



Soluble ST2 Predicts Delayed Cerebral Ischemia & Outcome after Subarachnoid Hemorrhage

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Disclosures

- National Institutes of Health
- American Heart Association
- Andrew David Heitman
Neurovascular Research Foundation

Introduction

Aneurysmal Subarachnoid Hemorrhage

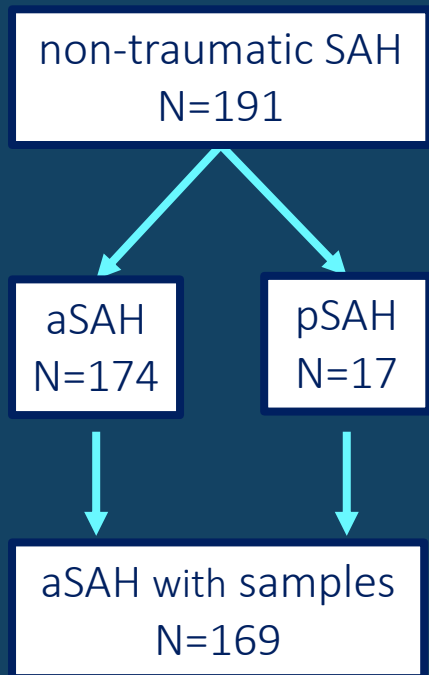
- Approximate incidence is 1 per 10,000
- Mortality rate is approximately 30%
- Poor functional outcome in 10-20% of patients
- Several factors contribute:
 - Age
 - Initial aSAH severity
 - Delayed cerebral ischemia (DCI)

Background

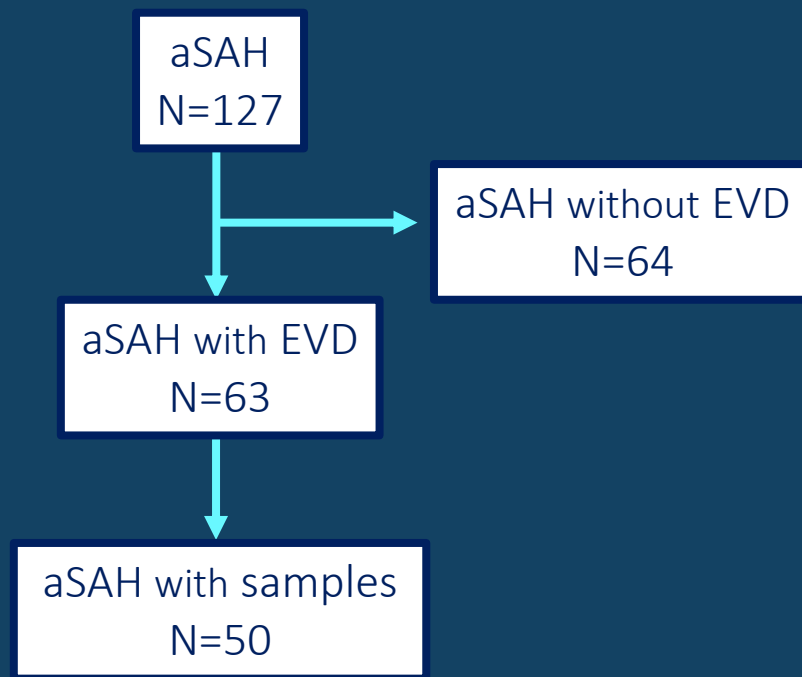
- Neuroinflammatory responses have been implicated in the sequelae of aSAH
- sST2 is a decoy receptor that promotes immune activation of Th1 pro-inflammatory cells
- We have previously shown sST2 is linked to outcome after ischemic stroke
- We hypothesized that sST2 is a marker for neuroinflammation induced secondary injury in aSAH

