Lumbar Drainage of Cerebrospinal Fluid After Aneurysmal Subarachnoid Hemorrhage

A Prospective, Randomized, Controlled Trial (LUMAS)

Yahia Z. Al-Tamimi, MRCS; Deepti Bhargava, MRCS; Richard G. Feltbower, PhD; Gregory Hall, PhD; Anthony J.P. Goddard, FRCR; Audrey C. Quinn, FFARCSI; Stuart A. Ross, FRCS(SN)

Background and Purpose—A single-center prospective randomized controlled trial has been conducted to determine if lumbar drainage of cerebrospinal fluid after aneurysmal subarachnoid hemorrhage reduces the prevalence of delayed ischemic neurological deficit and improves clinical outcome.

Methods—Patients with World Federation of Neurological Surgeons Grade 1 to 3 aneurysmal subarachnoid hemorrhage and modified Fisher Grades 2, 3, 4, and 3+4 were randomized to either the study group of standard therapy plus insertion of a lumbar drain or the control group of standard therapy alone. The primary outcome measure was the prevalence of delayed ischemic neurological deficit.

Results—Two hundred ten patients with aneurysmal subarachnoid hemorrhage (166 female, 44 male; median age, 54 years; interquartile range, 45–62 years) were recruited into the control (n=105) and study (n=105) groups of the trial. World Federation of Neurological Surgeons grade was: 1 (n=139), 2 (n=60), and 3 (n=11); Fisher grade was: 2 (n=87), 3 (n=85), and 4 (n=38). The prevalence of delayed ischemic neurological deficit was 35.2% and 21.0% in the control and study groups, respectively (P=0.021). The prevalence of a modified Rankin Scale score of 4, 5, or 6 at Day 10 and 6 months, respectively, was 62.5% and 18.6% in the control group and 44.8% and 19.8% in the study group (P=0.009 and 0.83, respectively).

Conclusions—Lumbar drainage of cerebrospinal fluid after aneurysmal subarachnoid hemorrhage has been shown to reduce the prevalence of delayed ischemic neurological deficit and improve early clinical outcome but failed to improve outcome at 6 months after aneurysmal subarachnoid hemorrhage.

Clinical Trial Registration—URL: www.clinicaltrials.gov. Unique identifier: NCT00842049.

(Stroke. 2012;43:677-682.)

Key Words: aneurysmal subarachnoid hemorrhage ■ cerebrospinal fluid drainage ■ delayed ischemic neurological deficit ■ lumbar drain ■ randomized controlled trial ■ vasospasm

Delayed ischemic neurological deficit (DIND) is a serious and poorly understood complication of aneurysmal subarachnoid hemorrhage (aSAH). This is characteristically defined as deterioration in neurological function seen at least 3 to 4 days posthemorrhagic ictus and is also known as clinical/symptomatic vasospasm or delayed cerebral ischemia. DIND remains a significant cause of morbidity and mortality in survivors of the initial hemorrhage. The reported prevalence of DIND is 20% to 35%, although in those with a higher blood load, this may be as high as 40%. It is thought to result in cerebral infarcts in approximately 20% of patients and cause 13% of all death and disability after aSAH. Although the underlying pathophysiological process is not known, the presence of blood or its breakdown products within the subarachnoid space and cisterns is clearly associated with DIND. An association between the size of the blood clot and the prevalence of angiographic vasospasm and DIND has been observed. Thick subarachnoid clot completely filling any cistern or fissure has been shown to be an independent predictor of DIND.

It follows from this that attempts at clearing the subarachnoid space of blood may potentially reduce the prevalence and severity of DIND. Numerous techniques have been described to reduce the blood load. Studies investigating cisternal drainage have reported mixed results. Cisternal drains and intrathecal thrombolysis are difficult to administer and not without morbidity. There has been some evidence to suggest that drainage of cerebrospinal fluid (CSF) through the

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lumbar cistern may be of some benefit in reducing the prevalence of DIND.\(^2,12\) A lumbar drain is less invasive than other forms of CSF drainage and is a device that is regularly used for other clinical purposes. In a retrospective nonrandomized study, the prevalence of DIND was 17\% in those patients with a lumbar drain in situ and 51\% in those without a drain.\(^2\) There were numerous limitations to this study and a call for a randomized controlled trial to investigate this further.\(^2\)

The aim of this trial was to determine whether insertion of a lumbar drain after aSAH with subsequent CSF drainage results in a lower prevalence of DIND and improvement in clinical outcome compared with standard therapy.

