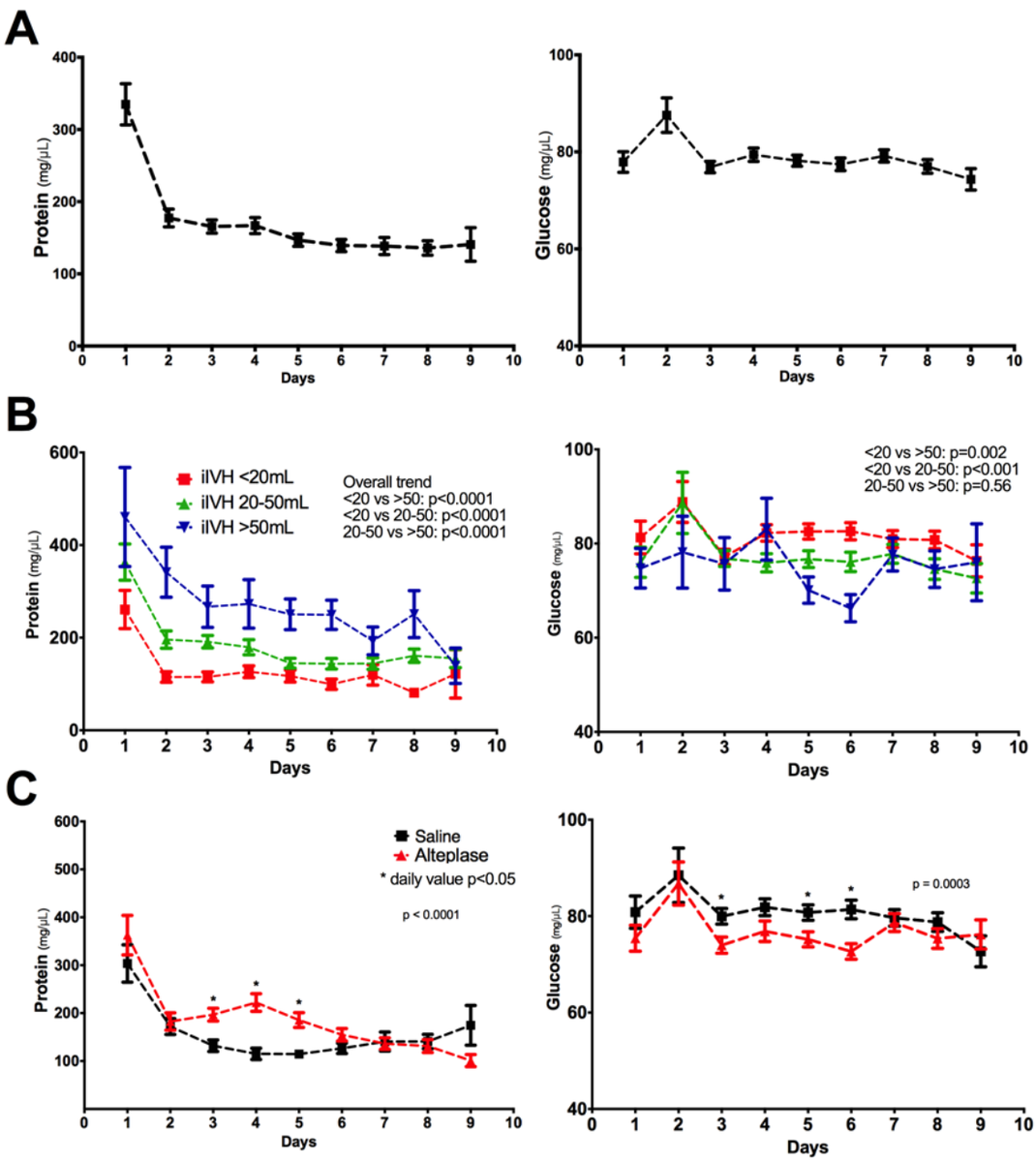
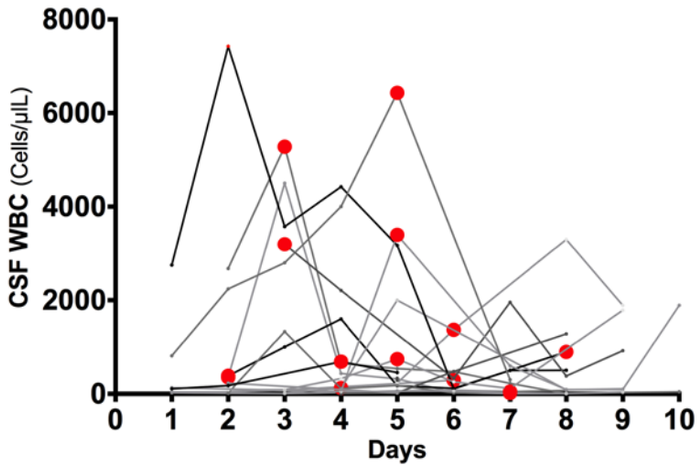
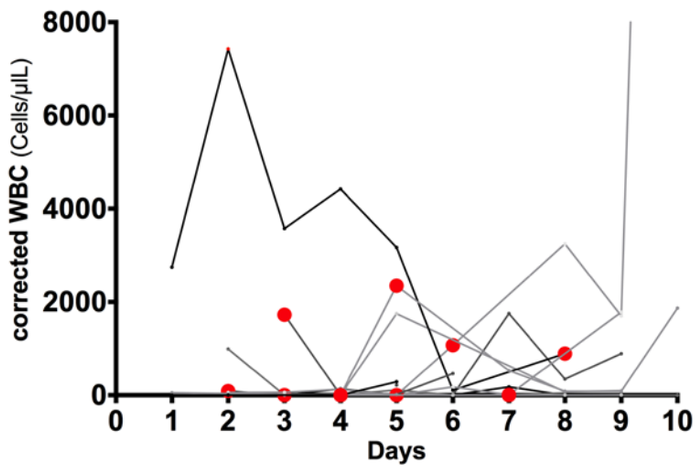
Figure e-1. Temporal trends of CSF protein and glucose levels.

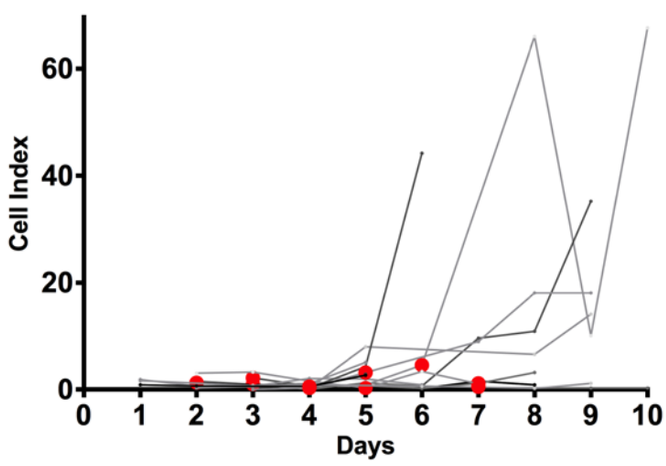


(A) General pattern over days 1-9 post-ictus. (B) Differences among cases with smaller versus larger iIVH volumes. (C) Differences among cases treated with alteplase versus saline. The p value listed with each panel refers to the difference in overall trends for the respective parameter. * refers to significantly different daily values

Figure e-2: Timing of positive culture and the temporal trends of CSF inflammatory parameters.

