes more than one. The percentage of rebleeding varied between the studies. The highest rebleeding rate, 53.57%, was seen in a retrospective study where external ventricular drain (EVD) was placed preoperatively [28]. Average rebleeding rates varied between 30% and 13.46% measured using the following 8 studies [6-8,14,15,19,20,21]. EVD were used in all these studies except one study where an external lumbar drain was used and the rebleeding rate was 27.8% [14]. The Lowest rates, 4.44% (EVD) and 4.76% (LP), were seen in two retrospective studies [8] and [6] respectively.

**Associated factors**

We identified 3 factors affecting rebleeding rate in aSAH patients after drain placement before surgery in 3 studies [14,19,21] only (Table 2). In one study, prolonging the drainage more than 24 hours was found to be associated with increased risk of rebleeding [19]. An additional factor was excessive CSF drainage found in another study [14]. On the other hand, we identified a study where no significant association was found between the amount of CSF drained and rates of rebleeding [7]. Added research concluded that in aSAH patients limited to WFNS grade V, delayed aneurysmal repair is associated with higher risk of rebleeding after drain placement due to less stable aneurysmal wall [21]. Another study showed that increased risk of rebleeding and degree of ventriculomegaly are not related [28]. Four studies [6,8,10,28] found no evidence of association between preoperative drain placement and increased risk of rebleeding. Two studies highlighted the increase in transmural pressure around the aneurysmal wall as a possible mechanism of rebleeding during CSF drainage [15,28].

**Control group comparison**

In addition to aSAH patients who had rebleeding after preoperative drain placement, 7 studies [6-8,14,15,20,21] included the number of aSAH patients who had rebleeding without any drains. This subset of patients was used as our control group throughout the review. We compared the rate of bleeding in control group to the rate of rebleeding in patients with preoperative drain placement. In six studies (85.7%) [6,7,14,15,20,21] the rate of bleeding was lower in the control group. It was slightly higher in only one study (5.4%) compared to (4.44%) in patients who had rebleeding after drain placement before surgery. In one study [6], the results were heterogenous. We found that the rate of rebleeding in control group (14.54%) was higher than in patients who had lumbar puncture (4.76%) but lower than in patients who had EVD insertion (20.5%) (Table 2).

**Mortality rate**

Four studies [14,19,20,21] reported the number of deaths in aSAH patients after drain placement before undergoing aneurysmal repair. The highest mortality rate (22.2%) was calculated using a retrospective study [14] where external lumbar drain was used. 1.92% was found to be the lowest mortality rate after EVD placement in a different study [19] (Table 2).

**EVD-related hemorrhage in patients on dual antiplatelet therapy**

Although not the primary goal of our study, we identified 7 studies [5,12,18,23,24,25,27] among qualified publications that assessed the risk of EVD-related hemorrhage in patients on dual antiplatelet therapy who are candidates for aneurysmal repair surgery as a major outcome of their research. Four studies showed that EVD placement before endovascular coiling and DAPT/Aspirin loading is associated with lower risk of EVD-related hemorrhage [5,12,18,23]. However, two different studies concluded that EVD placement before or after endovascular procedure and ADAPT/Aspirin loading is generally safe with no significant risk factor of EVD-related hemorrhage [24,27]. A single study demonstrated that the hemorrhage rate is the same irrespective of the timing of antiplatelet therapy [25].

**Table 2:** Primary findings.

| Author | Total nb of patients with aSAH (n=5492) | Acute hydrocephalus | Pre-op drain placement | Type of drain | Rebleeding after drain placement in patients with unsecured aneurysm (%) | Potential risk of rebleeding in patients with pre-op drain placement | Rebleeding in patients without drain placement (%) | Post-op drain placement | Mortality rate after drain placement before securing (%) |
|---|---|---|---|---|---|---|---|---|---|
| Bruder et al. [12] | 444 | 444 | 418 | EVD# | NA ǂ | _ | _ | _ | _ |
| Lenschow et al. [5] | 328 | 328 | 114 | EVD# | NA ǂ | _ | _ | 84 | _ |
| Sims-Williams et al. [13] | 1 | 1 | 1 | EVD | NA ǂ | _ | _ | _ | _ |
| Ruijs et al. [14] | 107 | 18 | 18 | ELD | 5/18 (27.8%) | Excessive CSF drainage | 44/324 (13.85%) | _ | 4/18 (22.2%) |
| Pare et al. [7] | 128 | 49 | 20[1] | EVD | 6/20 (30%) | No significant relation between the amount of CSF drained and rates of rebleeding | 9/108 (8.33%) | _ | _ |
| Lu et al. [15] | 471 | NA | 147 | EVD | 22/147 (14.96%) | Increase in transmural pressure around the aneurysm wall | 11/324 (3.39%) | _ | _ |
| Oppong et al. [16] | 939 | 921 | _ | EVD | NA ǂ | _ | _ | 663‡ | _ |
| Kirmani et al. [17] | 55 | 9 | 9‡ | EVD | NA ǂ | _ | _ | _ | _ |
| Zachariah et al. [18] | 241 | 241 | 241‡ | EVD# | NA ǂ | _ | _ | _ | _ |
| Hellingman et al. [6] | 546 | 271 | 55[1] | 34/EVD 21/LP | 7/34 (20.5%) 1/21 (4.76%) | No evidence of association | 16/110 (14.54%) | _ | _ |
| Rajshekhar et al. [19] | 194 | 52 | 52 | EVD | 7/52 (13.46%) | Prolonging the drainage more than 24 hours | _ | _ | 1/52(1.92%) |
| Lu et al. [20] | 152 | 27 | 10[2] | EVD | 4/19** (21.05%) | _ | 4/19** (21.05%) | _ | 4/19**(21.05%) |
| van den Berg et al. [21] | 126* | 71 | 103 | EVD | 23/103 (22.33%) | -Less stable aneurysms in WFNS grade V patients. -Delayed securing | 3/24 (12.5%) | _ | 6/103 (5.82%) |
| Maas et al. [22] | 211 | _ | 146 | EVD | _ | _ | _ | _ | _ |
| Evans et al. [23] | 355 | 130 | 104 | EVD# | NA ǂ | _ | _ | 26 | _ |
| Leschke et al. [24] | 93 | 93 | 93 | EVD*# | NA ǂ | _ | _ | _ | _ |
| Scholz et al.[25] | 27 | 27 | _ | EVD ICP gauge EVD+ICP gauge | NA ǂ | _ | _ | 17/EVD## 7/ICP gauge 3/EVD+ ICP gauge | _ |
| Gard et al. [26] | 112 | 112 | 112 | EVD | NA ǂ | _ | _ | _ | _ |
| Lim et al. [10] | 122 | 55 | 67 | EVD | 19/67 (28.35%) | Pre-op EVD placement did not increase the risk of rebleeding | _ | 55 (Rebleeding in 23 patients) 23/55 (41.81%) | _ |
| Hudson et al. [27] | 443 | 298 | 298‡ | EVD*# | NA ǂ | _ | _ | _ | _ |
| Kawai et al. [28] | 93* | 28 | 28 | EVD | 15/28 (53.57%) | -Increase in transmural pressure around the aneurysm wall -No significant relation between the degree of ventriculomegaly and increase rebleeding rates | _ | _ | _ |
| Mclver et al.[8] | 304 | 45 | 45 | EVD | 2/45 (4.44%) | No evidence of association between pre-op EVD and increase rebleeding rates | 14/259 (5.4%) | _ | _ |

