NIH StrokeNet

PREVENTION | TREATMENT | RECOVERY

Funded by a Grant from the National Institutes of Health

Clinical Study Concept Synopsis

Is On-Demand Cerebral Spinal Fluid Drainage Associated with Lower Complications in Aneurysmal Subarachnoid Hemorrhage

" SPLASH "

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Primary Aim:

To determine how EVD management strategies impact hospital associated outcomes including complications, ventriculoperitoneal shunt placement, and length of stay.

Primary hypothesis:

In patients with aSAH, the proportion with any complication* during ICU stay is higher for the continuous group compared to the on-demand group.

***complications include:**

- ❑ Non-Patent EVD
- ❑ Ventriculitis
- ❑ CSF Leak
- ❑ EVD tract hemorrhage

To determine how EVD management strategies impact patient associated outcomes including complication rates, ventriculoperitoneal shunt placement rates, and ICU length of stay.

Hypothesis 2: When compared to continuous drainage, on-demand CSF drainage is associated with less V-P shunt requirement.

Hypothesis 3: When compared to continuous drainage, on-demand CSF drainage is associated with shorter length of stay in the ICU.

Exploratory Hypothesis: When compared to continuous drainage, on-demand CSF drainage is associated with shorter hospital length of stay.

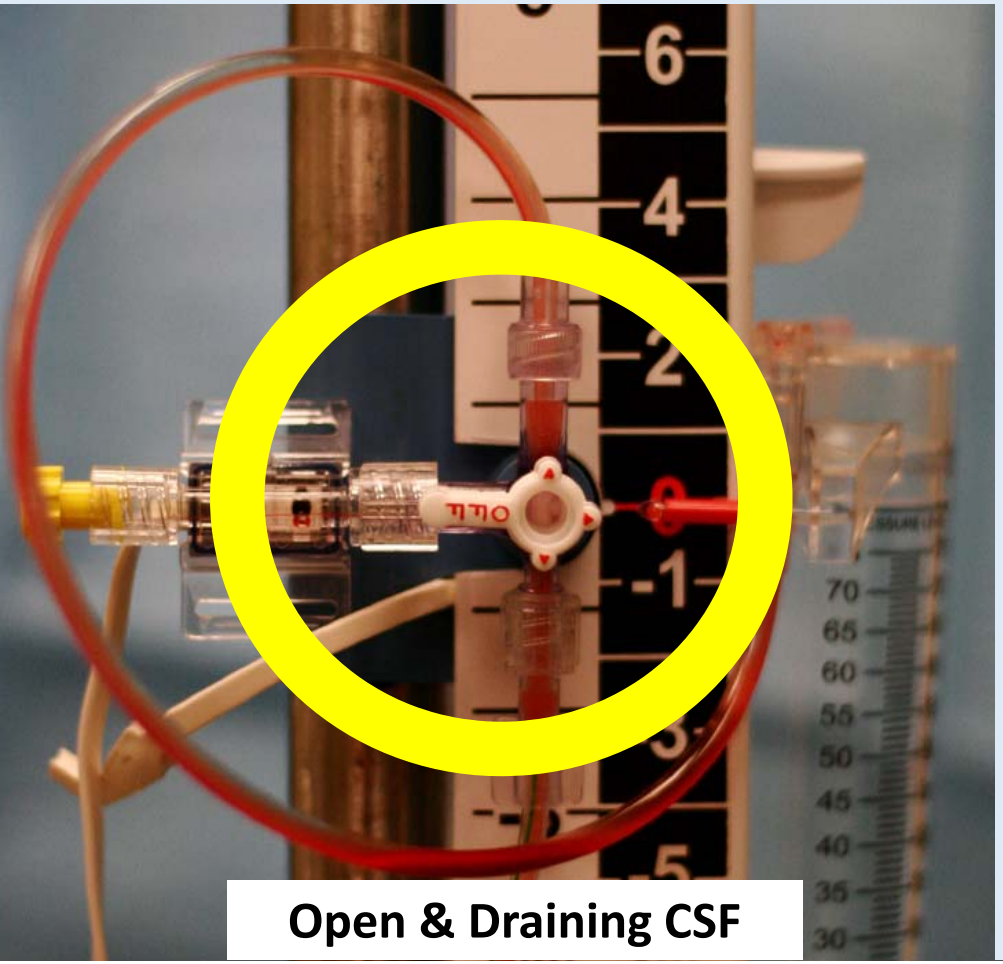
Secondary Aim(s):

To explore the impact of on-demand vs continuous CSF drainage on short and long term functional outcomes.