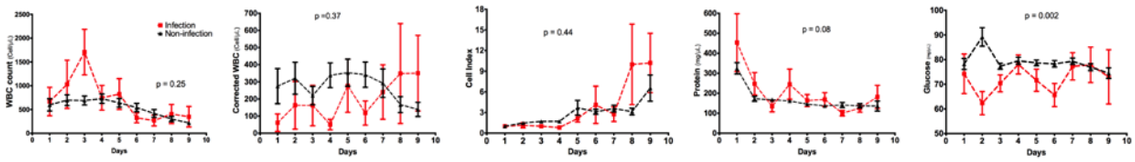






Individual patterns of CSF WBC, cWBC and Cell index in cases with CSF bacterial infection during the study period (within 10 days post-ictus, n=21). Red spot indicates the time of positive culture.

Figure e-3: Association with bacterial infection within 30 days of ictus.



Temporal trend of CSF WBC, cWBC, CI, protein and glucose over days 1-9 post-ictus in cases with and without bacterial infection manifested during the first month (within 30 days post-ictus, n=31). The p value listed with each panel refers to the difference in overall trends for the respective parameter.

Table e-1

Baseline demographics and characteristics of participants in the CLEAR III trial

	Saline (N=251)	**Alteplase (N=249)**	**All (N=500)**
Demographic variables			
Age in Years: Median [IQR]	59 [51, 67]	59 [51, 66]	59 [51, 67]
Gender: Female	117 (46.6%)	105 (42.2%)	222 (44.4%)
Race			
White	161 (64.1%)	144 (57.8%)	305 (61.0%)
African American	78 (31.1%)	92 (36.9%)	170 (34.0%)
American Indian or Alaskan Native	1 (0.4%)	0 (0.0%)	1 (0.2%)
Other	11 (4.4%)	13 (5.2%)	24 (4.8%)
Ethnicity			
Hispanic/Latino	32 (12.7%)	28 (11.2%)	60 (12.0%)
Baseline variables			
Tobacco Use	59 (23.5%)	73 (29.3%)	132 (26.4%)
Cocaine Use	18 (7.2%)	12 (4.8%)	30 (6.0%)
Anticoagulated at Registration	29 (11.6%)	20 (8.0%)	49 (9.8%)
Antihypertensive Med Compliant	202 (80.5%)	168 (67.5%)	370 (74.0%)
Hyperlipidemia Med Compliant	245 (97.6%)	240 (96.4%)	485 (97.0%)
On Antiplatelet at Registration	72 (28.7%)	56 (22.5%)	128 (25.6%)
Presentation Blood Pressure			
	(N=244)	**(N=244)**	**(N=488)**
Systolic BP (mmHg): Median [IQR	191 [166, 221.5]	197 [1698.2, 220.0]	193 [167.0, 220.0]
	(N=243)	**(N=242)**	**(N=485)**
Diastolic BP (mmHg): Median [IQR]	104 [90.0, 120.0]	110 [90.2, 125.8]	107 [90.0, 124.0]
Enrollment GCS	**(N=237)**	**(N=233)**	**(N=470)**
Total: Median [IQR]	10 [7,14]	10 [7,14]	10 [7,14]
Enrollment NIHSS	**(N=168)**	**(N=175)**	**(N=343)**
Enrollment NIHSS: Median [IQR]	19 [11, 34]	21 [11, 32.5]	20 [11, 33]
Stability CT (last CT prior to enrollment)			
IVH Volume (mL): Median [IQR]	22.4 [12.7, 38.9]	21.2 [12.7, 35.8]	21.8 [12.7, 36.9]
ICH Volume (mL): Median [IQR]	7.2 [2.3, 14.6]	8.2 [2.8, 15.2]	7.9 [2.5, 15.0]
Index Clot Location			
Thalamus	144 (57.4%)	149 (59.8%)	293 (58.6%)
Primary IVH	27 (10.8%)	18 (7.2%)	45 (9%)
Ictus to Randomization: Median [IQR]	52.2 [41.2, 66.7]	51.8 [36.4, 65.8]	52.1 [39.1, 66.5]
Average Before Dosing			
	(N=251)	**(N=247)**	**(N=498)**
Systolic BP (mmHg): Mean (95% CI)	143.4 (141.9, 144.9)	144.5 (142.7, 146.4)	144.0 (142.8, 145.1)
Diastolic BP (mmHg): Mean (95% CI)	70.0 (68.6, 71.3)	71.8 (70.1, 73.4)	70.9 (69.8, 71.9)
ICP (mmHg): Mean (95% CI)	**(N=249)** 9.6 (9.1, 10.2)	**(N=246)** 9.0 (8.5, 9.5)	**(N=495)** 9.3 (8.9, 9.7)

Table e-2

Distribution of data-point frequency of CSF inflammatory parameters used in the final analyses

	WBC	cWBC (Negative data points corrected to zero)	CI	Protein	Glucose	Total
Day 1	131	109 (70)	109	140	139	628
Day 2	262	226 (129)	226	262	265	1241
Day 3	355	313 (189)	313	378	374	1733
Day 4	367	325 (201)	325	387	383	1787
Day 5	350	306 (155)	306	370	370	1702
Day 6	310	273 (128)	273	315	318	1489
Day 7	284	242 (110)	242	291	293	1352
Day 8	211	175 (79)	175	213	212	986
Day 9	105	88 (32)	88	111	108	500
Total	2375	2057 (1093)	2057	2467	2462	11418
					Outliers	42
					Final	11,376

Table e-3
Demographic, clinical and treatment characteristics in groups with lower versus higher data-points frequency (<5 vs. ≥ CSF WBC readings)

Variable	<5 CSF WBC readings	≥ 5 CSF WBC readings	P
N	203	297	
Demographic variables			
Age in Years: Median [IQR]	59 [52-67]	59 [51-66]	0.40
Gender: Female	86 (42.4%)	136 (45.8%)	0.45
Race			
White	125 (61.58%)	180 (60.6%)	0.44
African American	66 (32.5%)	104 (35.0%)	
Ethnicity			
Hispanic/Latino	29 (14.3%)	31 (10.4%)	0.19
Clinical Variables			
Enrollment GCS Total: Median [IQR]	10 [7 – 11]	11 [6 – 14]	0.27
Diagnosis IVH Volume (mL): Median [IQR]	34.0 [22.7-49.4]	36.1 [22.9-49.4]	0.73
Stability IVH Volume (mL): Median [IQR]	20.7 [12.0-34.9]	22.6 [13.8-37.6]	0.54
Diagnosis ICH Volume (mL): Median [IQR]	8.8 [4.0-14.6]	7.3 [2.4-13.3]	0.06
Diagnosis ICH location: Thalamus (%)	130 (64.0%)	163 (54.9%)	0.04
Treatment Variables			
Treatment (tPa)	109 (53.7%)	140 (47.1%)	0.15
Diagnosis to first EVD (hrs): Median [IQR]	4.4 [4.0-14.6]	4.2 [2.4-13.3]	0.04
Ictus to first EVD (hrs): Median [IQR]	7.1 [5.0-12.8]	7.7 [4.9-11.5]	0.40
Ictus to first dose (hrs): Median [IQR]	56.1[44.6-70.5]	58.3[46.3-70.9]	0.96
ICU stay (days): Median [IQR]	14.0 [11.0-22.0]	15.0 [12.0-21.0]	0.61
Mortality (%)	54 (26.6%)	65 (21.9%)	0.22