SAH Cohort Design

MGH cohort 2013-2016



Copenhagen cohort 2014-2015

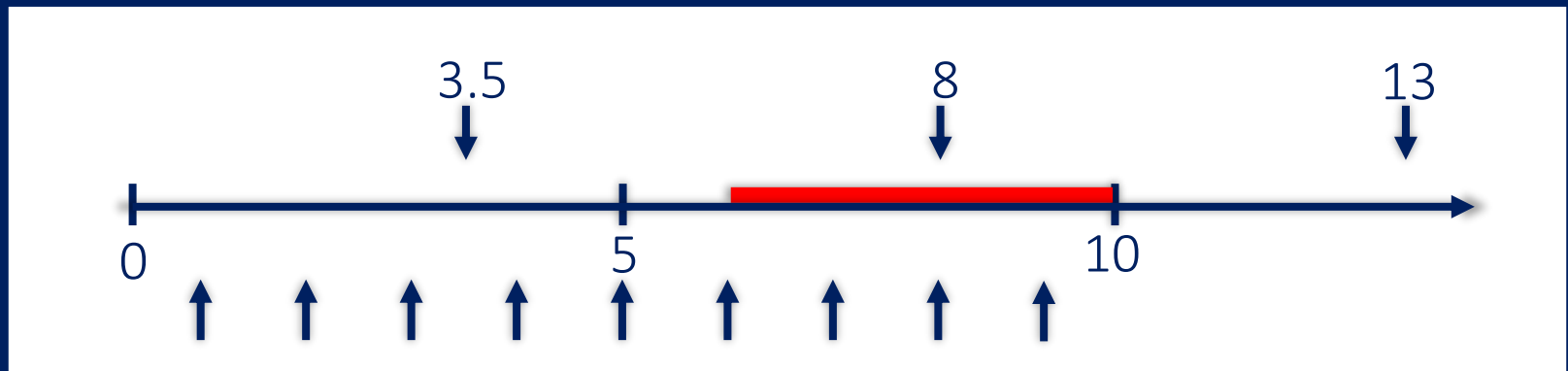


SAH Cohort Design

MGH cohort

*

2014-2015



Copenhagen cohort

*

2014-2015

Cohort characteristics

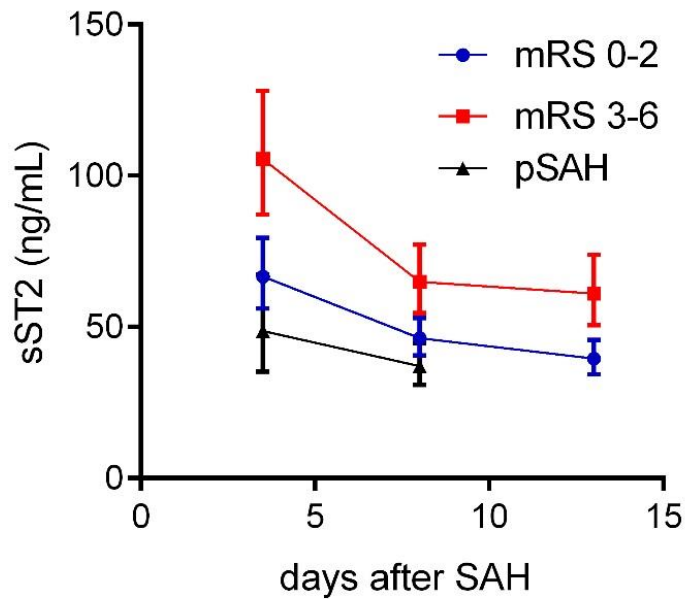
* Boston *

	MGH aSAH cohort N=169	MGH pSAH cohort N=17
Age (yrs.)	57 ± 12	58 ± 8
Sex (F)	108 (64%)	7 (41%)
HH grade	2 [1, 4]	1 [1, 2]
modified Fisher score	3 [3, 4]	3 [2, 3]
Clipping	73 (43%)	0 (0%)
mRS, 90 day	2 [1, 4]	1 [0, 1]
DCI	61 (47%)	0 (0%)
Age (yrs.)	57 ± 12	58 ± 8