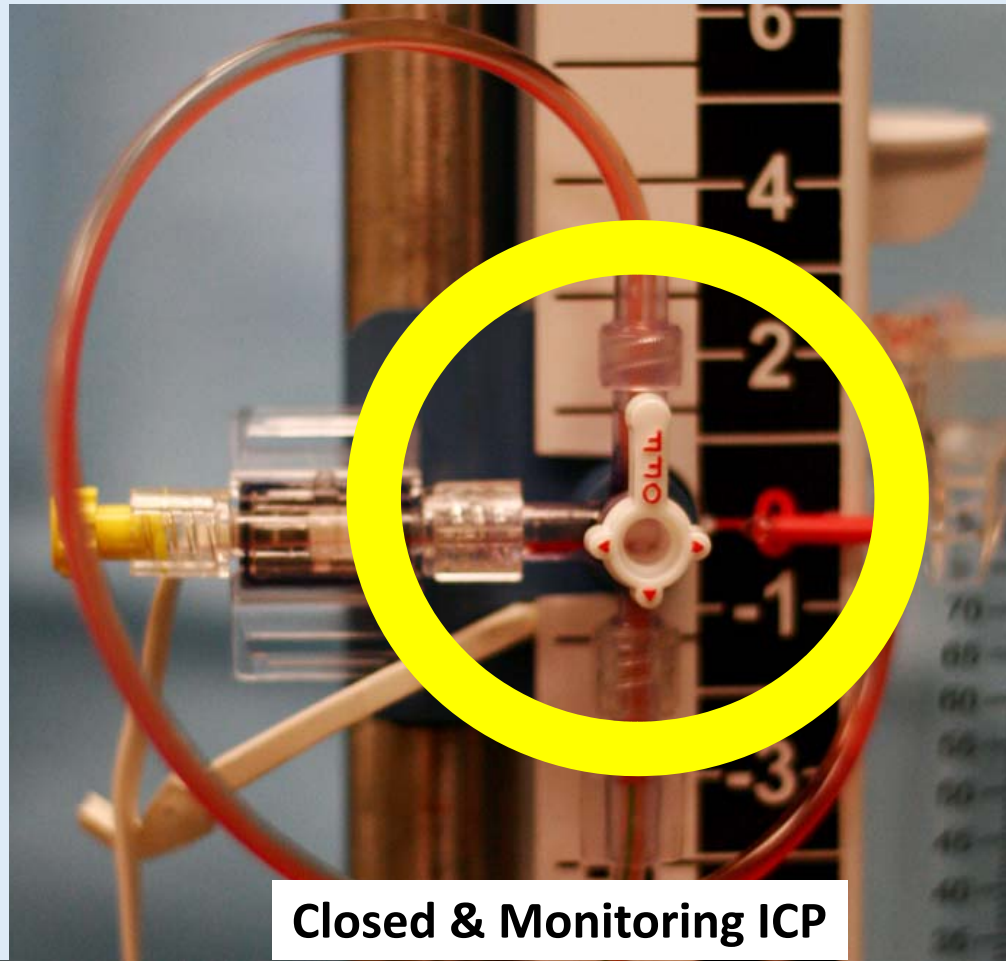
- Hypothesis : Compared to continuous drainage, on-demand drainage is associated with lower mRS scores at discharge day 14 (whichever is first), & 90 days post randomization.

- Hypothesis : Compared to continuous drainage, on-demand drainage is associated with lower GOSE scores at discharge day 14 (whichever is first), & 90 days post randomization.