Table e-4
Association of alteplase treatment and CSF WBC (Days 1-9, mean, median and maximum), analysis repeated with correction for initial IVH volume (iIVH)

	CSF WBC				CSF WBC adjusted for iIVH Volume			
Parameter	**Diff**	**95% Confidence Limits**		**P**	**Diff**	**95% Confidence Limits**		**P**
WBC D1	-20.9	-498.9	457.09	0.93	-36.01	-520.1	448.1	0.88
WBC D2	41.6	-391.8	475.1	0.85	75.6	-354.7	511.8	0.72
WBC D3	645.2	282.9	1007.5	0.0005	672.6	312.9	1032.4	0.0003
WBC D4	646.4	282.1	1010.7	0.0005	694.4	335.2	1053.5	0.0002
WBC D5	527.0	186.4	867.6	0.0025	555.0	218.2	891.7	0.001
WBC D6	370.5	46.6	694.4	0.03	411.9	93.0	730.9	0.01
WBC D7	8.7	-300.4	317.7	0.96	14.8	-296.5	326.1	0.93
WBC D8	-23.3	-229.0	182.4	0.82	-8.6	-214.5	197.4	0.93
WBC D9	-111.5	-291.4	68.4	0.22	-108.9	-287.2	69.5	0.23
WBC mean	316.6	258.9	374.2	< 0.0001	350.5	294.0	407.0	< 0.0001
WBC median	261.4	216.1	306.7	< 0.0001	285.6	241.0	330.2	< 0.0001
WBC max	80.0	514.6	845.4	< 0.0001	766.8	603.8	929.8	< 0.0001

Table e-5
Association of alteplase treatment and cWBC (Days 1-9, mean, median and maximum), analysis repeated with correction for initial IVH volume (iIVH)

	cWBC				cWBC adjusted for iIVH Volume			
Parameter	**Diff**	**95% Confidence Limits**		**P**	**Diff**	**95% Confidence Limits**		**P**
cWBC D1	-4.5	-378.5	387.6	0.98	-1.6	-390.4	387.2	0.99
cWBC D2	-17.4	-374.7	340.0	0.92	-10.3	-370.4	349.8	0.96
cWBC D3	233.1	31.6	434.6	0.02	237.6	35.3	440.0	0.02
cWBC D4	327.2	60.5	594.0	0.02	341.5	74.6	608.4	0.01
cWBC D5	233.7	-61.6	529.0	0.10	246.4	-47.3	540.2	0.10
cWBC D6	253.4	-20.0	526.8	0.07	274.5	3.6	545.4	0.05
cWBC D7	-90.7	-408.8	223.5	0.57	-91.7	-408.5	225.2	0.56
cWBC D8	-80.6	-266.1	105.0	0.39	--75.4	-261.4	110.6	0.42
cWBC D9	-118.9	-301.6	63.8	0.20	-132.1	-313.4	49.2	0.15
cWBC mean	125.8	85.0	166.6	< 0.0001	141.3	100.7	181.9	< 0.0001
cWBC median	63.3	35.4	91.1	< 0.0001	68.9	41.0	96.8	< 0.0001
cWBC max	300.8	172.5	429.1	< 0.0001	350.0	222.4	477.4	< 0.0001

Table e-6
Association of alteplase treatment and cell index (Days 1-9, mean, median and maximum), analysis repeated with correction for initial IVH volume (iIVH)

	CI				CI adjusted for iIVH Volume			
Parameter	**Diff**	**95% Confidence Limits**		**P**	**Diff**	**95% Confidence Limits**		**P**
CI D1	-0.02	-0.37	0.42	0.91	-0.001	-0.395	0.40	0.99
CI D2	-0.06	-0.60	0.48	0.83	-0.04	-0.59	0.50	0.88
CI D3	0.24	-0.46	0.95	0.50	0.22	-0.49	0.93	0.54
CI D4	0.8	0.15	1.44	0.02	0.79	0.14	1.44	0.02
CI D5	4.01	0.02	8.0	0.05	4.02	0.01	8.03	0.05
CI D6	1.56	0.08	3.03	0.04	1.57	0.08	3.05	0.04
CI D7	2.28	0.45	4.12	0.02	2.2	0.36	4.06	0.02
CI D8	-0.5	-2.86	1.86	0.68	-0.57	-2.94	1.81	0.64
CI D9	2.17	-4.9	9.28	0.54	2.15	-5.05	9.36	0.56
CI mean	1.11	0.78	1.43	< 0.0001	1.10	0.76	1.43	< 0.0001
CI median	1.09	0.76	1.43	< 0.0001	0.82	0.65	0.99	< 0.0001
CI max	2.57	1.41	3.73	< 0.0001	2.51	1.35	3.68	< 0.0001

Table e-7

Association of CSF bacterial infection during the study period (10 days post-ictus) and CSF inflammatory parameters (Days 1-9, mean, median and maximum)

CSF WBC

Effect	Diff	95% Confidence Limits		P
WBC D1	165.8	-1079.6	1411.1	0.79
WBC D2	547.3	-530.9	1625.4	0.32
WBC D3	1121.8	109.4	2134.2	0.03
WBC D4	209.0	-697.3	1115.3	0.65
WBC D5	518.8	-302.9	1340.5	0.22
WBC D6	-235.1	-1114.2	644.0	0.60
WBC D7	-36.9	-837.8	763.9	0.93
WBC D8	308.0	-152.8	768.7	0.19
WBC D9	300.3	-71.9	672.4	0.11
WBC mean	234.8	87.7	382.0	0.002
WBC median	256.3	140.7	372.0	< 0.0001
WBC max	642.9	223.2	1062.6	0.003

cWBC

Effect	Diff	95% Confidence Limits		P
cWBC D1	-246.0	-1415.4	923.4	0.68
cWBC D2	-157.7	-1191.0	875.6	0.76
cWBC D3	-18.7	-626.1	588.8	0.95
cWBC D4	-310.2	-1024.8	404.5	0.39
cWBC D5	51.4	-713.8	816.6	0.89
cWBC D6	-142.7	-912.9	627.5	0.72
cWBC D7	65.7	-877.3	1008.8	0.89
cWBC D8	310.9	-132.5	754.4	0.17
cWBC D9	328.8	-0.6	658.2	0.05
cWBC mean	-13.5	-124.3	97.3	0.81
cWBC median	36.1	-39.2	111.4	0.35
cWBC max	-118.8	-466.0	228.4	0.50