sST2 over time

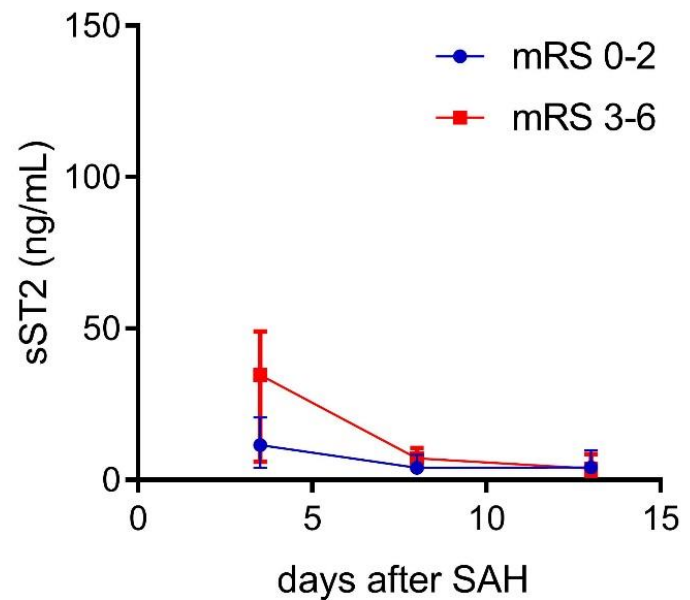
Plasma

Plasma sST2 time course



CSF

CSF sST2 time course



sST2 predicts poor outcome (mRS 3-6) independent of clinical risk factors

	OR	Confidence Interval		<i>P</i> value
		Lower 95%	Upper 95%	
sST2*	3.02	1.58	5.76	0.001
+ Age, Sex, HH	2.50	1.22	5.11	0.012
+ Age, Sex, HH, mF	2.43	1.17	5.06	0.017
+ Age, Sex, HH, mF, Clip	2.58	1.20	5.56	0.015
+ Age, Sex, HH, mF, Clip, CHF	2.56	1.19	5.52	0.017
+ Age, Sex, HH, mF, Clip, CHF, Afib	2.54	1.17	5.49	0.018