*: Limited to patients with WFNS grade V only; **: In this study 4 out of 19 patients had rebleeding (10/19) with EVD and 9/19 without EVD); 1: The rest of patients have been monitored or their acute hydrocephalus has resolved spontaneously; 2: In this study 7 patients underwent FLT during clipping and only one patient needed a VPS placement after surgery; #: This study shown that EVD placement before endovascular coiling and ADAPT/Aspirin loading is associated with lower risk of EVD-related hemorrhage; *#: This study has shown that EVD placement before or after endovascular procedure and ADAPT/Aspirin loading is generally safe with no significant risk factor of EVD-related hemorrhage; ##: This study has shown that EVD-related hemorrhage rates are the same before or after anticoa/antiplatelet therapy with endovascular coiling; †: These studies did not aim to investigate EVD-related rebleeding of an unsecured ruptured aneurysm; ‡: Data on the exact timing of EVD placement were missing.

## Discussion

Aneurysmal rupture can be followed with serious complications including subarachnoid hemorrhage which in turn has its own complications. aSAH induced HCP is a serious complication that requires urgent medical intervention with CSF drainage due to the elevation of the ICP and decrease in cerebral perfusion before the securing the aneurysm. EVD is used to manage elevated ICP [11]. As seen from the literature review, CSF drainage can differ in type and timing. Among the 22 relevant papers, we found that the highest rebleeding rate with pre-operative CSF drainage via EVD was 53.47% while 27.8% via ELD compared to the 14.57% in the control group without pre-operative drainage. Only 1 out of the 22 papers assessed the rebleeding rate with drainage via ELD (Table 2) so further studies should be done to evaluate the difference between ventricular and lumbar CSF drainage when it comes to patient safety and risk of re-bleed. Only a few studies reported the number of mortalities among patients with pre-operative drainage and the highest mortality rate was 22%.

There are several risk factors that can be associated with the risk of rebleeding. However, no significant statistical data was reported by any of the studies. It was theorized that the prolongation of drainage, amount of CSF drained, and the time between drainage and securing the aneurysm were the most associated risk factors [7,14]. The mechanism for the rebleed is theorized to be the difference in pressure across the aneurysmal wall leading to the re-rupture. More studies should be done to evaluate the rate of CSF drainage and the maximum safe time delay before securing the aneurysm.

## Conclusion

The risk of aneurysmal re-rupture with CSF drainage can reach up to 53.47% compared to 14.57% without drainage. The mortality rate can reach up to 22% based on the limited data reported. More studies should be done to assess the safety profile of EVD vs. Lumbar drainage. It was also shown that dual antiplatelet therapy has no significant risk of causing EVD associated hemorrhage. According to what was observed in the literature, CSF drainage in cases of aSAH before securing the aneurysm could be safe with decreased risk of re-bleed if CSF drainage was done minimally in order not to cause any tension on the aneurysmal that could induce its rupture; however, more data is needed to prove that, and to indicate the adequate amount of CSF drainage per hour.

**Abbreviations:** aSAH: Aneurysmal Subarachnoid Hemorrhage; CSF: Cerebrospinal Fluid; EVD: External Ventricular Drain; ELD: External Lumbar Drain; FLT: Fenestration of Lamina Terminalis; HCP: Hydrocephalus; ICP: Intracranial Pressure; NA: Not Available; PDP: Preoperative Drain Placement; VPS: Ventriculoperitoneal Shunt; WFNS: World Federation of Neurological Surgeons.

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