The Problem



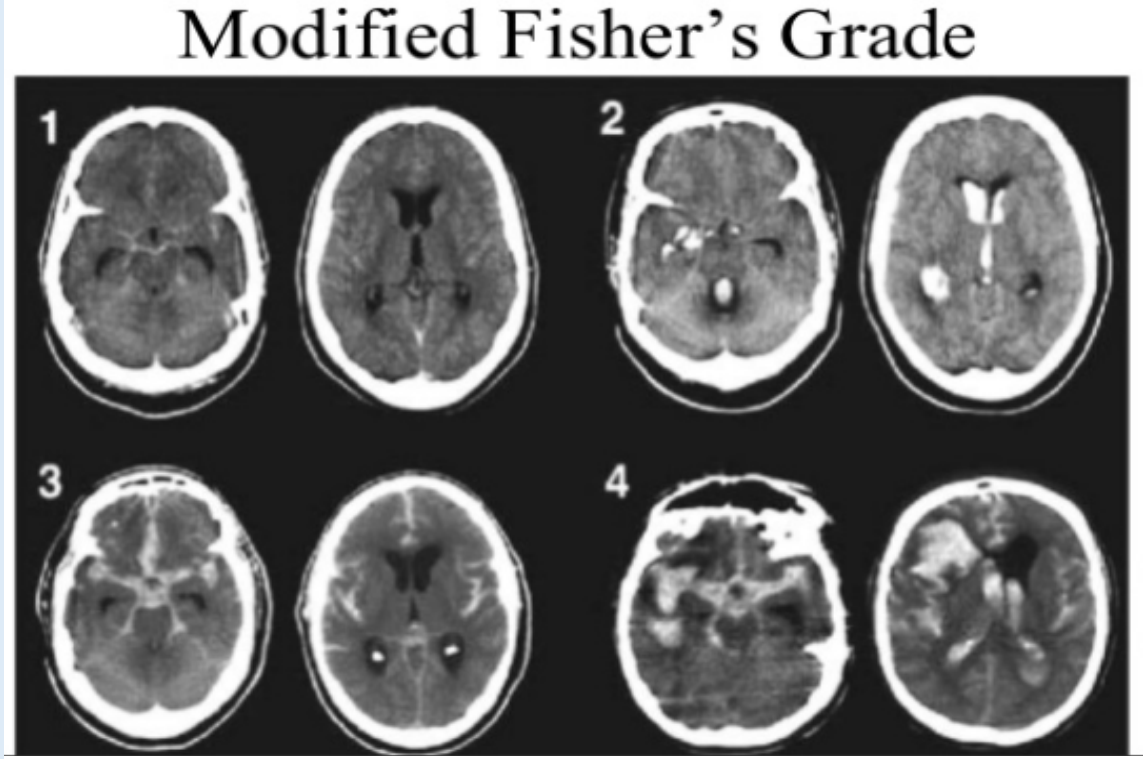
Open & Draining CSF



Closed & Monitoring ICP

Background & Significance

Approximately 25,000 EVDs / year in the USA



Aneurysmal SAH results in blood within the tissues and often in the ventricular system. This may be the catalyst for elevated cerebral artery vasospasm, hydrocephalus, or increased ICP.

It has become common practice to place an EVD to: 1) facilitate removal of blood from the ventricles, 2) monitor ICP, and 3) provide external shunting of CSF in the setting of hydrocephalus.

Background & Significance

- 2004 Klopfenstein et al “no advantage to gradual EVD weaning”
- 2009 Hickey et al “ICP waveform varies by respiratory cycle”
- 2010 Olson et al “nursing care impacts ICP”
- 2010 Gigante et al “there are no definitive guidelines”
- 2011 Amato et al “Continuous CSF drainage might be a bad idea”
- 2011 Kim et al “Continuous vs on-demand does not impact vasospasm rates”
- 2013 Olson et al “there is large variance in EVD management practice”
- 2013 Olson et al “nursing care impacts ICP”
- 2013 Nwachuku et al “5.66 mmHg difference in TBI patients favoring continuous drainage”
- 2013 Olson et al “continuous EVD drainage is associated with increased complications in SAH”
- 2014 Olson et al “there is no agreement on what to do with the EVD stopcock”
- 2015 Olson et al “The EMR cannot be used for ICP research”
- 2016 Mahdavi et al “EVD and Bolt are not equivalent in ICP measures”
- 2017 Olson et al “nursing care impacts ICP”
- 2017 Chung et al “EVD management in SAH is not standardized but leans towards continuous”
- 2017 Rogers et al “ICP values vary significantly & unpredictably after EVD is closed”

Observational study (2011)

	On-Demand (N = 13)	Continuous (N = 24)	P-value
Max ICP	43.92 (19.87)	49.88 (25.32)	0.4687
CSF Volume	1796 (1501)	1975 (1324)	0.7146
EVD Days	13.38 (5.98)	15.0 (5.43)	0.4099
CSF/day	134.99 (109.48)	128.90 (67.29)	0.8348
# of EVDs	1.31 (.48)	1.38 (.65)	0.7445
LOS (days)	18.92 (10.57)	21.33 (9.07)	0.4715
mRS	3.62 (2.02)	3.75 (1.57)	0.8232
			OR (95% C.I.)
Vasospasm	54 %	66.67 %	.58 (.14-2.32)
Shunt Required	8 %	29.17 %	.20 (.02-1.87)
Complications	23 %	**58.33 %**	**.21** (.05-.98)

Amato A, Britz GW, James ML, Graffagnino C, Zomorodi AR, Zomorodi ME, Olson DM. An observational pilot study of CSF diversion in subarachnoid haemorrhage. Nursing in critical care. 2011;16(5):252-60.