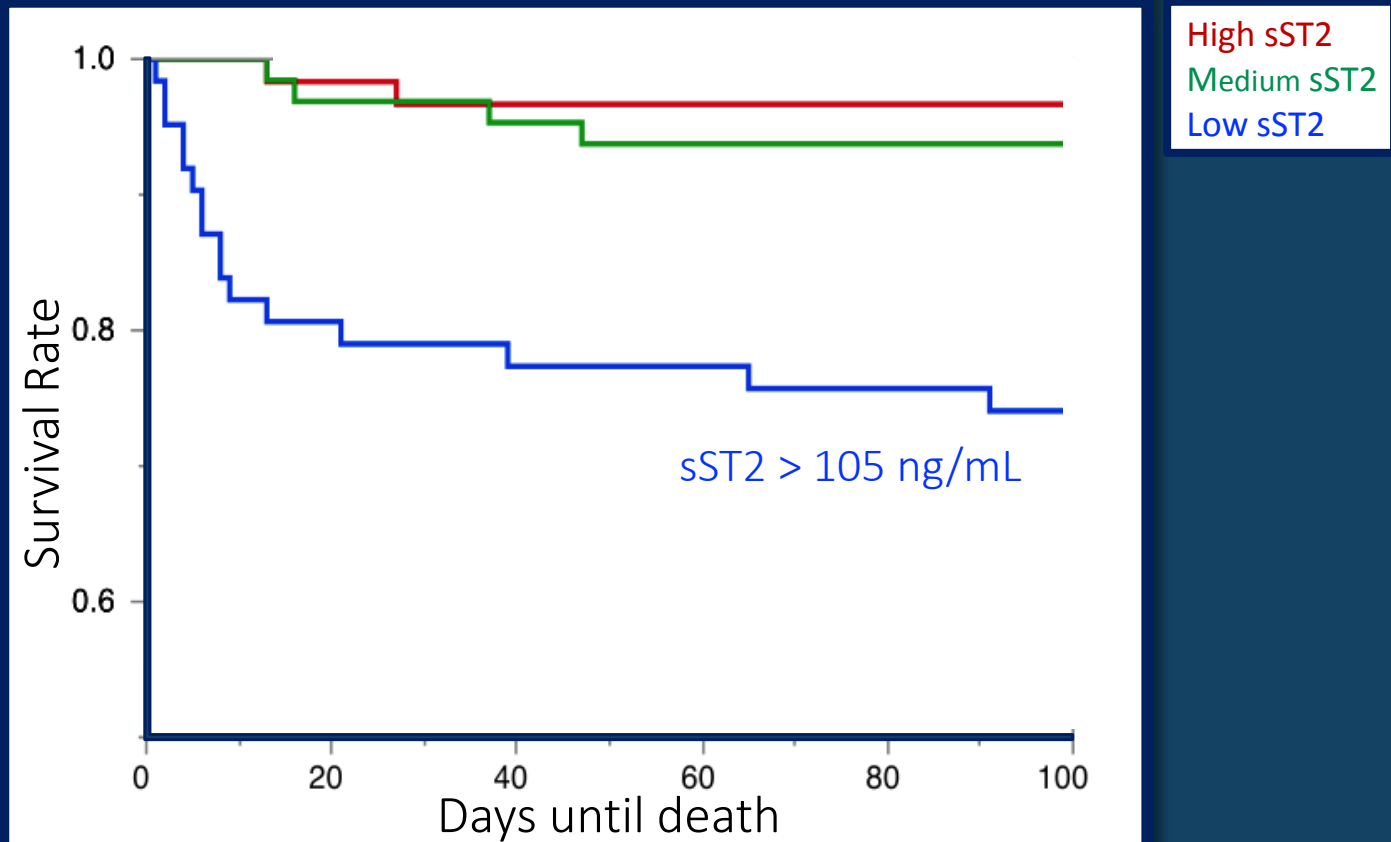
* sST2 measured at day 3.5

sST2 predicts mortality independent of clinical risk factors

	OR	Confidence Interval		<i>P</i> value
		Lower 95%	Upper 95%	
sST2*	4.62	1.92	11.10	0.001
+ Age, Sex, HH	4.43	1.56	12.56	0.005
+ Age, Sex, HH, mF	4.38	1.49	12.86	0.007
+ Age, Sex, HH, mF, Clip	4.13	1.38	12.40	0.011
+ Age, Sex, HH, mF, Clip, CHF	3.90	1.30	11.73	0.015
+ Age, Sex, HH, mF, Clip, CHF, Afib	3.79	1.24	11.64	0.020