**Materials and Methods**

**Patients**

This single-center prospective randomized controlled trial started recruitment of patients with aSAH in October 2006 and closed recruitment in July 2010 as per protocol. Patients admitted to the neurosurgery department at Leeds General Infirmary with aSAH were assessed for suitability according to inclusion criteria: World Federation of Neurological Surgeons (WFNS) Grade 1 to 3; modified Fisher Grade 2, 3, 4 or 5\+ on initial CT scan; and recruitment before 96 hours posthemorrhage (see protocol). The protocol was approved by the Leeds West Research Ethics Committee (October 2006).

**Procedure and Interventions**

After written consent/assent, the patient was randomized to the control arm of standard therapy alone (described in the study protocol) or the study arm of standard therapy plus insertion of a Medtronic lumbar intrathecal catheter. After screening and recruitment, patients were not subjected to further DIND prevention trials.

**Outcome Measure**

The primary outcome measure was the prevalence of DIND. This was defined as a drop in consciousness (1 motor score or 2 eye/verbal scores of the Glasgow Coma Score) or a new focal neurological deficit within 24 hours of treatment (confirmed established infarct (as assessed by CT and MRI when available). DIND were made by a multidisciplinary neurovascular team and confirmed established infarct (as assessed by CT and MRI when available). DIND were prospectively and retrospectively verified by the investigators blinded to the treatment allocation. Neuroradiologists blinded to the treatment allocation reported radiologically confirmed infarcts as part of routine clinical care.

**Statistical Analysis**

The initial power calculation was based on an expected DIND prevalence of 40\% in the control arm and 20\% in the study group. For an 85\% power, 105 patients were required in each arm of the trial. Planned interim analyses were performed after recruitment of 40 patients (to establish adverse effects only) and 100 patients. The data monitoring committee/statistical consultation advocated continuation of the trial to completion following these analyses. Baseline data on all patients with aSAH was collected prospectively on confirmation of the aneurysmal cause of the hemorrhage. The primary analysis was performed on an intention-to-treat basis. The analysis of the primary outcome was a categorical frequency comparison with the \(\chi^2\) test. All numeric data were assessed for normality using the Shapiro-Wilk test and Q-Q plots. Normal numeric data were tested with the independent \(t\) test and data not normally distributed with the Mann-Whitney \(U\) test. Categorical frequencies were compared using the \(\chi^2\) test or Fisher exact test when a cell size was \(<5\). \(P<0.05\) was considered statistically significant.

Relative risk was calculated as the ratio of 2 conditional probabilities using \(2 \times 2\) crosstabsulation. All statistical tests were performed with SPSS Version 19 (IBM).

**Results**

The trial profile is shown in the Figure. From a total of 426 patients with aSAH, 210 were recruited and randomized to the trial. The main reasons for exclusions were poor WFNS grade and delayed presentation after ictus. The primary analysis followed intention-to-treat principles and included all 210 patients.

Table 1 shows baseline patient characteristics including age, gender, WFNS grade, Fisher grade, aneurysm type, and treatment modality in the 2 groups.

Table 2 shows the primary intention-to-treat analysis of primary and secondary outcome measures. There was a significantly lower prevalence of DIND and a better outcome at 10 days postictus for those in the study group. There were no significant differences noted in the other outcome measures including modified Rankin Scale at 6 months.

A secondary analysis was performed that excluded those patients in the study group who could not receive lumbar drain/CSF drainage therapy due to an inability to place a functioning drain and those patients in the control and study groups who were treated for hydrocephalus with early external ventricular drainage (within 14 days of ictus). This demonstrates similar findings to the primary analysis (data in the Data Supplement; http://stroke.ahajournals.org).

Complications associated with lumbar drains are detailed in the Data Supplement. Two patients with a lumbar drain developed meningitis and 1 patient developed a lumbar drain exit site infection (no permanent morbidity). There was 1 case of continued low-pressure headaches several weeks after removal of the lumbar drain. This required a dural blood patch. There were no cases of neurological deterioration/rebleed of aneurysm secondary to lumbar drain insertion.