Single-Center RCT continuous vs on-demand (2013)

Variable	Continuous (N=34)	On-Demand (N=26)	Odds Ratio	95% CI	p-value
Vasospasm*					
Any Method	22 (64.7%)	21 (80.8%)	0.44	0.13 – 1.45	0.1768
By TCD	21 (61.7%)	18 (69.2%)	0.72	0.24 – 2.12	0.5486
By Angiogram	7 (20.6%)	9 (34.6%)	0.49	0.15 – 1.56	0.2274
By CTA	13 (38.2%)	10 (38.5%)	0.99	0.347 – 2.831	0.9857
Complication*					
Complications	18 (52.9%)	6 (23.1%)	3.75	1.21 – 11.66	**0.0223**
Non-Patent EVD	15 (44.1%)	3 (11.5%)	4.35	1.18 – 16.10	**0.0276**
Ventriculitis	6 (17.6%)	1 (3.8%)	5.36	0.60 – 47.57	0.1322
Self Device Removal	2 (8.8%)	2 (7.7%)	1.16	0.18 – 7.51	0.8753
CSF leak/hemorrhage	5 (14.7%)	1 (3.8%)	4.31	0.47 – 39.39	0.1956
Shunt Placement	3 (8.8%)	19.2%	0.41	0.09	0.2503
Discharge mRS<2	7 (20.6%)	5 (19.2%)	1.09	0.30 3.92	0.8968
Discharge mRS <3	11 (32.3%)	9 (34.6%)	0.90	0.30 – 2.66	0.8539
Discharge mRS>4	15 (44.1%)	8 (30.8%)	1.78	0.61 – 5.20	0.2941
Died mRS = 6	8 (23.5%)	3 (11.5%)	2.36	0.56 – 9.96	0.2430

Olson DM, Zomorodi M, Britz GW, Zomorodi AR, Amato A, Graffagnino C. Continuous cerebral spinal fluid drainage associated with complications in patients admitted with subarachnoid hemorrhage. Journal of neurosurgery. 2013;119(4):974-80.

Approach

StrokeNet: multicenter prospective RCT

182 subjects

1:1 randomization

on-demand vs **continuous** CSF drainage.

The primary outcome is the proportion of subjects with any complication within ICU stay.

Complications considered for the primary outcome are: non-patent EVD, ventriculitis, CSF leak, and EVD tract hemorrhage

Approach

StrokeNet: multicenter prospective RCT

182 subjects

1:1 randomization

on-demand vs **continuous** CSF drainage.

Block Randomization by FISHER Score

Fisher II, II vs Fisher IV

The primary outcome is the proportion of subjects with any complication within ICU stay.

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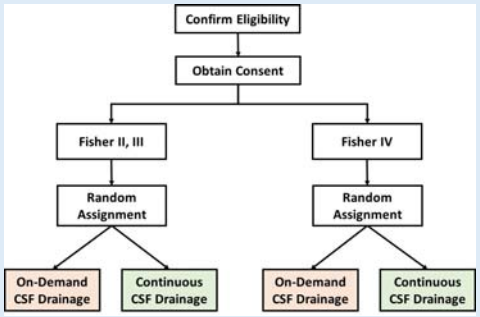