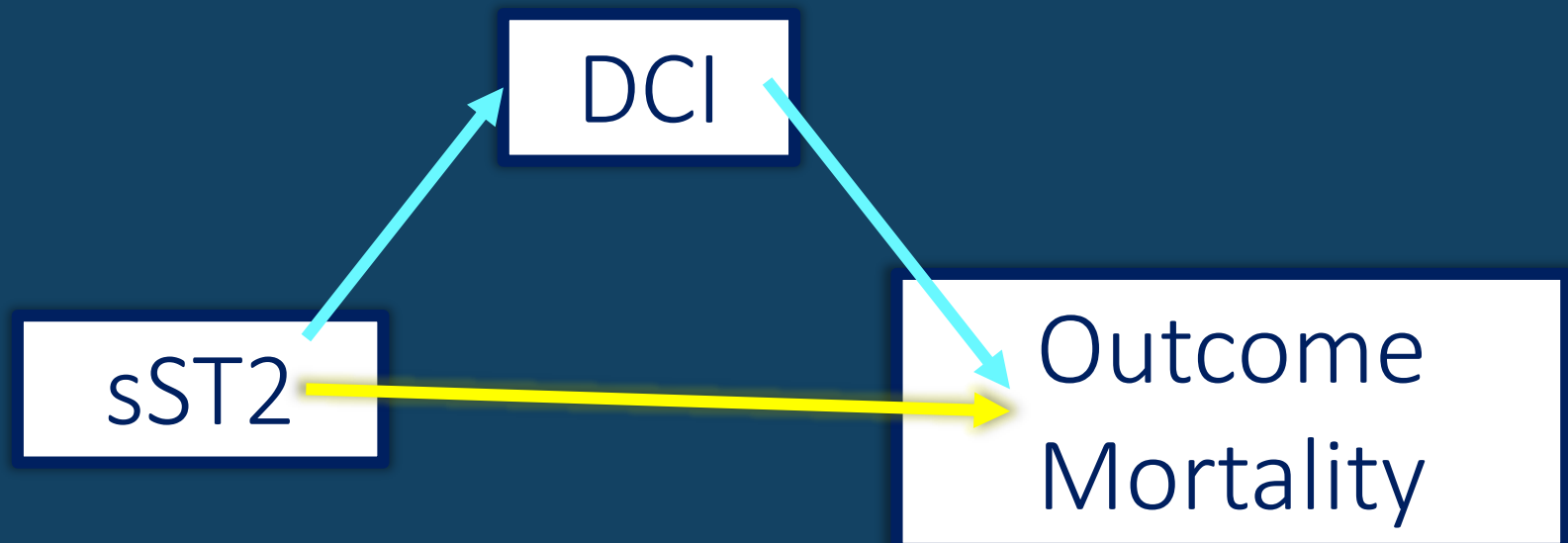
* sST2 measured at day 3.5

sST2 and Mortality



Log-Rank: $P < 0.0001$

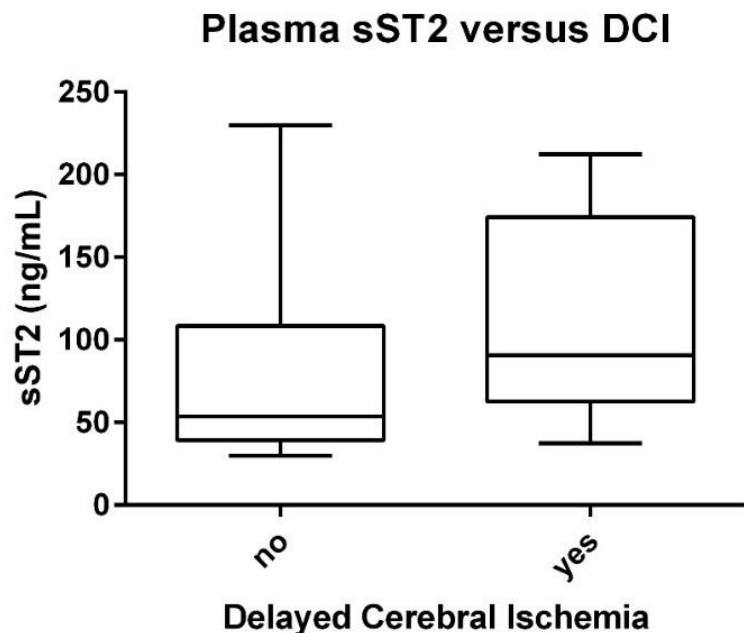
SAH and secondary injury



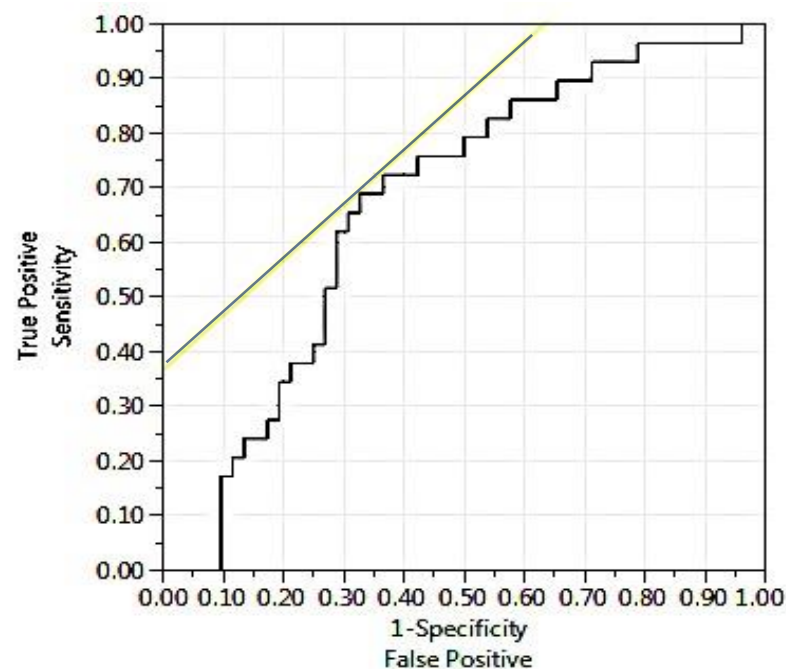
DCI definition

Delayed cerebral ischemia: Focal neurological impairment, or a decrease of at least 2 points on the GCS not apparent immediately after aneurysm occlusion, and cannot be attributed to other causes.