In those patients with lumbar drains, mean CSF drainage was 138 mL/24 hours (CI, 124–152 mL/24 hours; data missing in 16 patients). The mean duration of drainage was 5.0 days (CI, 4.5–5.6 days). Drain insertion occurred on Day 1 postictus in 31\%, Day 2 in 32\%, Day 3 in 26\%, and Day 4 in 11\% of patients. Drain insertion occurred before aneurysm
treatment in 31%, on the day of aneurysm treatment in 40% (approximately half immediately before treatment and half several hours after treatment), and after aneurysm treatment in 29% of patients. For the first 53 patients in the lumbar drain group, the opening pressure was recorded. Mean opening pressure (95% CIs) was 27.3 cm H2O (24.9–29.7 cm H2O). Approximately half the patients underwent insertion of a lumbar drain with an unprotected aneurysm.

There was a trend for a lower prevalence of DIND in the lumbar drain group in Fisher Grades 2, 3, and 4, although this was statistically significant in Fisher Grade 3 patients only ($P=0.013$; for data see online-only Data Supplement).

The relative risk of DIND for control versus study group was greater in those with drain insertion on Days 3 and 4 postictus (data in Data Supplement).

### Discussion

This study has demonstrated that the use of lumbar drainage of CSF after aSAH significantly reduces the prevalence of DIND and improves early clinical outcome. There is no significant difference noted in the clinical outcome at 6 months or in the need for permanent CSF shunting, although there is a nonsignificant decrease in radiologically confirmed infarct. The incidence of CSF infection in those with lumbar drains is <2% with no permanent morbidity associated with their use.

The hypothesis that lumbar drains confer benefit by reducing blood load has support from the current study. The trial protocol consisted of volume-driven CSF drainage with the aim of 5 to 10 mL CSF per hour until the CSF was visibly clear. This objective was achieved in most patients. Support-
Table 1. Baseline Characteristics for Patients in Both Arms of the Trial

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Group</th>
<th>Study Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort size</td>
<td>105</td>
<td>105</td>
</tr>
<tr>
<td>Mean age (95% CI), y</td>
<td>54.8 (52.3–57.2)</td>
<td>53.0 (50.6–55.4)</td>
</tr>
<tr>
<td>Sex, male:female</td>
<td>1:3.6</td>
<td>1:4</td>
</tr>
<tr>
<td>WFNS grade, percent of group</td>
<td>1:3.6</td>
<td>1:4</td>
</tr>
<tr>
<td>Modified Fisher grade, percent of group</td>
<td>1:3.6</td>
<td>1:4</td>
</tr>
</tbody>
</table>

Aneurysm type, no. of patients

Anterior circulation

- ICA: 6, 8
- OA: 1, 2
- PCOMA: 21, 16
- MCA: 17, 21
- ACA: 18, 8
- PA: 2, 5
- AComA: 26, 25

Posterior circulation

- VA: 0, 1
- BA: 3, 10
- SCA: 1, 1
- PICA: 6, 4
- PCA: 3, 3
- None: 1, 1

Multiple aneurysms/percent of group

- 18.1, 32.6

Aneurysm Treatment

- Coiling: 86, 78
- Clipping: 13, 16
- Both†: 4, 10
- None†: 2, 1

Procedural adverse events§

- Aneurysm rupture/coiling: 3, 3
- Ischaemia post procedure|: 9, 11
- Hydrocephalus requiring early external ventricular drainage: 15, 5

WFNS indicates World Federation of Neurological Surgeons; ICA, internal carotid artery; OA, ophthalmic; PCOMA, posterior communicating artery; MCA, middle cerebral artery; PA, pericallosal artery; AComA, anterior communicating artery; VA, vertebral artery; BA, basilar artery; SCA, superior cerebellar artery; PICA, posterior inferior cerebellar artery; PCA, posterior cerebral artery.

*Dense subarachnoid blood clot and intracerebral/intraventricular extension as previously described† see protocol.
†† If no treatment was offered due to patient deterioration or no aneurysm found on formal angiogram after initial diagnosis of an aneurysm on CT angiography.
§Adverse events noted during aneurysm treatment or immediately on recovery from general anaesthetic.