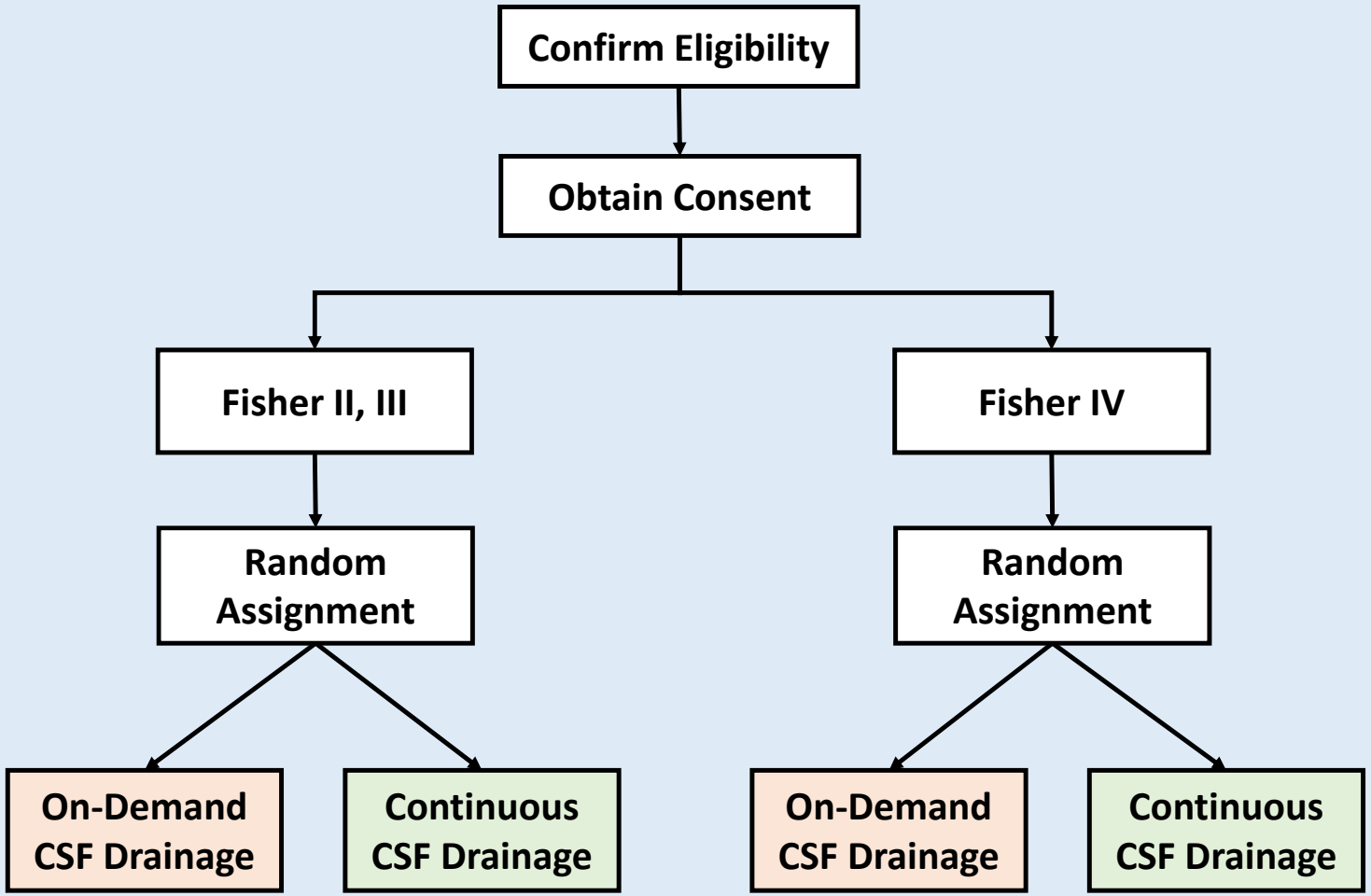
Confirm Eligibility
Obtain Consent
Fisher II, III
Fisher IV
Random Assignment
Random Assignment
On-Demand CSF Drainage
Continuous CSF Drainage
On-Demand CSF Drainage
Continuous CSF Drainage

EVD closed
unless and until ICP is elevated

If ICP is > 20 mm Hg for 5 minutes, the EVD stopcock will be opened at 15 cm above the tragus to allow CSF drainage for 1 minute.

On –Demand CSF drainage

Continuous CSF drainage
EVD left open to drain 10 cm above the tragus.

Once each hour, the stopcock will be closed for 5 minutes and ICP documented.

Inclusion & Exclusion Criteria

Inclusion

- Primary diagnosis of aSAH
- Admitted to ICU
- Adult (≥ 18 years of age)
- EVD catheter inserted

Exclusion

- Traumatic SAH
- SAH onset > 72 hours prior to admission
- EVD inserted > 72 hours prior to enrollment
- V-P shunt prior to enrollment

Data Analysis Plan

Statisticians: Renee' Martin, PhD and Jordan Elm, PhD

The primary analysis will be conducted on the intent-to-treat (ITT) analysis population. We will compare proportion with any complication by treatment group via an logistic regression adjusted for relevant, prespecified baseline covariates.

Primary Outcome is number of subjects experiencing any complication (Non-Patent EVD, Ventriculitis, CSF Leak, or EVD tract hemorrhage) within ICU stay

Secondary outcomes will be examined by group assignment based on intent-to-treat. V-P shunt rate, 90-day mRS & GOSE (control for baseline severity), volume of CSF drained, EVD dwell time (days), complications associated with ICP monitoring

SPLASH

collaborators

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Thank you