sST2 predicts future DCI



P=0.0026



ROC threshold: sST2 >77 ng/mL

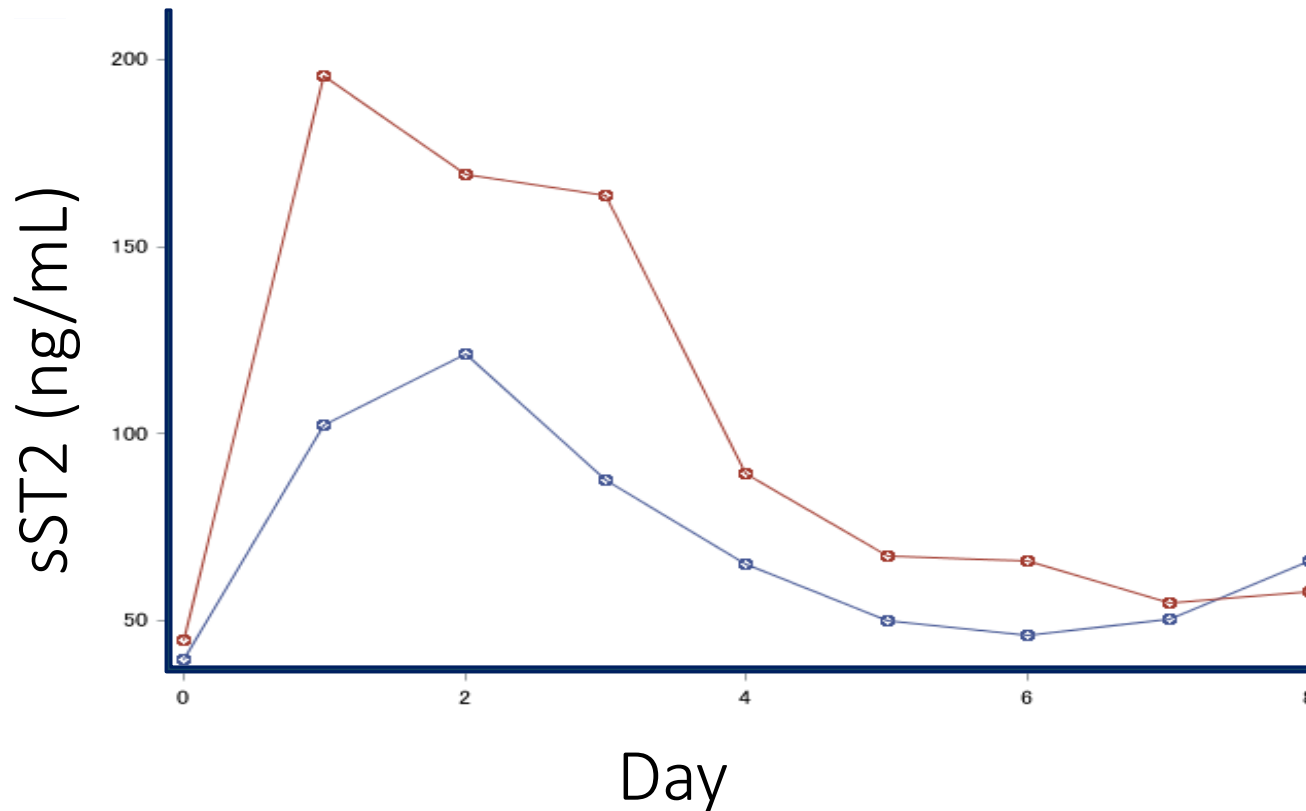
* sST2 measured at day 3.5

Copenhagen replication cohort

	Copenhagen aSAH cohort N=50	MGH aSAH cohort N=169	MGH pSAH cohort N=17
Age (yrs)	61 ± 11	57 ± 12	58 ± 8
Sex (F)	45 (90%)	108 (64%)	7 (41%)
WFNS grade	3 [1, 4]	2 [1, 4]	1 [1, 2]
modified Fisher score	3 [3, 3]	3 [3, 4]	3 [2, 3]
Clipping	14 (28%)	73 (43%)	0 (0%)
mRS, 90 day	1 [0, 3]	2 [1, 4]	1 [0, 1]
DCI	25 (50%)	61 (47%)	0 (0%)

sST2 replication cohort

sST2 predicts poor outcome (mRS 3-6)