## Additional Text

...ing this hypothesis is the finding that lumbar drains conferred the most benefit to patients with Fisher Grade 3 aSAH. A contradiction to this hypothesis is the lack of additional benefit that was observed for drains placed very early (ie, within 48 hours of hemorrhage). The lack of significant difference in long-term outcome in the current study and the demonstrable safety of lumbar drainage in this setting would support a future study investigating longer periods of drainage with larger volumes of drainage to determine if this increases the beneficial effects of lumbar drainage.

An alternative hypothesis regarding the mechanism of benefit conferred by lumbar drainage is intracranial pressure (ICP) control. In the current study, opening lumbar cisternal pressure was invariably raised in all of the patients administered with lumbar drains (when tested) and drainage resulted in immediate improvements in the severity of headaches in most patients. Although drainage of CSF was volume-driven, ICP was likely to have been lowered by the volumes of CSF drained through the lumbar cistern. Previous studies have demonstrated elevated ICP (as measured in the ventricle) several days after aSAH regardless of the volume of blood load. Although associated with poor clinical grade, elevated ICP has been seen in 50% to 90% of patients with good clinical grade and is associated with a poor clinical outcome. Severe angiographic vasospasm has been shown to be more common with high ICP, although the association with DIND is weak. A previously reported comparison of simultaneous lumbar and ventricular pressure in this setting demonstrated that both pressure readings reflect each other closely. Drainage of 5 to 20 mL of CSF through a lumbar drain has been shown to approximately halve ICP in patients with aSAH and those with brain injury. Additional benefits observed included an improvement in regional cerebral blood flow and brain tissue oxygen. Number of patients requiring treatment of hydrocephalus with external ventricular drainage was higher in the control group than in the study group. Some patients with lumbar drainage may have had this clinical effect masked by the presence of a lumbar drain. This adds further support to the hypothesis that patients with a lumbar drain in the current study would have been likely to benefit from a reduction in ICP. It is plausible that this may have improved ischemic thresholds by improving oxygenation and cerebral blood flow and thus reduce the prevalence of DIND.

Because the current study cohort consisted of good WFNS grade patients with aSAH (Grades 1–3), the benefits of lumbar drainage have been demonstrated in this cohort only. Although results cannot be extrapolated outside of the study cohort, there is no reason to suggest that poor-grade patients with aSAH (Grades 4–5) would not benefit from lumbar drainage. Patients of poor grade are more likely to have higher blood loads and a higher ICP. They are, however, also more likely to have an intracerebral and extensive intraventricular hemorrhage, which raises the issue of safety. Patients of poor grade were not included in this study due to the potential safety issues of lumbar drainage in comatose patients (given the lack of available data in the literature) and the difficulty in diagnosing DIND accurately. Neurological deterioration that has been reported after lumbar drain insertion is more difficult to assess in this cohort of ventilated and...
comatose patients. Although rebleed of the ruptured aneurysm has been reported after insertion of an external ventricular drain or lumbar puncture/drain insertion, this risk has not been proven.20 This problem was not encountered in the current study despite the fact that approximately half the patients underwent insertion of a lumbar drain with an unprotected aneurysm. One patient reported continued low-pressure headaches requiring a blood patch. This is consistent with the reported incidence of this complication with lumbar drain use after transsphenoidal surgery (1.3%).21 Meningitis secondary to lumbar drainage has been shown to be <2% in the current study, which is half that previously described.22 No permanent morbidity was associated with infection. This would support the use of lumbar drainage in a larger clinical trial investigating all clinical grades of aSAH.

Although lumbar drainage has previously been shown to reduce the need for permanent CSF diversion (24% with lumbar drain versus 36% without lumbar drain), this reduction has not been consistently demonstrated.12 In the current study, there was no significant difference in the need for permanent CSF diversion between the 2 groups (with a slight trend toward fewer permanent CSF diversion procedures in the lumbar drain group). In contrast, cisternal CSF drainage and irrigation has been associated with a higher rate of permanent CSF diversion with the volume of drainage proportional to this rate.10,11,23 It is unclear why lumbar drainage did not increase the occurrence of long-term hydrocephalus. Acute and chronic hydrocephalus is thought to result from tentorial/ventricular obstruction and blockage of arachnoid granulations with blood, respectively.24,25 Either mechanism is likely to be resisted and minimized by the negative downward pressure drawing CSF into the lumbar cistern, an advantage of lumbar drainage over supratentorial CSF drainage.