Cell Index

Effect	Diff	95% Confidence Limits		P
CI D1	0.5	-0.7	1.7	0.40
CI D2	-0.3	-1.9	1.2	0.68
CI D3	-0.6	-2.8	1.5	0.55
CI D4	-0.9	-2.6	0.8	0.31
CI D5	-1.0	-11.3	9.4	0.85
CI D6	3.1	-1.0	7.2	0.14
CI D7	-0.2	-5.7	5.3	0.94
CI D8	10.2	4.8	15.5	0.001
CI D9	6.8	-7.1	20.6	0.33
CI mean	2.3	1.4	3.1	< 0.0001
CI median	1.0	0.5	1.5	< 0.0001
CI max	6.4	3.3	9.5	< 0.0001

Table e-8
Univariate correlation of poor functional outcome (mRS 4-6) at 30 and 180 days with daily, mean, median and maximal CSF WBC, cWBC and cell index

Poor outcome vs WBC (Days 1-9, mean, median and maximum)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
WBC D1	0.0000	-0.0003	0.0003	0.93	0.0001	-0.0002	0.0004	0.47
WBC D2	0.0001	-0.0001	0.0003	0.22	0.0001	-0.0000	0.0003	0.15
WBC D3	0.0002	0.0000	0.0004	0.10	-0.0000	-0.0001	0.0001	0.87
WBC D4	0.0001	-0.0002	0.0003	0.66	0.0001	-0.0001	0.0004	0.20
WBC D5	0.0000	-0.0001	0.0001	0.98	0.0001	-0.0001	0.0002	0.35
WBC D6	0.0001	-0.0002	0.0003	0.67	0.0002	-0.0001	0.0004	0.14
WBC D7	0.0004	-0.0001	0.0009	0.15	0.0001	-0.0001	0.0003	0.26
WBC D8	0.0008	-0.0004	0.0019	0.18	0.0005	-0.0001	0.0010	0.12
WBC D9	0.0004	-0.0010	0.0018	0.58	0.0001	-0.0007	0.0009	0.73
WBC mean	0.0002	-0.0001	0.0006	0.23	0.0002	0.0000	0.0004	0.09
WBC median	0.0002	-0.0002	0.0007	0.26	0.0002	0.0000	0.0005	0.10
WBC max	0.0001	-0.0001	0.0002	0.30	0.0000	0.0000	0.0001	0.24

Poor outcome vs cWBC (Days 1-9, mean, median and maximum)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
cWBC D1	0.0000	-0.0004	0.0005	0.86	0.0001	-0.0003	0.0004	0.61
cWBC D2	0.0001	-0.0002	0.0004	0.49	0.0002	-0.0000	0.0005	0.11
cWBC D3	0.0004	-0.0002	0.0009	0.19	0.0001	-0.0002	0.0004	0.49
cWBC D4	0.0000	-0.0003	0.0003	0.97	0.0001	-0.0001	0.0003	0.44
cWBC D5	0.0000	-0.0002	0.0002	0.98	0.0001	-0.0001	0.0002	0.39
cWBC D6	0.0000	-0.0003	0.0002	0.75	0.0002	-0.0001	0.0004	0.26
cWBC D7	0.0003	-0.0001	0.0008	0.17	0.0001	-0.0001	0.0003	0.31
cWBC D8	0.0007	-0.0004	0.0018	0.21	0.0006	-0.0001	0.0013	0.11
cWBC D9	0.0013	0.0000	0.0026	0.05	0.0004	-0.0006	0.0013	0.46
cWBC mean	0.0002	-0.0002	0.0007	0.30	0.0003	0.0000	0.0007	0.05
cWBC median	0.0006	-0.0002	0.0014	0.12	0.0004	-0.0001	0.0008	0.10
cWBC max	0.0000	-0.0001	0.0002	0.65	0.0001	0.0000	0.0002	0.10

Poor outcome vs CI (Days 1-9, mean, median and maximum)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
CI D1	0.1533	-0.2504	0.5570	0.46	-0.1543	-0.5455	0.2369	0.44
CI D2	-0.0161	-0.1618	0.1296	0.83	0.0658	-0.0632	0.1947	0.32
CI D3	0.0509	-0.0408	0.1426	0.28	0.0499	-0.0218	0.1216	0.17
CI D4	-0.0257	-0.1079	0.0566	0.54	-0.0321	-0.1038	0.0397	0.38
CI D5	0.0014	-0.0089	0.0116	0.79	-0.0063	-0.0176	0.0049	0.27
CI D6	-0.0121	-0.0554	0.0313	0.59	-0.0146	-0.0537	0.0245	0.46
CI D7	0.0052	-0.0321	0.0425	0.78	-0.0201	-0.0593	0.0192	0.32
CI D8	0.0129	-0.0325	0.0584	0.58	0.0093	-0.0263	0.0450	0.61
CI D9	-0.0030	-0.0257	0.0198	0.80	-0.0420	-0.0926	0.0085	0.10
CI mean	0.0217	-0.0260	0.0694	0.37	-0.0311	-0.0715	0.0093	0.13
CI median	0.0499	-0.0378	0.1375	0.26	-0.0560	-0.1235	0.0114	0.10
CI max	0.0032	-0.0070	0.0135	0.54	-0.0076	-0.0186	0.0034	0.17

Table e-9
Univariate correlation of mortality at 30 and 180-days with daily, mean, median and maximum CSF WBC, cWBC and cell index

Mortality vs CSF WBC (Days 1-9, mean, median and maximum)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
WBC D1	0.0001	-0.0003	0.0006	0.51	0.0002	-0.0001	0.0006	0.17
WBC D2	0.0001	-0.0002	0.0004	0.56	0.0001	-0.0001	0.0004	0.29
WBC D3	0.0000	-0.0002	0.0002	0.92	-0.0000	-0.0001	0.0001	0.97
WBC D4	-0.0001	-0.0002	0.0001	0.25	-0.0001	-0.0002	0.0001	0.37
WBC D5	-0.0001	-0.0002	0.0001	0.26	0.0000	-0.0001	0.0002	0.66
WBC D6	-0.0001	-0.0002	0.0001	0.55	0.0000	-0.0001	0.0002	0.65
WBC D7	0.0004	-0.0002	0.0009	0.17	0.0001	-0.0002	0.0003	0.68
WBC D8	-0.0002	-0.0006	0.0002	0.28	-0.0003	-0.0006	0.0001	0.15
WBC D9	-0.0004	-0.0016	0.0009	0.57	-0.0005	-0.0013	0.0003	0.24
WBC mean	0.0000	-0.0003	0.0002	0.70	0.0000	-0.0002	0.0002	0.98
WBC median	0.0000	0.0002	0.0004	0.86	-0.0001	-0.0004	0.0002	0.54
WBC max	0.0000	-0.0001	0.0001	0.77	0.0000	-0.0001	0.0001	0.95