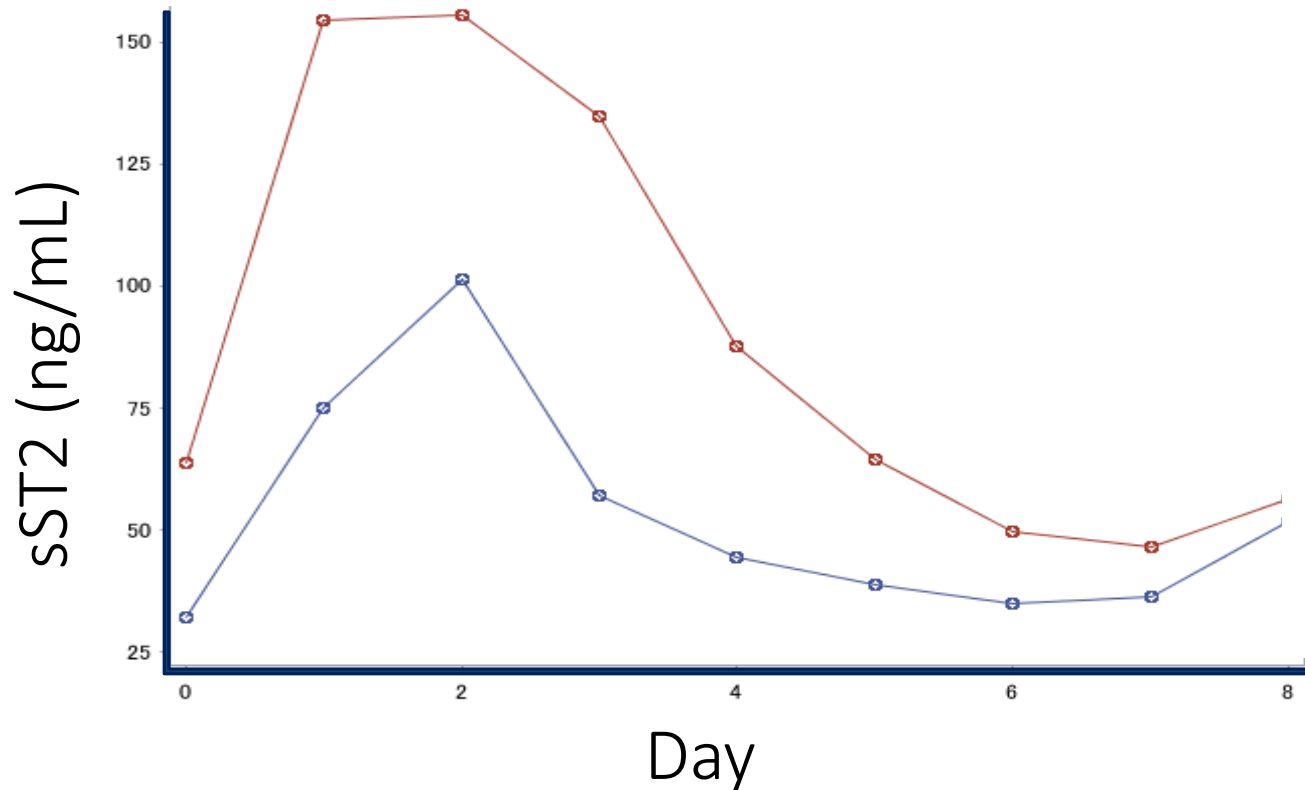


Good outcome
Poor outcome

$P=0.025$

sST2 replication cohort

sST2 predicts DCI



$P=0.0045$

Summary

- sST2 demonstrates an early rise in plasma and CSF that peaks at ~day 1-3
- Higher sST2 level predicts poor outcome and mortality
- Higher sST2 level predicts DCI
- sST2 is also linked to outcome after ischemic stroke and intracerebral hemorrhage*
- We hypothesize that sST2 is a marker for neuroinflammation induced secondary brain injury

*Poster #: WMP101; Wednesday 5:30-6:30 pm

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