Although patients in the study group demonstrated improved clinical outcome 10 days after ictus, this improvement was not maintained at 6 months (there was a trend for patients with lumbar drains to have improved 6-month outcome but this was only seen in the secondary analysis and was not statistically significant). It is well recognized that clinical trials powered to detect changes in DIND occurrence often report difficulties in detecting patient-centered “downstream” clinical outcome.26 The effect size of a treatment on DIND does not translate into the same effect size on the clinical outcome. In addition, the modified Rankin Scale score has been noted to lack specificity in detecting subtle yet meaningful changes in cognition and functioning. A demonstrable acceleration in recovery time after aSAH may have some bearing on inpatient stay and rehabilitation, length of disability status, time to return to work, and overall economic impact of aSAH. This is of course speculative.

Limitations of the study include a reliance on DIND as the primary end point, which can be a subjective end point.13 This subjectivity has been minimized by using a homogenous cohort of good WFNS grade patients with aSAH with very strict diagnostic criteria for DIND, objective investigations to exclude other causes of neurological deterioration, and multiple verification of the diagnosis of DIND. A second limitation to the study is the reliance on imaging performed as part of routine clinical care only; although there was a trend for fewer radiologically confirmed infarcts in the lumbar drain group, this is based on the incorrect assumption that those without clinical need for imaging will not have infarcts. This bias has been minimized with the inclusion of follow-up MRI in a number of patients, thus providing imaging data in approximately 90% of all patients and all patients exhibiting DIND with radiological data. A third limitation to this study is the difficulties associated with blinding treatment alloca-

Table 2. Primary Intention-to-Treat Analysis

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Control Group (n=105)</th>
<th>Study Group (n=105)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients with DIND (percent of group)</td>
<td>37 (35.2%)</td>
<td>22 (21.0%)</td>
<td>P=0.021</td>
</tr>
<tr>
<td>OR DIND for control versus study (95% CI)</td>
<td>1.7 (1.1–2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients diagnosed with a DIND and a persisting neurological deficit at discharge (percent of group)</td>
<td>13 (12.4%)</td>
<td>10 (9.5%)</td>
<td>P=0.51</td>
</tr>
<tr>
<td>Type of DIND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal</td>
<td>21</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Altered consciousness</td>
<td>9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>No. of patients with radiologically confirmed infarct/no. of patients imaged (missing data)</td>
<td>31/91 (missing 14)</td>
<td>23/94 (missing 11)</td>
<td>P=0.151</td>
</tr>
<tr>
<td>No. of patients with DIND and radiologically confirmed infarct/no. of patients with DIND imaged (missing data)</td>
<td>26/37 (missing 0)</td>
<td>14/22 (missing 0)</td>
<td>P=0.816</td>
</tr>
<tr>
<td>Percent patients with DIND and radiologically established infarct</td>
<td>70%</td>
<td>64%</td>
<td>P=0.816</td>
</tr>
<tr>
<td>No. of patients with mRS of 0–2 at Day 10 (percent of group)</td>
<td>39 (37.5%)</td>
<td>58 (55.2%)</td>
<td>P=0.009</td>
</tr>
<tr>
<td>No. of patients with mRS of 0–2 at 6 months (percent of group)</td>
<td>83 (81.4%)</td>
<td>81 (80.2%)</td>
<td>P=0.83</td>
</tr>
<tr>
<td>No. patients dead at 6 months (percent of group)</td>
<td>5 (4.8%)</td>
<td>4 (3.8%)</td>
<td>P=1.00</td>
</tr>
<tr>
<td>No. of patients requiring permanent cerebrospinal fluid shunting (percent of group)</td>
<td>8 (7.6%)</td>
<td>6 (5.7%)</td>
<td>P=0.58</td>
</tr>
</tbody>
</table>

DIND indicates delayed ischemic neurological deficit; mRS, modified Rankin Scale.
tion and obtaining unbiased outcome measures. Being a single-center trial has the advantage that only few clinicians were involved during the study period and so quality and consistency of diagnoses and treatment should be high. The disadvantage is the small size of the trial not powered to detect changes in clinical outcome and the lack of information regarding reproducibility in other neurosurgical centers, particularly those in other countries where management of patients is likely to be markedly different.