Mortality vs cWBC (Days 1-9, mean, median and maximum)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
cWBC D1	0.0004	-0.0004	0.0012	0.37	0.0009	-0.0006	0.0024	0.26
cWBC D2	0.0000	-0.0003	0.0002	0.86	0.0001	-0.0002	0.0003	0.58
cWBC D3	-0.0001	-0.0004	0.0002	0.54	-0.0001	-0.0003	0.0002	0.54
cWBC D4	-0.0001	-0.0003	0.0001	0.37	-0.0001	-0.0002	0.0001	0.52
cWBC D5	-0.0001	-0.0003	0.0001	0.21	0.0000	-0.0002	0.0002	0.98
cWBC D6	-0.0001	-0.0003	0.0001	0.50	0.0001	-0.0002	0.0003	0.62
cWBC D7	0.0007	-0.0005	0.0019	0.24	0.0001	-0.0003	0.0005	0.64
cWBC D8	-0.0003	-0.0009	0.0003	0.29	-0.0003	-0.0008	0.0001	0.15
cWBC D9	-0.0005	-0.0019	0.0009	0.48	-0.0007	-0.0017	0.0003	0.18
cWBC mean	-0.0002	-0.0005	0.0002	0.41	0.0000	-0.0003	0.0003	0.95
cWBC median	0.0000	-0.0006	0.0005	0.87	-0.0003	-0.0008	0.0003	0.40
cWBC max	0.0000	-0.0002	0.0001	0.45	0.0000	-0.0001	0.0001	0.87

Mortality vs CI (Days 1-9, mean, median and maximum)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
CI D1	0.1881	-0.2851	0.6614	0.44	0.4156	-0.0466	0.8778	0.08
CI D2	-0.0324	-0.2303	0.1655	0.75	0.0054	-0.1502	0.1611	0.95
CI D3	-0.0347	-0.1172	0.0478	0.41	-0.0447	-0.1276	0.0382	0.29
CI D4	-0.0445	-0.1293	0.0403	0.30	-0.0178	-0.0922	0.0566	0.64
CI D5	0.0145	-0.0166	0.0455	0.36	0.0271	-0.0078	0.0619	0.13
CI D6	0.0253	-0.0272	0.0779	0.35	-0.0012	-0.0453	0.0430	0.96
CI D7	0.0135	-0.0454	0.0725	0.65	0.0627	-0.0180	0.1434	0.13
CI D8	-0.0509	-0.0868	-0.0151	0.005	-0.0300	-0.0648	0.0049	0.09
CI D9	0.0432	-0.0285	0.1150	0.24	0.0790	0.0048	0.1531	0.048
CI mean	0.0027	-0.0433	0.0488	0.91	0.0134	-0.0282	0.0550	0.53
CI median	0.0018	-0.0947	0.0984	0.97	0.0296	-0.0518	0.1111	0.48
CI max	0.0008	-0.0119	0.0134	0.90	0.0054	-0.0076	0.0183	0.42

Table e-10
Multivariate modeling of poor functional outcome (mRS 4-6) at 30 and 180 days in relation to CSF mean, median and maximum WBC count, cWBC and cell index

CSF WBC (mean per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0713	0.0472	0.0954	< 0.0001	0.0523	0.0364	0.0682	< 0.0001
IVH evacuation	-0.7254	-1.7846	0.3339	0.18	-0.3265	-0.8766	0.2236	0.24
ICH volume	0.2305	0.1513	0.3097	< 0.0001	0.1192	0.0808	0.1577	< 0.0001
ICH: thalamus	1.2893	0.5731	2.0054	0.0004	1.1041	0.4925	1.7157	0.0004
GCS: presentation	-0.0269	-0.1084	0.0545	0.52	-0.0722	-0.1259	-0.0184	0.009
CSF WBC mean	-0.0001	-0.0005	0.0002	0.40	-0.0001	-0.0003	0.0002	0.59

CSF WBC (median per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0722	0.0480	0.0963	< 0.0001	0.0516	0.0357	0.0674	< 0.0001
IVH evacuation	-0.7164	-1.7619	0.3292	0.18	-0.3550	-0.9165	0.2066	0.22
ICH volume	0.2328	0.1523	0.3133	< 0.0001	0.1179	0.0794	0.1565	< 0.0001
ICH: thalamus	1.2876	0.5717	2.0035	0.0004	1.1177	0.5058	1.7297	0.0003
GCS: presentation	-0.0284	-0.1101	0.0533	0.50	-0.0705	-0.1240	-0.0169	0.01
CSF WBC median	-0.0003	-0.0007	0.0002	0.25	-0.0000	-0.0003	0.0003	0.94

CSF WBC (maximum per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0701	0.0464	0.0937	< 0.0001	0.0529	0.0370	0.0689	< 0.0001
IVH evacuation	-0.7587	-1.8251	0.3077	0.16	-0.2953	-0.8324	0.2418	0.28
ICH volume	0.2290	0.1506	0.3074	< 0.0001	0.1210	0.0825	0.1594	< 0.0001
ICH: thalamus	1.2954	0.5768	2.0140	0.0004	1.0777	0.4658	1.6895	0.0006
GCS: presentation	-0.0243	-0.1047	0.0561	0.55	-0.0738	-0.1274	-0.0201	0.007
CSF WBC maximum	-0.0000	-0.0001	0.0001	0.74	-0.0001	-0.0001	0.0000	0.29

cWBC (mean per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0691	0.0452	0.0931	< 0.0001	0.0496	0.0332	0.0660	< 0.0001
IVH evacuation	-0.7867	-1.8938	0.3203	0.16	-0.4650	-1.0847	0.1547	0.14
ICH volume	0.2322	0.1494	0.3149	< 0.0001	0.1133	0.0742	0.1524	< 0.0001
ICH: thalamus	1.3353	0.5855	2.0850	0.0005	1.0665	0.4320	1.7010	0.001
GCS: presentation	-0.0150	-0.0960	0.0659	0.72	-0.0612	-0.1170	-0.0054	0.03
cWBC mean	-0.0001	-0.0006	0.0005	0.84	0.0001	-0.0003	0.0006	0.58

cWBC (median per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0690	0.0449	0.0930	< 0.0001	0.0498	0.0334	0.0662	< 0.0001
IVH evacuation	-0.7968	-1.8995	0.3060	0.16	-0.4441	-1.0520	0.1638	0.15
ICH volume	0.2322	0.1489	0.3155	< 0.0001	0.1137	0.0746	0.1528	< 0.0001
ICH: thalamus	1.3399	0.5920	2.0878	0.0004	1.0548	0.4246	1.6850	0.001
GCS: presentation	-0.0142	-0.0941	0.0657	0.73	-0.0626	-0.1181	-0.0070	0.03
cWBC median	-0.0001	-0.0010	0.0009	0.90	0.0001	-0.0006	0.0008	0.79

cWBC (maximum per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0691	0.0453	0.0929	< 0.0001	0.0497	0.0333	0.0661	< 0.0001
IVH evacuation	-0.7859	-1.8926	0.3207	0.16	-0.4638	-1.0844	0.1568	0.14
ICH volume	0.2319	0.1494	0.3144	< 0.0001	0.1138	0.0747	0.1528	< 0.0001
ICH: thalamus	1.3327	0.5803	2.0851	0.0005	1.0691	0.4327	1.7055	0.001
GCS: presentation	-0.0150	-0.0952	0.0651	0.71	-0.0612	-0.1169	-0.0056	0.03
cWBC maximum	-0.0000	-0.0002	0.0001	0.82	0.0000	-0.0001	0.0002	0.58