Conclusions

Lumbar drainage of CSF after aSAH has been successfully administered and shown to reduce the prevalence of DIND and improve early clinical outcome in this cohort of patients with WFNS Grade 1 to 3 aSAH without space-occupying hematomas and significant intraventricular blood. A larger trial investigating all grades of patients with aSAH and powered to detect changes in radiological infarct and long-term clinical outcome is warranted.

Acknowledgments

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Disclosure

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References

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Supplemental Material
Lumbar drainage of cerebrospinal fluid following aneurysmal subarachnoid haemorrhage: A prospective, randomised and controlled trial (LUMAS)

Data Supplement
Method

Randomisation

Randomisation to treatment group was performed by randomly permuted blocks of 20 with an allocation ratio of 1:1 using an online package (http://www.randomization.com). Instructions on the next intervention were sealed in an envelope and numbered at the start of the study. The research team were blinded to any information about block size and the envelopes were prepared independently from the research team involved in recruiting patients and managing the trial. The research team opened the envelopes sequentially at the time of randomisation only.

Blinding

Although treatment allocation could not be blinded, clinicians/investigators were masked to outcomes when possible. MRS at six months were obtained by the investigators (YA/DB) blinded to the treatment allocation via a structured telephone interview directly with the patient (or their primary carer if the patient was unable to communicate on the phone) as previously described. Blinding of treatment allocation was not always possible for MRS obtained at ten days post haemorrhage. All diagnoses of DIND were made by a multidisciplinary neurovascular team (neurosurgeons, neurointensive care anaesthetists and neuroradiologists) and were prospectively and retrospectively verified (from prospectively collected clinical parameters and electronically recorded blood results/picture archiving and communication system) by the investigators blinded to the treatment allocation. With the exception of a few additional clinicians, the multidisciplinary team had remained largely unchanged over the four-year study period. No disagreements occurred between prospective and retrospective assessments due to the relative ease of assessing the neurology of good grade patients, the absolute diagnostic criteria for DIND and the objective investigations required to exclude other causes of neurological deterioration. Neuroradiologists blinded to the treatment allocation reported radiologically confirmed infarcts as part of routine clinical care.

Results

Table 1 demonstrates the results of the secondary analysis that reflect those findings in the primary analysis.

Table 2 illustrates all the complications associated with the use of lumbar drains.

Table 3 shows the prevalence of DIND in the control and study groups stratified by Fisher grade. There was a trend for a lower prevalence of DIND in Fisher grades 2, 3 and 4 although this was statistically significant in Fisher 3 patients only. Table 4 shows the prevalence of DIND in the study group stratified by the day of drain insertion relative to the haemorrhagic ictus. The relative risk of DIND for control versus study group was greater in those with drain insertion on days 3 and 4 post ictus. Approximately 94% of all patients had presented to the neurosurgery department within 48 hours of ictus.

References

### Table 1—Secondary analysis with exclusions

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Control Group (n=89)</th>
<th>Study Group (n=87)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with DIND (% of group)</td>
<td>32 (36.0%)</td>
<td>14 (16.1%)</td>
<td>p=0.003</td>
</tr>
<tr>
<td>Relative risk of DIND for control versus study (95% confidence interval)</td>
<td>2.2 (1.3-3.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients diagnosed with a DIND and a persisting neurological deficit at discharge (% of group)</td>
<td>10 (12.2%)</td>
<td>7 (8.0%)</td>
<td>p=0.47</td>
</tr>
<tr>
<td>Type of DIND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal</td>
<td>20</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Altered consciousness</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Number of patients with radiologically confirmed infarct/number of patients imaged (missing data)</td>
<td>26/77 (missing 12)</td>
<td>16/77 (missing 10)</td>
<td>p=0.07</td>
</tr>
<tr>
<td>Number of patients with DIND and radiologically confirmed infarct/number of patients with DIND imaged (missing data)</td>
<td>22/32 (missing 0)</td>
<td>8/14 (missing 0)</td>
<td>p=0.447</td>
</tr>
<tr>
<td>% Patients with DIND and radiologically established infarct</td>
<td>69 %</td>
<td>57 %</td>
<td>p=0.447</td>
</tr>
<tr>
<td>Number of patients with MRS of 0-2 at day ten (% of group)</td>
<td>38 (42.7%)</td>
<td>52 (59.8%)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Number of patients with MRS of 0-2 at six months (% of group)</td>
<td>71 (82.6%)</td>
<td>72 (86.7%)</td>
<td>p=0.45</td>
</tr>
<tr>
<td>Number of patients dead at six months (% of group)</td>
<td>3 (3.4%)</td>
<td>3 (3.3%)</td>
<td>p=1.00</td>
</tr>
<tr>
<td>Number of patients requiring permanent CSF shunting (% of group)</td>
<td>3 (3.4%)</td>
<td>3 (3.4%)</td>
<td>p=0.98</td>
</tr>
<tr>
<td>Description of complication</td>
<td>No of patients involved</td>
<td>Consequence of complication</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>CSF infection/meningitis</td>
<td>2</td>
<td>Required intravenous antibiotics as per microbiology protocol. No permanent morbidity. Delay in discharge.</td>
<td></td>
</tr>
<tr>
<td>Local lumbar drain exit site infection</td>
<td>1</td>
<td>Required intravenous antibiotics as per protocol. No permanent morbidity. Delay in discharge.</td>
<td></td>
</tr>
<tr>
<td>Organism grown on CSF/lumbar drain tip culture</td>
<td>13</td>
<td>No clinical relevance and no treatment required. Likely to be contaminant from the skin.</td>
<td></td>
</tr>
<tr>
<td>Inability to place drain/non functioning drain in-situ</td>
<td>9</td>
<td>CSF drainage not possible. Excluded from the secondary analysis.</td>
<td></td>
</tr>
<tr>
<td>Concern about post-operative haematoma resulting in cessation of lumbar CSF drainage</td>
<td>3</td>
<td>No drainage during theatre or in the immediate post-operative period but due to the presence of a post-operative haematoma requiring evacuation (in two cases), subsequent CSF drainage was stopped. Excluded from the secondary analysis.</td>
<td></td>
</tr>
<tr>
<td>Symptomatic non-communicating hydrocephalus despite the presence of a functioning lumbar drain</td>
<td>1</td>
<td>Required external ventricular drainage</td>
<td></td>
</tr>
<tr>
<td>Continued low pressure headaches following removal of the lumbar drain</td>
<td>1</td>
<td>Required a lumbar blood patch several weeks after removal of the lumbar drain. Symptoms improved.</td>
<td></td>
</tr>
<tr>
<td>Neurological deterioration/re-bleed of aneurysm secondary to lumbar drain insertion</td>
<td>0</td>
<td>This problem was not encountered.</td>
<td></td>
</tr>
</tbody>
</table>
Table 3-Prevalence of DIND stratified by Fisher grade

<table>
<thead>
<tr>
<th>Fisher Grade</th>
<th>Control Group: Number of patients with DIND/Total number in subset (% of subset)</th>
<th>Study Group: Number of patients with DIND/Total number in subset (% of subset)</th>
<th>Significance</th>
<th>Relative Risk of DIND for control versus study (95% confidence intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>8/46 (17.3)</td>
<td>3/39 (7.7)</td>
<td>p=0.21</td>
<td>2.53 (0.62-10.3)</td>
</tr>
<tr>
<td>3</td>
<td>22/44 (50)</td>
<td>9/41 (22.0)</td>
<td>p=0.013</td>
<td>3.56 (1.38-9.16)</td>
</tr>
<tr>
<td>4</td>
<td>6/13 (46.2)</td>
<td>3/11 (27.3)</td>
<td>p=0.42</td>
<td>2.29 (0.41-12.7)</td>
</tr>
<tr>
<td>3+4</td>
<td>1/2 (50)</td>
<td>7/14 (50)</td>
<td>p=1.00</td>
<td>0.50 (0.036-6.86)</td>
</tr>
</tbody>
</table>

Table 4-Prevalence of DIND in the study group stratified by day of lumbar drain insertion following ictus

<table>
<thead>
<tr>
<th>Day of insertion post ictus</th>
<th>Number of patients in each sub-group</th>
<th>Prevalence of DIND (% of sub-group)</th>
<th>Relative Risk of DIND for control versus study (95% confidence intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>26.7</td>
<td>1.5 (0.9-2.6)</td>
</tr>
<tr>
<td>2</td>
<td>31</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>15.4</td>
<td>2.2 (1.0-4.7)</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>18.2</td>
<td></td>
</tr>
</tbody>
</table>