Cell Index (mean per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0696	0.0460	0.0932	< 0.0001	0.0495	0.0332	0.0658	< 0.0001
IVH evacuation	-0.8264	-1.9051	0.2523	0.13	-0.3812	-0.9625	0.2002	0.20
ICH volume	0.2375	0.1514	0.3236	< 0.0001	0.1172	0.0769	0.1575	< 0.0001
ICH: thalamus	1.3070	0.5611	2.0529	0.0006	0.9939	0.3682	1.6196	0.002
GCS: presentation	-0.0153	-0.0956	0.0650	0.71	-0.0626	-0.1178	-0.0075	0.03
CI mean	0.0609	-0.0164	0.1383	0.12	-0.0283	-0.0794	0.0229	0.28

Cell Index (median per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0695	0.0462	0.0929	< 0.0001	0.0496	0.0333	0.0658	< 0.0001
IVH evacuation	-0.8157	-1.8981	0.2666	0.14	-0.3869	-0.9713	0.1975	0.19
ICH volume	0.2354	0.1503	0.3206	< 0.0001	0.1175	0.0773	0.1578	< 0.0001
ICH: thalamus	1.3229	0.5750	2.0709	0.0005	0.9979	0.3727	1.6231	0.002
GCS: presentation	-0.0196	-0.1004	0.0613	0.64	-0.0613	-0.1164	-0.0061	0.03
CI median	0.1107	-0.0003	0.2216	0.05	-0.0370	-0.1280	0.0541	0.43

Cell Index (maximum per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	0.0690	0.0453	0.0927	< 0.0001	0.0495	0.0331	0.0658	< 0.0001
IVH evacuation	-0.8207	-1.9075	0.2661	0.14	-0.3843	-0.9658	0.1972	0.20
ICH volume	0.2374	0.1514	0.3234	< 0.0001	0.1171	0.0766	0.1575	< 0.0001
ICH: thalamus	1.3096	0.5622	2.0571	0.0006	0.9918	0.3651	1.6185	0.002
GCS: presentation	-0.0136	-0.0933	0.0660	0.74	-0.0633	-0.1185	-0.0082	0.02
CI maximum	0.0110	-0.0058	0.0277	0.20	-0.0087	-0.0233	0.0058	0.24

Table e-11
Multivariate Modeling of Mortality at 30 and 180 days in relation to CSF WBC count, cWBC and Cell Index

CSF WBC (mean per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0523	-0.0692	-0.0353	< 0.0001	-0.0382	-0.0518	-0.0246	< 0.0001
IVH evacuation	0.2713	-0.2283	0.7708	0.29	0.1801	-0.3232	0.6834	0.48
ICH volume	-0.0202	-0.0717	0.0313	0.44	-0.0501	-0.0879	-0.0123	0.009
ICH: thalamus	-1.5827	-2.6065	-0.5590	0.002	-0.7279	-1.3764	-0.0794	0.03
GCS: presentation	0.0908	0.0060	0.1755	0.04	0.0851	0.0262	0.1439	0.005
CSF WBC mean	0.0001	-0.0003	0.0004	0.71	0.0002	-0.0001	0.0004	0.22

CSF WBC (median per subject)

	30 days				**180 days**			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0529	-0.0698	-0.0360	< 0.0001	-0.0385	-0.0519	-0.0251	< 0.0001
IVH evacuation	0.2400	-0.2634	0.7435	0.35	0.1665	-0.3330	0.6660	0.51
ICH volume	-0.0214	-0.0724	0.0296	0.41	-0.0503	-0.0876	-0.0130	0.008
ICH: thalamus	-1.5659	-2.5808	-0.5511	0.003	-0.7342	-1.3774	-0.0910	0.03
GCS: presentation	0.0924	0.0077	0.1771	0.03	0.0860	0.0267	0.1452	0.005
CSF WBC median	0.0002	-0.0002	0.0006	0.30	0.0003	-0.0001	0.0006	0.11

CSF WBC (maximum per subject)

	30 days				**180 days**			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0520	-0.0690	-0.0351	< 0.0001	-0.0377	-0.0513	-0.0242	< 0.0001
IVH evacuation	0.2837	-0.2145	0.7818	0.26	0.1922	-0.3149	0.6994	0.46
ICH volume	-0.0194	-0.0708	0.0319	0.46	-0.0496	-0.0871	-0.0120	0.01
ICH: thalamus	-1.5925	-2.6233	-0.5618	0.003	-0.7224	-1.3708	-0.0740	0.03
GCS: presentation	0.0896	0.0051	0.1741	0.04	0.0838	0.0252	0.1424	0.005
CSF WBC maximum	0.0000	-0.0001	0.0001	0.88	0.0001	-0.0000	0.0001	0.25

cWBC (mean per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0463	-0.0643	-0.0284	< 0.0001	-0.0316	-0.0457	-0.0176	< 0.0001
IVH evacuation	0.3112	-0.1777	0.8002	0.21	0.1458	-0.3494	0.6410	0.56
ICH volume	-0.0223	-0.0738	0.0292	0.40	-0.0502	-0.0879	-0.0125	0.009
ICH: thalamus	-1.6943	-2.7947	-0.5939	0.003	-0.7354	-1.3943	-0.0765	0.03
GCS: presentation	0.0764	-0.0099	0.1627	0.08	0.0741	0.0141	0.1342	0.02
cWBC mean	-0.0001	-0.0006	0.0003	0.56	0.0000	-0.0003	0.0004	0.81

cWBC (median per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0467	-0.0648	-0.0287	< 0.0001	-0.0319	-0.0459	-0.0179	< 0.0001
IVH evacuation	0.2862	-0.2015	0.7739	0.25	0.1268	-0.3637	0.6173	0.61
ICH volume	-0.0236	-0.0753	0.0281	0.37	-0.0518	-0.0896	-0.0140	0.007
ICH: thalamus	-1.6733	-2.7613	-0.5853	0.003	-0.7308	-1.3878	-0.0737	0.03
GCS: presentation	0.0803	-0.0052	0.1658	0.07	0.0773	0.0171	0.1376	0.01
cWBC median	-0.0000	-0.0006	0.0006	0.99	0.0003	-0.0002	0.0009	0.23

cWBC maximum per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0463	-0.0642	-0.0284	< 0.0001	-0.0314	-0.0454	-0.0174	< 0.0001
IVH evacuation	0.3118	-0.1777	0.8013	0.21	0.1554	-0.3424	0.6532	0.54
ICH volume	-0.0223	-0.0736	0.0290	0.39	-0.0497	-0.0871	-0.0123	0.009
ICH: thalamus	-1.7067	-2.8251	-0.5884	0.003	-0.7426	-1.4023	-0.0828	0.03
GCS: presentation	0.0765	-0.0094	0.1624	0.08	0.0728	0.0130	0.1327	0.02
cWBC maximum	-0.0000	-0.0002	0.0001	0.50	-0.0000	-0.0001	0.0001	0.96

Cell Index (mean per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0469	-0.0650	-0.0287	< 0.0001	-0.0314	-0.0452	-0.0175	< 0.0001
IVH evacuation	0.2988	-0.1873	0.7850	0.23	0.1557	-0.3380	0.6493	0.54
ICH volume	-0.0243	-0.0755	0.0269	0.35	-0.0469	-0.0847	-0.0090	0.02
ICH: thalamus	-1.6866	-2.7940	-0.5791	0.003	-0.7405	-1.4072	-0.0738	0.03
GCS: presentation	0.0782	-0.0064	0.1628	0.07	0.0768	0.0170	0.1366	0.01
CI mean	-0.0206	-0.0613	0.0201	0.32	-0.0059	-0.0413	0.0295	0.74

Cell Index (median per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0467	-0.0646	-0.0287	< 0.0001	-0.0313	-0.0451	-0.0175	< 0.0001
IVH evacuation	0.3026	-0.1799	0.7851	0.22	0.1523	-0.3408	0.6455	0.54
ICH volume	-0.0248	-0.0757	0.0261	0.34	-0.0469	-0.0848	-0.0090	0.02
ICH: thalamus	-1.6649	-2.7510	-0.5788	0.003	-0.7369	-1.4023	-0.0715	0.03
GCS: presentation	0.0787	-0.0061	0.1635	0.07	0.0769	0.0169	0.1369	0.01
CI median	-0.0382	-0.1489	0.0725	0.50	-0.0026	-0.1004	0.0952	0.96

Cell Index (maximum per subject)

	30 days				180 days			
Parameter	**Estimate**	**95% Confidence Limits**		**P**	**Estimate**	**95% Confidence Limits**		**P**
IVH volume	-0.0470	-0.0652	-0.0288	< 0.0001	-0.0313	-0.0452	-0.0175	< 0.0001
IVH evacuation	0.2955	-0.1911	0.7821	0.23	0.1525	-0.3409	0.6458	0.54
ICH volume	-0.0242	-0.0756	0.0272	0.36	-0.0469	-0.0848	-0.0090	0.02
ICH: thalamus	-1.6926	-2.8041	-0.5811	0.003	-0.7382	-1.4051	-0.0713	0.03
GCS: presentation	0.0780	-0.0064	0.1625	0.07	0.0768	0.0171	0.1365	0.01
CI maximum	-0.0060	-0.0168	0.0048	0.27	-0.0007	-0.0104	0.0090	0.89

Table e-12

Characteristics of IVH cases with high inflammatory response based on CSF WBC count

Variable	Quartile with Highest WBC	Rest of subjects	P
n	116	348	
Demographic variables			
Age in Years: Median [IQR]	59 [51-67]	56 [48-65]	0.07
Gender: Female	62 (53.5%)	148 (42.5%)	0.04
Race			
White African American	63 (54.3%) 46 (39.7%)	207 (59.5%) 124 (34.6%)	0.82
Ethnicity Hispanic/Latino	19 (16.4%)	39 (11.2%)	0.15
Clinical Variables			
Enrollment GCS Total: Median [IQR]	9 [5 – 14]	11 [7 – 14]	0.02
Diagnosis IVH Volume (mL): Median [IQR]	43.9 [31.1-58.1]	32.3 [21.3-45.9]	< 0.0001
Stability IVH Volume (mL): Median [IQR]	28.1 [19.3-40.5]	20.2 [11.3-33.1]	0.0006
Diagnosis ICH Volume (mL): Median [IQR]	9.27 [3.8-16.0]	7.52 [3.0-13.3]	0.18
Diagnosis ICH location: Thalamus (%)	56 (48.3%)	216 (62.07%)	0.009
Treatment Variables			
Treatment (alteplase)	78 (67.2%)	156 (44.8%)	< 0.0001
IVH clearance (%): Median [IQR]	68.0 [42.6-83.8]	55.7 [33.3-75.0]	0.04
Diagnosis to first EVD (hrs): Median [IQR]	3.8 [2.6-6.0]	4.3 [2.9-6.5]	0.19
Ictus to first EVD (hrs): Median [IQR]	7.5 [4.6-11.4]	7.5 [5.0-11.9]	0.56
Ictus to last EVD removal (hrs): Median [IQR]	292.6 [231.4-368.7]	268.0 [210.4-354.4]	0.68
Ictus to first dose (hrs): Median [IQR]	57.8 [46.2-71.1]	57.9 [46.0-71.2]	0.97
ICU stay (days): Median [IQR]	16.0 [12.0-22.5]	15.0 [11.0-21.0]	0.42
Mortality (%, at 30 days)	14 (12.1)	37 (10.6)	0.67
Mortality (%, at 180 days)	24 (20.7)	83 (23.9)	0.48
mRS 0-3 (%, at 30 days)	17 (14.7)	74 (21.3)	0.12
mRS 0-3 (%, at 180 days)	53 (45.7)	170 (48.9)	0.56

Table e-13

Characteristics of IVH cases with high inflammatory response based on CSF cWBC

Variable	Quartile with Highest cWBC	Rest of subjects	P
n	106	317	
Demographic variables			
Age in Years: Median [IQR]	55 [49-64]	59 [51-67]	0.11
Gender: Female	50 (47.2%)	144 (45.4%)	0.76
Race			
White African American	61 (57.6%) 37 (34.9%)	182 (57.4%) 120 (37.9%)	0.86
Ethnicity Hispanic/Latino	16 (15.1%)	35 (11.0%)	0.15
Clinical Variables			
Enrollment GCS Total: Median [IQR]	9 [6 – 13]	11 [7 – 14]	0.01
Diagnosis IVH Volume (mL): Median [IQR]	40.1 [27.8-52.0]	33.4 [21.8-48.2]	0.01
Stability IVH Volume (mL): Median [IQR]	26.5 [17.4-37.6]	20.4 [11.6-36.3]	0.02
Diagnosis ICH Volume (mL): Median [IQR]	7.19 [2.1-14.4]	8.14 [3.2-13.4]	0.18
Diagnosis ICH location: Thalamus (%)	54 (50.9%)	120 (37.9%)	0.02
Treatment Variables			
Treatment (alteplase)	70 (66.0%)	146 (46.1%)	0.0004
IVH evacuation (%): Median [IQR]	69.4 [46.0-82.7]	54.7 [32.0-75.0]	0.001
Diagnosis to first EVD (hrs): Median [IQR]	3.9 [2.7-6.1]	4.3 [2.9-6.4]	0.79
Ictus to first EVD (hrs): Median [IQR]	7.9 [5.0-13.5]	7.5 [5.0-11.8]	0.49
Ictus to last EVD removal (hrs): Median [IQR]	302.9 [231.4-368.7]	274.0 [210.4-354.4]	0.78
Ictus to first dose (hrs): Median [IQR]	58.2 [46.1-71.5]	57.6 [46.0-70.5]	0.61
ICU stay (days): Median [IQR]	16.0 [12.0-21.0]	15.0 [11.0-21.0]	0.47
Mortality (%, at 30 days)	13 (12.3)	34 (10.7)	0.67
Mortality (%, at 180 days)	23 (21.7)	76 (24.0)	0.63
mRS 0-3 (%, at 30 days)	25 (23.6)	63 (19.9)	0.42
mRS 0-3 (%, at 180 days)	54 (50.9)	154 (48.6)	0.67

Table e-14

Characteristics of IVH subjects with high inflammatory response based on CSF cell index

Variable	Quartile with Highest CI	Rest of subjects	P
n	105	317	
Demographic variables			
Age in Years: Median [IQR]	56 [51-66]	58 [50-66]	0.89
Gender: Female	41 (39.1%)	153 (48.3%)	0.10
Race			
White African American	68 (64.8%) 35 (33.3%)	174 (54.9%) 122 (38.5%)	0.29
Ethnicity Hispanic/Latino	13 (12.4%)	37 (11.7%)	0.85
Clinical Variables			
Enrollment GCS Total: Median [IQR]	9 [5 – 13]	11 [7 – 14]	0.06
Diagnosis IVH Volume (mL): Median [IQR]	35.65 [21.8-46.9]	35.4 [23.7-49.9]	0.64
Stability IVH Volume (mL): Median [IQR]	21.7 [11.8-35.8]	21.9 [13.3-37.6]	0.33
Diagnosis ICH Volume (mL): Median [IQR]	6.5 [2.9-13.3]	8.3 [3.1-13.8]	0.40
Diagnosis ICH location: Thalamus (%)	46 (43.8%)	128 (30.3%)	0.54
Treatment Variables			
Treatment (alteplase)	63 (60.0%)	153 (48.3%)	0.04
IVH evacuation (%): Median [IQR]	65.2 [45.7-80.7]	55.2 [32.2-76.4]	0.003
Diagnosis to first EVD (hrs): Median [IQR]	3.9 [2.7-6.1]	4.3 [2.9-6.4]	0.78
Ictus to first EVD (hrs): Median [IQR]	7.7 [4.5-14.1]	7.6 [5.0-11.5]	0.29
Ictus to last EVD removal (hrs): Median [IQR]	302.9 [231.4-368.7]	274.0 [210.4-354.4]	0.18
Ictus to first dose (hrs): Median [IQR]	58.8 [47.0-72.4]	57.6 [45.4-69.4]	0.13
ICU stay (days): Median [IQR]	15.0 [11.0-21.0]	14.0 [11.0-21.0]	0.91
Mortality (%, at 30 days)	13 (12.4)	34 (10.7)	0.64
Mortality (%, at 180 days)	24 (22.9)	75 (23.7)	0.87
mRS 0-3 (%, at 30 days)	20 (19.1)	68 (21.5)	0.60
mRS 0-3 (%, at 180 days)	56 (53.3)	151 (47.6)	0.31

Table e-15: Systematic literature review of CSF inflammation in relation to hemorrhagic stroke*

Study	Subjects	Design	Data	n	Samples	Methods	Results
Kramer 2015[1]	IVH (IVT 50%)	Pro	Cell count, ILs, TNF, CBC	12	48	Subjects randomized to IVT or saline, CSF at baseline and daily for 3 days	Inflammatory markers and WBC increased in the first 2 days before dropping at 72 hours. CSF pleocytosis (WBC, RBC) was more evident with IVT but no significant Diff.
Kaestner 2013[2]	SAH/IVH	Pro	CSF Albumin, TGF-beta	42	420	Patient reviewed after 6 months and categorized for development of hydrocephalus	CSF albumin is more than three times higher in IVH. No correlation with hydrocephalus development
Hallevi 2012[3]	IVH (62% IVT)	Retro	Chemistry, corrected WBC, CBC	29	551	Excluded ventriculitis, compared trends with/out IVT	Following IVH a brisk and transient cellular inflammation arises within the ventricles. This response seems to be attenuated by IVT therapy
King 2012[4]	IVH (44% IVT)	Pro	CSF hemoglobin	16	80	Subjects randomized to Uk vs placebo, CSF drawn daily for 5 days	Increase in the drained CSF Hb concentration with Uk
Boeer 2011[5]	IVH included	Retro	Cell count, chemistry, ture and ILs, CBC, CRP	50	50+6	Only 1 sample/patient (trends for 1 and 1 subjects were plotted), WBC not corrected for blood. ROC aluation of each parameter in predicting +ve culture.	Pilot study, both IL1β and IL8 should be further evaluated
Simard 2011[6]	IVH	In Vitro	NK-kB, p65		N/M	Immuno-labelling	An inflammatory response is upregulation and activation of NF- κB signaling by the CSF barrier cells of the choroid plexus and ependymal lining
Ducruet 2010[7]	IVH (IVT 43%)	Retro	Edema, aseptic meningitis	30	N/M	IVT (n=13) vs control (n=17), comparing hematommal edema, CSF inflammatory response and shunt dependency	Increase in perihematomal edema in this cohort as well as worsening rates of sterile meningitis
Muttaiyah 2008[8]	IVH included	Retro	Protein, glucose	60	454	454 samples over 1 year, comparing EVD with and without ventriculitis	Median glucose is lower, no Diff in protein
Boeer 2008[9]	IVH included	Retro	Cell count, protein	264	724	ROC analysis performed using absolute count and adjusted counts using two formulas	Acceptable sensitivity and specificity for absolute WBC and granulocyte count. Blood-contaminated samples should not be corrected for the RBC count
Wong 2008[10]	SAH/IVH	Pro	CSF lactate	16	34	Comparing CSF lactate levels in IVH with/out ventriculitis	CSF lactate cutoff of 4mmol/L has a 60% positive predictive value and 100% negative predictive value for CSF infection
Pfausler 2004[11]	IVH	Pro	Cell count, corrected WBC, chemistry, CBC	13	N/M	Consecutive IVH, daily CSF. Culture +ve in n=7 med day 0, trends in pleocytosis was plotted for both groups	CI is highly indicative for nosocomial ventriculostomy-related ventriculitis in IVH. Preceding the diagnostic capacity by conventional means on average by 3 days.
Gordon 2014[12]	IVH	Pro	Cell count, chemistry and sTREM-1	73	73	3/wk sampling, comparing EVD with and without ventriculitis	Significantly different glucose and protein
Savmann 2002[13]	Neonatal IVH	Pro	Cytokines	43	43	IVH group Vs Control group tested for inflammatory cytokines	Intense and prolonged inflammatory reaction with high levels of pro-inflammatory cytokines (TNF-a, IL-1b, IL-6 and IL-8) in CSF from preterm infants with neonatal IVH compared with preterm controls.
Hudgins 1997[14]	Neonatal IVH	Pro	Cell count, protein, glucose and cultures	18	126	7 day treatment with low Vs high dose urokinase	No Diff in RBC count or protein between groups. RBC count occasionally demonstrated a rise during treatment caused by clot lysis.
Lee 1975[15]	Stroke (lumbar puncture)	Retro	Cell count, chemistry	61	61	Compared CSF characteristics for ICH, Ischaemic and hemorrhagic strokes.	CSF leukocyte pleocytosis is common after acute cerebral hemorrhage or infarction, and peaks three to four days after onset. CSF neurophils may be increased sufficiently to simulate infection.

*Literature search was performed using Medline PubMEd, Scopus and Ovid databases for English publications using the keywords “cerebrospinal fluid (CSF)” or “CSF pleocytosis” or “CSF Inflammation” and “Intracerebral hemorrhage” or “Intraventricular hemorrhage”. No timeframe, species or study type filters were used in our search. All articles in the English literature published through June 2015 were included in the search. The bibliographies of included articles were reviewed and cross-referenced for articles that may have been missed in the initial search. Titles of included articles were then screened to exclude those with irrelevant content. Abstracts were reviewed to exclude articles whose methodology did not include CSF analysis

IVH= intraventricular hemorrhage; SAH= subarachnoid hemorrhage; CSF= cerebrospinal fluid; IVT= intraventricular thrombolysis

Pro= prospective; Retro=retrospective

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